

Bicyclo[1.1.1]pentanes, [*n*]Staffanes, [1.1.1]Propellanes, and Tricyclo[2.1.0.0^{2,5}]pentanes

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I. Introduction

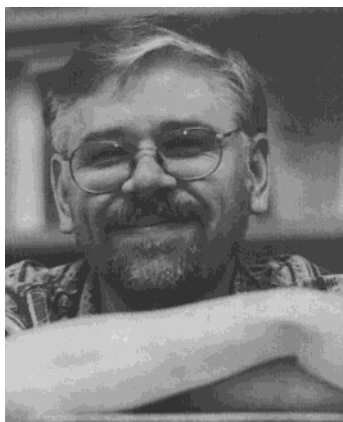
Highly strained yet remarkably stable, the bicyclo[1.1.1]pentane cage endows the derivatives of bicyclo[1.1.1]pentane (**1**, Chart 1), tricyclo[1.1.1.0^{1,3}]pentane ([1.1.1]propellane, **2**), and tricyclo[2.1.0.0^{2,5}]pentane (**3**) with unusual geometries and properties. The first synthesis of **1** was reported by Wiberg et al.¹ in 1964. It took 18 more years before Wiberg and Walker reported the preparation of **2**.² Three years later a seminal paper appeared from the laboratory of Szeimies³ and provided facile access to **2**, which has since then served as the port of entry into the chemistry of **1** and [*n*]**1**. In 1986, Wiberg et al.⁴ noted the formation of [*n*]staffanes (**[n]1**), oligomers of **2** (see structure in Table 1). Another claimed formation of a [2]staffane derivative⁵ was later shown⁶ to be incorrect (section IV.B.2.b.iii). The first derivatives of tricyclo[2.1.0.0^{2,5}]pentane (**3**) were reported in 1964,^{7,8} and the parent **3** was isolated in 1977.⁹ More highly cyclized cages based on the bicyclo[1.1.1]pentane skeleton, such as tetracyclo[2.1.0.0^{2,4}.0^{2,5}]pentane (**4**), tetracyclo[2.1.0.0^{1,3}.0^{2,5}]pentane (also known as [3.3.3.3]fenestrane and pyramidane, **5**), pentacyclo[2.1.0.0^{1,3}.0^{2,5}.0^{3,5}]pentane (**6**), and hexacy-

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Michael Levin was born in 1965 in Moscow, Russia. He graduated with honors from the Moscow Institute of Fine Chemical Technology in 1990 and spent one year as a junior research associate at the Nesmeyanov Institute of Organometallic Compounds in Moscow before attending graduate school at the University of Colorado at Boulder. He obtained his Ph.D. degree in 1997 under supervision of Professor Josef Michl and spent two years as a postdoctoral scholar first with Professor Seth R. Marder (Caltech) and then with Professor Peter J. Stang (University of Utah). He is interested in physical organic chemistry and organic synthesis as it applies to creation of materials with useful properties.



Piotr Kaszynski is an Assistant Professor of Chemistry at Vanderbilt University. He received his Master's degree from Warsaw Polytechnic in Poland in 1985 and his Ph.D. degree in Organic Chemistry in 1991 at the University of Texas at Austin under the supervision of Professor Josef Michl. He spent the subsequent two years at Caltech as a postdoctoral fellow with Professor Dennis A. Dougherty working in the area of organic magnetic materials before joining the faculty at Vanderbilt University in 1993. His research is focused on design, synthesis, and characterization of organic materials for electrooptic and molecular electronics applications and for studying molecular magnetism in liquid-crystalline media.

clo[2.1.0.0^{1,3}.0^{2,4}.0^{2,5}.0^{3,5}]pentane (**7**), are not known although the compounds **4–6** have been predicted to be at least marginally stable as isolated molecules.^{10–13} Recent calculations for **6** showed that it is considerably less stable than other C₅H₂ isomers.¹⁴

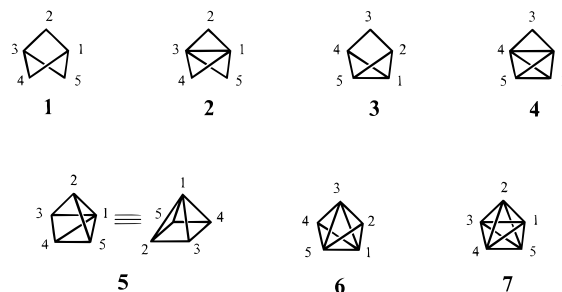
The synthesis and properties of bicyclo[1.1.1]pentanes,¹⁵ [*n*]staffanes,¹⁶ [1.1.1]propellanes,^{15,17,18} and tricyclo[2.1.0.0^{2,5}]pentanes¹⁹ have been the subject of prior reviews. Presently, we provide a comprehensive review of work dealing with all compounds containing the bicyclo[1.1.1]pentane skeleton and published through mid-1999.

Charts 2, 3, and 4, respectively, give the structures and formula numbers of the substituted [1.1.1]propellanes **8–12**, bicyclo[1.1.1]pentanes **13–97**, and tricyclo[2.1.0.0^{2,5}]pentanes **98–110** that will be referred to explicitly.



Josef Michl was born in 1939 in Prague, Czechoslovakia. He received his M.S. in Chemistry in 1961 under V. Horák and P. Zuman at Charles University, Prague, and his Ph.D. in 1965 under R. Zahradnik at the Czechoslovak Academy of Sciences, also in Prague. He left Czechoslovakia in 1968. He did postdoctoral work with R. S. Becker at the University of Houston, with M. J. S. Dewar at the University of Texas at Austin, with J. Linderberg at Aarhus University, Denmark, and with F. E. Harris at the University of Utah, where he stayed and became a full professor in 1975 and served as chairman in 1979–1984. In 1986–1990 he held the M. K. Collie-Welch Regents Chair in Chemistry at the University of Texas at Austin and subsequently moved to the University of Colorado at Boulder. He is a member of the National Academy of Sciences, the American Academy of Arts and Sciences, and the International Academy of Quantum Molecular Science. Dr. Michl's current research interests are the development of a molecular-size "Tinkertoy" construction set for the assembly of giant molecules and new solids, photochemistry, chemistry of silicon and boron, preparation and study of reactive organic and main-group organometallic molecules, and use of quantum chemical and experimental methods for better understanding of electronic structure. He has been the Editor of *Chemical Reviews* since 1984.

Chart 1. Bicyclo[1.1.1]pentane and Related Compounds



II. Properties

A. General

1. Bulk Properties

At ambient temperature and atmospheric pressure most known [1.1.1]propellanes are liquids, while most known bicyclo[1.1.1]pentanes and all known [*n*]staffanes are solids. The parent bicyclo[1.1.1]pentane (**1**) boils at the same temperature as *n*-pentane, but melts almost 100 °C higher than the latter. [*n*]Staffanes (**[*n*]**1****) and their derivatives melt at much higher temperatures than alkanes with the same number of carbons and the same functional groups.^{20,21} This has been attributed to a very efficient crystal packing and a low entropy of melting for the rigid rods compared to flexible chains.²⁰ Some derivatives of [*n*]staffanes give liquid-crystalline phases before melting into an isotropic liquid (see section V).

Tricyclo[2.1.0.0^{2,5}]pentane (**3**) derivatives are liquids or solids at ambient temperature and pressure.

Derivatives of **1**, **2**, and **3** are soluble in common organic solvents. The solubility of [*n*]staffanes and their derivatives rapidly decreases with increasing number of bicyclo[1.1.1]pentane units in the molecule. A table of solubilities of representative derivatives is available.²⁰

2. Stability

Bicyclo[1.1.1]pentane (**1**) and parent [*n*]staffanes (**[*n*]**1****) are thermally stable up to about 300 °C.²⁰ [*n*]-Staffanes with *n* ≥ 4 usually decompose at their melting point. Neat [1.1.1]propellane (**2**) is stable for several minutes in the gas phase at 110 °C,² and there are indications that **2** and its derivatives may be stable at even higher temperatures in the absence of electrophiles (see also section IV.B.7).^{22,23}

The parent **2** polymerizes spontaneously in liquid phase at temperatures above 0 °C, but can be stored as a solid in liquid nitrogen. Dilute solutions of **2** in ether may be stored in a refrigerator for several days, but spontaneous polymerization reduces the amount of **2** in the solution noticeably after about a week. It is best to store **2** in the form of the easily prepared and nearly indefinitely stable adduct, 1,3-diiodobicyclo[1.1.1]pentane (**13**, Chart 3), from which **2** is readily regenerated by reaction with an alkali cyanide in DMSO.^{24,25}

Tricyclo[2.1.0.0^{2,5}]pentane (**3**) is stable at -20 °C and survives purification in a preparative gas chromatograph, although with low recovery.⁹ Tricyclo[2.1.0.0^{2,5}]pentan-3-one (**98**, Chart 4) can be stored for months as a neat liquid at -5 °C.²⁶

[1.1.1]Propellane (**2**) has a strain energy of 98 kcal/mol,²⁷⁻²⁹ compared to 65^{30,31} or 68²⁹ kcal/mol for bicyclo[1.1.1]pentane (**1**) and 27.5 kcal/mol for cyclopropane.²⁹ The relatively high stability is therefore surprising until it is realized that there is no easy way to release strain. Breaking of the central C-C bond releases less than a third of the strain energy since **1** is still highly strained, and the breaking of a peripheral C-C bond is symmetry-forbidden. An RHF/6-31G* calculation predicts the strain energy of **3** to be 3.7 kcal/mol higher than that of **2**.³² Breaking of the C(1)-C(5) bond leads to the strained structure **1**, as in the case of **2**. Thus, derivatives of **3** are moderately stable.

B. Molecular and Electronic Structure

1. Molecular Geometry and Electronic Structure

a. Bicyclo[1.1.1]pentane (1). Structural properties of the derivatives of **1** and of [*n*]staffanes (**[*n*]**1****) have been studied by X-ray diffraction,³³⁻⁴⁹ electron diffraction,^{50,51} and microwave spectroscopy.^{52,53} Interatomic distances and valence angles in bicyclo[1.1.1]pentanes and [*n*]staffanes are collected in Table 1. Two electron-diffraction values have been published for the H-C-H angle in **1**: 103.9⁵⁰ and 111.7°.⁵¹ Calculations and analysis of vibrational spectra favor the latter value.⁵⁴ The nonbonded interbridgehead distance in the parent **1** has been reported as 1.845⁵⁰ and 1.874⁵¹ Å, much shorter than

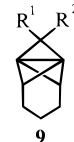
Chart 2. Substituted [1.1.1]Propellanes

2,4-Ethylene[1.1.1]propellanes

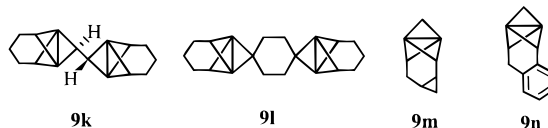


compd	R ¹	R ²
8a	H	H
8b	Ph	Ph
8c	CH=CH ₂	H
8d	<i>E</i> -CH=CHMe	H
8e	<i>p</i> -C ₆ H ₄ OMe	H
8f	1-naphthyl	H
8g	Ph	<i>o</i> -C ₆ H ₄ Br

2,4-Trimethylene[1.1.1]propellanes



compd	R ¹	R ²
9a	H	H
9b	Me	H
9c	<i>i</i> -Pr	H
9d	<i>c</i> -C ₆ H ₁₁	H
9e	<i>E</i> -CH=CHMe	H
9f	Ph	H
9g	Me	Me
9h	Me	CH ₂ OPh
9i		-(CH ₂) ₄ -
9j		-(CH ₂) ₅ -



Monosubstituted [1.1.1]Propellanes

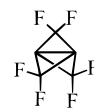


compd	R	compd	R
10a	Et	10k	CH ₂ CH(Me)- <i>n</i> -Pr
10b	<i>n</i> -Pr	10l	CH ₂ Ph
10c	(CH ₂) ₄ Me	10m	CH ₂ CH ₂ Ph
10d	(CH ₂) ₆ Me	10n	CH ₂ OH
10e	(CH ₂) ₁₀ Me	10o	CH ₂ OCH ₂ OMe
10f	(CH ₂) ₃ OMe	10p	CH ₂ OSi(<i>t</i> -Bu)Me ₂
10g	(CH ₂) ₅ OMe	10q	CH ₂ OAc
10h	CH(Me)Et	10r	CH ₂ O ₂ CNHCH ₂ Ph
10i	CH ₂ CH(Me) ₂	10s	(CH ₂) ₂ OCH ₂ OMe
10j	CH ₂ CH(Me)Et		

Other Substituted [1.1.1]Propellanes



compd	R ¹	R ²
11a	Et	Et
11b		-(CH ₂) ₃ -
11c	Cl	Cl



12

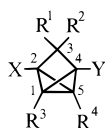
Chart 3. Bridgehead-Substituted Bicyclo[1.1.1]pentanes

	X	Y		X	Y		X	Y		X	Y		X	Y
13	I	I	18b	Br	Br	20b	CO ₂ H	Cl	29	SPh	H	42	CO ₂ H	CO ₂ H
14	CO ₂ H	H	18c	Br	F	20c	CO ₂ H	CF ₃	30a	SPh	SPh	43	COCl	COCl
15	NH ₂	H	18d	I	Br	20d	CO ₂ H	Ph	30b	SMe	SMe	44	CH ₂ Cl	H
16	F	F	18e	I	Cl	20e	CO ₂ H	CO ₂ Me	31	Sn(<i>n</i> -Bu) ₃	H	45	NO ₂	NO ₂
17a	F	H	18f	Br	Cl	20f	CO ₂ H	Br	32	COPh	H	46	CO ₂ Me	CO ₂ Me
17b	Cl	H	18g	Br	F	21	D	H	33	CONH ₂	H	47	SO ₂ Me	Cl
17c	OH	H	19a	CO ₂ ⁻	F	22	D	D	34	SePh	H	48	CF ₃	I
17d	CF ₃	H	19b	CO ₂ ⁻	I	23	C≡CH	C≡CH	35	Ph	Li	49	CO ₃ - <i>t</i> -Bu	CO ₂ Me
17e	PH ₂	H	19c	CO ₂ ⁻	Br	24	Me	H	36	Ph	F	50	CO ₂ Me	CO ₂ H
17f	CH ₃	H	19d	CO ₂ ⁻	Cl	25	Me	Me	37	Ph	H	51	SiMe ₃	SiMe ₃
17g	SiH ₃	H	19e	CO ₂ ⁻	H	26a	CO ₂ Me	H	38	CH(OH)Ph	CH(OH)Ph	52	Br	SiMe ₃
17h	I	H	19f	CO ₂ ⁻	CF ₃	26b	CO ₂ Me	Et	39	SH	SH	53	SiEt ₃	H
17i	Br	H	19g	CO ₂ ⁻	CO ₂ Me	27	CHO	H	40	Cl	Cl	54	CH(Me)SiHEt ₂	H
18a	I	F	20a	CO ₂ H	F	28	Li	Li	41	COCl	H	55	I	CCl ₃

	X	Y		X	Y		X	Y
56	NO ₂	H	67	CH ₂ CO ₂ NC ₅ H ₄ S	H	82	O ₂ CPh	O ₂ CPh
57	NO ₂	SCN	68	CMe ₂ CH ₂ C≡CH	H	83	SCOMe	SH
58	(EtO) ₂ PO	(EtO) ₂ PO	69	$\overline{\text{-CMeCH}_2\text{C(=CH}_2\text{)CH}_2\text{-}}$	H	84	SH	H
59a	CF ₃	CF ₃	70	CH(OEt)Ph	H	85	SO ₂ Me	SO ₂ Me
59b	Ph	Ph	71	C(=N ₂)Ph	H	86	SO ₃ H	H
60	(CH ₂) ₂ CN	(CH ₂) ₂ CN	72	CHCl ₂	H	87	SO ₃ H	SO ₃ H
61	Ph	I	73	CCl ₃	D	88	Ph	NH ₂
62	(CH ₂) ₂ CO ₂ H	I	74	CH(NH ₂)CO ₂ H	CO ₂ Me	89	NH ₂	NH ₂
63	CF ₃	Me	75	CO ₂ CO- <i>t</i> -Bu	CO ₂ Me	90	NH ₂	NC
64	CF ₃	Ph	76	CH ₂ OH	CO ₂ Me	91	NC	NC
65a	OMe	I	77	CHO	CO ₂ Me	92	COMe	COMe
65b	N ₃	I	78	CH(CN)NHCHPhCH ₂ OH	CO ₂ Me	93	C ₄ H ₉ S	C ₄ H ₉ S
66a	NEt ₃ ⁺ I ⁻	I	79a	Ph	COMe	94	C ₄ H ₉	CO ₂ Me
66b	DABCO ⁺ I ⁻	I	79b	Ph	COBu	95	MeCOS	SOCMe
66c	NC ₄ H ₈ O ⁺ I ⁻	I	80a	Ph	CH ₂ Me	96	SRu(NH ₃) ₅	SH
66d	NC ₅ H ₅ ⁺ I ⁻	I	80b	Ph	CH ₂ Bu	97	SAg	SH
66e	(NC ₅ H ₄) ₂ ⁺ I ⁻	I	81	OAc	CO ₂ H			

the 1,3-distance in cyclobutane (2.14 Å).⁵⁵ In the absence of bridge substituents, it varies from 1.80⁴⁷ to 1.91 Å⁴⁵ depending on substitution in the bridgehead positions. Upon hexafluorination on the bridges it increases to 1.979 Å in **111** (Chart 5).⁴⁸ This large increase is attributed to the tendency of the C–CF₂–C

valence angle to be larger than the C–CH₂–C angle, in agreement with Bent's rules.⁵⁶ In [**n**]**1** and their derivatives the intracage interbridgehead distances are around 1.88 Å.⁴⁵ These distances may or may not vary from cage to cage along the staffane chain depending on the bridgehead substituents and the

Chart 4. Tricyclo[2.1.0.0^{2,5}]pentanes

Compound	R ¹	R ²	R ³	R ⁴	X	Y
98		=O	H	H	H	H
99a		=O	Me	Me	H	H
99b		=O	Ph	Ph	H	H
99c		=O	CH ₂ OAc	CH ₂ OAc	H	H
99d		=O	CO ₂ Me	CO ₂ Me	H	H
99e		=O	CH ₂ I	CH ₂ I	H	H
99f		=O	CH ₂ Br	CH ₂ Br	H	H
99g		=O	CH ₂ OH	CH ₂ OH	H	H
99h		=O	CH ₂ Cl	CH ₂ Cl	H	H
99i		=O	SiMe ₃	SiMe ₃	H	H
99j		=O	<i>n</i> -Pr	<i>n</i> -Pr	H	H
99k		=O	CH ₂ N(BOC)N(BOC)CH ₂		H	H
99l		=O	CH ₂ NHNHCH ₂		H	H
100a	OCH ₂ CH ₂ O		CO ₂ Me	CO ₂ Me	H	H
100b	OCH ₂ CH ₂ O		CH ₂ OAc	CH ₂ OAc	H	H
100c	OCH ₂ CH ₂ O		CH ₂ OH	CH ₂ OH	H	H
101a	H	O ₂ CC ₆ H ₅	Me	Me	H	H
101b	H	O ₂ CC ₆ H ₅	Ph	Ph	H	H
101c	H	O ₂ CC ₆ H ₄ Br	Ph	Ph	H	H
101d	H	O ₂ CC ₆ H ₅	Me	H	Me	H
102a	OEt	OEt	CH ₂ OAc	CH ₂ OAc	H	H
102b	OEt	OEt	CH ₂ Cl	CH ₂ Cl	H	H
102c	OEt	OEt	CH ₂ N(BOC)N(BOC)CH ₂		H	H
102d	OEt	OEt	CH ₂ OH	CH ₂ OH	H	H
103	=CH ₂		H	H	H	H
104a	=O		<i>t</i> -Bu	<i>t</i> -Bu	<i>t</i> -Bu	<i>t</i> -Bu
104b	=O		<i>t</i> -Bu	<i>t</i> -Bu	<i>t</i> -Bu	Et
104c	=O		<i>t</i> -Bu	<i>t</i> -Bu	<i>t</i> -Bu	<i>i</i> -Pr
104d	=O		<i>t</i> -Bu	<i>t</i> -Bu	<i>t</i> -Bu	1-adamantyl
105a	H	OH	Me	Me	H	H
105b	H	OH	CH ₂ OAc	CH ₂ OAc	H	H
105c	H	OH	Ph	Ph	H	H
105d	Me	OH	Me	Me	H	H
106	H	H	H	H	Me	Me
107	Me	Me	Ph	Ph	Me	<i>t</i> -Bu
108a	H	OH	Me	H	Me	H
108b	Me	OH	Me	H	H	H
109	=CH ₂		Me	Me	H	H
110	=O		<i>t</i> -Bu	<i>t</i> -Bu	H	<i>t</i> -Bu

number of bicyclo[1.1.1]pentane units in the chain. The intercage C–C bonds are very short, 1.46–1.50 Å,⁴⁵ as expected from Bent's rules⁵⁶ for bonds made by carbon hybrids with high *s* character (see below). The endocyclic C–C bonds have a normal length of 1.545–1.56 Å.⁴⁵ The length of [*n*]staffane rods measured between the farthest bridgehead carbons in-

creases in increments of 3.4 Å per bicyclo[1.1.1]pentane unit, and it is 12.0 Å for *n* = 4.⁴⁵

Difference electron density was determined in the bicyclo[1.1.1]pentane derivative **112** (Chart 5).⁵⁷ It demonstrated the presence of bent bonds and the absence of a bond between the bridgehead atoms.

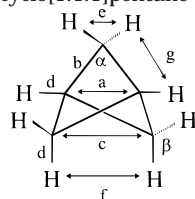
b. [1.1.1]Propellane (2). This molecule contains three fused cyclopropane rings with structural parameters similar to those of the parent cyclopropane. The experimentally determined structural properties of [1.1.1]propellanes **2**, **8a,b**, and **9a,k,l** are summarized in Table 2.¹⁷ The C(1)–C(2) bond length in the parent **2** has been measured by different methods to be 1.512–1.555 Å,^{58–60} compared to that of 1.514 Å in cyclopropane.^{62,63} The length of the central bond is 1.593–1.605 Å.^{58–60} Valence angles in the three-membered rings are 58° for C(1)–C(3)–C(2) and 63° for C(1)–C(2)–C(3). The C(2)–C(1)–C(4) angles are about 95°. The H–C–H angle is 116°, significantly larger than that in **1**.

Experimentally determined electron density distributions in two [1.1.1]propellane derivatives, **8a** and **9a**,⁶⁴ indicate the presence of bent bonds and positive (excess) electron density in the region outside of the inverted bridgehead carbon atoms. Electron density between these carbons is slightly less than would correspond to the sum of contributions from two spherically symmetrical neutral atoms, but since these are not an appropriate reference, no conclusions about the presence or absence of an interbridgehead bond were drawn from this result.

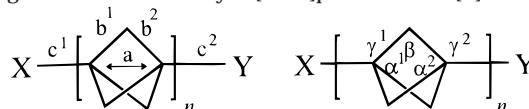
c. Tricyclo[2.1.0.0^{2,5}]pentane (3). Structures of compounds **99a–d**, **100a,b**, **101a**, and **102a** have been studied by X-ray diffraction on single crystals (Table 3).^{65–72} The methylene bridge between C(2) and C(4) provides a fixed angle α between the planes C(1)–C(2)–C(5) and C(1)–C(4)–C(5) of 94–99°, compared to 113–130° in analogous unbridged bicyclo[1.1.0]butanes.¹⁹ Such a small angle α forces the hybrid orbitals on C(1) and C(5) that point toward each other to form an extraordinarily short bent bond (1.408–1.509 Å). The valence angles β between the C(1)–C(5) bond and the bonds to substituents attached to these two carbons are larger than the angles between the carbon hybrids forming the bonds.¹⁹ The largest experimental value for the angle β is 145° in **99a**. π -Acceptor substituents in positions 1 and 5 cause the value of the angle β to decrease, and the C(1)–C(5) bond to lengthen. The bridging carbonyl group in the ketones **99** has the opposite effect, and the C(1)–C(5) bond is shorter in **99** than in the corresponding ketals **100** and **102**, while the value of the angle β is larger in the ketones **99** (see also section II.B.1.d).¹⁹

d. Hybridization. Qualitative assessment of hybridization in the simple valence-electron basis set model often provides useful insight. Different methods agree in the assignment of hybridization in derivatives of **1**. The ¹*J*_{HC} spin–spin coupling constant analysis yields hybridizations of sp^{2.5} and sp^{2.1} for the hybrids used by C(2) and C(1), respectively, to bind hydrogens, and an average hybridization of sp^{3.7} for the hybrids used in the endocyclic C–C

Table 1. Structural Properties of Bicyclo[1.1.1]pentanes and [n]Staffanes

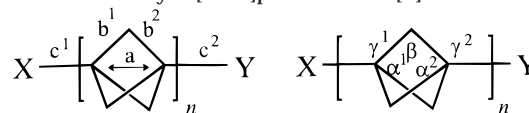
Bicyclo[1.1.1]pentane (1)^a

distances (Å)							angles (deg)		ref
a	b	c	d	e	f	g	α	β	
1.845(160)	1.545(60)	2.147(53)	1.110(10)	1.732 ^b	2.455 ^b	2.918 ^b	73.3(10)	103.9(50)	50
1.874(4)	1.557(2)	2.151(3)	1.109(4)	1.835(20)	2.340(28)	2.817(7)	74.2(2)	111.7(18)	51

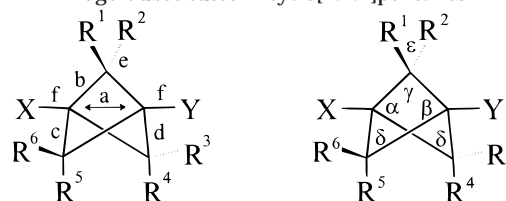
Bridge-Unsubstituted Bicyclo[1.1.1]pentanes and [n]Staffanes^c

compd			distances (Å)					angles (deg)					ref
[n]	X	Y	a	b ^{1d}	b ^{2d}	c ¹	c ²	α ^{1d}	α ^{2d}	β ^d	γ ^{1d}	γ ^{2d}	
[1]	COMe	COMe	1.874(6)										45
[1]	CO ₂ Ti ^e	CO ₂ Ti ^e	1.858(4)										34
[1]	Cl	H	1.850	1.536(7)	1.556(7)	1.761(12)	1.102 ^f	88.63	87.20	73.47(50)	126.2		52
[1]	g	H	1.884(3)	1.561(4)	1.547(4)	1.474(3)		86.6(2)	87.6(2)	74.6(2)	127.4(2)		44
[1]	CO ₂ H	CH ₃	1.873(2)	1.549(2)	1.557(2)	1.486(2)	1.498(3)	87.2(1)	86.7(1)	74.2(1)	126.4(2)	127.1(2)	38
[1]	CCl ₃	Cl	1.83(2)	1.53(1)	1.51(1)	1.46(2)	1.81(2)	86.7(6)	88.5(6)	73.9(5)	127.6(7)	126.3(6)	37
[1]	CCl ₃	I	1.835(7)	1.547(8)	1.555(7)	1.498(7)	2.109(5)	88.7(3)	88.3(4)	h	126.0(4)	126.3(3)	37
[1]	I	C ₅ H ₅ N ⁺	1.80(2)	1.55(2)	1.54(2)	2.12(1)	1.47(2)	88.8(9)	90.2(10)	71.2(7)	126.1(8)	125.2(12)	47
[1]	t-Bu	Ph	1.891(2)	h	1.546(2)	1.518(2)	1.493(2)	h	86.81(9)	75.21	127.2(1)	h	49
[2]	Br	Br	1.824(9)	1.538(5)	1.555(5) ⁱ	1.933(9)	1.478(9) ^j	89.4(2)	88.1(2) ⁱ	72.7(2)	125.7(2)	126.6(3) ⁱ	45
[2]	SMe	SMe	1.861(4)	1.553(4)	1.546(3) ⁱ	1.784(2)	1.480(3) ^j	86.9(2)	87.4(2) ⁱ	73.9(2)	126.7(2)	127.1(2) ⁱ	41
[2]	SO ₂ Me	SO ₂ Me	1.856(5)	1.548(6)	1.558(6) ⁱ	1.762(4)	1.469(6) ^j	88.3(2)	87.6(2) ⁱ	73.4(2)	126.4(1)	127.0(2) ⁱ	41
[2]	CO ₂ Me	H	1.871(4)	1.539(2)	1.558(2) ⁱ	1.487(4)	1.487(4) ^j	87(1)	86.7(1) ⁱ	74.3(1)	126.9(1)	127.2(1) ⁱ	45
			1.871(4)	1.548(3) ⁱ	1.546(3)			86.6(1) ⁱ	87.1(1)	74.5(1)	127.0(1) ⁱ		
[2]	SAc	SAc	1.858(5)	1.547(3)	1.557(3) ⁱ	1.798(4)	1.476(4) ^j	88.2(2)	87.6(2) ⁱ	73.6(1)	120.8(3)	124.6(4) ⁱ	45
[2]	CCl ₃	H	1.872(3)	1.558(3) ⁱ	1.547(3)	1.490(3)	1.473(3) ^j	87.8(2)	87.0(2) ⁱ	74.2(2)	126.8(2)	127.3(2) ⁱ	40
			1.877(3)	1.541(3)	1.551(3) ⁱ			86.7(2) ⁱ	87.3(2)	74.8(2)	127.6(2) ⁱ		
[2]	Cl	CCl ₃	1.828(8)	1.519(9)	1.542(8) ⁱ	1.786(6)	1.481(8) ^j	88.8(5)	87.1(5) ⁱ	73.3(4)	126.1(5)	127.2(5) ⁱ	40
			1.843(7)	1.551(8) ⁱ	1.538(8)		1.508(7)	87.6(4) ⁱ	88.5(4)	73.2(4)	126.9(5) ⁱ	126.3(5)	
[2]	CN	H	1.863(11)	1.546(11)	1.545(11) ⁱ	1.447(11)	1.497(11) ^j	87.4(6)	87.5(6) ⁱ	74.1(5)	127.1(7)	127.0(6) ⁱ	46
			1.854(12)	1.543(12) ⁱ	1.531(13)			86.9(6) ⁱ	87.8(7)	74.2(6)	127.4(7) ⁱ		
[3]	H	H	1.866(9)		1.536(5) ^{k,l}		1.458(8) ^{j,l}		87.0(3) ^{k,l}	74.7(4) ⁱ		127.2(4) ^{k,l}	42 ⁱ
			1.869(9)		1.555(3) ^{i,j}			86.4(3) ^{i,k,l}		75.9(4) ⁱ		127.5(2) ^{i,k,l}	
[3]	SAc	SAc	1.869(7)	1.535(11)	1.557(12) ⁱ	1.783(5)	1.465(7) ^j	88.0(6)	86.4(6) ⁱ	74.4(5)	126.5(6)	127.8(6) ⁱ	45
			1.893(7)	1.514(12) ⁱ	1.514(10) ⁱ		1.468(7) ^j	85.0(6) ⁱ	85.1(6) ⁱ	77.4(5)	128.7(5) ⁱ	128.7(6) ⁱ	
			1.881(7)	1.538(1) ⁱ	1.541(14)		1.781(5)	86.6(6) ⁱ	86.4(6)	75.4(6)	127.6(7) ⁱ	127.7(6)	
[3]	SAc	SAc	1.864(7)	1.541(9)	1.555(11) ⁱ	1.792(6)	1.476(7) ^j	88.0(5)	87.0(5) ⁱ	74.0(5)	126.5(5)	127.3(5) ⁱ	45
			1.887(7)	1.550(11) ⁱ	1.547(8) ⁱ		1.464(7) ^j	86.6(5) ⁱ	86.8(5) ⁱ	75.1(4)	127.6(5) ⁱ	127.4(5) ⁱ	
			1.866(8)	1.562(8) ⁱ	1.539(11)		1.785(6)	86.7(5) ⁱ	88.3(5)	74.0(5)	127.6(6) ⁱ	126.4(4)	
[3]	SAc	SAc	1.860(6)	1.536(4)	1.551(4) ⁱ	1.784(4)	1.470(6) ^j	87.9(2)	86.9(2) ⁱ	74.2(2)	125.4(2)	127.3(2) ⁱ	45
			1.902(6)		1.556(4) ⁱ				86.4(2) ⁱ	75.4(3)		127.4(3) ⁱ	

Table 1. (Continued)

Bridge-Unsubstituted Bicyclo[1.1.1]pentanes and [n]Staffanes^c (Continued)

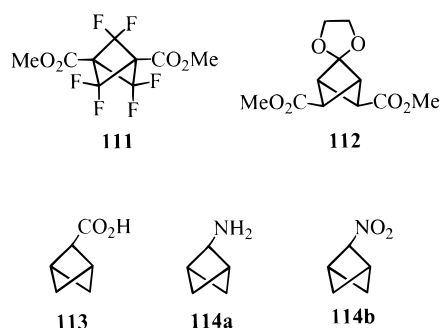
compd			distances (Å)					angles (deg)					ref
[n]	X	Y	a	b ^{1d}	b ^{2d}	c ¹	c ²	α ^{1d}	α ^{2d}	β ^d	γ ^{1d}	γ ^{2d}	
[4]	H	H	1.886(9) 1.888(6)	1.552(3) ^{k,l} 1.555(3) ^{k,l}		1.473(6) ^{j,l} 1.498(8) ^{j,l}		86.9(2) ^{k,l} 87.0(1) ^{i,k,l}		74.8(2) ^l 74.7(2) ^l	127.3(3) ^{k,l} 127.6(1) ^{i,k,l}		42 ^l
[4]	SAc	SAc	1.866(6) 1.900(6)	1.544(5) 1.559(4) ⁱ	1.558(5) ⁱ 1.556(4) ⁱ	1.798(5)	1.477(6) ^j 1.480(6) ^j	88.4(2) 87.0(2) ⁱ	87.5(2) ⁱ 87.1(2) ⁱ	73.9(2) 75.1(2)	126.3(2) 127.7(2) ⁱ	127.2(2) ⁱ 127.4(2) ⁱ	45
[4]	SAc	SAc	1.854(6) 1.891(6)	1.546(4) 1.558(4) ⁱ	1.555(4) ⁱ 1.558(4) ⁱ	1.795(5)	1.485(6) ^j 1.479(9) ^j	87.9(3) 86.6(2) ⁱ	87.1(2) ⁱ 86.9(2) ⁱ	73.4(2) 74.7(2)	127.7(2) 127.5(2) ⁱ	127.1(2) ⁱ 127.3(2) ⁱ	45

Bridge-Substituted Bicyclo[1.1.1]pentanes^c

compd				distances (Å)						angles (deg)					ref
X	Y	R ¹ , R ²	R ³⁻⁶	a	b	c	d	e	f	α	β	γ	δ ^k	ε	
H	H	Ph, OR ^m	H	1.89	1.55	1.54		1.45 (C–O) 1.47 (C–C)		87.5	87	75.5	75	108	33
H	H	=O	H	1.955	1.524	1.573		1.201 (C=O)		<i>n</i>	<i>n</i>	79.8	76.9		53
Me	CO ₂ H	Cl, Cl	H	1.903(3)	1.530(2)	1.557(2)		1.784(2) [C–Cl]	1.493(3) ^o 1.492(3) ^p	86.1(2)	85.9(2)	76.9(2)	75.3(2)	106.1(2)	37
H	H	O(CH ₂) ₂ O	CO ₂ Me ^{q,r}	1.903(3)	1.541(3)	1.554(3)	1.554(3)	1.402(3) [C–O]	1.498(3) ^s	85.4(2)	87.9(2)	76.2(2)	75.5(2)	106.8(2)	35, 36
H	H	O(CH ₂) ₂ O	CO ₂ Me ^{q,t}	1.902(3)	1.543(3)	1.554(3)	1.555(3)	1.404(3) [C–O]	1.497(3) ^s	85.4(2)	88.0(2)	76.1(2)	75.4(2)	106.7(2)	36
H	H	O(CH ₂) ₂ O	CO ₂ Me ^u	1.898(3)	1.532(3)	1.547(3)		1.398(2) [C–O]	1.498(3) ^s	86.3(1)	85.6(2)	76.5(1)	75.6(1)	107.3(2)	36
H	H	O(CH ₂) ₂ O	CO ₂ Me ^{r,v}	1.907(3)	1.545(5)	1.557(6)	1.556(4)	1.400(6) [C–O]	1.492(6) ^s	86.0(1)	86.6(3)	76.2(2)	75.5(2)	107.1(3)	36
H	H	O(CH ₂) ₂ O	CO ₂ Me ^{t,v}	1.903(6)	1.544(6)	1.553(6)	1.554(5)	1.402(4) [C–O]	1.502(4) ^s	86.1(3)	86.6(3)	76.1(2)	75.5(3)	107.0(2)	36
CO ₂ Me	CO ₂ Me	F, F	F	1.976(2)		1.562(2)		1.347(2) [C–F]	1.503(2)	84.2(8)		78.6(1)		106.5(3)	48

^a Electron diffraction. ^b No error margins have been reported for the calculated values. ^c X-ray diffraction. ^d Average values of distances or angles related by appropriate symmetry. ^e Each titanium atom carries two Cp ligands. ^f An assumed value for the C–H distance. ^g 4-(Bicyclo[1.1.1]pent-1'-yl)cub-1-yl. ^h The value is not listed. ⁱ C–C distance or CCC angle at a bridgehead carbon facing another cage. ^j Interchange CC bond lengths. ^k Average values of distances or angles. ^l The value is taken from reference 45. ^m R = 4-CONHC₆H₄Br. ⁿ Not reported. ^o Distance C–CO₂Me. ^p Distance C–CH₃. ^q R⁴ = R⁵ = CO₂Me, R³ = R⁶ = H. ^r Molecule I as a part of the asymmetric unit. ^s Average distance C(bridge)–CO₂Me. ^t Molecule II as a part of the asymmetric unit. ^u R³ = R⁶ = CO₂Me, R⁴ = R⁵ = H. ^v R³ = R⁵ = CO₂Me, R⁴ = R⁶ = H.

Chart 5



bonds.^{73,74} These numbers are in reasonable agreement with *ab initio*^{48,75} and semiempirical⁷⁶ calculations. As noted above, short length and high strength of the intercage bonds in [*n*]1 derivatives agree with the high *s* character of the bridgehead carbon hybrids used for exocyclic bonds.¹⁶

The substituent properties of the bicyclo[1.1.1]pentyl and related groups relative to alkyl and cycloalkyl groups are largely dictated by their unusual hybridization. The high *s* character of exocyclic hybrid orbitals causes both the bicyclo[1.1.1]pent-1-yl and the bicyclo[1.1.1]pent-2-yl groups to represent substituents with an inductively electron-withdrawing effect.^{16,78} Thus, bicyclo[1.1.1]pentane-1-carboxylic acid (**113**, Chart 5) and bicyclo[1.1.1]pentane-2-carboxylic acids (**113**, Chart 5) are significantly more acidic (Table 4) than pivalic acid ($pK_a = 5.05$).^{77,78} Bicyclo[1.1.1]pent-1-ylamine (**15**)⁷⁷ is less basic than ammonia, and both **15** and bicyclo[1.1.1]pent-2-ylamine (**114a**) are less basic than other cycloalkylamines.^{77,78} 2-Nitrobicyclo[1.1.1]pentane (**114b**) is, however, much less acidic than nitrocyclohexane or nitrocyclopentane,⁷⁸ and this is undoubtedly related to the reluctance of carbon 2 to accept sp^2 hybridization and the resulting increase in strain.

Table 2. Selected Interatomic Distances and Angles in [1.1.1]Propellane and Its Derivatives

	distances (Å)			angles (deg)				method	ref
	C1–C3	C1–C2	C2–C(R)	C1–C4–C3	C1–C2–C3	C2–C1–C3	C4–C3–C5		
2	1.60	1.522	<i>a</i>	<i>a</i>	<i>a</i>	<i>a</i>	<i>a</i>	<i>b</i>	58
	1.596	1.525	<i>a</i>	63.1	<i>a</i>	<i>a</i>	95.1	<i>c</i>	59
	1.605 ^d	1.525–1.555 ^d	<i>a</i>	63.0–63.7 ^d	<i>a</i>	57.9–58.8 ^d	92.4–99.0 ^d	<i>e</i>	60
	1.593 ^f	1.512–1.539 ^f	<i>a</i>	62.4–62.8 ^f	<i>a</i>	57.9–59.7 ^f	94.4–96.9 ^f	<i>e</i>	60
8a	1.587	1.529	1.517	62.48, 62.50	62.95	58.69–58.84	98.04, 98.03	<i>e</i>	64
8b	1.592 ^d	1.517–1.534 ^d	1.521, 1.529 ^d	62.7, 62.9 ^d	62.9 ^d	58.7, 59.1 ^d	97.2–98.4 ^d	<i>e</i>	169
	1.586 ^f	1.524–1.526 ^f	1.517, 1.524 ^f	62.7 ^f	62.9 ^f	58.7 ^f	97.8–98.2 ^f	<i>e</i>	169
9a	1.585	1.524–1.538	1.519, 1.522	62.31, 62.36	62.81	58.43–59.22	95.42, 96.08	<i>e</i>	64
9k	1.577	1.513–1.529	1.515	62.46	62.72	58.30	96.20	<i>e</i>	208
9l	1.587 ^g	1.499–1.599 ^g	1.531, 1.532 ^g	60.7, 63.7 ^g	62.4 ^g	57.8, 58.7 ^g	94.7–97.1 ^g	<i>e</i>	169
	1.601 ^h	1.508–1.560 ^h	1.534, 1.552 ^h	62.5, 63.4 ^h	<i>a</i>	57.4, 59.8 ^h	<i>a</i>	<i>e</i>	169

^a Not reported. ^b IR/Raman spectroscopy. ^c Electron diffraction. ^d Molecule A in the crystal. ^e X-ray diffraction. ^f Molecule B in the crystal. ^g One of the propellane cages in the molecule. ^h The other propellane cage in the molecule.

Table 3. Selected Interatomic Distances and Angles in Tricyclo[2.1.0.0^{2,5}]pentane and Its Derivatives (Adapted from Ref 19)

compd	R ¹	R ²	C1–C5 (Å)	C1–C2 (Å)	C2–C4 (Å)	α (deg)	β (deg)	ref
99a	=O	Me	1.408	1.539	2.003	94.1	144.5	66
99a	=O	Me	1.417	1.545	2.024	95.0	145.0	67
99b	=O	Ph	1.444	1.526	2.001	96.1	142.1	66
99c	=O	CH ₂ OAc	1.416	1.528	2.006	95.7	144.1	71, 72
99d	=O	CO ₂ Me	1.453	1.521	2.031	98.9	137.9	70
100a	OCH ₂ CH ₂ O	CH ₂ OAc	1.455	1.515	1.987	96.8	132.9	69
100b	OCH ₂ CH ₂ O	CO ₂ Me	1.485	1.509	1.993	98.7	131.4	70
101a	H, OCOC ₆ H ₄ Br	Ph	1.44	1.53	1.99	95	139	68
102a	OEt, OEt	-CH ₂ N(BOC)N(BOC)CH ₂ -	1.509	1.511	1.986	98.6	120.0	65

Table 4. Acidities of Bicyclo[1.1.1]pentane Derivatives

position of substituent	substituent				
	H gas phase ^a	CO ₂ H pK _a (H ₂ O)	NH ₃ Cl pK _a (H ₂ O)	NH ₃ Cl pK _a (50% aq EtOH)	NO ₂ pK _a (50% aq MeOH)
1	411 ± 3.5 ^b	4.09 ^c	8.58 ^c	8.2 ^{d,e}	
2		4.27 ^e		8.90 ^e	11.20 ± 0.11 ^e

^a kcal/mol. ^b Reference 100. ^c Reference 77. ^d Estimated value based on the pK_a in water. ^e Reference 78.

Consideration of hybridization alone would suggest that proton acidity and CH bond strength in position 1 are considerably higher than in position 2. However, as we shall see below, matters are complicated by strong 1–3 transannular interactions.

The hybridization of atomic orbitals in [1.1.1]-propellane (**2**) is controversial. One-bond spin–spin coupling constants were used to estimate the character of the hybrids used by carbons for bonding in **2** with the use of empirical equations.^{17,73} In **2**, ¹J_{CH} is 163.7 Hz^{2,58,73} (159 and 162 Hz in **9a**⁷⁹), and this corresponds to sp^{2.1} hybridization of the hybrids used by the bridge carbon C(2) for C–H bonds. The other two mutually equivalent hybrids used by C(2) to bind the bridgehead carbons C(1) and C(3) therefore are sp^{4.7}. The ¹J_{C(1)C(2)} spin–spin coupling constant of 9.9 ± 0.1 Hz⁷³ then requires sp^{8.6} hybridization for the hybrids used by the bridgehead carbons for C(1)–C(2) bonds. This analysis leaves an sp^{0.5} hybrid on each bridgehead carbon to be used for the central C(1)–C(3) bond. Another set of empirical equations²⁷ yielded hybridizations of sp^{2.1} for the C(2)–H hybrid, sp^{4.5} and sp^{4.6} for the hybrids used by C(2) and C(1), respectively, to form the C(1)–C(2) bond, and sp^{1.2} for the hybrids that form the central bond. This very high s character of the bridgehead carbon orbitals used for the central bond agrees with the interpretation proposed for e,2e (electron momentum) spectra.⁶¹

In contrast, the recently measured⁸⁰ and calculated⁸¹ ¹J_{C(1)C(3)} constants suggest a very high p character for the central bond in **2**. Analysis of quantum mechanical results¹⁷ shows that the hybrids forming the central C–C bond are essentially purely p in character, and the hybrids used by the bridgehead carbon for the peripheral C(1)–C(2) bonds are sp². The fact that the central bond is heavily represented in the HOMO according to photoelectron⁸² and electron energy loss⁸³ spectra agrees with the latter evaluation of orbital hybridization.¹⁷

We consider it likely that the latter interpretation is correct and that the best simple description of the electronic structure of **2** is based on a pair of sp² hybridized carbons, bound to each other by a single bond formed from their p orbitals, and using the three pairs of equivalent sp² hybrids to make bent bonds to three methylene groups. It seems to us that the empirical equations relating NMR coupling constants to hybridization are invalid in this highly strained system. It is more difficult to account for the discrepancy with the interpretation of the electron-momentum spectra. Many other discussions of the nature of bonding in **2** from different points of view have appeared in a number of publications and we provide leading references.^{17,61,84–86}

The strength of the central C–C bond in **2** is about 60 kcal/mol,^{2,87,88} much less than usual in alkanes,

and some biradicaloid character is present in it.¹⁷ Natural bond orbital analysis⁸⁹ predicts the occupancy for the central bonding orbital to be 1.83, and for the antibonding orbital this number is 0.15.¹⁷

Very high values of ¹J_{C(1)H} in tricyclo[2.1.0.0^{2,5}]pentane derivatives (>200 Hz, see also section II.C.5) indicate a large share of s orbital in the carbon hybrid.⁹⁰ The hybrid is estimated to be sp^{1.5} in **3** and sp^{1.1} in **98**.⁹¹ The exocyclic orbital of C(2) is sp^{1.7} hybridized.⁹¹ The hybrids forming the C(1)–C(5) bond are sp^{4.6} in **3** and sp^{4.0} in **98** according to natural bond orbital calculations.⁸⁹ This result is in agreement with high CH acidity⁹⁰ and with the strong influence that π-accepting substituents have on the length of this bond.^{19,69,70,92} It also makes it clear why the bond is so strongly bent: the p orbitals do not point at each other.

The [1.1.1]propell-2-yl and tricyclo[2.1.0.0^{2,5}]pent-1-yl groups most likely have an even stronger electron-withdrawing inductive effect than the bicyclo[1.1.1]pent-1-yl group. The Walsh orbitals of these substituents are well set up for strong electron-donating hyperconjugative effects as well, but no experimental evidence seems to be available so far.

2. Interactions within the Bicyclo[1.1.1]pentane Cage

a. Interbridgehead Interactions. The short interbridgehead distance in bicyclo[1.1.1]pentane (**1**) and its derivatives (1.80–1.98 Å) provides for a strong 1–3 nonbonded interaction between the two high s character exocyclic hybrids on the bridgehead carbons across the bicyclo[1.1.1]pentane cage (Figure 1). The interaction between two closed shells of the two exocyclic bridgehead bonds is expected to destabilize the bicyclo[1.1.1]pentane cage in the ground state. Such repulsion between the back lobes of the exocyclic bridgehead hybrids has been proposed to be one of the main contributors to the strain energy of the bicyclo[1.1.1]pentane cage.^{88,93} Electronegative bridgehead substituents should relieve the strain to some extent by decreasing the coefficient of the exocyclic bond orbital on carbon and thus reducing electron occupancy on the interacting hybrids. Indeed, early ab initio calculations (3-21G, presumably HF) predicted that the interbridgehead distance in the bicyclo[1.1.1]pentanes with electronegative bridgehead substituents is smaller than that in the parent **1** (1.849 Å in 1,3-difluorobicyclo[1.1.1]pentane (**16**) compared to 1.916 in **1**).⁹³ Subsequently it was shown that the MP2/6-31G* optimized interbridgehead distance in 1-substituted bicyclo[1.1.1]pentanes **15** and

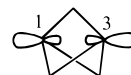


Figure 1. Orientation of the exocyclic hybrid orbitals on bridgehead carbon atoms in the bicyclo[1.1.1]pentane cage.

Table 5. Calculated (MP2/6-31G*) Interbridgehead Distances in Parent Bicyclo[1.1.1]pentane (1) and 1-Substituted Bicyclo[1.1.1]pentanes (Adapted from Ref 94)

compd	substituent	calculated C1–C3 distance (Å)
17a	F	1.826
17b	Cl	1.836
17c	OH	1.849
17d	CF ₃	1.857
15	NH ₂	1.867
1	H	1.872
17e	PH ₂	1.876
17f	CH ₃	1.878
17g	SiH ₃	1.890

Table 6. Electrode Potentials for Reduction of 1-Halo and 1,3-Dihalobicyclo[1.1.1]pentanes and Oxidation of 3-Substituted Bicyclo[1.1.1]pentane-1-carboxylate Anions in Acetonitrile

X	Y	compd	E° (V vs SCE)	ref
H	I	17h	-1.09 ^a	95
H	Br	17i	-1.12 ^a	95
F	I	18a	-1.17 ^a	95
F	Br	18c	-1.15 ^a	95
Cl	I	18e	-0.84 ^a	95
Cl	Br	18f	-0.89 ^a	95
Br	I	18d	-0.74 ^a	95
Br	Br	18b	-0.70 ^a	95
I	I	13	-0.64 ^a	95
CO ₂ ⁻	I	19b	0.39 ^b	96
CO ₂ ⁻	Br	19c	0.90 ^b	96
CO ₂ ⁻	Cl	19d	1.38 ^b	96
CO ₂ ⁻	F	19a	1.47 ^b	96
CO ₂ ⁻	H	19e	1.15 ^b	96
CO ₂ ⁻	CF ₃	19f	1.37 ^b	96
CO ₂ ⁻	CO ₂ Me	19g	1.22 ^b	96

^a Reduction potential. ^b Peak of oxidation potential at 0.2 V/s. Accurate to ±5 mV.

17a–g decreases considerably with increasing σ -electron-withdrawing strength of the substituent (Table 5).⁹⁴

An additional factor contributing to the decrease in the interbridgehead distance is that a more electronegative substituent favors a larger endocyclic valence angle at the bridgehead carbon and a shorter endocyclic C–C bond according to Bent's rules.⁵⁶

Overlap of the back lobes of the exocyclic bridgehead hybrids provides for enhanced transmission of spin–spin interactions through the bicyclo[1.1.1]pentane cage. The NMR coupling constants and EPR hyperfine splitting constants across the bicyclo[1.1.1]pentane cage or $[n]$ staffane chain are very large (see sections II.C.4 and II.C.5).

Additional evidence for relief of strain by electronegative substituents in bridgehead positions resulted from an electrochemical study of 1-halo- and 1,3-dihalobicyclo[1.1.1]pentanes (13, 17h,i, and 18).⁹⁵ Electrode reduction potentials in 0.1 M *n*-Bu₄NBF₄ solution in acetonitrile at a glassy carbon electrode range from -0.64 V for 1,3-diiodobicyclo[1.1.1]pentane (13) to -1.17 V for 18a (Table 6). The dissociation energy of the C–I bond in iodides has been estimated to vary from 43.6 kcal/mol in 13 to 56.0 kcal/mol in 18a. For the C–Br bond, the value varies from 58.8 kcal/mol in 18b to 69.1 kcal/mol in 18c. Stabilization of C–I and C–Br bonds in 3-fluorobicyclo[1.1.1]pentanes 18a and 18c has been at-

Table 7. Acidities of 3-Substituted Bicyclo[1.1.1]pentane-1-carboxylic Acids in 50% (by Weight) Aqueous Ethanol at 25 °C (Adapted from Ref 96)

R	compd	pK _a ^{a,c}	pK _a ^{b,c}	σ_F ^d
H	14	5.63 ± 0.05 (0)	5.71 ± 0.06 (0)	0
F	20a	4.84 ± 0.04 (0.79)	4.90 ± 0.07 (0.81)	0.41
Cl	20b	4.69 ± 0.14 (0.94) ^e	4.66 ± 0.08 (1.05)	0.43
CF ₃	20c	4.75 ± 0.06 (0.88)	4.82 ± 0.05 (0.89)	0.42

^a Determined by conductivity. ^b Determined by potentiometric titration. ^c ΔpK_a values in parentheses. ^d Polar field effects of substituents in methanol. Adcock, W.; Abeywickrema, A. N. *J. Org. Chem.* **1982**, *47*, 2957. ^e The compound slowly solvolyzes. The value is extrapolated to time zero.

tributed to withdrawal of electron density from the bridgehead carbon by the electronegative fluorine, significantly reducing the interbridgehead nonbonded repulsion. An electrostatic stabilization of the C–I (Br) bond through an induced dipole generation by the C–F dipole has also been proposed.⁹⁵ The same factors determine the ease of electrochemical oxidation of 3-substituted bicyclo[1.1.1]pentane-1-carboxylate anions (19a–g).⁹⁶ Thus, the peak potential of an irreversible oxidation wave of the 3-fluorobicyclo[1.1.1]pentane-1-carboxylate anion (19a) is 1.08 V higher than that for 3-iodobicyclo[1.1.1]pentane-1-carboxylate anion (19b).

In 3-substituted bicyclo[1.1.1]pentane-1-carboxylic acids (20), the inductive/field effect of substituents is the dominant factor governing the differences in their pK_a values (Table 7).⁹⁶

b. Other Interactions. Bridge substitution in bicyclo[1.1.1]pentane (1) has several effects: rehybridization of the exocyclic and endocyclic hybrid orbitals, electrostatic interaction of dipoles and multipoles, van der Waals repulsion and electronic interactions between proximate substituents on the bridges, and interactions between the back lobes of exocyclic hybrids arranged in a W relationship (Figure 2).^{48,97} Rehybridization and electrostatic interactions involve both interbridge and bridge-bridgehead interactions, while the proximate and the back-lobe-

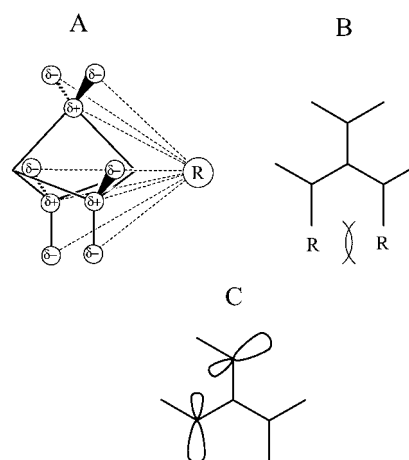
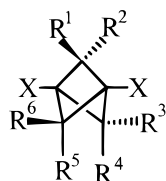


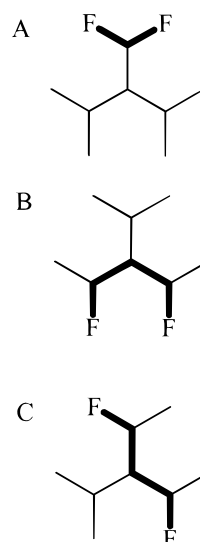
Figure 2. (A) Interaction of the multipole formed by the atoms on the bridges of the bicyclo[1.1.1]pentane cage with a bridgehead substituent; (B) van der Waals repulsion of two proximate substituents on the bridges of the bicyclo[1.1.1]pentane cage; (C) Orientation of the exocyclic hybrid orbitals of the bridge carbon atoms in the bicyclo[1.1.1]pentane cage.

Chart 6. Bridge-Fluorinated Bicyclo[1.1.1]pentane Derivatives

Compound	X	R ¹	R ²	R ³	R ⁴	R ⁵	R ⁶
115a	H						
116a	CO ₂ Me	F	H	H	H	H	H
115b	H	F	H	F	H	H	H
116b	CO ₂ Me	F	H	F	H	H	H
115c	H	F	F	H	H	H	H
116c	CO ₂ Me	F	F	H	H	H	H
115d	H	F	H	H	F	H	H
116d	CO ₂ Me	F	H	H	F	H	H
115e	H	F	H	H	H	H	F
116e	CO ₂ Me	F	H	H	H	H	F
115f	H	F	H	F	H	F	H
116f	CO ₂ Me	F	H	F	H	F	H
115g	H	F	H	H	F	F	H
116g	CO ₂ Me	F	H	H	F	F	H
115h	H	F	F	F	H	H	H
116h	CO ₂ Me	F	F	F	H	H	H
115i	H	F	F	H	H	F	H
116i	CO ₂ Me	F	F	H	H	F	H
115j	H	F	F	F	H	F	H
116j	CO ₂ Me	F	F	F	H	F	H
115k	H	F	F	F	F	H	H
116k	CO ₂ Me	F	F	F	F	H	H
115l	H	F	F	H	F	F	H
116l	CO ₂ Me	F	F	H	F	F	H
115m	H	F	F	F	H	H	F
116m	CO ₂ Me	F	F	F	H	H	F
115n	H	F	F	F	F	F	H
116n	CO ₂ Me	F	F	F	F	F	H
115o	H	F	F	F	F	F	F
111	CO ₂ Me	F	F	F	F	F	F

to-back-lobe interactions are of purely interbridge nature. These interactions manifest themselves in large long-range spin–spin coupling constants, an increased strain energy, and modified reactivity.

A computational study of the strain energies of bridge-fluorinated bicyclo[1.1.1]pentanes (**115a–o**, Chart 6) suggested that three types of fluorine arrangement significantly contribute to strain: geminal, proximate, and W-related (Figure 3).^{97,98} A CF₂ group introduces strain via angular distortions, as it attempts to increase the C–C–C valence angle at the bridge. The proximate arrangement of fluorines causes a nonbonded van der Waals repulsion since in **111** they are about 0.3 Å closer to each other than the sum of their van der Waals radii.^{48,97} The energy increase due to the interaction between W-related

**Figure 3.** Highly strained arrangements of fluorines of the bridges of the bicyclo[1.1.1]pentane cage: (A) geminal; (B) proximate; (C) W-type.

fluorines has been tentatively attributed to electrostatic repulsion between C–F dipoles,⁹⁷ but it could also be related to back-lobe orbital interactions (Figure 2C), and it is not obvious that it is properly described as strain.

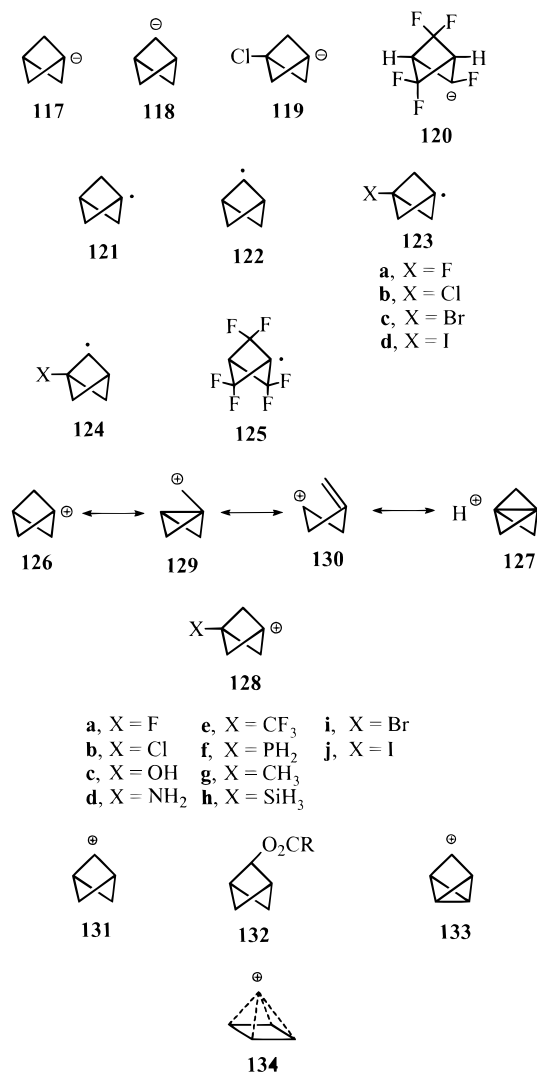
No direct experimental evidence is available for comparison with these computational results. A hint is given by the results of direct fluorination of dimethyl bicyclo[1.1.1]pentane-1,3-dicarboxylate (**46**),^{98,99} which yields a mixture of partially fluorinated diesters **116a–n** after reesterification (**116l** has not been detected). Fluorinated esters whose bicyclo[1.1.1]pentane cages **115a–o** have lower calculated strain energies tend to be formed in higher yields, presumably because the bridge radical intermediates prefer to abstract a fluorine atom in a way that minimizes strain in the product, but the situation is complicated by the concurrent formation and destruction of each product in the multiple fluorination process, and a detailed analysis is currently not available.^{98,99}

c. Charge Transmission. Charge transmission through [*n*]staffanes is related to electronic coupling between the two termini. Information about such interactions has been obtained from photoelectron and electron transmission spectra, as well as NMR and EPR spectra, all of which will be discussed in Section II.C. It has also been studied computationally, and the general consensus of all these studies is that [*n*]staffanes are very effective at transmitting electronic interactions over long distances, considering that they are saturated systems. We shall discuss the computational results along with the experiments in Section II.C.

3. Anions, Radicals, and Cations

Intramolecular interactions in the bicyclo[1.1.1]pentane cage play an essential role in determining the structure and properties of reactive intermediates containing this moiety. The interbridgehead interactions are the best studied to date and seem to be the most important. The interbridge and bridge–bridge-

Chart 7. Reactive Intermediates



head interactions have been studied less thoroughly, but are of some interest for heavily bridge-substituted bicyclo[1.1.1]pent-1-yl and for bicyclo[1.1.1]pent-2-yl reactive intermediates. This section is devoted to a discussion of molecular and electronic structure, intramolecular interactions, and enthalpies of formation of the bicyclo[1.1.1]pent-1-yl and -2-yl anions, radicals, and cations. Reactivity patterns of these and other reactive intermediates are discussed in section IV. The intermediates **117**–**134**, referred to explicitly, are shown in Chart 7.

a. Carbanions. (i) *Bicyclo[1.1.1]pent-1-yl (117) and Bicyclo[1.1.1]pent-2-yl (118) Anions.* Gas-phase proton affinity of **117** (Chart 7) is 411 ± 3.5 kcal/mol,^{100,101} close to that of the cyclopropyl anion (408 ± 5 kcal/mol¹⁰²) and the vinyl anion (407 ± 3 kcal/mol¹⁰²), in agreement with MP3/6-31+G* calculations.⁸⁸ Indeed, the high *s* character of exocyclic carbon hybrids would be expected to increase the acidity of protons on the bicyclo[1.1.1]pentane cage and to favor the formation of anions. However, this is partially mitigated by a transannular interaction between the back lobes of the axially directed hybrid orbitals at the bridgehead carbons, which destabilizes completely filled orbitals containing these hybrids. This destabilization is particularly important in the

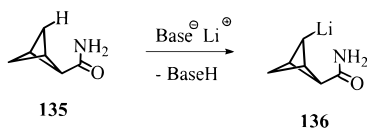
case of bicyclo[1.1.1]pent-1-yl anion (**117**) in which the electron occupancy of the exocyclic bridgehead hybrid is the highest. Thus, MP2/6-31G* calculations predict a much larger interbridgehead distance in the bridgehead anions compared to that in neutral species (1.970 Å has been calculated for the parent anion **117**, cf. 1.872 Å in **1**).⁸⁸ The calculated proton affinity of **117** is lower than that of **118** (Chart 7) by 5.4 kcal/mol at the MP2/6-31+G* level of theory (4.9 kcal/mol at RHF/6-31+G*),¹⁰³ and the higher *s* character of the bridgehead exocyclic hybrid in **117** apparently outweighs the importance of the destabilization due to 1–3 interactions. The calculated 1,3-distance in bicyclo[1.1.1]pent-2-yl anion (**118**, 1.85 Å, RHF/6-31+G*) is very close to that in **1**,¹⁰³ which is reasonable considering that no additional 1,3-repulsion is present in **118** compared to **1**.

The 1–3 interaction would be expected to permit electronegative substituents in position 3 to stabilize negative charge on the other bridgehead carbon, C(1), by offering a low-energy σ^* bond orbital with a large coefficient on the bridgehead carbon, C(3), for interaction with the bridgehead lone pair in position 1. Indeed, semiempirical calculations on 3-chlorobicyclo[1.1.1]pent-1-yl anion (**119**, Chart 7) predict a 10% increase in C–Cl bond length relative to the neutral molecule (1.797 Å) and a high negative charge on chlorine ($-0.479 e$).¹⁰⁴

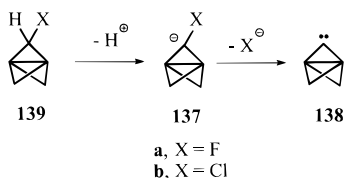
(ii) *Bridge-Substituted Bicyclo[1.1.1]pent-1-yl and Bicyclo[1.1.1]pent-2-yl Anions.* In bridge-substituted bicyclo[1.1.1]pentanes the C–substituent bond dipoles lie in a plane perpendicular to the C(bridgehead)–H bonds. In 2,2,4,4,5,5-hexafluorobicyclo[1.1.1]pentane (**115o**), the assembly of charges on the bridges produces no net dipole moment, and its effect on the acidity of the C(1)–H bond might be expected to be limited to a small classical σ -inductive effect. However, the calculated gas-phase acidity of **115o** (366.4 kcal/mol, MP2/6-31+G*) is much higher than that of **1**.⁴⁸ The calculated acidity of the C(1)–H bond in 2,2,4,4,5-pentafluorobicyclo[1.1.1]pentane (**115n**) is somewhat lower (374.4 kcal/mol, MP2/6-31+G*).⁴⁸ Such a pronounced increase in the acidity of **115o** and **115n** can be explained by a combination of a favorable rehybridization of the orbitals in the bicyclo[1.1.1]pentane cage, leading to a high *s* character of the exocyclic bridgehead hybrid, and a multipole–dipole interaction between the system of charges on the bridges and the C(1)–H dipole.⁴⁸ Calculated enthalpy of bridge proton abstraction from **115n** (384.3 kcal/mol, MP2/6-31+G*)⁴⁸ is substantially higher than that from the bridgehead, presumably because the electrostatic and hybridization stabilization are much less effective in the bridge-borne anion **120** (Chart 7).

Theoretical investigation of bicyclo[1.1.1]pentane-2-carboxamide (**135**) and its lithio derivative **136** suggested that intramolecular complexation of the metal enhances the stability of **136** tremendously, by up to 38.3 kcal/mol (Scheme 1).¹⁰⁵ The predicted effect is close to that computed for the analogous cubane derivative (37.7 kcal/mol), known to form a chelated anion easily.

Scheme 1



Scheme 2



The generation of the α -halo anions **137** and subsequently the carbenes **138** from chloro- and fluoro[1.1.1]propellane (**139b** and **139a**, respectively) has also been studied theoretically (Scheme 2).¹⁰⁶ MINDO/3 level calculations led to the conclusion that the anion can be generated under relatively mild phase transfer conditions.¹⁰⁶

b. Radicals. (i) *Bicyclo[1.1.1]pent-1-yl (121) and Bicyclo[1.1.1]pent-2-yl (122) Radicals.* The C(1)–H bond in bicyclo[1.1.1]pentane (**1**) is calculated to be as strong as the CH bond in methane (102–106 kcal/mol).^{2,30,87,107} The effect of the high *s* character of the exocyclic bridgehead hybrid appears to be partly mitigated by three-electron 1–3 transannular interactions in the bicyclo[1.1.1]pent-1-yl radical (**121**, Chart 7), which is less destabilizing than in **1**, or perhaps even stabilizing, as evidenced by the substantially shorter calculated interbridgehead distance in the radical **121** (1.797 Å at UMP2/6-31G* level⁸⁸ and 1.815 Å at UHF/6-31G* level^{108,109}) compared with **1** (1.872 Å at MP2/6-31G* level⁸⁸ and 1.870 Å at HF/6-31G* level¹⁰⁹). The removal of the bridgehead hydrogen atom from **121** with formation of [1.1.1]propellane (**2**) has been calculated to be much easier than abstraction of hydrogen atom from **1** and requires only 47 kcal/mol.⁸⁷ Enthalpy of formation of the bridge radical **122** (Chart 7) has been calculated (MINDO/3,¹¹⁰ UHF/6-31G*,¹⁰⁸ PUMP2/6-31G*¹⁰⁸) to be very close to that of **121**. MINDO/3 calculations provided a value of 99 kcal/mol.¹¹⁰ As in the case of bicyclo[1.1.1]pent-2-yl anion (**118**), 1–3 interaction is not expected to affect the stability of **122** compared to that of **1**. An increase in the interbridgehead distance (1.887 Å, UHF, 6-31G*)¹⁰⁸ is caused presumably by rehybridization at C(2). In this respect the half-filled orbital acts as an electron-withdrawing group (see also section II.B.1).

The high *s* character of the singly occupied bridgehead carbon hybrid orbital in the radical **121** and its unhindered geometry makes it more reactive than the *tert*-butyl radical in addition reactions to α -methylstyrene (absolute rate constant $1.4 \times 10^7 \text{ M}^{-1} \text{ s}^{-1}$ at 25 °C) and 1,4-cyclohexadiene ($4.6 \times 10^5 \text{ M}^{-1} \text{ s}^{-1}$ at 25 °C).¹¹¹

(ii) *Substituted Bicyclo[1.1.1]pent-1-yl and Bicyclo[1.1.1]pent-2-yl Radicals.* Electron-withdrawing bridgehead substituents are calculated to reduce the interbridgehead distance in the 3-substituted bicyclo[1.1.1]pent-1-yl radicals **123a,b** (Chart 7). The shortest distance occurs in the 3-fluorobicyclo[1.1.1]pent-1-yl

radical (**123a**, 1.766 Å).¹¹² As in the case of 1,3-difluorobicyclo[1.1.1]pentane (**16**, see section II.B.2), two explanations are plausible: reduction of electron density between the bridgehead carbons and rehybridization effect of the fluorine.

Substitution of one bridgehead position in **1** does not affect significantly the stability of the bridge-borne radicals **124** (Chart 7), presumably because of insignificant rehybridization.¹⁰³

Upon fluorination of the bridges the C(bridgehead)–H bond strength is expected to increase along with the contribution of *s* orbital in the exocyclic bridgehead hybrid.⁹⁷ Thus, the bridge-fluorinated bicyclo[1.1.1]pent-1-yl radical **125** (Chart 7) is expected to abstract hydrogen atoms more readily than the parent radical **121**.

c. Carbocations. (i) *Bicyclo[1.1.1]pent-1-yl Cation (126).* This bridgehead cation is highly unusual. Despite the high *s* character of the exocyclic hybrid of the bridgehead carbon in **1**, solvolysis to **126** (Chart 7) is very facile. Thus, in 80% ethanol, 1-chlorobicyclo[1.1.1]pentane (**17b**) undergoes solvolysis 3 times faster than *tert*-butyl chloride.^{94,113} The stabilization of the bicyclo[1.1.1]pent-1-yl cation **126** is attributed to the transannular interaction of the vacant orbital in position 1 with the full shell of the C–H bond on position 3.^{88,114–117} The calculated interbridgehead distance in **126** is 1.525 Å (MP2/6-31G*),⁸⁸ which is lower than that in **1** and even in [1.1.1]propellane (**2**). Abstraction of hydride from the tertiary position of **1** has been calculated to be easier by about 2 kcal/mol than from the tertiary position of isobutane.⁸⁸ The calculated (HF/4-31G) proton affinity of **2** is 229 kcal/mol, very close to that of ammonia,¹¹⁴ and protonation of **2** is possible even with acetic acid.^{2,58} Analysis of the calculated charge density between C(1) and C(3) indicates that a bond has been formed between the bridgehead carbons.⁸⁸ Thus, the cation **126** can be viewed as a protonated [1.1.1]propellane (structure **127**, Chart 7).^{88,93,118–120}

There is a good linear correlation between substituent inductive/field constants and the logarithm of the rates of solvolysis of 3-substituted bicyclo[1.1.1]pent-1-yl bromides,¹²¹ and similar substituent effects were found for several 3-substituted bicyclo[1.1.1]pent-1-yl iodides.⁹⁴ The reaction constant ρ extracted from the correlation for the bromides is the largest recorded to date in the solvolysis of γ -substituted substrates.¹²¹ A Hammett σ/ρ study of *p*-substituted 3-phenylbicyclo[1.1.1]pent-1-yl iodides likewise found a strong retardation of solvolysis by σ -electron withdrawal.⁹⁴ Calculated enthalpies of hydride transfer between bridgehead-substituted bicyclo[1.1.1]pentanes and the parent cation **126** also suggest that σ -electron-withdrawing bridgehead substituents (F, Cl, OH, NH₂, and CF₃) strongly destabilize the corresponding bicyclo[1.1.1]pent-1-yl cations **128a–e** (Chart 7), while σ -electron donor groups (SiH₃, PH₂, CH₃) stabilize the cations **128f–h**.⁹⁴

Ab initio calculations (MP2/6-31G**) provide evidence that the cation **126** is also stabilized by hyperconjugation between the strained C(1)–C(2) and C(2)–C(3) bonds and the vacant cationic *p* orbital.¹²² It has been shown that resonance struc-

Table 8. Selected Vibrational Transitions in Bicyclo[1.1.1]pentane (1) and [n]Staffanes ([n]1, Intracage Only) and Their Assignment

vibrational transitions in 1 (cm ⁻¹) ^a					assigned symmetry	description ^b	analogous IR transitions in [n]1 (cm ⁻¹) ^{b,e}
IR _(g) ^b	IR _(g) ^{c,d}	IR _(m) ^b	Raman _(g) ^{c,d}	Raman _(l) ^{c,d}			
2976 (vs)	2976 (vs)	2962 (vs)			a ₂ ''	out-of-phase CH stretch	3005–2994
2973 (vs) ^f		2956 (s)	2978 (vs) ^g	2968 (vs) ^g	e'	CH ₂ asymmetric stretch	2978–2962
2920 (s)	2919 (s)	2911, 2914 (s)			e'	Fermi resonance: CH ₂ symmetric stretch and 2 CH ₂ scissors	2915–2864
2888 (s)	2887 (vs)	2882 (s)	2886 (s) ^g	2876 (s) ^g			
1455 (s)	1455 (m)	1452 (s)	1455 (vw)	1450 (w)	e'	CH ₂ scissors	1456–1431
1228 (m) ^f	1232 (w)	1227, 1229 (m)	1232 (w)	1229 (w)	e'	CH in-phase deformation	1254–1241
1218 (vs)	1220 (s)	1216 (vs)			a ₂ ''	CH ₂ wag	1219–1203
967 (w)	1098 (w)	992 (w)			e'	CH ₂ rock	994–890
885 (m)	886 (w)	888, 885 (w)			e'	CCC symmetric stretch	1077–891 ^b
832 (s)	832 (m)	833 (s)			a ₂ ''	CCC asymmetric stretch	830–834 ^{b,h}
539 (m)	540 (w)	538 (w)		538 (w)	e'	CCC bend	570–541 ⁱ

^a Spectra recorded in (g) gas phase, (m) Ar matrix, (l) liquid phase. ^b Reference 133. ^c Reference 54. ^d Only the assigned peaks are listed. ^e Observed in an Ar matrix. Symmetry of the vibrations may vary depending on the symmetry group of the molecule.

^f The peak is buried under a stronger peak of different symmetry. ^g Another transition may contribute to intensity of the peak.

^h The transition has not been observed or assigned for **[5]1**. ⁱ The transition has not been observed or assigned for **[4]1**.

tures **129** and **130** (Chart 7) are important contributors to the overall structure of **126**.

Calculations at all levels suggest that the cation **126** with C_{3v} symmetry is at best only a shallow local minimum or a transition state on the ground state potential energy surface. For details on the pathways of rearrangement of cations **126** and **128**, see section IV.B.3.

(ii) *Bicyclo[1.1.1]pent-2-yl Cation (131, Chart 7)*. No theoretical studies of the cation have been published to the best of our knowledge, and little experimental information is available. The solvolysis of bicyclo[1.1.1]pentan-2-ol esters (**132**, Chart 7) is much slower than that of 1-chlorobicyclo[1.1.1]pentane (**17b**), which is consistent with absence of the stabilizing interaction of the empty shell with any filled orbital across the cage.²⁸⁷

(iii) *Tricyclo[2.1.0.0^{2,5}]pent-3-yl Cation (133, Chart 7)*. According to semiempirical^{123–126} and ab initio (4-31G)¹²⁷ calculations on the C₅H₅⁺ potential surface, the nonclassical cation **134** with D_{4v} symmetry has the lowest energy. Its calculated heat of formation is 269.7 kcal/mol, comparable to that calculated for cyclopentadienyl cation (268.5 kcal/mol).¹²⁵ The theoretical prediction of considerable stability for **134** and its derivatives has been strongly supported by the results of low-temperature ¹H and ¹³C NMR experiments and mechanistic studies (see section IV.B.3.f).^{128–132}

C. Spectra

1. Vibrational Spectra

a. Bicyclo[1.1.1]pentane (1). The assignment of vibrational transitions in bicyclo[1.1.1]pentane (Table 8) is based on IR spectra of **1**^{54,133} and bridgehead-deuterated bicyclo[1.1.1]pentanes (**21** and **22**)^{54,134} in the gas phase^{54,133,134} and in Ar matrix,¹³³ and on Raman spectra of **1** in the gas and liquid phases.⁵⁴

Analysis of the rotational structure of the a₂'' IR bands of **1** and **22** yielded moments of inertia, which are in excellent agreement with the more recent set of the structural parameters determined by electron diffraction and with calculated (MP2/6-31G*) parameters.⁵⁴

b. [n]Staffanes ([n]1). IR transitions of these oligomers have been examined in matrix isolation

and in stretched polyethylene as solvent. Their polarization has been established¹³³ and used in the determination of [n]staffane rod orientation in supramolecular assemblies (section V). Detailed analysis was based on comparison with HF/3-21G calculations. Intracage and intercage vibrations can be distinguished.^{16,133}

Intracage vibrations in **[n]1** are similar to the vibrations of **1**¹³³ (Table 8). The extent of cage-to-cage coupling depends on the degree to which the bridgehead carbons participate in the motion. If they are only weakly involved, the coupling is weak and the frequencies of all the normal modes of a particular type are similar. Both the frequencies and their intensities can then be accounted for by a simple Hückel-like theory, which readily accounts for the fact that only one of the modes of a particular type is very intense in the IR, namely the one in which the motion in all the cages occurs in phase. For those modes in which the bridgehead atoms move significantly, intercage coupling is strong and the frequencies of the normal modes of a particular type then differ substantially.

The most characteristic and useful intracage mode is the very intense long-axis polarized in-phase combination of all the CH₂ wagging motions near 1215 cm⁻¹. The doubly degenerate out-of-phase combination of symmetric CH₂ stretching motions interacts with two quanta of a CH₂ scissor fundamental and occurs as a Fermi doublet near 2880 and 2915 cm⁻¹, polarized perpendicular to the long axis. An intense peak between 3000 and 2960 cm⁻¹ contains contributions from CH and CH₂ stretches and is of mixed polarization. The long-axis polarized stretch of the terminal CH group occurs near 3000 cm⁻¹. It is weak and usually buried under the peaks due to the more numerous CH bonds of the bridges.¹³³

Intercage vibrations are of four types: accordion, rod-bending, rolling, and internal rotation. Only accordion intercage vibrations have been observed by IR spectroscopy in **[n]1** with n = 2–5. Their frequencies are relatively high (1333–1385 cm⁻¹),¹³³ considering that these are primarily single-bond CC stretching motions. This is due in part to the high force constant of the short exocyclic bonds and in part to

Table 9. Main Vibrational Transitions in [1.1.1]Propellane (2) and Their Assignment

vibrational transitions (cm ⁻¹) ^a			assigned sym	description
IR _(g)	Raman _(g) ^b	Raman _(l) ^b		
3079.9 (s)	3083.0 (m)	3075.2 (m)	e'	CH ₂ sym stretch
3019.6 (s)			e'	CH ₂ asym stretch
2980.7 (w)				
2949.0 (w)				
2924.0 (w)				
1458.9 (m)				
1186 (w)	1182.4 (vw)	1178 (vw)	e'	C–C–C bend
1096.4 (m)			a ₂ ''	CH ₂ scissors
1083 (vw) ^c	1084.7 (vw)	1078 (vw)	e'	CH ₂ wag
611.7 (vs)			e'	CH ₂ rock
529 (w)		529.4 (w)	a ₂ ''	C–C–C asym stretch
			e'	C–C–C sym stretch

^a Spectra recorded in (g) gas phase, (l) liquid phase. ^b Only the assigned peaks are listed. ^c Observed in a matrix.

an interaction with a low-frequency symmetric CC stretching intracage motion that modulates the intracage interbridgehead distance. This type of vibration can be thought of as defining the longitudinal vibrations of a structureless rodlike object.

Rod-bending defines the transverse vibration of a rod. It is calculated to appear in the far IR (160–35 cm⁻¹)¹³³ and has so far eluded detection. In crystals the substituted rods deviate from linearity,⁴⁵ suggesting that the force constant for rod-bending is low. This has been attributed to the very high degree of s character in the exocyclic bridgehead orbital and the resulting small restoring force for a bending displacement. Thus, [*n*]staffane rods resemble rubber sticks rather than steel rods.

Rolling modes correspond to rotations of the cages around axes that are perpendicular to the long axis of the rod. Their frequencies are calculated to lie at 300–400 cm⁻¹.

Rotation around the intercage CC bonds has been calculated to have a barrier of about 2 kcal/mol.¹³³ Such a low barrier is reasonable even for a hexa-substituted ethane if angles of attachment of substituents are taken into account.

c. [1.1.1]Propellane (2). Like other small-ring propellanes, **2** exhibits an intense IR band at a low frequency, 603 cm⁻¹. In an initial MNDO-based analysis,¹³⁵ this was assigned to an antisymmetric combination of peripheral CC stretching motions (a “bobbing” mode, in which the central CC bond oscillates relative to the three bridges). The striking intensity of this vibration can be qualitatively attributed⁵⁴ to the development of a large dipole across the polarizable central CC bond due to formation of atomic dipoles at the bridgehead carbons as their valence angles and hybridization change in opposite directions during the normal mode motion. Also CH stretching vibrations at 3000 cm⁻¹ (symmetric) and 3060 cm⁻¹ (asymmetric), similar to those in cyclopropane, are characteristic of the [1.1.1]propellane structure. Selected observed vibrational transitions are given in Table 9.

A later, more detailed HF/6-31G*-based analysis⁵⁸ of the IR and Raman spectra of the parent **2** and its perdeuterated derivative, including an analysis of the rotational components of a₂' vibrational bands, provided moments of inertia, and these agreed with the more recent⁵¹ of the two electron-diffraction analyses. A comparison of the force field derived from the

results with those of related molecules led the authors to conclude that, with regard to structural data, force constants, and dipole moment derivatives, **2** strongly resembles cyclopropane, while **1** resembles cyclobutane. Regardless of its unusual geometry, **2** is best thought of as three fused cyclopropane rings.

A more recent MP2/6-31G* calculation of the IR and Raman spectra agrees very well with observations.¹³⁶ An HF/D95** calculation of Raman intensities of CH stretching vibrations predicts a significantly higher value for the bridgehead CH bond in **1** than for most CH bonds in hydrocarbons; it is about twice higher than the intensity calculated for a bridgehead CH bond in **1** or **2**.¹³⁷ Additional information on the vibrations of **2** was obtained from its electron energy loss spectrum.⁸³

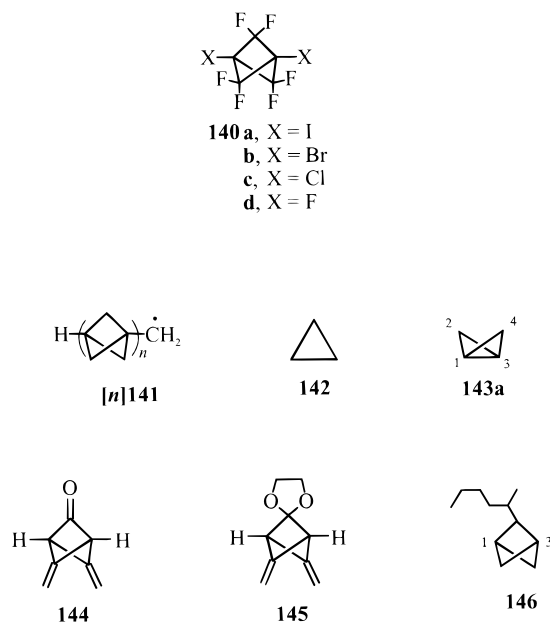
2. Photoelectron and Electron Transmission Spectra

These types of spectra relate the ground state of a molecule to those of its radical cation and radical anion. Through Koopmans' theorem, they provide semiquantitative indicators of the nature of the occupied and the unoccupied molecular orbitals of the neutral species, respectively.

a. Bicyclo[1.1.1]pentane (1) and [*n*]Staffanes ([*n*]1). The first ionization potentials (IPs) of **1** and [2]staffane ([**2**]1) are 10.6 and 9.5 eV, respectively.¹³⁸ For higher [*n*]staffanes the IPs converge to the rather low value of about 8.5 eV as the chain grows longer.²⁰ All attempts to observe the radical cations directly have failed so far, presumably due to their instability, and the symmetry of the HOMO is not known with certainty. The low ionization potential and its decrease with the length of the [*n*]staffane rod are compatible with strong σ homoconjugation, but do not prove it unambiguously. If the HOMO is of σ symmetry, they could simply be due to the high degree of strain. More direct evidence for σ homoconjugation is provided by the EPR spectra discussed below.

If the HOMO is of π symmetry, the low ionization potential could be a reflection of long-range through-bond π interactions. Good evidence for such interactions is provided by the photoelectron spectra of bicyclo[1.1.1]pentanes and [*n*]staffanes carrying bridgehead substituents with lone pairs of π symmetry. Initial work¹³⁸ showed that the bicyclo[1.1.1]pentane cage is a relatively good conductor of transannular interaction between occupied π MOs. The splitting of the IPs of the substituent lone pairs in

Chart 8



1,3-dibromobicyclo[1.1.1]pentane (**18b**) and 1,3-diethynylbicyclo[1.1.1]pentane (**23**) was found to be 0.7 eV. A splitting across two cages is smaller, but still observable. For 3,3'-dibromo[2]staffane (**[2]18b**) it is 0.4 eV.¹³⁸ Computational studies of the interaction of σ and π symmetry radical centers¹³⁹ and of ethynyl substituents¹⁴⁰ located in the terminal positions permitted a detailed analysis of the origin of the surprising efficiency with which $[n]$ staffane transmits electronic interactions over considerable distances.

More recently,¹⁴¹ photoelectron spectra of a larger series of the parent 1,3-dihalobicyclo[1.1.1]pentanes **18** have been compared with those of 1,3-dihaloheptafluorobicyclo[1.1.1]pentanes **140a–d** (Chart 8). Hexafluorination was found to affect not only the values of the ionization potentials but also the fine vibrational structure. The spectra are in excellent agreement with the results of SAC-CI calculations that include spin–orbit coupling explicitly and have been interpreted qualitatively in terms of a simple model for interactions between the two bridgehead halogen atoms mediated by the cage.

Resonances in the electron transmission spectra of bicyclo[1.1.1]pentane (**1**) and [2]staffane (**[2]1**) are not sufficiently resolved to permit an unambiguous analysis but the electron affinity appears to be about -4 to -5 eV, and the interaction between neighboring cages causes a relatively large splitting of 1.6 eV.¹⁴² In the same study,¹⁴² the bridgehead-substituted ethynyl and diethynyl derivatives of **1** were examined as well, and the latter displays the effects of a cage-mediated interaction between the two acetylene π^* orbitals corresponding to a splitting of at least 1.1 eV. This is even larger than the 0.7 eV splitting in the corresponding π orbital energies observed in the photoelectron spectra.¹³⁸ Clearly, the bicyclo[1.1.1]pentane cage has an excellent capacity for transmission of π interactions and for the delocalization of both holes and electrons. This has obvious consequences for the rate of charge transfer through $[n]$ -staffane rods, and detailed theoretical examina-

tions^{143,144} have been published. However, few experimental data on these rates exist, and they do not separate σ and π interactions. Preliminary measurements¹⁴⁵ of charge transfer bands in incompletely characterized mixed-valence Ru(II)–Ru(III) $[n]$ staffanes with $(\text{NH}_3)_5\text{RuS}$ -bridgehead substituents on both rod ends yielded the rather high rate constants $1 \times 10^7 \text{ s}^{-1}$ for $n = 1$ and $2 \times 10^6 \text{ s}^{-1}$ for $n = 2$, comparable with those measured previously for spiro-linked cyclobutanes,¹⁴⁶ but additional work is clearly required.

b. [1.1.1]Propellane (2). The first IP of **2** is 9.74 eV,⁸² unusually low for a saturated hydrocarbon. According to molecular orbital calculations, it corresponds to an ionization from a symmetric MO localized predominantly on the central C–C bond.^{2,82} The narrow Franck–Condon allowed shape of this band suggests little change in equilibrium geometry upon ionization, in agreement with calculations,^{88,91} which suggest that the central bond is actually a little shorter in the radical cation (much of the electron density removed upon ionization is located in the regions outside of the central bond). The ionization potential calculated⁸⁸ at the MP3/6-311G* level agrees well with the observed value.

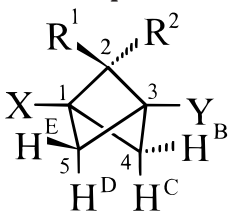
Although calculations⁸² suggest that the softest totally symmetric vibration will have a higher frequency in the radical cation than in neutral **2**, the first two vibrational peaks in the first band in the photoelectron spectrum are separated by only $360 \pm 20 \text{ cm}^{-1}$, much less than the lowest vibrational frequency in **2** (529 cm^{-1}), let alone the frequency of its lowest totally symmetric vibration (908 cm^{-1}). This puzzle remains unresolved and is perhaps due to vibronic mixing with the lowest excited state of the radical cation.

The electron transmission spectrum of **2**⁸³ reveals an electron affinity of -2.04 eV , to be compared with the values around -6 eV common for ordinary saturated hydrocarbons. The low LUMO energy agrees with calculations, which suggest that this orbital is dominated by the antibonding combination of axial p orbitals at the two bridgehead carbons.⁸⁷ The length of the central C–C bond is significantly increased in the radical anion in agreement with the 1.88 Å value calculated at the UHF/6-31G** level, and the peripheral bonds also are longer.

c. Tricyclo[2.1.0.0^{2.5}]pentane (3). Photoelectron spectrum of **3** has not been measured, but for 3-methylenetricyclo[2.1.0.0^{2.5}]pentane (**103**) the first IP is 8.54 eV.¹⁴⁷ It has been assigned to ionization out of a symmetric MO localized primarily on the carbon atoms of the bicyclo[1.1.0]butane fragment. The first IP of tricyclo[2.1.0.0^{2.5}]pentan-3-one (**98**) is 9.15 eV.¹⁴⁷

3. Electronic and Electron Momentum Spectra

Unsubstituted **1** and $[n]$ staffanes absorb UV light only at relatively high energies, and it is not known whether the vacuum UV spectra contain any signs of strong σ homoconjugation. UV spectra of $[n]$ -staffanes carrying identical bridgehead substituents at both ends provide at best weak indications of through-cage interactions.^{20,145}

Table 10. Selected NMR Chemical Shifts of Bicyclo[1.1.1]pentanes (ppm)


	X	Y	R ¹	R ²	H ^A	H ^B	H ^C	H ^D	H ^E	H ^F	C ¹	C ²	C ³	C ⁴ , C ⁵	ref
1	H ^F	H ^F	H ^A	H ^A	1.84	1.84	1.84	1.84	1.84	2.44	33.59	50.75	33.59	50.75	160, 161
17a	F	H ^F	H ^A	H ^A	<i>a</i>	<i>a</i>	<i>a</i>	<i>a</i>	<i>a</i>	<i>a</i>	74.93	53.18	14.79	53.18	161
17b	Cl	H ^F	H ^A	H ^A	2.27	2.27	2.27	2.27	2.27	2.77	49.84	56.99	24.87	56.99	77, 236
17h	I	H ^F	H ^A	H ^A	2.37	2.37	2.37	2.37	2.37	3.26	10.46	60.19	35.91	60.19	236
17i^b	Br	H ^F	H ^A	H ^A	2.42	2.42	2.42	2.42	2.42	3.10	38.30	58.73	28.98	58.73	275
18b	Br	Br	H ^A	H ^A	2.57	2.57	2.57	2.57	2.57		30.50	64.63	30.50	64.63	239
24	Me	H ^F	H ^A	H ^A	1.67	1.67	1.67	1.67	1.67	2.40	42.17 ^c	52.18 ^c	27.39 ^c	52.18 ^c	77, <i>d</i>
115o	H ^F	H ^F	F ^e	F ^e	<i>f</i>	<i>f</i>	<i>f</i>	<i>f</i>	<i>f</i>	3.74	63.41	109.9	63.41	109.9	97
207	H ^F	H ^F	Cl	H ^A	4.19	1.61	2.07	1.91	2.78	2.62	<i>g</i>	<i>g</i>	<i>g</i>	<i>g</i>	77

^a ¹H NMR spectrum has been reported as a multiplet δ 2.01–2.07 ppm.²³² ^b In CFCl₃. ^c ¹³C enriched methyl group. ^d Della, E. W.; Pigou, P. E. *J. Am. Chem. Soc.* **1982**, *104*, 862. ^e ¹⁹F NMR δ –117.18 ppm.⁹⁷ ^f Fluorines instead of hydrogens. ^g Not reported.

The parent **2** is likewise transparent in the near UV region. Detailed information about its electronically excited states has been obtained by electron energy loss spectroscopy (EELS).⁸³ The first excited singlet is located at 7.26 eV, corresponds roughly to a HOMO–LUMO excitation, and is partly of Rydberg character. The equilibrium geometry of the excited state is similar to that of the ground state. Like other ¹ $\sigma\sigma^*$ excited states, this excited state can be viewed as a resonance combination of two contact ion-pair structures with oppositely charged bridgehead carbons, not dissociative but bound by their electrostatic attraction, and the absence of a large geometric distortion upon excitation is not surprising.¹⁴⁸

Pyrene fluorescence is quenched by **2** at a rate that is smaller than diffusion-controlled but still quite high ($k_q = 1.4 \times 10^8 \text{ M}^{-1}\text{s}^{-1}$),¹⁴⁹ although the pyrene vertical excitation energy is much lower than that of **2**, and the authors suggest that the quenching is due to thermally vibrationally excited molecules of **2**. This is not very compatible with the above conclusion that the ground and first excited singlet state have similar equilibrium geometries, and the issue must be considered open.

The equilibrium geometry is very different for the lowest triplet state, observed by EELS at 4.1 eV (first peak) to 4.70 eV (peak maximum), in whose excited state the central C–C bond is greatly stretched. This again agrees with simple expectations for a ³ $\sigma\sigma^*$ excited bond, with a strongly antibonding repulsive interaction and with the 1.83 Å interbridgehead separation calculated at the UHF/6-31G* level,⁵⁸ a value characteristic of bicyclo[1.1.1]pentanes. More recently, the MP2/6-311G** and BLYP/6-311G** methods were used to simulate the vibrational envelope of the excitation into the triplet state, for which a 1.82 Å central bond length was obtained¹⁵⁰ in excellent agreement with the earlier results. Absolute differential cross-sections for electron-impact triplet excitation as a function of the scattering angle have been calculated¹⁵¹ and measured¹⁵² and agreed within a factor of 2.

A somewhat different set of assignments of the singlet and triplet transitions was proposed in a SAC-CI study using a double- ζ plus polarization basis set

augmented by diffuse functions,¹⁵³ and the disagreement has not yet been settled.

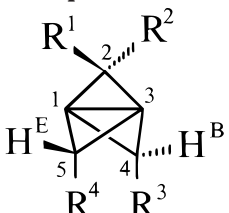
The MP3/6-31G* triplet excitation energy of **2**, 3.2 eV,⁵⁸ appears to be much too low, but it is quite possible that the agreement with observations is better than it appears to be, since the origin of the transition could well be too weak and may have been missed in the experiment. This would be compatible with the rather high quenching constants observed for various triplet sensitizers.¹⁴⁹

Finally, electron momentum spectroscopy of [1.1.1]-propellane (**2**) has received considerable experimental and theoretical attention and the results provided insight into the nature of its molecular orbitals.^{154–156}

4. EPR Spectra

An unpaired electron located in the bridgehead orbital of the parent and 3-substituted bicyclo[1.1.1]-pent-1-yl radicals (**121** and **123a,b**, Chart 7) interacts strongly with magnetically active nuclei in a substituent located on the other bridgehead, as reflected in a very high hyperfine splitting (hfs) constant in the EPR spectrum. The hfs splitting constant in the parent radical **121** due to γ -coupling with the hydrogen across the cage is 69.6 G.¹⁵⁷ In **123a** the splitting due to γ -coupling to fluorine is 167 G.¹¹² In **123b** the γ -Cl splitting constants, 26.2 G (³⁵Cl) and 21.7 G (³⁷Cl), are larger than the α -Cl and β -Cl hfs constants of ordinary chloroalkyl radicals.¹¹² Hyperfine splitting due to coupling of bridge β -H atoms in the bridgehead-borne radicals **121** and **123** is relatively small (≤ 1.2 G), and electron-withdrawing substituents in position 3 appear to reduce it further.¹¹²

The extent and the mechanism of spin density propagation from a bridgehead position across a series of bicyclo[1.1.1]pentane cages have been studied in the parent [*n*]staff-3-yl radicals [*n*]**121** ($n = 1–3$).¹⁰⁹ Measurable spin density has been detected on γ , ζ , and ι hydrogens, transmitted through up to three cages and attenuated by a factor of about 25 per added cage. A Hückel-type analysis suggests that the transannular resonance integrals are about five times smaller than the intercage resonance integrals in the σ -homoconjugated system. It is interesting to ask whether the transannular resonance integral is

Table 11. Selected NMR Chemical Shifts in [1.1.1]Propellanes (C₆D₆, ppm)


compd	R ¹	R ²	R ³	R ⁴	H ^A	H ^B	H ^C	H ^D	H ^E	C ¹ , C ³	C ²	C ⁴	C ⁵	ref
2	H ^A	H ^A	H ^C	H ^D	1.77	1.77	1.77	1.77	1.77	1.23	73.91	73.91	73.91	24
2^a	H ^A	H ^A	H ^C	H ^D	2.06	2.06	2.06	2.06	2.06	1.0	74.1	74.1	74.1	2, 58
8a^b	H ^A	H ^A	(CH ₂) ₂		2.32	2.73	2.73	2.06	2.06	11.78	70.73	84.11	84.11	3
8b	Ph	Ph	(CH ₂) ₂			3.05			3.05	22.75	110.71	82.27	82.27	169
8c	CH=CH ₂	H ^A	(CH ₂) ₂		3.47	2.59			3.44	17.42	89.23	83.05	79.33	169
8d	<i>E</i> -CH=CHMe	H ^A	(CH ₂) ₂		3.53	2.59			3.45	17.33	88.87	82.93	78.78	169
8e	<i>p</i> -C ₆ H ₄ OMe	H ^A	(CH ₂) ₂		4.22	2.74			3.37	17.75	90.75	84.50	79.36	169
8f	1-naphthyl	H ^A	(CH ₂) ₂		4.38	2.83			3.18	<i>c</i>	<i>c</i>	<i>c</i>	<i>c</i>	169
8g	<i>o</i> -C ₆ H ₄ Br	Ph	(CH ₂) ₂			2.89			3.19	<i>c</i>	<i>c</i>	<i>c</i>	<i>c</i>	169
9a	H ^A	H ^A	(CH ₂) ₃		1.55	2.75			2.75	9.42	66.55	86.51	86.51	169
9b	Me	H ^A	(CH ₂) ₃		2.10	2.52			3.56	15.05	76.23	84.66	81.90	169
9c	<i>i</i> -Pr	H ^A	(CH ₂) ₃		1.90	2.49			3.48	14.21	91.96	85.05	81.78	169
9d	<i>c</i> -C ₆ H ₁₁	H ^A	(CH ₂) ₃		1.98	2.50			3.50	13.75	90.56	85.17	81.84	169
9e	<i>E</i> -CH=CHMe	H ^A	(CH ₂) ₃		2.73	2.62			3.65	15.14	85.51	83.42	81.99	169
9f	Ph	H ^A	(CH ₂) ₃		3.41	2.72			3.41	14.96	87.26	86.11	82.46	169
9g	Me	Me	(CH ₂) ₃			3.48			3.48	19.26	83.86	79.87	79.87	208
9h	CH ₂ OPh	Me	(CH ₂) ₃			3.48			3.48	19.48	86.57	81.45	80.39	208
9i	-(CH ₂) ₄ -		(CH ₂) ₃			3.25			3.25	19.55	94.38	82.13	82.13	169
9j	-(CH ₂) ₅ -		(CH ₂) ₃			3.55			3.55	17.90	93.35	79.33	79.33	169
9k	<i>d</i>	H ^A	(CH ₂) ₃		2.13	2.50 ^e			4.10 ^e	16.02	75.15	87.14 ^e	82.02 ^e	208
9l	<i>f</i>		(CH ₂) ₃			3.48			3.48	18.54	92.88	79.75	79.75	169
9m	H ^A	H ^A	<i>g</i>		1.40	2.49			3.28	9.45	65.30	83.45	88.72	169
9n	H ^A	H ^A	<i>h</i>		1.63, 1.76	2.73			3.18	7.57	67.42	86.23	84.29	169
10a	Et	H ^A	H ^C	H ^D	2.40	2.50	1.94	1.52–1.57	5.54		92.79	71.70	69.75	80
10b	<i>n</i> -Pr	H ^A	H ^C	H ^D	2.43	2.52	1.95	1.54–1.58	5.47		90.76	71.86	69.23	80
10c–g^{a,i}	alkyl	H ^A	H ^C	H ^D	2.60	2.69	2.16	1.74	1.74	5.3	91.0	71.9	69.2	80
10h	CHMeEt	H ^A	H ^C	H ^D	2.20	2.49	1.93	1.51–1.54	4.06, 6.14		98.29	72.06	69.12	80
10i	CH ₂ CHMe ₂	H ^A	H ^C	H ^D	2.44	2.52	1.99	1.54–1.58	5.44		89.47	72.02	69.30	80
10j	CH ₂ CHMeEt	H ^A	H ^C	H ^D	2.45	2.54	1.96	1.55–1.59	5.29, 5.79		89.40	72.05	69.27	80
10k	CH ₂ CH(<i>n</i> -Pr)Me	H ^A	H ^C	H ^D	2.46	2.55	1.93	1.56–1.60	5.29, 5.83		89.38	72.06	69.29	80
10l	CH ₂ Ph	H ^A	H ^C	H ^D	2.56–2.64	1.96	1.54	1.52	5.68		91.14	72.01	69.41	80
10m	(CH ₂) ₂ Ph	H ^A	H ^C	H ^D	2.43	2.51/	1.93	1.46–1.54	5.73		90.39	71.95	69.24	80
10n	CH ₂ OH	H ^A	H ^C	H ^D	2.70	2.48	1.88	1.45	1.55	5.0	92.4	72.3 ^k	70.0 ^k	211
10o	CH ₂ OCH ₂ OMe	H ^A	H ^C	H ^D	2.71	2.45	1.85	1.53	1.58	4.7	88.7	72.3	70.3	211
10p	CH ₂ OSiMe ₂ (<i>t</i> -Bu)	H ^A	H ^C	H ^D	2.73	2.43	1.88	1.49	1.55	5.1	92.0	72.3	70.0	211
10q	CH ₂ OAc	H ^A	H ^C	H ^D	2.65	2.48	1.83	1.45	1.50	4.6	86.8	72.1 ^k	70.0 ^k	211
10r^j	CH ₂ OR ^m	H ^A	H ^C	H ^D	2.85	2.80	2.27	1.85	1.90	4.9	87.7	78.8 ^k	70.7 ^k	211
10s	(CH ₂) ₂ OCH ₂ OMe	H ^A	H ^C	H ^D	2.58; 2.46; 1.92; 1.46–1.57 ^{n,o}				5.4		87.6 ⁿ	72.0, 69.5, 67.4 ^{n,o}		212
11a	Et	Et	H ^C	H ^D		1.57	2.30	2.30	1.57	11.78	107.16	67.77	67.77	211
11b	-(CH ₂) ₃ -		H ^C	H ^D		2.03	1.98	1.98	2.03	11.55	95.09	67.19	67.19	211
11c	Cl	Cl	H ^C	H ^D		3.06	2.26	2.26	3.06	<i>c</i>	<i>c</i>	<i>c</i>	<i>c</i>	254

^a Recorded in CDCl₃. ^b Recorded in THF-*d*₆. ^c Not reported. ^d Two [1.1.1]propellane cages are connected through this bond. ^e The shifts may be reversed. ^f Two [1.1.1]propellane cages spiro connected through two CH₂CH₂ bridges. ^g R = *c*-C₃H₄CH₂. ^h R = 2-C₆H₄CH₂. ⁱ NMR shifts for nuclei in the same relative positions in [1.1.1]propellanes **10c–g** are the same within ±0.1 ppm for protons and ±0.5 ppm for carbons. ^j Signal from a different proton overlaps with the one observed, the multiplet is 2.48–2.54 ppm. ^k Assignment is based on analogy with [1.1.1]propellanes **10o** and **10p**. ^l Recorded in CD₂Cl₂. ^m R = CONHCH₂Ph. ⁿ The signals have not been assigned to nuclei; the presented assignment is based on the reported multiplicity of the signals and on analogy with spectra of other [1.1.1]propellanes. ^o Signals from different nuclei overlap with the one been assigned.

due mostly to through-space or through-bond interactions. According to maximally spin-paired NBO (MSPNBO) analysis, the major mechanism of spin density propagation through the bicyclo[1.1.1]pentane cage is through-space polarization, with all through-space interactions accounting for two-thirds to three-quarters of the total spin density on the bridgehead hydrogen and through-bond interactions accounting for the rest.¹⁰⁹

Measurement of the ¹³C hyperfine tensors for the bicyclo[1.1.1]pent-1-yl radical (**121**)¹⁵⁸ allowed an estimation of the “experimental” C(2)–C(1)–C(4) angles to be 110° based on the assumption of “complete orbital following”. Comparison with the angle of the optimized geometry (UHF/6-31G*), which is

20° smaller, reveals the “bent” nature of the C(1)–C(2) bonds in the radical **121**.

In bicyclo[1.1.1]pent-1-ylmethyl (**141**, Chart 8) radical, hfs due to couplings with the bridge and bridgehead hydrogens are equal in absolute value (~1.2 G).³⁰⁴ In [2]staff-3-ylmethyl radical (**2**)[**141**] hfs due to the bridgehead hydrogen has not been detected.¹⁵⁹ Clearly, propagation of spin density along the [*n*]staffane rod is much less efficient when it is held in a π-symmetry orbital compared to a σ-symmetry orbital.

5. NMR Spectra

a. Chemical Shifts. Unsubstituted bicyclo[1.1.1]pentane (**1**) gives two singlets in ¹H NMR (at δ 1.84

Table 12. ^{13}C NMR Shielding Tensors of [1.1.1]Propellane (Adapted from Ref 167)

tensor component	δ (ppm)
Bridge CH_2 Group	
σ_A (bisecting the HCH angle)	43
σ_B (perpendicular to the HCH plane)	57
σ_C (perpendicular to the CCC plane)	138
σ_{iso}	79.3
Bridgehead C	
σ_{\parallel} (parallel to the central C–C bond)	35
σ_{\perp} (degenerate component perpendicular to the C–C bond)	–11
σ_{iso}	4.3

for the bridge protons and at δ 2.44 for the bridgehead protons, Table 10).¹⁶⁰ In [*n*]staffanes signals of the bridge protons are shifted to a higher field as the length of the chain grows and appear between δ 1.35 and 1.55.⁴² The $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of unsubstituted **1** consists of two signals at δ 33.59 (bridgehead) and 50.75 (bridge).^{161,162} In the parent [*n*]staffanes (**[*n*]**1****), the chemical shift of the methine protons is δ 2.36. The methylene protons on the outer cages resonate at δ 1.57–1.61, while those of the inner cages have chemical shifts of δ 1.34–1.38.⁴² ^{13}C NMR chemical shifts for unsubstituted **1** and some bridgehead-substituted derivatives have been calculated at IGLO HF/6-31G** level of theory, and the results are within 6 ppm of the observed shifts.^{163,164}

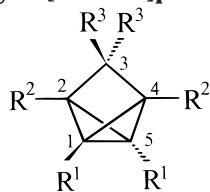
Selected NMR chemical shifts in [1.1.1]propellanes **2**, **8a–g**, **9a–n**, **10a–s**, and **11a–c** are collected in Table 11. The ^1H NMR spectrum **2** in CDCl_3 consists of a singlet at δ 2.06, and the chemical shift is solvent sensitive.^{2,60} The isotropic ^{13}C chemical shifts for the unsubstituted bridge carbons are about δ 65–74,^{17,80} which is shifted significantly downfield compared to

cyclopropane (**142**, δ –4,¹⁶⁵ Chart 8) and bicyclo[1.1.0]butane (**143a**, δ 33¹⁶⁶). Individual components of the ^{13}C shielding tensor in **2** (Table 12) suggest that this difference in chemical shifts is mainly due to the tensor component perpendicular to the CCC plane.¹⁶⁷ Chemical shifts for the bridgehead carbons are about δ 1–23.^{17,80} Alkyl and aryl substituents shift the resonance of the adjacent bridge carbon to lower field, up to δ 111 ppm.^{17,80}

Selected chemical shifts in tricyclo[2.1.0.0^{2,5}]pentanes **3**, **98**, **99–102**, and **104–106** are collected in Table 13. Signals from protons in position 1 and 5 are shifted downfield (δ 3–4), which is probably a consequence of an increased electronegativity of the adjacent carbons.

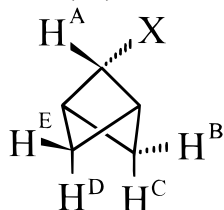
b. Coupling Constants. Absolute values of ^1H – ^1H geminal coupling constants in bridge-substituted bicyclo[1.1.1]pentanes vary from 1.9 to 3.5 Hz (Table 14).⁷⁷ The corresponding constants in the monosubstituted [1.1.1]propellanes **10** (Table 15) and in the tricyclo[2.1.0.0^{2,5}]pentane derivative **106** have similar values (Table 16). A huge spin–spin coupling constant $^4J_{\text{HH}}$ between the two bridgehead protons in **1** (18 Hz) has been observed.^{160,168} The coupling constants between the W-related protons on bridges are also quite large (6–10 Hz, Table 14).^{77,160,168} Similar coupling constants in substituted [1.1.1]propellanes **8** and **10** vary between 4 and 8 Hz (Table 15).^{169,170} They are large in substituted **3** as well (Table 16).

The coupling constants $^1J_{\text{CH}}$ in **1** are 144.5 Hz (methylene group) and 167.8 Hz (bridgehead).^{160,161} The latter constant increases upon substitution on the bridges and can be very large: 184 Hz in the ketone **144** (Chart 8),¹⁷¹ 180 Hz in 2,2,4,4,5,5-hexafluorobicyclo[1.1.1]pentane (**115o**, Chart 6),⁹⁹

Table 13. NMR Chemical Shifts of Selected Tricyclo[2.1.0.0^{2,5}]pentanes (ppm)

compd	R ¹	R ²	R ³	H ^A	H ^B	H ^C	C1	C2	C3	ref
3	H ^A	H ^B	H ^C , H ^C	3.46	1.55	2.65	20.8	24.6	56.8	9
98	H ^A	H ^B	=O	3.99	2.06	<i>a</i>	<i>a</i>	<i>a</i>	<i>a</i>	26
99a	Me	H ^B	=O		1.73	14.6 ^b	42.3 ^b	185.3 ^b		7, 129
99b	Ph	H ^B	=O		2.88	25.6 ^c	46.8 ^c	181.7 ^c		8, 129
99c	CH ₂ OAc	H ^B	=O		2.16	15.33	43.01	181.4		72
99e	CH ₂ I	H ^B	=O		2.34	<i>a</i>	<i>a</i>	<i>a</i>		204a
99f	CH ₂ Br	H ^B	=O		2.37	31.11	45.69	180.41		204a
99g	CH ₂ OH	H ^B	=O		2.32	18.19	41.32	185.05		72, 204a
100c	CH ₂ OH	H ^B	OCH ₂ CH ₂ O		2.21	22.17 ^d	32.70 ^d	111.34 ^d		72
101a	Me	H ^B	H ^C , O ₂ CPh		<i>a</i>	<i>a</i>	14.8, 28.1 ^e	28.6 ^e	85.5 ^e	129
101b	Ph	H ^B	H ^C , O ₂ CPh		<i>a</i>	<i>a</i>	30, 44.0 ^c	35.9 ^c	84.9 ^c	129
102a	CH ₂ OAc	H ^B	OEt, OEt		2.40	20.75	34.75	112.08		72
102d	CH ₂ OH	H ^B	OEt, OEt		2.39	22.17 ^d	32.70 ^d	111.34 ^d		72
104a	<i>t</i> -Bu	<i>t</i> -Bu	=O			<i>f</i>	<i>f</i>	188.71		197
105a	Me	H ^B	H ^C , OH		<i>a</i>	<i>a</i>	12.9, 27.5 ^e	33.6 ^e	84.4 ^e	129
105c	Ph	H ^B	H ^C , OH		<i>a</i>	<i>a</i>	30, 44.9 ^c	40.1 ^c	84.1 ^c	129
105d	Me	H ^B	OH, Me		1.50	14.45, 22.52	35.77	90.48		130
106	H ^A	Me	H ^C , H ^C	2.98		2.09	<i>a</i>	<i>a</i>	<i>a</i>	90

^a Not reported. ^b Spectra measured in CD_2Cl_2 . ^c Spectra measured in $(\text{CD}_3)_2\text{CO}$. ^d Identical ^{13}C NMR spectra have been reported for **100c** and **102d**. ^e Spectra measured in CS_2 . ^f Four signals for quaternary carbons have been reported without assignment: δ 60.58, 33.42, 30.24, 29.32 ppm.

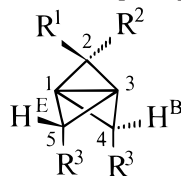
Table 14. ^1H – ^1H NMR Coupling Constants Between Bridge Protons in Monosubstituted Bicyclo[1.1.1]pentanes (Hz)^a

X	$^4J_{AC}$	$^4J_{BE}$	$^2J_{BC}$	$^4J_{DE}$
Cl	7.4	10.1	-3.0	-3.0
OH	6.3	10.1	-2.7	-3.0
OCOEt	6.9	9.8	-2.7	-3.2
COEt	6.7	9.8	-3.0	-2.3
CO ₂ Me	7.2	9.6	-3.2	-1.9
CO ₂ H	7.3	10.0	-3.2	-2.2
CH ₂ OH	6.7	10.0	-3.5	-2.5

^a Adapted from ref 77.

and 172.6 Hz in the ketal **145** (Chart 8).¹⁷¹ The $^1J_{CH}$ constants in [1.1.1]propellanes are around 160 Hz.^{2,11,60} In tricyclo[2.1.0.0^{2,5}]pentane (**3**) and its derivative **106** the constants $^1J_{C(1)H}$ are the highest (210 Hz⁹ and 212 ± 2 Hz,⁹⁰ respectively) and exceed the analogous constant in bicyclo[1.1.0]butane (**143a**, 205 Hz).^{166,172} $^1J_{C(2)H}$ coupling constants in substituted **3** are somewhat smaller, but they are still huge for a methine group (Table 16).

Detectable long-range ^{13}C – ^1H coupling constants in **1** are $^2J_{CH} = 3.0$ Hz and $^3J_{CH} = 10.0$ Hz for bridgehead carbons, and *cisoid*- $^3J_{CH} = 7.8$ Hz and *transoid*- $^3J_{CH} = 15.5$ Hz¹⁶⁸ for the bridge carbons. Long-range coupling constants $^3J_{C(2)H(4)}$ in substituted **3** are also remarkably large (Table 16).

Table 15. Selected Spin–Spin NMR Coupling Constants in [1.1.1]Propellanes (Hz)

^1H – ^1H Coupling Constants								ref
	R ¹	R ²	R ³	$^4J_{HH}$		$^2J_{HH}$		
				AC	BE	BC		
8c	CH=CH ₂	H(A)	(CH ₂) ₂		4			79
8d	<i>E</i> -CH=CHMe	H(A)	(CH ₂) ₂		4			79
8e	<i>p</i> -C ₆ H ₄ OMe	H(A)	(CH ₂) ₂		4.5			79
8f	1-naphthyl	H(A)	(CH ₂) ₂		4			79
8g	<i>o</i> -C ₆ H ₄ Br	Ph	(CH ₂) ₂		4.5			79
10a	Et	H(A)	H(C,D)	4.4	7.2	2.2		80
10b	<i>n</i> -Pr	H(A)	H(C,D)	4.6	7.8	2.2		80
10d	<i>n</i> -C ₇ H ₁₅	H(A)	H(C,D)	4.5	7.6	2.3 ^a		170
10h	CH(Me)Et	H(A)	H(C,D)	4.4	7.8	2.1		80
10i	CH ₂ CHMe ₂	H(A)	H(C,D)	4.5	7.8	2.2		80
10j	CH ₂ CH(Me)Et	H(A)	H(C,D)	4.4	7.8	2.1		80
10k	CH ₂ CH(<i>n</i> -Pr)Me	H(A)	H(C,D)	4.4	7.8	2.1		80
10l	CH ₂ Ph	H(A)	H(C,D)	4.3	7.2	2.4		80
10m	CH ₂ CH ₂ Ph	H(A)	H(C,D)	4.4		2.1		80

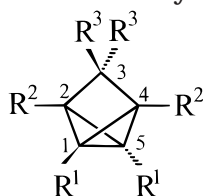
^{13}C – ^{13}C Coupling Constants (R ² = R ³ = H)								ref	
	R ¹	$^1J_{CC}$							
		C1C3	C1C2	C2C3	C1C4	C3C4	C1C5		C3C5
10h	CH(Me)Et	0.53	10.6	10.4	9.7	9.6	10.4	10.4	80
10j	CH ₂ CH(Me)Et	0.47	10.5	10.5	9.9	9.6	10.1	10.3	80

^a $^2J_{H(D)H(E)} = 1.7$ Hz.

The effect of bridgehead substituents on $^3J_{C(1)H}$ coupling constants is surprisingly large.¹⁷³ The observed constants varied from 10 Hz for the unsubstituted **1** to 33.8 Hz for 1-bromobicyclo[1.1.1]pentane (**17i**). Electronegativity of the substituent appears to be the dominant influence compared to contributions of field/inductive and resonance effects, particularly in bicyclo[1.1.1]pentanes with a second-row element attached to a bridgehead. IPPP-CLOPPA-INDO¹⁷⁴ analysis suggests that more than three-quarters of spin information is transmitted through bonds, primarily through the polarization propagator factor, and only one-quarter is transmitted through space. The share of through-space transmission mechanism has been found to be independent of the bridgehead substituent,¹⁷³ and a rationalization in terms of the polarizability of the bridgehead bond has been offered.¹⁷⁵

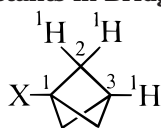
The ^{13}C – ^{13}C coupling constant through one bond is 25.1 Hz in unsubstituted **1**¹⁶⁸ and varies from 25.1 to 25.4 in 2-(*sec*-hexyl)bicyclo[1.1.1]pentane (**146**, Chart 8).⁸⁰ The coupling constant between the bridge and the bridgehead carbons range from 9.6 to 10.6 Hz for substituted [1.1.1]propellanes **10h** and **10j** (Table 15)⁸⁰ and is 9.9 Hz in the parent **2**.⁷³

J_{CC} coupling constants between the bridgehead carbons in bicyclo[1.1.1]pentane (**1**, $^2J_{CC}$) and in [1.1.1]propellane (**2**, $^1J_{CC}$) have been calculated at the EOM-HF (DZP) level of theory and compared to those calculated for propellanes of different ring sizes.⁸¹ A remarkably small number (1.59 Hz) has been predicted for $^1J_{CC}$ in **2**, contrary to a value predicted by INDO calculations¹⁷⁶ (213.8 Hz). The former number is in excellent agreement with recently measured

Table 16. Selected Spin–Spin NMR Coupling Constants in Tricyclo[2.1.0.0^{2,5}]pentanes (Hz)

compd	R ¹	R ²	R ³	² J _{H(3)H(3')}	³ J _{H(1)H(6)}	⁴ J _{H(1)H(3)}	¹ J _{C(1)H}	¹ J _{C(2)H}	⁴ J _{H(2)H(4)}	³ J _{C(2)H(4)}	ref
3	H(1) H(5)	H(2) H(4)	H(3) H(3')	<i>a</i>	<i>a</i>	<i>a</i>	210	<i>a</i>	<i>a</i>	<i>a</i>	9
99b	Ph	H(2) H(4)	=O					190.1	14	<i>a</i>	8
99c	CH ₂ OAc	H(2) H(4)	=O					190.5	<i>a</i>	14.7	72
99f	CH ₂ Br	H(2) H(4)	=O					192.46	<i>a</i>	14.66	204a
100c	CH ₂ OH	H(2) H(4)	-OCH ₂ CH ₂ O-					173.34 ^b	<i>a</i>	10.5 ^b	72
102a	CH ₂ OAc	H(2) H(4)	OEt, OEt					185.0	<i>a</i>	10.83	72
102d	CH ₂ OH	H(2) H(4)	OEt, OEt					173.34 ^b	<i>a</i>	10.5 ^b	72
106	H(1) H(5)	Me	H(3) H(3')	3.13	7.66	5.80, 0.90	212(2)				90

^a Coupling constants have not been reported. ^b Identical ¹³C NMR spectra have been reported for **102d** and **100c**.

Table 17. Selected Spin–Spin NMR Coupling Constants in Bridgehead-Substituted Bicyclo[1.1.1]pentane (Hz)

X	⁴ J _{XH(3)}	³ J _{XC(3)}	³ J _{C(1)H(3)}	³ J _{XH(2)}	² J _{XC(2)}	¹ J _{XC(1)}	ref
¹ H	18		10	<i>a</i>	<i>a</i>	167.8	160, 168
¹³ CO ₂ H	14.22	9.68	13.2 ^b	<i>a</i>	<i>a</i>	64.55	248
¹⁵ NH ₂	6.11	4.63	17.1 ^b	<i>a</i>	1.46	1.33	181, 173
¹⁵ NH ₃ Cl	8.18	5.49	21.4 ^b	<i>a</i>	0.31	<i>a</i>	181, 173
¹⁹ F	70.6	42.5	27.4 ^c	2.8	20.5	332.5	161, 179, 173
³¹ PO(OMe) ₂	55.92	<i>d</i>	<i>d</i>	2	<i>d</i>	<i>d</i>	91, 180
¹¹⁹ SnPh ₃	225.9	<i>d</i>	13.5 ^e	2.0 ^e	<i>d</i>	<i>d</i>	182
¹¹⁷ SnPh ₃	216.1	<i>d</i>	<i>d</i>	<i>d</i>	<i>d</i>	<i>d</i>	182
¹¹⁵ SnPh ₃	198.5	<i>d</i>	<i>d</i>	<i>d</i>	<i>d</i>	<i>d</i>	182

^a No coupling has been observed. ^b Value obtained at natural abundance. ^c Value obtained from deuterated compound. ^d Value has not been reported. ^e Average for different magnetically active isotopes.

values for [1.1.1]propellanes **10j** and **10h**, 0.47 and 0.53 Hz, respectively.⁸⁰ This result has been attributed to the high *p* character of the central C–C bond in [1.1.1]propellanes (section II.B.1.d), which is unfavorable for transmission of spin information by the Fermi contact mechanism, the major contributor to large coupling constants at this level of theory. The magnitude calculated for ²J_{C(1)C(3)} in **1** is –25.45 Hz, and its absolute value is remarkably close to the values observed in bicyclo[1.1.1]pentane-1-carboxylic acid (**14**, 25.16 Hz^{177,178}) and in **146** (25.1 Hz⁸⁰). The large value is presumably due to a very strong transannular interaction capable of transmitting a large Fermi contact term, even though there is no formal bond.

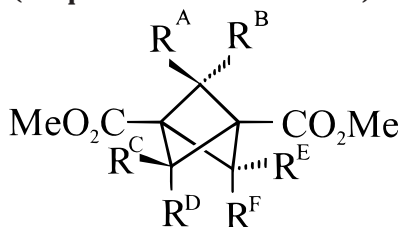
In bridgehead-substituted bicyclo[1.1.1]pentanes the transannular coupling constants between magnetically active nuclei in substituents are also very large.^{91,179–183} Some representative examples of coupling constants in bridgehead-substituted bicyclo[1.1.1]pentanes are listed in Table 17. Spin–spin coupling between nuclei in the bridgehead positions across more than one cage in [*n*]staffanes is noticeable if at least one of the nuclei is heavier than proton (⁷J_{PH} = 1.7 Hz,^{21,91} ⁷J_{FF} = 11 Hz,⁹⁸ ⁷J_{HF} = 2.9 Hz,⁹⁸ ⁶J_{CF} = 2.9 Hz⁹⁸).

The large long-range spin–spin coupling constants ⁴J_{HH}, ⁴J_{HF}, and ⁴J_{FF} observed in bridge-fluorinated

bicyclo[1.1.1]pentane derivatives **111** and **116a–k,m,n** are very stereospecific.^{48,98} This is illustrated in Table 18, which collects the long-range coupling constants in the dimethyl esters **111** and **116a–k,m,n**.⁴⁸ The ⁴J_{HH} and ⁴J_{HF} constants are large across the W pathway. Presumably, the spin–spin interaction between H and F nuclei is promoted by overlapping back lobes of the exocyclic bridge hybrids. In contrast, the ⁴J_{FF} constants are the largest between the proximate F nuclei, most likely due to an interaction between lone pairs of the proximate F atoms. For several of these molecules, the coupling constants were calculated by the EOM-CCSD/6-311G* method and very good agreement with the observed values was found.⁹⁸

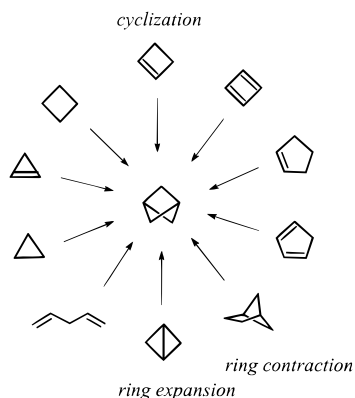
III. Synthesis of the Bicyclo[1.1.1]pentane Framework

Since the original low-yield synthesis,² better synthetic approaches to [1.1.1]propellane (**2**) have been developed. The seminal discovery³ of an efficient two-step preparation of **2** and several improvements^{20,79,169,184–186} have opened an exciting period of rapidly expanding chemistry and application of derivatives of **1** and [*n*]**1** (in our experience, the

Table 18. ^1H – ^1H , ^1H – ^{19}F , and ^{19}F – ^{19}F Spin–Spin NMR Coupling Constants (Hz) in Fluorinated Dimethyl Bicyclo[1.1.1]pentane-1,3-dicarboxylates (Adapted from Refs 48 and 98)

compd	2J (geminal constants) ^a			4J (long-range constants) ^a											
	A–B	C–D	E–F	A–F ^b	B–D ^b	C–E ^b	A–E ^c	A–D ^c	B–F ^c	B–C ^c	D–E ^c	C–F ^c	A–C ^d	B–E ^d	D–F ^d
116a ^e	70.5	2.7	3.3	27.6	6.6	9.6	2.1	3.1	<i>f</i>	<i>f</i>	<i>f</i>	<i>f</i>	<i>f</i>	<i>f</i>	<i>f</i>
116b ^e	68.6	4.0	66.3	19.4	6.7	28.0	8.3	3.4	<i>f</i>	<i>f</i>	2.0	<i>f</i>	<i>f</i>	0.5	<i>f</i>
116c ^g	144.2	2.5	2.5	19.6	19.6	10.1	3.2	0.2	0.2	3.2	<i>f</i>	<i>f</i>	1.5	1.5	<i>f</i>
116d ^g	68.9	3.3	68.9	29.8	6.6	6.6	2.1	4.7	2.1	0.4	0.4	4.7	0.9	<i>f</i>	0.9
116e ^g	65.5	65.5	4.6	26.0	7.6	26.0	2.2	1.5	0.4	1.5	0.4	2.2	48.9	<i>f</i>	<i>f</i>
116f ^g	64.6	64.6	64.6	18.6	18.6	18.6	8.1	<i>f</i>	<i>f</i>	8.1	<i>f</i>	<i>f</i>	<i>f</i>	<i>f</i>	<i>f</i>
116g ^e	64.4	63.6	63.6	31.0	18.2	7.4	1.6	6.9	2.0	<i>f</i>	0.9	0.9	<i>f</i>	<i>f</i>	63.2
116h ^e	141.5	4.4	65.2	22.7	17.3	28.4	<i>f</i>	1.3	<i>f</i>	3.3	1.0	<i>f</i>	1.2	52.2	<i>f</i>
116i ^e	148.3	4.0	69.8	14.7	18.7	7.0	1.2	1.0	1.0	3.4	<i>f</i>	6.0	1.7	<i>f</i>	<i>f</i>
116j ^e	159.0	64.8	63.2	22.7	16.6	19.2	<i>f</i>	2.3	<i>f</i>	<i>f</i>	8.5	<i>f</i>	1.1	63.2	<i>f</i>
116k ^g	144.7	4.3	144.7	9.7	18.1	18.1	6.0	2.7	6.0	3.3	3.3	2.7	1.6	56.2	1.6
116m ^g	143.0	62.8	62.8	21.1	21.1	33.5	1.3	<i>f</i>	<i>f</i>	1.3	2.1	2.1	66.4	66.4	<i>f</i>
116n ^{e,h}	156.2	162.0	62.7	22.6	11.4	14.7	<i>f</i>	4.8	<i>f</i>	7.8	<i>f</i>	1.4	70.6	85.4	1.3
111 ^g	160	160	160	10	10	10	9	9	9	9	9	9	98	98	98

^a ^1H – ^1H coupling constants are in plain font; ^1H – ^{19}F coupling constants are in italics; ^{19}F – ^{19}F coupling constants are in bold. ^b Coupling through a W-shaped path. ^c Coupling through a sickle-shaped path. ^d Coupling between proximate nuclei. ^e Absolute values of coupling constants were obtained from first-order spectra. ^f No coupling was observed. ^g Values were obtained from computer simulation of experimental spectra. ^h Signs of the coupling constants were determined by spin tickling experiments.

Scheme 3

presently best procedure for the synthesis of **2** is a slight modification⁹⁸ of that described in refs 185 and 186). More than 30 [1.1.1]propellanes and tricyclo[2.1.0.0^{2,5}]pentanes each and several hundred bicyclo[1.1.1]pentane derivatives are known to date.

The synthetic approaches to compounds with bicyclo[1.1.1]pentane framework, from precursors without such framework, can be divided into three general categories: (1) cyclizations, (2) ring expansions, and (3) ring contractions. Scheme 3 summarizes all known general classes of precursors to compounds containing the bicyclo[1.1.1]pentane framework: acyclic, monocyclic, and bicyclic compounds.

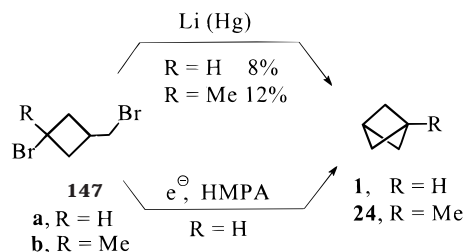
Photochemical cyclization and decarbonylation, intramolecular and intermolecular carbene insertion, and anionic annelation are the typical key reactions leading to derivatives of **1**, **2**, and **3**, although radical cyclization as well as thermal rearrangements have also been used.

A. Cyclizations**1. Wurtz Coupling**

Wurtz-type cyclization of 3-bromo(bromomethyl)cyclobutane (**147a**, Scheme 4) was the first successful approach to the parent bicyclo[1.1.1]pentane (**1**).¹ A variety of metals and solvents were tried,¹⁶⁰ but the best yield of **1** is only 8%. In a similar fashion, the dibromide **147b** gives 1-methylbicyclo[1.1.1]pentane (**24**) in 12% yield. The lithium dehalogenation method was used in the synthesis¹³⁴ of 1-deuterio- and 1,3-dideuteriobicyclo[1.1.1]pentane (**21** and **22**, 95% and 92% isotopic purity, respectively), starting from the properly labeled dibromides **147a**. Electrochemical^{187,188} cyclization of the dibromide **147a** produced some bicyclo[1.1.1]pentane, as well as typical¹ side products such as 1,4-pentadiene, methylcyclobutane, and 1-pentene.

2. Photochemical Transformations

Photochemical cyclization^{189–191} of cyclobutylaryl ketones **148** represents a direct path to 2-substituted bicyclo[1.1.1]pentanes **149** (Scheme 5 and Table 19). Irradiation of the ketone **148a** in benzene gave two products of the Norrish II type: the major cyclic

Scheme 4

Scheme 5

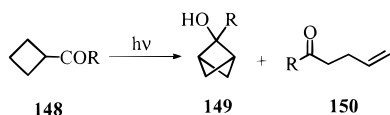


Table 19. Photochemical Cyclization of Cyclobutyl Aryl Ketones

substrate	Ar	yield of 149	yield of 150	ref
148a	Ph	38	24	189, 190
148a	Ph	36	^a	191
148b	1,3-imidazol-2-yl	20	15	192
148c	1,3-imidazol-4-yl	40	19	192

^a Not reported.

product **149a** and the fragmentation product **150a**. The products of Norrish I cleavage are also present in the reaction mixture. Irradiation of **148a** in 2-propanol gave only a pinacol,¹⁹⁰ and irradiation of the imidazolyl ketones **148b** and **148c** in acidic methanol yielded mostly the Norrish II products **149b** and **149c**, respectively.¹⁹² The quantum yield of the cyclization process in a series of para-substituted derivatives of **148a** depends strongly on the substituent and ranged from extremely small for CH₃O to 0.089 for CF₃.¹⁹³ Chemical yields were not reported. The low quantum yield has been attributed to an unfavorable conformational equilibrium in the excited state.^{190,193} Irradiation of cyclobutyl ketones with *o*-, *m*-, and *p*-anisyl, 2-furyl, and vinyl substituents did not yield any significant amount of bicyclo[1.1.1]pentane derivatives, presumably because these substituents red-shifted the $\pi-\pi^*$ transition and made the $n-\pi^*$ state photochemically ineffective.⁷⁸

Norrish II cyclization also permits the generation of a bicyclo[1.1.1]pentane skeleton within the bicyclo[2.1.1]hexane (**151a**) and even the bicyclo[1.1.1]pentane (**151b**) ring system, leading to phenyl derivatives of tricyclo[3.2.0.0^{2,6}]heptan-7-ol (**152a**)¹⁹⁴ and tricyclo[2.1.0.0^{2,5}]hexan-2-ol (**152b**),¹⁹⁵ respectively (Scheme 6 and Table 20). The quantitative chemical yield and relatively high quantum yield in the former reaction have been attributed to the proximity of the carbonyl group to the CH₂ bridge.¹⁹⁶

Irradiation of the substituted cyclobutylphenyl ketones **153a** and **153b** did not lead to the expected derivatives of **1**, and the benzylic bond cleaved instead (Scheme 7). The ketone **153a**, a monocyclic analogue of **151b**, yielded only the cyclobutyl derivative **154**, attributable to Norrish I cleavage followed

Scheme 6

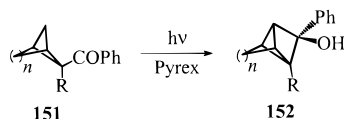
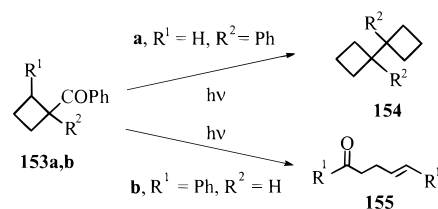


Table 20. Norrish II Photocyclization of Bicyclic Aryl Ketones

151, 152	R	<i>n</i>	solvent	yield (%)	ref
a	H	2	PhH	11	194
b	Ph	1	<i>t</i> -BuOH	100	195

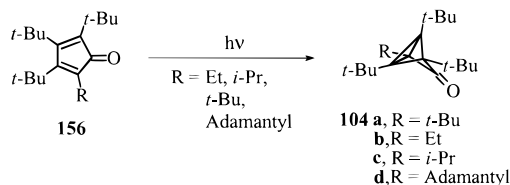
Scheme 7



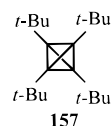
by dimerization.⁹¹ Irradiation of the ketone **153b** gave the Norrish II product **155**.¹⁹⁰

Certain cyclopentadienones **156** have been found to photocyclize to the corresponding tricyclo[2.1.0.0^{2,5}]pentan-3-ones **104** (Scheme 8), which serve as inter-

Scheme 8



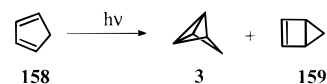
mediates in the synthesis of other strained compounds (for instance, tetra-*tert*-butyltetrahydrene **157**, see also discussion in section IV.B.6).^{197,198}



The photochemistry of differently substituted ketones **156** has been examined, and it is established that only fully alkyl-substituted compounds, preferably with bulky alkyl groups, undergo this criss-cross cycloaddition.^{199,200}

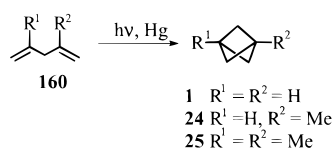
Irradiation of cyclopentadiene (**158**) produces the parent tricyclo[2.1.0.0^{2,5}]pentane (**3**) and bicyclo[2.1.0]pent-2-ene (**159**) in a 1:7 ratio (Scheme 9).⁹

Scheme 9



Mercury (³P₁)-sensitized cyclization of penta-1,4-dienes **160** yields the bicyclo[1.1.1]pentanes **1**, **24** (R¹ = H, R² = Me) and **25** (R¹ = R² = Me) only as minor products, difficult to separate out of the complex reaction mixture (Scheme 10).²⁰¹

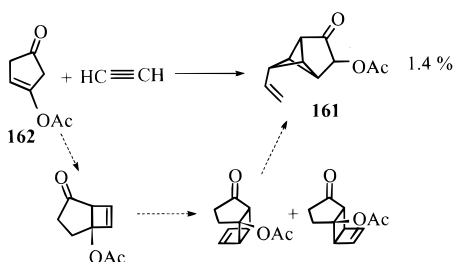
Scheme 10



The compound **161**, containing the bicyclo[1.1.1]pentane skeleton, has been isolated unexpectedly as a very minor product from an intermolecular photocycloaddition of 3-acetoxycyclopent-2-ene (**162**) and

acetylene. The mechanism proposed for this reaction is shown in Scheme 11.²⁰²

Scheme 11



3. Intramolecular Carbene Addition (for intermolecular carbene insertion, see section III.B)

Carbene addition to exo- and endocyclic double bonds represents an efficient path to derivatives of **2**¹⁸ and **3**.¹⁹ Carbenes generated either thermally^{7,71,72,203,204a} or photochemically^{8,205} from the cyclopropenyldiazoketones **163** cyclize to substituted tricyclo[2.1.0.0^{2,5}]pentan-3-ones **99**, albeit in low yields (Scheme 12 and Table 21). The efficiency of the

Scheme 12

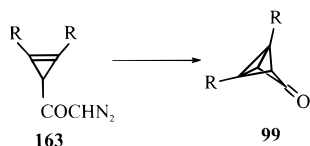
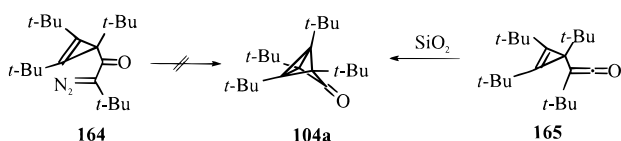


Table 21. Generation of Tricyclo[2.1.0.0^{2,5}]pentan-3-ones from Cyclopropenones by Intramolecular Carbene Insertion (Scheme 12)

substrate	R	product	yield (%)	ref
163a	Me	99a	1	7
163b	CH ₂ Cl	99h	37	204a
163c	CH ₂ OAc	99c	37	71, 72
163d	SiMe ₃	99i	203	
163e	Ph	99b	10–15	8, 205
163f	<i>n</i> -Pr	99j	10–15	205

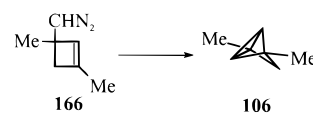
transformation of **163** to **99** has been improved by using a rhodium(II) catalyst.^{71,72,204a} No 1,2,4,5-tetra-*tert*-butyltricyclo[2.1.0.0^{2,5}]pentan-3-one (**104a**) is obtained from **164**, a tetra-*tert*-butyl-substituted analogue of **163**, presumably because of steric hindrance.²⁰⁶ However, the ketone **104a** may be obtained from ketene **165** upon treatment with silica gel, in a thermal reversal of the photochemical isomerization of **104a** into **165** (Scheme 13, see also section IV.B.6).

Scheme 13



In an analogous intramolecular reaction, a carbene intermediate generated from the diazo compound **166** adds to the cyclobutene double bond and gives the

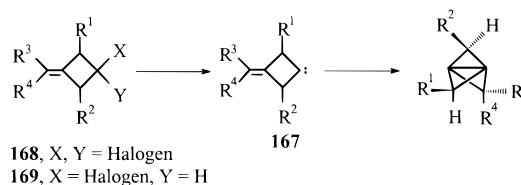
Scheme 14



tricyclo[2.1.0.0^{2,5}]pentane **106** (Scheme 14).⁹⁰

An intramolecular cyclization of 3-alkylidenecyclobutylcarbenes **167** to bridge-substituted [1.1.1]propellanes has been suggested² and found to be efficient.^{23,169,207,208} The carbenes are generated either by metal–halogen exchange^{23,169,207} in the corresponding 1,1-dihalides **168** or by deprotonation^{169,207} of the monohalides **169** followed by α -elimination (Scheme 15). The reaction appears to be general, and

Scheme 15

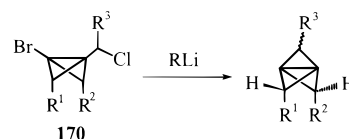


several tetracyclic and spirocyclic propellanes have been prepared in good yields (Table 22).

4. Anionic Cyclization

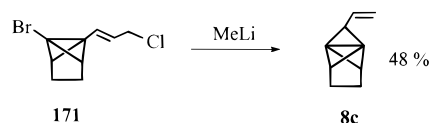
Anionic cyclization of derivatives of bicyclo[1.1.0]butane (**170**) represents another powerful method for the synthesis of [1.1.1]propellanes (Scheme 16 and Table 23).^{3,23,169,209} Metal–halogen exchange at the

Scheme 16



relatively acidic bridgehead position of **170**, followed by intramolecular nucleophilic substitution, provides high yields of the [1.1.1]propellanes. An interesting case of this reaction is the reaction of the bicyclo[1.1.0]butane derivative **171** with MeLi, which apparently proceeds via S_N2' substitution by an initially formed bridgehead anion and leads to the [1.1.1]propellane **8c** (Scheme 17). Sequential dilithiation of

Scheme 17



bicyclo[1.1.0]butanes **172** and **173** and treatment with iodochloromethane yields [1.1.1]propellanes **8a** and **9n**, respectively (Schemes 18 and 19).

Scheme 18

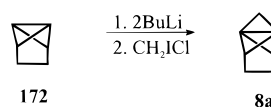


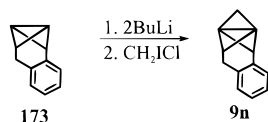
Table 22. Generation of [1.1.1]Propellanes from Cyclobutanes (Scheme 15)

substrate	reagent	X	Y	R ¹	R ²	R ³	R ⁴	product	yield (%)	ref
168a	MeLi	Br	Br	H	H	H	H	2	76	23, 208
168b	MeLi	I	I	(CH ₂) ₃	H	H	H	9a	43	208
168c	MeLi	Br	Cl	(CH ₂) ₂	Ph	Ph	Ph	8b	88	169
168d	MeLi	Br	Br	(CH ₂) ₂	H	CH=CH ₂	CH=CH ₂	8c	41	169
168e	MeLi	Br	Cl	(CH ₂) ₂	H	<i>E</i> -CH=CHMe	<i>E</i> -CH=CHMe	8d	56	169
168f	MeLi	Br	Cl	(CH ₂) ₂	H	<i>p</i> -C ₆ H ₄ OMe	<i>p</i> -C ₆ H ₄ OMe	8e	85	169
168g	MeLi	Br	Cl	(CH ₂) ₂	H	1-naphthyl	1-naphthyl	8f	35	169
168h	MeLi	Br	Cl	(CH ₂) ₂	<i>o</i> -C ₆ H ₄ Br	Ph	Ph	8g	77	169
168i	MeLi	Br	I	(CH ₂) ₃	H	<i>a</i>	<i>a</i>	9k	94	23, 208
168j	MeLi	Br	Cl	(CH ₂) ₃	H	<i>E</i> -CH=CHMe	<i>E</i> -CH=CHMe	9e	31	169
168k	MeLi	Br	Br	(CH ₂) ₃	H	Ph	Ph	9f	35	169
168l	MeLi	Br	Cl	(CH ₂) ₃	H	Ph	Ph	9f	48	207
168m	MeLi	Br	I	(CH ₂) ₃	Me	Me	Me	9g	57	208
168n	MeLi	Br	I	(CH ₂) ₃	CH ₂ OPh	Me	Me	9h	95	208
169a	LDA	Cl	H	(CH ₂) ₃	H	H	H	9a	62	169, 208
169b	LDA	Cl	H	(CH ₂) ₃	<i>b</i>	<i>b</i>	<i>b</i>	9l	18	208
169c	LDA	Br	H	(CH ₂) ₃	H	<i>i</i> -Pr	<i>i</i> -Pr	9c	77	169
169d	LDA	Cl	H	(CH ₂) ₃		(CH ₂) ₄		9i	44	169
169e	LDA	Cl	H	(CH ₂) ₃		(CH ₂) ₅		9j	50	169

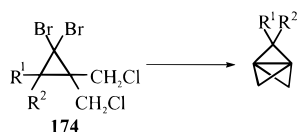
^a Two [1.1.1]propellane cages are connected through this bond. ^b Two [1.1.1]propellane cages are spiro connected through two -CH₂CH₂- bridges.

Table 23. Generation of [1.1.1]Propellanes from Bicyclo[1.1.0]butanes by Intramolecular Anionic Cyclization (Scheme 16)

substrate	R ¹	R ²	R ³	product	yield (%)	ref
170a	H	H	H	2	30	209
170b	-(CH ₂) ₂ -	H	H	8a	47	23, 169
170c	-(CH ₂) ₃ -	H	H	9a	71	3, 23, 169
170d	-(CH ₂) ₃ -	Me	H	9b	66	23, 169
170e	-(CH ₂) ₃ -	<i>i</i> -Pr	H	9c	60	23, 169
170f	-(CH ₂) ₃ -	<i>c</i> -C ₆ H ₁₁	H	9d	57	23, 169
170g	- <i>c</i> -C ₃ H ₄ CH ₂ -	H	H	9m	67	23, 169
170h	-2-C ₆ H ₄ CH ₂ -	H	H	9n	10	23, 169

Scheme 19

The tetrahalides **174** treated with alkyl-lithiums^{3,20,41,79,80,98,169,170,180,184–186,210–212} or lithium metal doped with sodium⁷⁹ presumably undergo two sequential metal–halogen exchange and nucleophilic substitution processes via the bicyclo[1.1.0]butane derivative **170** and afford [1.1.1]propellanes (Scheme 20 and Table 24). This reaction is currently the best method for the preparation of the parent [1.1.1]-propellane (**2**) in solution, starting from a readily available^{184,213} precursor **174a** and giving an almost quantitative yield^{98,185,186} of **2**.

Scheme 20

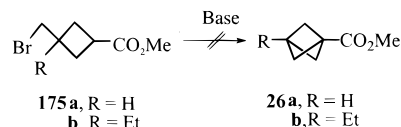
In contrast to the efficient base-induced cyclization of bicyclo[1.1.0]butanes **170**, the cyclobutane bromoesters **175** do not give the expected methyl bicyclo[1.1.1]pentane-1-carboxylates **26** (Scheme 21).^{160,214}

Table 24. Generation of [1.1.1]Propellanes from Cyclopropanes (Scheme 20)

substrate	R ¹	R ²	product	yield (%)	ref
174a	H	H	2	30–100	<i>a</i>
174a	H	H	2	25–38 ^b	79
174b	Et	H	10a	16	80
174c	<i>n</i> -Pr	H	10b	45	80
174d	<i>n</i> -C ₅ H ₁₁	H	10c	34–60	170, 210
174e	<i>n</i> -C ₇ H ₁₅	H	10d	54	170
174f	<i>n</i> -C ₁₁ H ₂₃	H	10e	21	170
174g	(CH ₂) ₃ OMe	H	10f	57	170
174h	(CH ₂) ₅ OMe	H	10g	40	170
174i	CHMeEt	H	10h	41	80
174j	CH ₂ CHMe ₂	H	10i	36	80
174k	CH ₂ CHMeEt	H	10j	48	80
174l	CH ₂ CHMe- <i>n</i> -Pr	H	10k	52	80
174m	CH ₂ Ph	H	10l	46	80
174n	CH ₂ CH ₂ Ph	H	10m	25	80
174o	CH ₂ OCH ₂ OMe	H	10o	57	211
174p	CH ₂ OSiMe ₂ (<i>t</i> -Bu)	H	10p	55	211
174q	(CH ₂) ₂ OCH ₂ OMe	H	10s	30	212
174r	Et	Et	11a	30	80
174s	-(CH ₂) ₃ -		11b	35	80

^a References 3, 20, 41, 79, 98, 180, 184, 185, 239. ^b Lithium metal has been used.

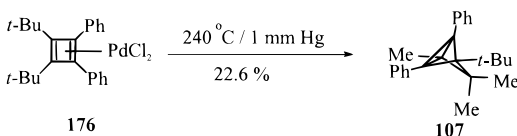
Several bases have been tried, but no bicyclo[1.1.1]-pentane products were obtained.

Scheme 21

5. Thermal Rearrangements

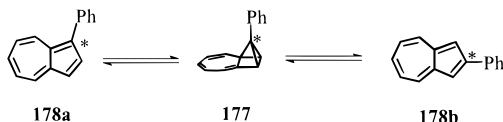
Thermal rearrangements leading to the bicyclo[1.1.1]pentane framework are represented by only one secure example. The heating of the cyclobutadiene palladium complex **176** at 240 °C gave a moderate yield of the tricyclo[2.1.0.0^{2,5}]pentane **107** (Scheme 22).²¹⁵

Scheme 22



The tricyclo[2.1.0.0^{2,5}]pentane **177** has been proposed as an intermediate in the thermal equilibration of the ¹³C labeled azulenes **178** (Scheme 23).²¹⁶

Scheme 23



B. Ring Expansions

Ring expansion of bicyclo[1.1.0]butanes **143** by addition of carbene leads to bicyclo[1.1.1]pentanes **1** and **179** functionalized at both bridgehead and bridge positions (Scheme 24 and Table 25). The reaction was

Scheme 24

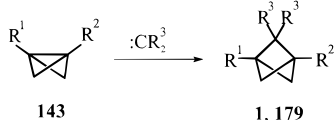


Table 25. Preparation of Bicyclo[1.1.1]pentanes from Bicyclo[1.1.0]butanes by Carbene Addition (Scheme 24)

substrate	R ¹	R ²	R ³	product	yield (%)	ref
143a	H	H	H	1	1	172
143b	Ph	CO ₂ Me	Cl	179a	46, 22	217, 218
143c	Ph	CN	Cl	179b	16	217, 218
143d	Me	CO ₂ Me	Cl	179c	20, 23	91, 217, 218
143e	CN	CN	Cl	179d	0	217
143f	CO ₂ Me	CO ₂ Me	Cl	179e	0	217
143g	H	CO ₂ Me	H	26a	0	172
143g	H	CO ₂ Me	Cl	179f	0	172
143h	Me	Me	Cl	179g	0–14	220

elaborated^{217,218} following the original observation¹⁷² of a successful addition of dihalocarbenes to bicyclo[1.1.0]butanes.²¹⁹ The structures of the products of the initially reported²¹⁹ addition of dichlorocarbene and dibromocarbene to methyl 3-methylbicyclo[1.1.0]butane-1-carboxylate (**143d**) have been later found to be misassigned.²¹⁸

The yield of the desired product depends strongly on the choice of substituents on both the bicyclo[1.1.0]butane **143** and the carbene.²²⁰ Generally, electron-withdrawing substituents promote the formation of the bicyclo[1.1.1]pentane **179**. However, derivatives of 1,4-pentadiene are always formed as by-products.^{50,172,217–220,221–226} The yield of the reaction also depends on the carbene generation method.²²⁰

A mechanism of the intermolecular carbene addition to bicyclo[1.1.0]butanes has drawn theoretical attention,^{223–226} and the addition of difluorocarbene, dichlorocarbene, and bis(carbomethoxy)carbene to bicyclo[1.1.0]butane and its 1,2,2-trimethyl derivative has also been studied experimentally.^{224–226} A top approach of the singlet carbene and its interaction

with HOMO of the bicyclo[1.1.0]butane, which is mainly localized at the C(1)–C(3) bond, has been calculated to lead to the formation of the bicyclo[1.1.1]pentane framework. In contrast, side attack is calculated to yield only 1,4-pentadiene derivatives. The experiments showed that the reactions of these three carbenes yielded only derivatives of 1,4-pentadiene, except that one of the minor products in the reaction with biscarbomethoxycarbene was tentatively assigned as a derivative of bicyclo[1.1.1]pentane.^{224,225} It was suggested that addition of carbenes to bicyclo[1.1.0]butanes would be an important route to derivatives of bicyclo[1.1.1]pentane and remains unexplored.²²⁷

C. Ring Contractions

The first ring contraction reaction to yield the bicyclo[1.1.1]pentane skeleton has been the Demjanov rearrangement of 1-amino-2-bicyclo[2.1.1]hexanol (**180a**), which produced some bicyclo[1.1.1]pentane-1-carboxaldehyde (**27**, Scheme 25 and Table 26).^{228–230}

Scheme 25

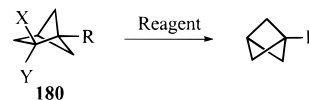


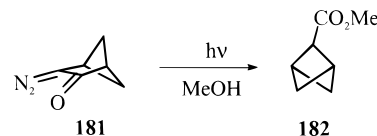
Table 26. Preparation of Bicyclo[1.1.1]pentanes from Bicyclo[2.1.1]hexanes (Scheme 25)

substrate	X	Y	R	reagent	R ¹	product	ref
180a	H	OH	NH ₂	HNO ₂	CHO	27	228
180b	=O	H	H	hν/Hg	H	1	231
180c	=O	F	H	hν	F	17a	232
180d	=O	Me	H	hν/Hg	Me	24	233
180e	=O	Cl	H	hν/Hg	Cl	17b	228
180e	=O	Cl	H	base	no rxn	17b	234

Photochemical extrusion of carbon monoxide from bicyclo[2.1.1]hexan-2-ones **180b–e** gave the parent bicyclo[1.1.1]pentane and its derivatives **17a**, **24**, and **17b** in about 10% yields.^{231–233}

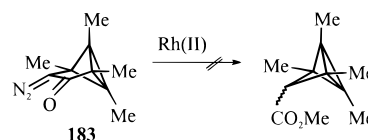
Wolff ring contraction of the diazoketone **181** produced small amounts of the expected ester **182** (Scheme 26).²³⁴ In contrast, **183** gave rearranged

Scheme 26



products unrelated to bicyclo[1.1.1]pentane (Scheme 27).²³⁵ Other attempts at ring contraction in the bicyclo[2.1.1]hexane skeleton, including a Favorskii reaction, failed, and only ring-opened products were isolated.²³⁴

Scheme 27



D. Summary

Out of over a dozen reported methods that lead to the formation of the bicyclo[1.1.1]pentane skeleton,

only three are general and practical: intramolecular carbene addition, anionic cyclization, and photocyclization of ketones. All three methods involve high-energy intermediates (carbenes, reactive carbanions, excited carbonyl compounds) and relatively low activation entropy, due to precursor geometry (bicyclo[1.1.0]butane, alkylidenecyclobutane). These appear necessary to build the highly strained bicyclo[1.1.1]pentane framework. The approach through [1.1.1]propellanes is particularly valuable, since the central bond in **2** and its derivatives reacts easily with a variety of radical and nucleophilic reagents, giving the broadest access to bridgehead-functionalized bicyclo[1.1.1]pentanes and their oligomers, [*n*]stafanes.

IV. Reactions

A. Introduction

Reactions of [1.1.1]propellanes, bicyclo[1.1.1]pentanes, [*n*]staffanes, and tricyclo[2.1.0.0^{2,5}]pentanes can be classified in several ways. For the purpose of this review we divide them into those involving a reactive center on the bicyclo[1.1.1]pentane cage (bridge or bridgehead carbon) and those involving a reactive center in a substituent. The rationale for such a classification is that the intermediates with a reactive center on the cage are the most affected by the properties of the bicyclo[1.1.1]pentane framework and often show unusual reactivity. The influence of the cage diminishes, and the chemistry changes as the reactive center is moved further away. Reactive intermediates can be further subdivided into anionic, radical, and cationic. Intermediates with cage-borne reactive centers are divided into those with the center on the bridge and those with the center on a bridgehead. This classification offers certain advantages, but requires an assignment of a mechanism before a reaction can be placed into one or another category. In some cases the assignment is not obvious, and for some reactions multiple mechanisms have been suggested.

Another possible classification is based on product structures (for instance, reactions preserving or opening the cage, or reactions producing a certain functionality). This classification is more practical for a strict compilation of synthetic methods and has been used to a larger extent in a prior review.¹⁵

B. Transformations Involving a Cage-Borne Reactive Center

Three major types of bicyclo[1.1.1]pentane species with a cage-borne reactive center can be distinguished: bicyclo[1.1.1]pentyl anions, radicals, and cations. Since all C–H bonds in bicyclo[1.1.1]pentane (**1**), [1.1.1]propellane (**2**), and tricyclo[2.1.0.0^{2,5}]pentane (**3**) generally have an enhanced acidity, the skeleton will promote the formation of carbanions. Perhaps surprisingly, it can also stabilize carbocations (see section II.B.3).

As a rule, bicyclo[1.1.1]pentyl anion and radical species are stable toward cage rearrangements and provide access to other compounds with bicyclo[1.1.1]-

pentane framework. Bicyclo[1.1.1]pentyl cations almost invariably lead to rearranged products in which the original bicyclic cage is lost. In the section on bicyclo[1.1.1]pentyl cations, we discuss all reactions involving an electrophilic attack on the bicyclo[1.1.1]pentane cage regardless of whether a bicyclo[1.1.1]pentyl cation is an intermediate.

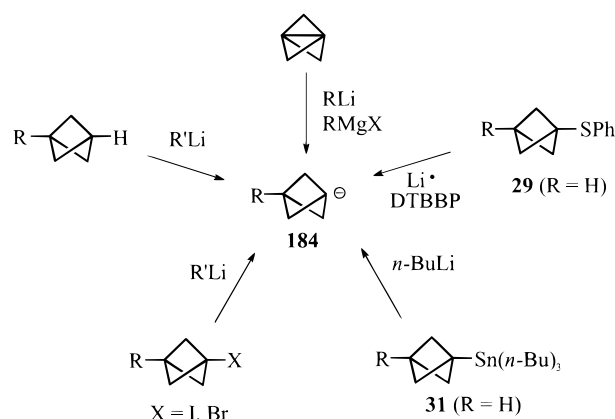
Addition of carbenes and electron-deficient olefins and acetylenes to [1.1.1]propellanes yields bicyclo[1.1.1]pentane biradicals with one cage-borne center. Unlike other bicyclo[1.1.1]pentyl radical intermediates, biradicals rearrange readily and are discussed separately. Transition-metal-catalyzed coupling and photochemical and thermal rearrangements of compounds related to bicyclo[1.1.1]pentane can proceed via intermediates of different polarity. They are discussed in three separate sections.

Chemical transformations of bicyclo[1.1.1]pentane derivatives usually occur with an initial scission of the bond to the skeletal carbon. Reactions of [1.1.1]propellanes and tricyclo[2.1.0.0^{2,5}]pentanes are different. These compounds contain an additional strained σ bond [C(1)–C(3) or C(1)–C(5), respectively] and undergo addition and elimination processes characteristic of olefinic double bonds.

1. Reactions Involving Bicyclo[1.1.1]pentyl Anions

a. Nucleophilic Attack (see section II.B.3.a for discussion of acidity of bicyclo[1.1.1]pentanes). The major methods for generation of bicyclo[1.1.1]pent-1-yl anions (**184**) are as follows: (i) metal–halogen exchange starting with 1-halobicyclo[1.1.1]pentanes; (ii) abstraction of a proton from the bridgehead position; (iii) addition of anionic species to [1.1.1]propellane (**2**); (iv) reduction of 1-alkylthiobicyclo[1.1.1]pentanes or [1.1.1]propellanes; (v) transmetalation of 1-tributylstannylbicyclo[1.1.1]pentanes (Scheme 28).¹⁵

Scheme 28

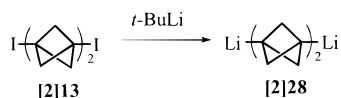


(i) *Li–Halogen and Li–H Exchange.* These reactions may compete for the substrate if both a halogen and a proton are available for the exchange. The parent **1** does not react with *t*-BuLi, but 1-iodo- and 1-bromobicyclo[1.1.1]pentanes (**17h** and **17i**, respectively) are relatively acidic. Metal–halogen exchange with *t*-BuLi in diethyl ether/pentane solution at -78 °C is faster in **17h**, and proton abstraction proceeds faster in **17i**.²³⁶ In solution of weakly basic and/or

polar solvents such as pyridine and acetonitrile or in the presence of KOH, abstraction of the bridgehead proton from 1-iodobicyclo[1.1.1]pentane competes successfully with solvolysis, which is very fast.¹¹³ 1-Chlorobicyclo[1.1.1]pentane (**17b**) does not react with *t*-BuLi. Thus, the increased acidity of **17h** and **17i** cannot be explained by an electrostatic effect of a bridgehead substituent alone. It is plausible that proton abstraction from **17h** and **17i** is promoted by a concerted departure of iodide or bromide anion and formation of [1.1.1]propellane (**2**). Chloride anion is not eliminated upon proton abstraction from **17b**, and it appears that the anchimeric assistance for proton abstraction is reduced or missing altogether.

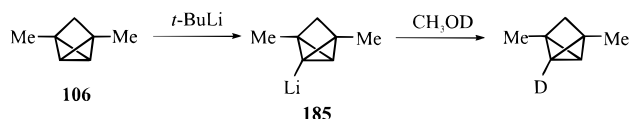
3,3'-Dilithio[2]staffane (**[2]28**) is formed upon treatment of 3,3'-diiodo[2]staffane (**[2]13**) with *t*-BuLi in THF at $-65\text{ }^{\circ}\text{C}$ (Scheme 29).¹⁴⁵ 2,4-Dimethyltricyclo-

Scheme 29



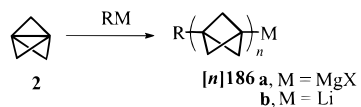
[2.1.0.0^{2,5}]pentane (**106**) is successfully lithiated with MeLi in ether solutions,⁹⁰ while **1** cannot be lithiated even with *t*-BuLi.²³⁶ The lithiated derivative **185** is trapped with CH₃OD (Scheme 30).⁹⁰

Scheme 30



(ii) *Addition of Anionic Species to [1.1.1]Propellanes.* Aliphatic²³ and some aromatic^{94,145} Grignard reagents add to [1.1.1]propellanes to give the bicyclo[1.1.1]pent-1-ylmagnesium reagents **186a** (Scheme 31). In contrast, organolithium reagents often yield

Scheme 31



mostly oligomerization products, the $[n]$ staffyllithium reagents **[n]186b** (Scheme 31),^{3,185,210,237–239} where the degree of oligomerization strongly depends on the RLi/propellane ratio.^{238,240} The course of the anion-induced oligomerization reaction is sensitive to reaction conditions and may also occur via a single-electron transfer radical-mediated process.^{49,240}

The organomagnesium addition reactions are rather slow and are performed in refluxing ether solution,^{23,145} while organolithiums react with [1.1.1]propellanes fast in hydrocarbon solutions at temperatures above $-30\text{ }^{\circ}\text{C}$. The rate of addition depends on the nature of the alkyllithium.^{3,238} Attempts to add allyl- and vinylmagnesium bromides to [1.1.1]propellane (**2**) have not been successful.²⁴¹

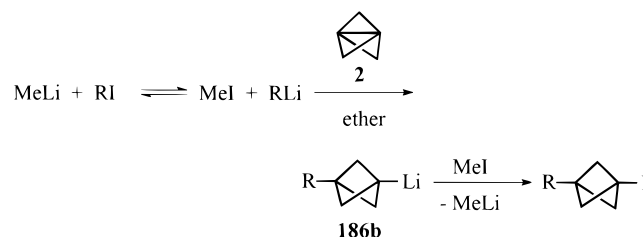
Methylithium was reported to catalyze the addition of alkyl iodides to **2** in diethyl ether (Scheme 32 and Table 27).²⁴¹ Presumably, a fast lithium–iodine

Table 27. Addition of Alkyl Iodides to [1.1.1]Propellane under Catalysis with MeLi (Scheme 32, Adapted from Ref 241)

R	yield (%)
Me	83
<i>n</i> -Pr	94
<i>n</i> -Bu	97
<i>n</i> -C ₇ H ₁₅	86
<i>n</i> -C ₈ H ₁₇	98
THP-O(CH ₂) ₃ ^a	98
THP-O(CH ₂) ₄ ^a	96
THP-O(CH ₂) ₈ ^a	97
Et-C≡C(CH ₂) ₂	25
CH ₂ =CH	0 ^b
CH ₂ =CHCH ₂	0 ^c
<i>c</i> -Hex	84
4- <i>cis</i> -Ph- <i>c</i> -Hex	95 ^d
4- <i>cis</i> -(4'-FC ₆ H ₄)- <i>c</i> -Hex	92 ^d
4- <i>cis</i> -(4'- <i>n</i> -PrC ₆ H ₄)- <i>c</i> -Hex	91 ^d

^a THP = tetrahydropyranyl. ^b 1-Methyl-3-iodobicyclo[1.1.1]pentane was obtained in 55% yield. ^c 1-Methyl-3-iodobicyclo[1.1.1]pentane was obtained in 60% yield. ^d A 2:1 mixture of *cis*- and *trans*-isomers was obtained.

Scheme 32

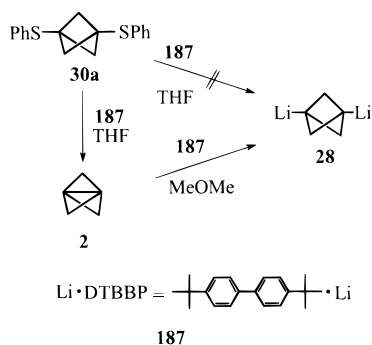


exchange between methylithium and an alkyl iodide takes place and yields the corresponding alkyllithium and methyl iodide. The alkyllithium adds to **2** faster than methylithium, and the resulting 1-lithiobicyclo[1.1.1]pentane derivative **186b** undergoes lithium–iodine exchange with methyl iodide or with excess alkyl iodide to produce the final product. The fact that vinyl iodide and allyl iodide do not add to **2** under methylithium catalysis²⁴¹ provides indirect evidence in favor of this mechanism since vinylithium and allyllithium should be less nucleophilic than alkyllithiums and, thus, less reactive in the addition to **2**. Addition of *t*-BuLi to [1.1.1]propellane (**2**) and subsequent trapping of the formed organolithium compound with CO₂,^{239,242} Me₃SiCl,²⁴² or CH₃OD¹⁷³ yielded monomeric products only.

(iii) *Reduction.* 1-Phenylthiobicyclo[1.1.1]pentane (**29**) represents another source of bicyclo[1.1.1]pent-1-yl anionic reagents. It is cleaved with lithium 4,4'-di-*tert*-butylbiphenyl (**187**) to give the bridgehead organolithium reagent **186b** and bicyclo[1.1.1]pent-1-ylthiolate in 2:1 ratio.^{180,243} 1,3-Bisphenylthiobicyclo[1.1.1]pentane (**30a**) treated with **187** in THF formed [1.1.1]propellane (Scheme 33) rather than 1,3-dilithiobicyclo[1.1.1]pentane (**28**).²⁴³ Formation of poorly soluble **28** in good yield has been reported, however, in the reaction of **2** with **187** in dimethyl ether.²⁴⁴ Under other conditions (lithium biphenyl, THF), the reaction gave much worse results.

(iv) *Transmetalation.* 1-(Tri-*n*-butylstannyl)bicyclo[1.1.1]pentane (**31**, Scheme 28) yields bicyclo[1.1.1]pent-1-yl anion upon treatment with *n*-BuLi in

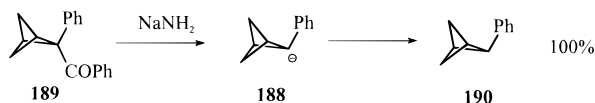
Scheme 33



THF.¹⁸² 1-(Tricyclohexylstannyl)- and 1-(triphenylstannyl)bicyclo[1.1.1]pentanes are completely inert toward *n*-BuLi under similar conditions, apparently due to steric congestion about the tin atom.¹⁸²

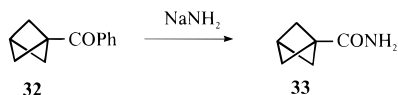
(v) *Bicyclo[1.1.1]pent-2-yl Anions*. The proton affinity of bicyclo[1.1.1]pent-1-yl anion (**117**) is higher than that of bicyclo[1.1.1]pent-2-yl anion (**118**, see section II.B.3.a). However, appropriate substitution may stabilize the bicyclo[1.1.1]pent-2-yl anion. 2-Phenylbicyclo[1.1.1]pent-2-yl anion (**188**) has been suggested as an intermediate in the debenzoylation of the phenyl ketone **189** with sodium amide (Scheme 34).²⁴⁵ The quantitative yield of 2-phenylbicyclo[1.1.1]-

Scheme 34



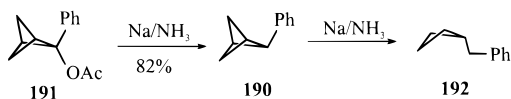
pentane (**190**) suggests that the transient anion **188** is considerably stabilized, since ordinarily the principal cleavage products from Haller–Bauer reactions of alkyl aryl ketones are alkylcarboxamides. Such stabilization is probably caused by the geminal phenyl group. In contrast to **189**, 1-benzoylbicyclo[1.1.1]pentane (**32**) treated with sodium amide produced only bicyclo[1.1.1]pentane-1-carboxamide (**33**, Scheme 35).²⁰

Scheme 35



Birch reduction of bridge-substituted bicyclo[1.1.1]pentanes may involve bridge-borne anions. The reduction may be carried out without ring opening in the case of 2-acetoxy-2-phenylbicyclo[1.1.1]pentane (**191**, Scheme 36).⁷⁸ One of the benzylic bonds in the

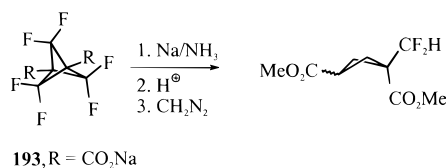
Scheme 36



resulting hydrocarbon **190** may be reduced to benzylcyclobutane (**192**) with excess sodium.⁷⁸ A ring opening is also observed in Birch reduction of 2,2,4,4,5,5-hexafluorobicyclo[1.1.1]pentane-1,3-dicarboxylate (**193**)⁴⁸ and is followed by defluorination of

the cyclobutane ring (Scheme 37).⁴⁸

Scheme 37



b. Reactions of Bicyclo[1.1.1]pentyl Carbanions.

(i) *Bicyclo[1.1.1]pent-1-yl Anions with a Leaving Group in Position 3*. Nucleophilic attack on 1,3-disubstituted bicyclo[1.1.1]pentanes or deprotonation of 1-iodobicyclo[1.1.1]pentane (**17h**) and 1-bromobicyclo[1.1.1]pentane (**17i**, see section IV.B.1.a) yields [1.1.1]propellane (**2**) and its derivatives (Scheme 38 and Table 28).^{2,24,94,95,236} The transient bicyclo[1.1.1]-

Scheme 38

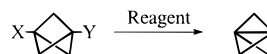


Table 28. Formation of [1.1.1]Propellanes from Bicyclo[1.1.1]pentanes upon Nucleophilic Attack (Scheme 38)

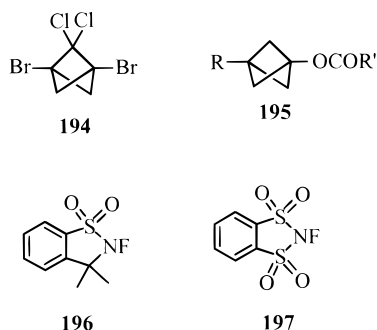
substrate	X	Y	reagent	product	yield (%)	ref
13	I	I	NaCN	2	88	24, 25
			MeO ⁻		<i>a</i>	94
			EtO ⁻		<i>a</i>	94
			<i>t</i> -BuLi		<i>b</i>	239
			PhMgBr		58	250
			R ₃ P		<i>b</i>	250
17i	H	Br	<i>t</i> -BuLi	2	40 ^a	242
			<i>t</i> -BuLi		2	46
18b	Br	Br	<i>t</i> -BuLi	2	46	2, 58, 239
			<i>t</i> -BuLi		2	<i>b</i>
30a	PhS	PhS	Li, DTBBP	2	<i>b</i>	243
194	Br ^d	Br ^d	MeLi	11c	18 ^a	246
140b	Br ^e	Br ^e	Cs ^f	12	<i>b</i>	247
65a	MeO	I	<i>t</i> -BuLi	2	<i>a</i>	239
66d	C ₅ H ₅ N ^{+c}	I	PhLi	2	<i>b</i>	250

^a A subsequent addition product has been isolated. ^b Formation of **2** has been observed. ^c The same reaction has been reported for other ammonium salts. ^d 2,2-Dichloro-1,3-dibromobicyclo[1.1.1]pentane (Chart 9). ^e 2,2,4,4,5,5-Hexafluoro-1,3-dibromobicyclo[1.1.1]pentane. ^f Gas phase.

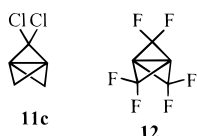
pent-1-yl anions with bromine, iodine, or another leaving group in position 3 cannot be trapped, and as noted above, a concerted 1,3-elimination appears to be taking place. A reaction of cyanides with 1,3-diiodobicyclo[1.1.1]pentane (**13**) in DMSO solution is of particular practical importance since it produces **2**, which can be isolated neat and pure in 88% yield by a trap-to-trap distillation.²⁴

Treatment of 1,3-dibromo-2,2-dichlorobicyclo[1.1.1]pentane (**194**, Chart 9) in solution with MeLi yields 2,2-dichloro[1.1.1]propellane (**11c**),²⁴⁶ and a reaction of 1,3-dibromo-2,2,4,4,5,5-hexafluorobicyclo[1.1.1]pentane (**140b**) with Cs in the gas phase provides 2,2,4,4,5,5-hexafluoro[1.1.1]propellane (**12**), judging

Chart 9



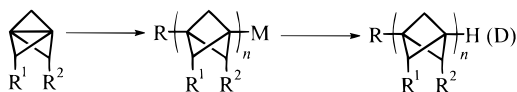
by the IR spectrum after trapping in an argon matrix.²⁴⁷



3-Aryl-, 3-methyl-, and 3-trifluoromethylbicyclo[1.1.1]pent-1-yl anions are quite stable and can be transformed into bicyclo[1.1.1]pentane derivatives by reaction with electrophiles.^{15,91,145,239,248–250}

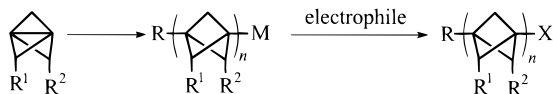
(ii) *Intermolecular Electrophilic Attack.* The reaction of carbanions with a proton represents the simplest case. Quenching of the carbanions with a proton source (water, alcohol) serves as a means to determine the yield of carbanion formation, and quenching with a deuterium source serves for deuterium labeling (Scheme 39 and Table 29).

Scheme 39



The bridgehead anions react with a typical range of electrophiles such as carbon dioxide, carbonyl compounds (aldehydes, esters, acid chlorides), and nitriles.^{20,23,145,180,243,244,248} Ketones are best obtained by reaction with nitriles^{180,243} since the reaction with esters and acid chlorides also gives tertiary alcohols, and this is not prevented even in the case of reaction with the bulky pivaloyl chloride^{180,243} (Scheme 40 and Table 30).

Scheme 40



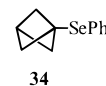
The anions may be silylated and stannylated with corresponding silyl or stannyl chlorides.^{180,182,239} Diphenyl disulfide and diphenyldiselenide convert the bicyclo[1.1.1]pent-1-yllithium compounds into the corresponding 1-phenylthio- (**29**) and 1-phenylselenobicyclo[1.1.1]pentanes (**34**).^{182,236} Treatment of the anion with lithium methoxylamide leads to the bridgehead primary amine **15**.¹⁸² Silylation, carboxylation with CO₂, acylation with butanedione, and hydrolysis with D₂O convert 1,3-dilithiobicyclo[1.1.1]-

Table 29. Formation and Hydrolysis of Bridgehead Lithio- and Magnesiobicyclo[1.1.1]pentanes (Scheme 39)

R ¹ , R ²	R	M	isotopic purity	yield (%)	ref
H,H	Li	Li	80	75	244
H,H	H	Li	>95	27	180
H,H	<i>t</i> -Bu	Li	<i>a</i>	78	242
H,H	<i>t</i> -Bu	Li	<i>a</i>	42	173
H,H	(CH ₂) ₈ OTHP	Li	<i>a</i>	93	241
H,H	cubyl	Li	<i>a</i>	<i>a</i>	44
H,H	1,4-cubanediyli	Li	<i>a</i>	<i>a</i>	44
H,H	C ₈ H ₁₃ -1-yl ^b	Li	<i>a</i>	<i>a</i>	44
H,H	C ₈ H ₁₂ -1,4-diyl ^c	Li	<i>a</i>	<i>a</i>	44
H,(CH ₂) ₄ Me	<i>t</i> -Bu	Li ^d	<i>a</i>	<i>a</i>	210
H,H	Ph	MgBr	<i>a</i>	80	241
H,H	4-(<i>n</i> -Pr)C ₆ H ₄	MgBr	<i>a</i>	70	241
H,H	4-(<i>n</i> -Bu)C ₆ H ₄	MgBr	<i>a</i>	65	241
H,H	4-FC ₆ H ₄	MgBr	<i>a</i>	60	241
H,H	4-(4'-EtC ₆ H ₄)C ₆ H ₄	MgBr	<i>a</i>	13	241
(CH ₂) ₃	Et	MgBr	<i>a</i>	21	23
(CH ₂) ₃	<i>i</i> -Pr	MgBr	<i>a</i>	46	23
(CH ₂) ₃	<i>t</i> -Bu	MgBr	<i>a</i>	67	23
(CH ₂) ₃	<i>t</i> -Bu	Li ^c	>96	43–96	237, 238
(CH ₂) ₃	CH ₂ Ph	MgBr	<i>a</i>	68	23
(CH ₂) ₃	CH ₂ CH=CH ₂	MgBr	<i>a</i>	67	23
(CH ₂) ₃	Ph	Li ^c	>96	34	237, 238
(CH ₂) ₃	Ph	MgBr	<i>a</i>	67	23

^a Not reported. ^b Bicyclo[2.2.2]octan-1-yl. ^c Bicyclo[2.2.2]octane-1,4-diyl. ^d Oligomers formed.

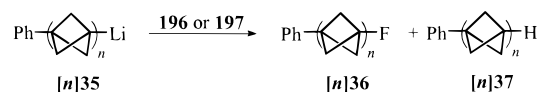
pentane (**28**) into the expected symmetrically substituted bicyclo[1.1.1]pentane derivatives.²⁴⁴



The bridgehead anions also react with peroxides^{23,180,243} and oxygen.^{180,243} The oxyanions formed in the latter reaction have been trapped with acyl chlorides and isolated as esters **195** (Chart 9).

A reaction of 3-phenyl-3'-lithio[*n*]staffanes (**[n]35**) and 3,3'-dilithio[2]staffane (**[2]28**) with *N*-fluorosulfonamides **196** and **197** (Chart 9) yields the bridgehead-fluorinated products **[n]36** and **[2]16**, respectively, with retention of the cage and in moderate yields (Schemes 41 and 42).⁹⁸ The major side products

Scheme 41



in these reactions are the reduced 3-phenyl[*n*]staffanes (**[n]37**) and 3-fluoro[2]staffane (**[2]17a**), respectively. The latter products apparently originate from partial hydrolysis of the lithiated species or from one-electron oxidation of the anionic bicyclo[1.1.1]pentane intermediates by F⁺ reagents, competing with the desired nucleophilic attack, and followed by hydrogen abstraction from the reactive bridgehead radical. No 1,3-difluorobicyclo[1.1.1]pentane (**[1]16**)

Scheme 42

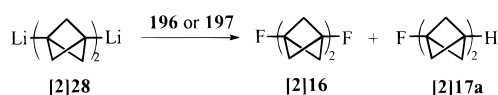


Table 30. Reactions of Bridgehead Organometallics with Electrophiles (Scheme 40)

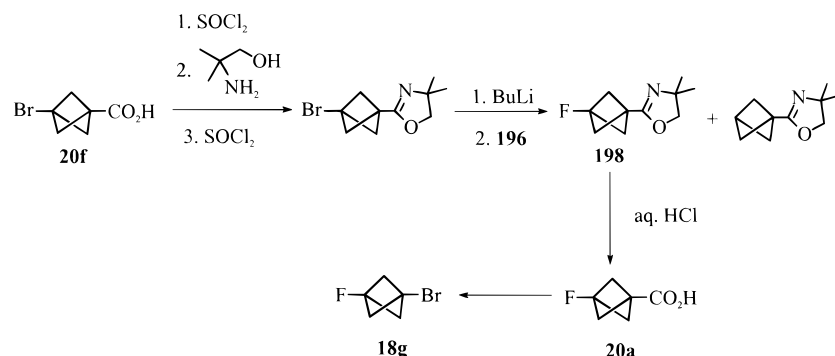
<i>a</i>	R	R ¹ , R ²	M	electrophile	X	yield (%)	ref
a	H	H	Li	CO ₂	CO ₂ H	75	236
b	H	H	Li	CO ₂	CO ₂ H	45	180, 243
a	CH ₃	H	Li	CO ₂	CO ₂ H	90	15
a	¹³ CH ₃	H	Li	CO ₂	CO ₂ H	<i>b</i>	15
a	<i>n</i> -Pr	H	Li	CO ₂	CO ₂ H	97	241
a	<i>n</i> -Bu	H	Li	CO ₂	CO ₂ H	60	241
c	<i>t</i> -Bu	H	Li	CO ₂	CO ₂ H	85, 40	239, 242
a	<i>n</i> -C ₇ H ₁₅	H	Li	CO ₂	CO ₂ H	54	241
a	<i>n</i> -C ₈ H ₁₇	H	Li	CO ₂	CO ₂ H	45	241
a	(CH ₂) ₄ OTHP	H	Li	CO ₂	CO ₂ H	56	241
a	(CH ₂) ₈ OTHP	H	Li	CO ₂	CO ₂ H	53	241
a	4-Ph- <i>c</i> -Hex	H	Li	CO ₂	CO ₂ H	44	241
a	Ph	H	Li	CO ₂	CO ₂ H	52	20
a	Ph	H	Li	CO ₂	CO ₂ H	66	248
d	Ph	H	MgX	CO ₂	CO ₂ H ^c	6 ^c	94
d	4-MeC ₆ H ₄	H	MgX	CO ₂	CO ₂ H ^c	18 ^c	94
d	4-ClC ₆ H ₄	H	MgX	CO ₂	CO ₂ H ^c	18 ^c	94
d	4-MeOC ₆ H ₄	H	MgX	CO ₂	CO ₂ H ^c	7 ^c	94
d	4-MeOC ₆ H ₄	H	Li	CO ₂	CO ₂ H	<i>b</i>	239
e	Li	H	Li	CO ₂	CO ₂ H ^d	36	244
e	Li	(CH ₂) ₃	Li	CO ₂	CO ₂ H ^d	63	244
a	<i>n</i> -Pr	H	Li	Me ₂ CO	Me ₂ C(OH)	52	241
a	<i>n</i> -Bu	H	Li	4-Ph- <i>c</i> -C ₆ H ₉ O	4-Ph- <i>c</i> -C ₆ H ₉ (OH)	70	241
b	H	H	Li	PhCHO	CH(OH)Ph	57	180
b	H	H	Li	<i>t</i> -BuCHO	CH(OH) <i>t</i> -Bu	60	180
e	Li	H	Li	PhCHO	CH(OH)Ph ^d	15	244
d	Et	(CH ₂) ₃	Li	PhCHO	CH(OH)Ph	40	23
b	H	H	Li	PhCOCl	CR ³ (OH)Ph ^e	52	180
a	<i>n</i> -C ₈ H ₁₇	H	Li	C ₂ H ₅ COCl	C ₂ H ₅ C(O)	74	241
a	(CH ₂) ₄ OTHP	H	Li	<i>n</i> -C ₃ H ₇ COCl	<i>n</i> -C ₃ H ₇ C(O)	76	241
a	4-Ph- <i>c</i> -Hex	H	Li	C ₂ H ₅ COCl	C ₂ H ₅ C(O)	74	241
d	<i>i</i> -Pr	(CH ₂) ₃	MgX	MeO ₂ CCl	CO ₂ Me	50	23
e	Li	H	Li	MeCOCl	MeCO ^d	0	244
b	H	H	Li	HCO ₂ Me	CHO	21	180
b	H	H	Li	<i>t</i> -BuCO ₂ Me	CR ³ (OH) <i>t</i> -Bu ^e	35	180
b	H	H	Li	PhCO ₂ Me	CR ³ (OH)Ph ^e	<i>b</i>	180
b	H	H	Li	<i>t</i> -BuCN	<i>t</i> -BuC(O)	60	180
b	H	H	Li	PhCN	PhC(O)	50	180
a	<i>n</i> -Bu	H	Li	<i>n</i> -PrCN	<i>n</i> -PrC(O)	17	241
a	<i>n</i> -Pr	H	Li	4-FC ₆ H ₄ CN	4-FC ₆ H ₄ C(O)	70	241
d	<i>n</i> -Pr	H	MgBr	4-FC ₆ H ₄ CN	4-FC ₆ H ₄ C(O)	31	241
d	<i>n</i> -Pr	H	MgBr	4-ClC ₆ H ₄ CN	4-ClC ₆ H ₄ C(O)	49	241
e	H	H	Li	SiMe ₃ Cl	SiMe ₃	61	180
a	<i>n</i> -Bu	H	Li	SiMe ₃ Cl	SiMe ₃	76	241
b	H	H	Li	SnBu ₃ Cl	SnBu ₃	50	180
c	<i>t</i> -Bu	H	Li	SiCl ₄	SiCl ₃	65	242
a	Ph	H	Li	SiMe ₃ Cl	SiMe ₃	92	239
a	Ph	H	Li	SnMe ₃ Cl	SiMe ₃	8	239
e	Li	H	Li	SiMe ₃ Cl	SiMe ₃ ^d	61	244
f	Li	H	Li	SiMe ₃ Cl	SiMe ₃ ^d	37	244
a	Li ^f	H	Li ^f	SiMe ₃ Cl	SiMe ₃ ^{d,f}	92	249
d	CH ₂ =CHCH ₂	(CH ₂) ₃	MgBr	CH ₂ =CHCH ₂ Br	CH ₂ =CHCH ₂	68	23
d	H	H	Li	<i>t</i> -BuOO(<i>t</i> -Bu)	<i>t</i> -BuO	15	180
b	PhCH ₂	(CH ₂) ₃	MgBr	PhCO ₂ O(<i>t</i> -Bu)	<i>t</i> -BuO	37	23
b	H	H	Li	O ₂ , R ³ COCl ^g	CO ₂ R ^{3 g}	<i>b</i>	180
d	4-FC ₆ H ₄	H	MgBr	CH ₂ =CHCH ₂ Br	CH ₂ =CHCH ₂	35	241
d	<i>n</i> -Bu	H	MgBr	Br ₂	Br	36	241
d	<i>n</i> -Pr	H	MgBr	<i>N</i> -chlorosuccinimide	Cl	24	241
g	H	H	Li	(PhS) ₂	PhS	40	182
a	H	H	Li	(PhSe) ₂	PhSe	76	236
g	H	H	Li	LiNHOMe	NH ₂	24	182

^a Method of generation of the anionic species: (a) Li-halogen exchange, (b) reduction of bicyclo[1.1.1]pent-1-yl sulfide with lithium 4,4'-di-*tert*-butylbiphenyl, (c) Li-proton exchange with subsequent generation of [1.1.1]propellane and addition of *t*-BuLi to the latter, (d) addition of an organometallic reagent to [1.1.1]propellane, (e) reduction of [1.1.1]propellane with lithium 4,4'-di-*tert*-butylbiphenyl, (f) reduction of [1.1.1]propellane with lithium biphenyl, (g) transmetalation of tributyl(bicyclo[1.1.1]pent-1-yl)stannane with alkyllithium. ^b Yield has not been reported. ^c Yield of a subsequent product. ^d In the product, R = X. ^e R³ = Bicyclo[1.1.1]pent-1-yl. ^f [2]Staffane derivatives. ^g R³ = *t*-Bu, Ph.

was produced upon reaction of 1,3-dilithiobicyclo[1.1.1]pentane (**1128**) with various F⁺ reagents.⁹⁸

Substitution of bromine in 1-bromobicyclo[1.1.1]pentane-1-carboxylic acid (**20f**) by fluorine was achieved by protection of the carboxylic acid group, bromine-lithium exchange, and treatment with the fluorinating agent **196** (Scheme 43). The protective

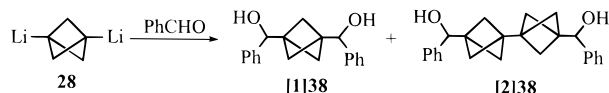
4,4-dimethyl-2-oxazolanyl group allows the resulting 3-fluorobicyclo[1.1.1]pentane derivative **198** to be converted into 3-fluorobicyclo[1.1.1]pentane-1-carboxylic acid (**20a**) and, subsequently, to 1-bromo-3-fluorobicyclo[1.1.1]pentane (**18g**).¹¹² An admixture of the parent bicyclo[1.1.1]pentane-1-carboxylic acid (**14**), formed along with **20a**, can be removed by

Scheme 43

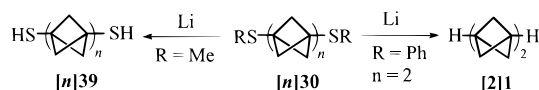
decarboxylation with XeF_2 since the fluorinated acid is much more stable to this reagent (see section IV.B.2.b.iii).⁹⁶

Attempts to produce bridgehead-fluorinated bicyclo[1.1.1]pentanes via reactions of 1,3-diiodobicyclo[1.1.1]pentane (**13**) or [1.1.1]propellane (**2**) with XeF_2 , CoF_3 , NO^+BF_4^- , and $(\text{Me}_2\text{N})_3\text{S}^+\text{Me}_3\text{SiF}_2^-$ have been unsuccessful.⁹⁸

(iii) *Oxidation.* The reaction of the dilithio derivative **28** with benzaldehyde gave the diol **[2]38** in addition to the expected diol **[1]38** (Scheme 44).²⁴⁴ This may be due to an initial one-electron transfer from the dianion to benzaldehyde and subsequent dimerization of the [1.1.1]propellane radical anion.

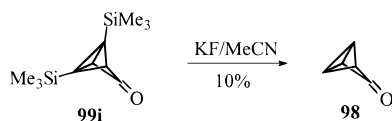
Scheme 44

(iv) *Other Reactions with Transient Bicyclo[1.1.1]pentyl Anions.* Reduction of the bisphenylthio compound **[2]30a** with lithium metal in ethylenediamine produced **[2]staffane ([2]1, Scheme 45).**⁴¹ In contrast,

Scheme 45

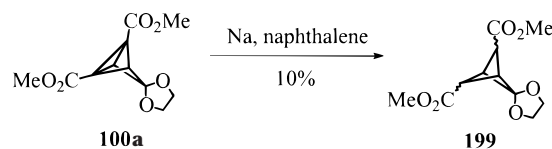
bismethyl analogues **[n]30b** give the bridgehead thiols **[n]39.**⁴¹

Potassium fluoride in acetonitrile cleaved trimethylsilyl groups off the ketone **99i** to yield the parent tricyclo[2.1.0.0^{2,5}]pentan-3-one (**98, Scheme 46).**²⁰³

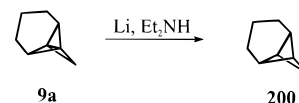
Scheme 46

The tricyclo[2.1.0.0^{2,5}]pentane derivative **100a** is reduced with sodium naphthalene to a mixture of bicyclo[1.1.1]pentanes **199** in moderate yield (Scheme

47).³⁶ Similarly, the central bond in 2,4-trimethylene-

Scheme 47

[1.1.1]propellane (**9a**) is reduced with lithium metal in diethylamine to the corresponding bicyclo[1.1.1]pentane **200** in 63% yield (Scheme 48).²⁰⁷

Scheme 48**2. Reactions Involving Bicyclo[1.1.1]pentyl Radicals**

a. Radical Attack and Photochemical Generation of Radicals (see section II.B.3.b for a discussion of stability and structure of bicyclo[1.1.1]pentyl radicals). The major ways to generate bicyclo[1.1.1]pentyl radicals are as follows: (i) addition of a radical to [1.1.1]propellanes; (ii) abstraction of hydrogen from bicyclo[1.1.1]pentanes with a halogen atom (chlorine or fluorine) or an oxygen-based radical; (iii) abstraction of halogen (usually bromine or iodine) from a halobicyclo[1.1.1]pentane with a silyl or stannyl radical, or by irradiation; (iv) homolytic decarboxylation of acid derivatives, such as Barton esters and carboxyl peroxides; and (v) abstraction of trimethylsilyl group by a halogen atom (Scheme 49). Radical addition to [1.1.1]propellanes yields bicyclo[1.1.1]pent-1-yl radicals, and the last four approaches may give access to both bicyclo[1.1.1]pent-1-yl and bicyclo[1.1.1]pent-2-yl radicals, depending on the precursor. Oxidative decarboxylation of a bridge carboxylic acid derivative has apparently not been attempted.

Compounds **201**–**[n]206**, which are referred to in this section but are not shown in reaction Schemes, are listed in Chart 10.

(i) *Radical Addition to [1.1.1]Propellane.* Radicals add across the central bond of [1.1.1]propellanes easily to form bridgehead radicals, with rate constants about 3 times larger than those for a similar

Scheme 49

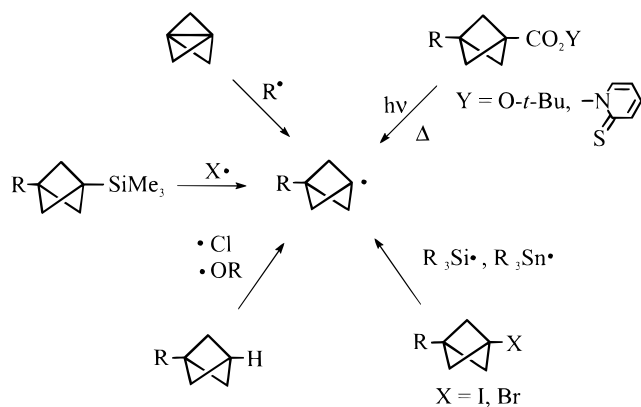
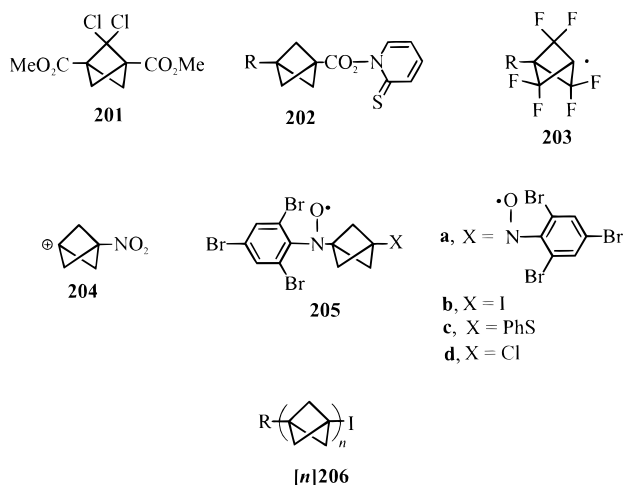


Chart 10



addition to styrene (Table 31),^{149,251–253} as determined by laser flash photolysis (for information on addition of carbenes, see section IV.B.4). Radical addition across the central bond of [1.1.1]propellanes is one of the most useful reactions for the synthesis of bicyclo[1.1.1]pentane and $[n]$ staffane derivatives.¹⁵ Even some of the reactions that nominally involve the addition of nucleophiles (e.g., Grignard reagents) probably proceed by a radical chain mechanism.^{49,240}

(ii) *Abstraction of Hydrogen*. Bicyclo[1.1.1]pentane (**1**) and its derivatives do not easily form radicals by abstraction, since the exocyclic bonds are unusually strong. The abstraction of hydrogen from **1** with *tert*-butoxy radical is much harder than the abstraction from cyclopropane, and it occurs preferentially at the bridgehead position.¹⁵⁷

Selectivity of radical abstraction of a bridge hydrogen versus a bridgehead hydrogen is an issue in using

Table 31. Rate Constants for Radical Attack on [1.1.1]Propellane and Styrene

radical	rate constants ($M^{-1} \times s^{-1}$) at ambient temperature	
	[1.1.1]propellane	styrene
<i>t</i> -BuO•	2.8×10^6	9.1×10^5
PhS•	6.2×10^7	2.2×10^7
Et ₃ Si•	6.0×10^8	2.0×10^8
Cl•{PhH} ^a	3.1×10^9	<i>b</i>
<i>p</i> -MeOC ₆ H ₄ CO ₂ •	1.0×10^7	5.5×10^6

^a Complex. ^b Not measured.

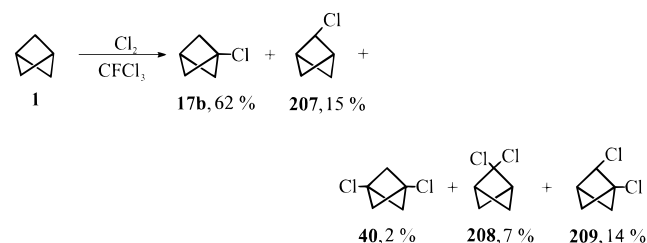
this method of radical generation in preparative procedures. Bicyclo[1.1.1]pent-1-yl and bicyclo[1.1.1]pent-2-yl radicals (**121** and **122**) have almost equal calculated enthalpies of formation (see section II.B.3.b), and in the parent bicyclo[1.1.1]pentane (**1**) the bridge hydrogens enjoy a 3-fold statistical advantage over the bridgehead hydrogens. The existing reports of radical attack on **1**, however, state that the bridgehead hydrogen is more susceptible to abstraction. Only the signal of the bridgehead radical **121** is observed in the ESR spectrum of a mixture of **1** and (*t*-BuO)₂ upon irradiation. Chlorination of the parent hydrocarbon **1** with neat *t*-BuOCl¹⁶⁰ and Cl₂ in CFCl₃⁷⁷ gives mostly 1-chlorobicyclo[1.1.1]pentane (**17b**) along with some 2-chlorobicyclo[1.1.1]pentane (**207**, Schemes 50 and 51) and the doubly chlorinated

Scheme 50



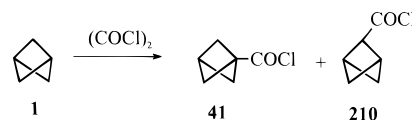
products **40**, **208**, and **209**. The relative reactivity of the bridgehead to bridge hydrogens is 23:1 and 7:1, respectively, for *t*-BuOCl and Cl₂. UV-promoted chlo-

Scheme 51



rocarbonylation of **1** with oxalyl chloride led to a 73% yield of a 85:15 mixture of the bridgehead and bridge acyl chlorides **41** and **210** (Scheme 52).⁷⁷ This corre-

Scheme 52

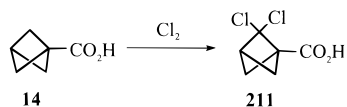


sponds to a ratio of 17:1 of bridgehead vs bridge hydrogen abstractions. At least two factors favor the preferential attack on the bridgehead hydrogen. First, the bridgehead hydrogens are less sterically hindered than the secondary hydrogens on the bridges.⁷⁷ Second, electronegative radicals are expected to form a polarized transition state upon an attack on a hydrogen with a partial positive charge on the adjacent carbon. The bridgehead carbon strongly stabilizes positive charge through inter-bridgehead interactions (see section II.B.3.c),¹¹⁰ while the bridge carbon does not provide such a mechanism for stabilization.

The selectivity of chlorination changes upon substitution of one bridgehead position in bicyclo[1.1.1]pentane (**1**). In chlorination of **1** in CFCl₃, 1,3-dichlorobicyclo[1.1.1]pentane (**40**) and 1,2-dichlorobicyclo[1.1.1]pentane (**209**) are formed in the ratio

1:7, presumably primarily from 1-chlorobicyclo[1.1.1]pentane (**17b**, Scheme 51). Chlorination of the monoacid **14** yielded only the bridge-substituted acid **211** (Scheme 53).²⁵⁴ These effects of the bridgehead sub-

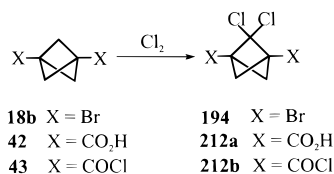
Scheme 53



stituent on the relative ease of hydrogen abstraction in the bridge and the bridgehead positions require further examination. Electron-withdrawing substituents in position 3 appear to stabilize the bridgehead radical (see section II.B.3.b), and might have been expected to favor hydrogen abstraction in position 1, but they also destabilize positive charge on the bridgehead carbon 1, which may be present in the transition state for an attack of an electronegative radical on the bridgehead hydrogen (see section II.B.3.c).

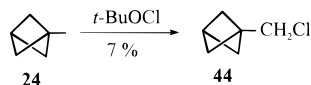
1,3-Disubstituted bicyclo[1.1.1]pentanes **18b**, **42**, and **43** are easily photochlorinated with elemental chlorine to give good yields of 2,2-dichloro derivatives (**194**, **212a,b**, Scheme 54).²⁵⁴ Attempts to isolate a

Scheme 54



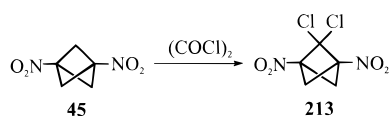
good yield of monochlorinated products have failed, apparently due to the radical-stabilizing effect of the first chlorine atom. Introduction of more than two chlorine atoms at bridge positions has not been achieved, and under forcing conditions the cage is destroyed. Chlorination of 1-methylbicyclo[1.1.1]pentane (**24**) with *tert*-butyl hypochlorite yielded 7% of 1-(chloromethyl)bicyclo[1.1.1]pentane (**44**, Scheme 55).¹⁶⁰ No other products have been reported.

Scheme 55



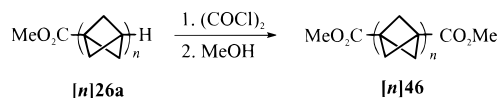
Chlorocarbonylation of 1,3-dinitrobicyclo[1.1.1]pentane (**45**) unexpectedly gave 2,2-dichloro-1,3-dinitrobicyclo[1.1.1]pentane (**213**) as the main product (Scheme 56).⁷⁸

Scheme 56



The chlorocarbonylation reaction has been applied in the first synthesis of dimethyl [*n*]staffane-3,3^(*n*-1)-dicarboxylates¹⁶³ (**[*n*]46**). Reaction of the monoesters **[*n*]26a** with oxalyl chloride yields about 10% of the desired products (Scheme 57).²⁰ The reaction pro-

Scheme 57

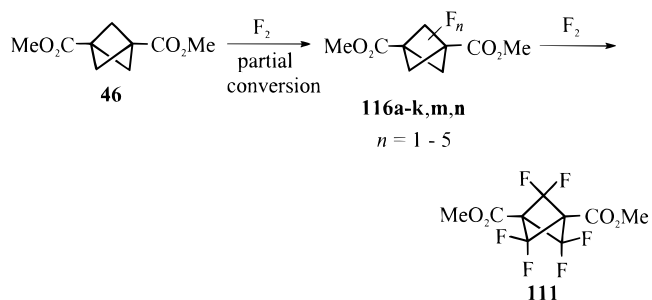


duces more of the bridgehead than the bridge derivative, but with increasing number *n* in **[*n*]26a** the ratio of bridgehead to bridge positions becomes too unfavorable and a complex mixture of products is formed. The reaction becomes impractical for *n* > 2, and better access to **[*n*]46** is available now²⁰ (see section IV.B.2.b.iii).

Attempts at radical bromination of a variety of bicyclo[1.1.1]pentanes with various reagents invariably failed.¹⁴⁵

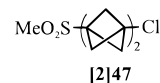
Fluorination of dimethyl bicyclo[1.1.1]pentane-1,3-dicarboxylate (**46**) with diluted fluorine gas with He or N₂ starts at room temperature (Scheme 58).⁹⁸

Scheme 58



Discontinuing fluorination at different degrees of conversion provides all but one (**116l**) of the possible isomers of partially fluorinated bicyclo[1.1.1]pentane derivatives **116**.⁹⁸ Deep fluorination provides access to 2,2,4,4,5,5-hexafluorobicyclo[1.1.1]pentane-1,3-dicarboxylic ester **111**.⁴⁸

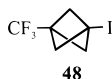
(iii) *Abstraction of a Halogen Atom.* Homolytic cleavage of the bridgehead carbon-halogen bond is also difficult. The bridgehead chloride **[2]47** is resistant to reduction with Bu₃SnH even in boiling xylene, bromides undergo slow reduction in boiling benzene, and only the bridgehead iodides are synthetically useful sources of bridgehead radicals in tin hydride



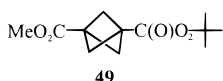
reactions.⁶ The low homolytic reactivity of the bridgehead bicyclo[1.1.1]pentyl chlorides may be anticipated from experimental data for other bicyclic chlorides. In the series of the tertiary chlorides, 1-methylcyclohexyl, adamantyl, bicyclo[2.2.2]octyl, and bicyclo[2.2.1]heptyl, the relative rates of the chlorine abstraction are 1.0, 0.24, 0.12, and 0.010, respectively.²⁵⁵ Thus the reactivity of the chlorides decreases significantly with increase in the *s* character of the exocyclic carbon hybrids. In contrast to the case of hydrogen abstraction just discussed above, in halogen abstraction by an electropositive Si radical, the ability of the bridgehead carbon in bicyclo[1.1.1]pentane to accommodate positive charge is presumably not particularly helpful.

The bridge C–Cl bond displays relatively low reactivity as well. Thus the reaction of dimethyl 2,2-dichlorobicyclo[1.1.1]pentane-1,3-dicarboxylate (**201**, Chart 10) with 1 equiv of *n*-Bu₃SnH selectively removes one chlorine atom,²⁵⁴ but full reduction of this and other 2,2-dichlorobicyclo[1.1.1]pentanes is slow.²¹⁸ The selectivity is attributed to stabilization of the 2-chlorobicyclo[1.1.1]pent-2-yl radical by the geminal chlorine substituent.

Only the bridgehead iodides can be converted into radicals with *n*-Bu₃SnH or under UV light irradiation easily. Bridgehead iodo[*n*]staffane can be used as a source of radicals for conversion into other functionalized derivatives.^{6,20} However, 1-trifluoromethyl-3-iodobicyclo[1.1.1]pentane (**48**) does not react with *n*-Bu₃SnH at 70 °C for 24 h.²⁵⁰

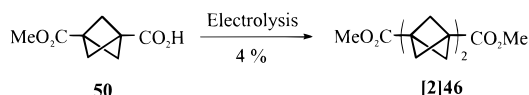


(iv) *Homolytic Decarboxylation.* Bridgehead carboxylic acids and their derivatives decarboxylate much more slowly than ordinary alkanolic acids. The *tert*-butyl perester **49** decomposes very slowly in boiling benzene and appreciably only at temperatures above 100 °C.⁶ The rather slow decarboxylation of the



Barton ester **202** (Chart 10) in boiling benzene is significantly accelerated by a tungsten lamp.^{6,239,248,256,257} Also, Kolbe oxidative dimerization of the acid **50** gave mostly ring-opened products and only 4% of the desired product **[2]46** (Scheme 59).⁶

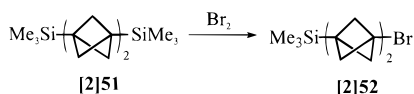
Scheme 59



The bridgehead radicals have been generated from bridgehead carboxylic acids by silver-catalyzed ammonium persulfate oxidations⁶ and, with much better results, under Hunsdiecker reaction condition.^{58,218}

(v) *Abstraction of a Trimethylsilyl Group with a Halogen Atom.* Bromination of 3,3'-bis(trimethylsilyl)-[2]staffane (**[2]51**) to yield 3-bromo-3'-(trimethylsilyl)-[2]staffane (**[2]52**, Scheme 60) has been reported recently,²⁴⁹ but other examples of this reaction are not known.

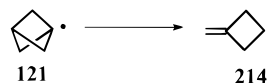
Scheme 60



b. Reactions of Radicals. (i) *Ring-Opening (β -Scission).* In principle, the bicyclo[1.1.1]pent-1-yl and bicyclo[1.1.1]pent-2-yl radicals (**121** and **122**, respectively) can rearrange to ring-opened cyclobutyl radi-

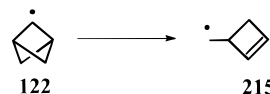
cals **214** and **215** (Schemes 61 and 62), but this

Scheme 61



process is remarkably difficult. Stability of both **121** and **122** toward β -scission to ring-opened products has been studied both experimentally^{112,258} and com-

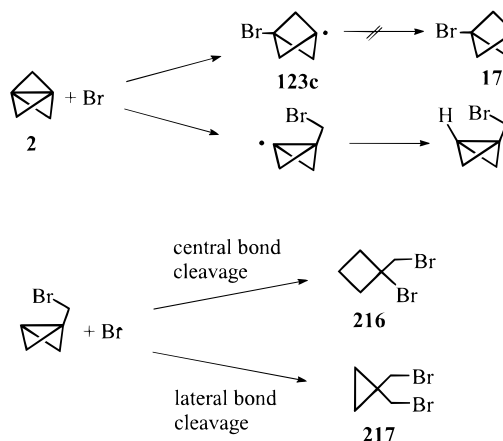
Scheme 62



putationally.^{108,112,157,258} The transition states of the ring-opening reactions of **121** and **122** are destabilized by antibonding interaction between the two atomic orbitals in which the SOMO is largely localized.¹⁰⁸ This interaction is enhanced in **121** and **122** by the forced proximity of the carbon atoms in the bridgehead (interbridgehead distance in **121** is calculated to be 1.815 Å,¹⁰⁸ UHF/6-31G*) and bridge carbons (interbridge distance in **122** is calculated to be 2.099 Å,¹⁰⁸ UHF/6-31G*). Such destabilization of the transition states is analogous to that in the high-energy cyclopropenyl radical, and it drives activation energies for β -scission up to 26 kcal/mol in the case of **121** (PUMP2/6-31G*).¹⁰⁸ Measured activation energies for the rearrangement of 3-methoxycarbonyl- and 3-phenylbicyclo[1.1.1]pent-1-yl radicals are in the range 21–25 kcal/mol.²⁵⁸

Radical addition of HBr to [1.1.1]propellane (**2**) yields two unexpected products, **216** and **217**, in a 3:2 ratio and 80% combined yield (Scheme 63).²⁰⁹ The

Scheme 63

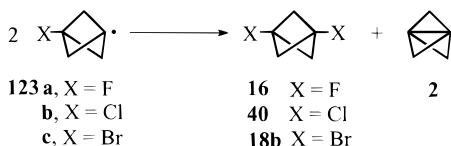


proposed mechanism involved cleavage of the lateral instead of the central bond of **2**.²⁰⁹ The fact that the addition of bromine radical to **2** with the cleavage of the central bond to give **123c** may be reversible in the absence of an efficient trap may be the reason for the reaction course.

(ii) *Elimination (γ -Scission).* Bicyclo[1.1.1]pent-1-yl radicals with a leaving group in position 3 undergo intramolecular S_H2 substitution, which leaves the bicyclo[1.1.1]pentane cage intact. Thus, the addition of the phenylthiyl radical to [1.1.1]propellane (**2**) is

reversible at room temperature.²⁵¹ 3-Iodobicyclo[1.1.1]pent-1-yl radical (**123d**) loses an iodine atom readily, and **2** is formed.⁶ The same reaction is observed under mild conditions for 3-bromobicyclo[1.1.1]pent-1-yl radical (**123c**), but the radical is stable enough to be partially intercepted by abstraction of iodine from 1,1,1-trifluoroiodoethane solvent.²³⁹ The propensity of **123c** toward disproportionation has been noticed.²³⁹ As a result, 1,3-dibromobicyclo[1.1.1]pentane (**18b**) is a common side product (in some cases the major product) of reactions involving **123c**.²³⁹ Similar processes have been observed for 3-chloro- (**123b**), and even for 3-fluorobicyclo[1.1.1]pent-1-yl (**123a**) radicals (Scheme 64),¹¹²

Scheme 64

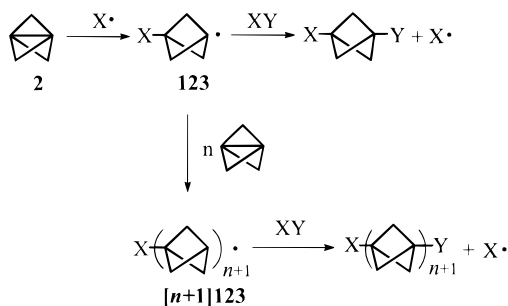


but they are less favored. The radical **123b** abstracts bromine atoms from CF_3CHBrCl in solution, giving the expected mixed 1-bromo-3-chlorobicyclo[1.1.1]pentane (**18f**) in excellent yield, while under the same conditions the radical **123c** gives only the dibromide **18b** in the presence of CF_3CCl_3 (see also section IV.B.2.b.iii).²³⁹ Most of the C(substituent)–C(3) bonds in 3-substituted radicals appear to be stable toward γ -scission. However, the 3-*tert*-butylbicyclo[1.1.1]pent-1-yl radical dissociates at an appreciable rate even at 25 °C ($k = 6 \times 10^3 \text{ s}^{-1}$).²⁵⁹ Sn–C(3), Si–C(3), and Se–C(3) bonds in the corresponding 3-substituted bicyclo[1.1.1]pentyl radicals break easily with formation of [1.1.1]propellane (**2**).²³⁹

Perfluorination of the bicyclo[1.1.1]pentane cage stabilizes the bridgehead radical toward γ -scission, presumably because of an increased interbridgehead distance and reduced strength of the new central bond.⁹⁷ No hexafluoro[1.1.1]propellane or products of its rearrangement have been found among the products of reactions in which the formation of 3-substituted 2,2,4,4,5,5-hexafluorobicyclo[1.1.1]pent-1-yl radical (**203**, Chart 10) is expected.⁹⁷

(iii) *Additions*. Photochemical or thermally induced radical chain addition of reagents across the central σ bond in [1.1.1]propellanes **2** and **9** produces either derivatives of bicyclo[1.1.1]pentane or oligomeric or polymeric [*n*]staffanes. The course of the reaction (Scheme 65) depends on the nature of the reagent, its concentration, and relative molar ratio to the

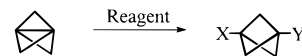
Scheme 65



[1.1.1]propellane,^{20,21,23,41,180,260} as well as on the solvent used for the reaction.²⁰ In many cases the net effect of the reaction is an insertion of a bicyclo[1.1.1]pentane moiety into a bond of the reagent X–Y. These reactions are listed in Table 32.

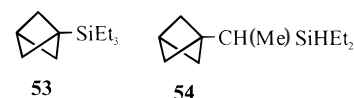
Some unexpected addition products may form when the initial radical undergoes transformations before it reacts with [1.1.1]propellane (**2**, Scheme 66)

Scheme 66



or if the chain is transferred to another reagent or the solvent. Such reactions are listed in Table 33.

The parent [*n*]staffanes have been prepared by a radical oligomerization of [1.1.1]propellane induced by hydrogen atoms generated in a microwave discharge. [*n*]Staffanes (**[n]1**) have been individually isolated up to $n = 6$.⁴² Many active C–H compounds, such as malonic esters and their derivatives, oligomerize with propellanes in ethereal solution.^{20,21,91,163,261–263} However, since diethyl ether itself can add [1.1.1]propellanes **2**^{20,180} or **9a**²⁰⁷ across its C–H bonds, some of the oligomerization reactions need to be performed in a hydrocarbon solution^{20,21} or without solvent.^{4,180,207} Compounds with P–H bonds^{21,91,163,180} also react with **2**, giving series of oligomers,^{21,91} while S–H reagents (thiophenol^{3,91,180} and thiolacetic acid⁹¹) yield only monomeric products. Hydrosilylation of **2** afforded a 3:1 mixture of bicyclo[1.1.1]pentanes **53** and **54** (see discussion below).¹⁸⁰ Tin hydrides react with neat [1.1.1]propellanes faster than silanes, and provide bridgehead stannanes in much better yields.^{182,207}



Although the kinetics of the reactions of R–H compounds with propellane have not been measured (except for PhSH ²⁵¹ and an estimate for THF ¹⁸⁰), a certain pattern of reactivity emerges from a consideration of the successful and unsuccessful reactions. It appears that the abstraction of hydrogen by a bridgehead bicyclo[1.1.1]pent-1-yl radical is a slow process, despite the relatively high bridgehead C–H bond dissociation energy in the bicyclo[1.1.1]pentane product. This allows the oligomerization of [1.1.1]propellanes to occur. However, some seemingly good hydrogen donors (dimethyl acetal, methyl isobutyrate) do not undergo radical addition to [1.1.1]propellane (**2**),¹⁸⁰ and others, like methoxyacetonitrile and methylthioacetonitrile, give only marginal yields of bicyclo[1.1.1]pentanes.⁹¹ In contrast, **2** reacts much more easily with chloroform ($D_{\text{C-H}} = 96 \text{ kcal/mol}$), and the reaction with triethylsilane ($D_{\text{Si-H}} = \sim 90 \text{ kcal/mol}$) yields unexpectedly mostly the C–H insertion product rather than the expected Si–H.¹⁸⁰ The difference in reactivity of **2** toward R–H radical sources is certainly due primarily to R–H bond strength (hydrogen abstraction), but the electro-negativity effect clearly also plays a role.

Table 32. Reactions of Radical "Insertion" of [1.1.1]Propellanes into X–Y Bonds (Scheme 65)

bond	X	Y	sol ^a	n ^b	yield (%) ^c	ref	
H–C	H	CH(CO ₂ Me) ₂	N	<i>d</i>	<i>d</i>	180	
	H	CH(CO ₂ Et) ₂	E	>1	<i>d</i>	21, 163	
	H	C(CO ₂ Et) ₃	E	4	28, 11, 1, 0.2	21, 163	
	H	CPh(CO ₂ Et) ₂	E	>1	<i>d</i>	21, 163	
	H	CH(COMe)CO ₂ Me	E	>1	<i>d</i>	21, 163	
	H	CH(COMe)CO ₂ Me	N	1	45	180	
	H	CH(CN)CO ₂ Me	E	>1	<i>d</i>	21, 163	
	H	CH(CN)CO ₂ Me	N	1	45	180	
	H	CH(Me)OEt	E	5	>22, 16, 6, 4, 2 ^e	20	
	H	CH(Me)OEt	E	3	13, 12, 5 ^f	207	
	D	CCl ₃	N	2	43	4, 180	
	H	CCl ₃	P	2	70, 20	209, 260	
	H	CCl ₃	P	3	35, 26, 9	40	
	H	CCl ₂ Me	E	3	>21, 14, 2	261	
	H	CH ₂ COMe	N	4	33	180	
	H	CH(Me)COMe	N	1	72	180	
	H	CH ₂ COCH ₂ COMe	N		0	180	
	H	CH ₂ CO ₂ Me	N		0	180	
	H	CH(Me)CO ₂ Me	N	4	45, 18	180	
	H	CMe ₂ CO ₂ Me	N		0	180	
	H	CH(Cl)CO ₂ Me	N	2	75	180	
	H	CCl(Me)CO ₂ Me	N	1	65	180	
	H	CO ₂ Me	N	1	40	180	
	H	CO ₂ Me	P	5	21, 18, 9, 3, 1	20, 21	
	H	2-THF-yl	N	5	44, 24	180	
	H	2- and 4-dioxolanyl	N	3	50 ^g	180	
	H	CH(Me)NEt ₂	N	1	22	180	
	H	CH(Me)SiHEt ₂	N	1	40 ^g	180	
	H–H	H	H	P	6	<i>d</i> , 13, 9, 6, 2, 0.3	42
	H–P	H	PO(OR') ₂	E	3	45, 23, 5	21, 91, 163
H		PO(OR') ₂	N	1	58	180	
H		PPh ₂	D	1	<i>d</i>	180	
H–S	H	SPh	E	1	98	91, 180	
	H	SPh	E	1	50	173	
	H	SCOMe	E	<i>d</i>	<i>d</i>	91	
H–Si	H	SiEt ₃	N	1	40 ^g	180	
H–Sn	H	SnMe ₃	E	1	50–57	182	
	H	SnBu ₃	E	1	28	209	
	H	SnBu ₃	E	1	60	182	
	H	SnBu ₃	E/P	1	52	173	
	D	SnBu ₃	E/P	1	49	278	
	H	SnBu ₃	E	1	72 ^f	207	
	H	Sn(<i>c</i> -C ₆ H ₁₁) ₃	E	1	56	182	
	H	SnPh ₃	E	1	58	182	
	H	SnPh ₃	E	1	73	173	
	Cl–C	Cl	CCl ₃	N	1	79	180
Cl		CCl ₃	P	2	70, 20	209, 260	
Cl		CCl ₃	T	2	54, 4 ^f	207	
Cl		CCl ₂ Me	E	2	>18, 18	261	
Cl–S	Cl	SO ₂ Me	E	2	<i>d</i> , 50	20	
	Cl	SO ₂ Me	O	2	15, 2	268	
	Cl	SO ₂ Ph	E	1	72	20	
	Cl	SO ₂ (<i>p</i> -C ₆ H ₄ Me)	O	2	19, 32	268	
	Cl	SO ₂ Cl	O	2	20, 10	268	
Cl–O	Cl	O(<i>t</i> -Bu)	N	1	41	4, 180	
	Br–C	<i>t</i> -Bu	P	2	50	20	
Br–C	Br	<i>t</i> -Bu	E	1	30	138	
	Br	<i>t</i> -Bu	N	1	36 ^f	207	
	Br	CH ₂ Ph	E	1	<i>d</i>	20, 21	
	Br	CH ₂ Ph	N	1	50 ^f	207	
	Br	CH ₂ Cl	N	1	31 ^f	207	
	Br	CCl ₃	C- <i>d</i>	1	<i>d</i>	4, 180	
	Br	CH(CO ₂ Et) ₂	E	1	>60 ^e	6	
	Br	CH(CO ₂ Et) ₂	E	1	68 ^h	209	
	Br	CH ₂ CO ₂ Me	E	1	>60 ^e	6, 20	
	Br	CH ₂ CO ₂ Me	P	3	>6, 11, 4	20	
	Br	CN	P	3	0, 45, 11 ^h	4, 180	
	Br	CHBr ₂	P		88	209	
	Br	CBr ₃	P		83	209	
	Br	CF ₂ Br	P	2	85, 10	264	
	Br	(CF ₂) ₂ Br	P	2	40, 20 ⁱ	264	

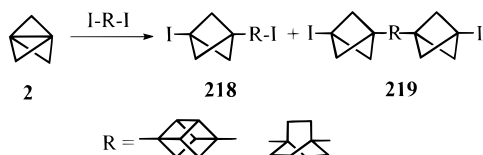
Table 32. (Continued)

bond	X	Y	sol ^a	n ^b	yield (%) ^c	ref
I-C	I	Me	N	1	42	261
	I	Me	E	1	68	94
	I	Me	N	1	25 ^f	207
	I	Me	P	1	65	209
	I	CF ₃	E	1	75	250
	I	Et	E	1	90	94
	I	<i>n</i> -Bu	E	1	46	20
	I	<i>n</i> -Bu	P	3	14, 16, 8 ^e	20
	I	<i>s</i> -Bu	E	1	47	20
	I	alkyl	E	d	>60 ^e	6
	I	Ph	P	2	>20 ^e	20
	I	C ₈ H ₆ ^j	O	1	55, ^{k,l} 78 ^{l,m}	44
	I	C ₈ H ₁₂ ⁿ	O	1	74, ^{k,l} 81 ^{l,m}	44
	I	C ₅ H ₆ ^p	P	2	95	20
	I		P	2	60	266
	I	3-(<i>n</i> -Bu)C ₅ H ₆	P	4	>27, 12, 4.7, 1.4 ^e	20
	I	3-PhC ₅ H ₆	P	2	<i>d</i>	20
	I	CH ₂ CH ₂ CO ₂ H	E	1	31 ^p	6
	I	<i>n</i> -Hex ₃ SiC ₂ B ₁₀ H ₁₀ ^q	P	1	88	249
I	H(C ₂ B ₈ H ₈) ₂ ^r	P	1	<i>d</i>	265	
P-C	(Me ₂ O) ₂ P(O)	<i>n</i> -C ₅ H ₁₁	B- <i>d</i>	1	12	270
	(Me ₂ O) ₂ P(O)	CH ₂ Ph	B- <i>d</i>	1	46	270
	(-OCH ₂ CHMeO-)P(O)	CH ₂ Ph	B- <i>d</i>	1	40 ^g	270
P-N	(Me ₂ O) ₂ P(O)	Me ₂ N	B- <i>d</i>	1	7	270
S-S	SMe	SMe	E	4	40, 12, 0.4, 0.1	20, 23, 41
	SEt	SEt	E	2	18, 4	41
	SPh	SPh	E	1	45	4, 180
	SPh	SPh	E	2	63, 27	23, 41
	S(CH ₂) ₂ CO ₂ Et	S(CH ₂) ₂ CO ₂ Et	E	1	5	41
	SCOMe	SCOMe	E	5	3, 14, 3, 0.3, 0.05	20, 21, 163
Se-Se	SePh	SePh	E	1	38	4, 180
N-N	NO ₂	NO ₂	E	1	25 ^h	180
P-P	P(OEt) ₂	P(OEt) ₂	E	1	27	20, 163
Br-Br	Br	Br	E	1	13	20
	Br	Br	E	1	37	209
I-I	I	I	E	1	88	4, 20, 180
	I	I	E	1	61	24
	I	I	E	1	18 ^s	246
C-C	MeCO	MeCO	E	1	58	185, 274
	MeCO	PhCO	E	1	24 (11, ^t 12 ^u)	20
	PhCO	PhCO	E	4	3, 8, 1	20

^a Solvents: B, benzene; C, chloroform; D, dichloromethane; E, diethyl ether; N, none; P, pentane; T, carbon tetrachloride.

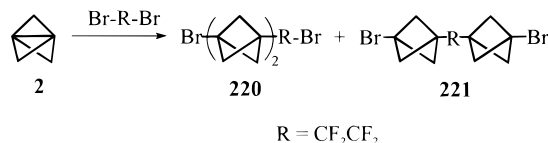
^b Maximum degree of oligomerization observed. ^c Yields of [*n*]staffanes based on [1.1.1]propellane are given in the sequence *n* = 1, 2, ^d Not reported. ^e Yields of the isolated subsequent products. ^f 2,4-Trimethylene[1.1.1]propellane. ^g Combined yield of two isomers. ^h Yield of the major product. A side reaction takes place. See Table 33. ⁱ Two 2:1 adducts formed: Br(CF₂)₂(C₅H₆)₂Br and BrC₅H₆(CF₂)₂C₅H₆Br. ^j Cubane-1,4-diyl from 1,4-diiodocubane. ^k 1:1 Adduct. ^l Yields based on the starting diiodide. ^m 2:1 adduct. ⁿ Bicyclo[2.2.2]octane-1,4-diyl from 1,4-diiodobicyclo[2.2.2]octane. ^o Bicyclo[1.1.1]pentane-1,3-diyl from 1,3-diiodobicyclo[1.1.1]pentane. ^p Yield of the rearranged product. ^q 12-(Tri-*n*-hexylsilyl)-1,12-dicarba-*closo*-dodecaboran-1-yl. ^r 1,1'-Bis(1,10-dicarba-*closo*-decaborane)-10-yl. ^s 2,2-Dichloro[1.1.1]propellane. ^t 1,3-Diacetylbicyclo[1.1.1]pentane is a side product. ^u 1,3-Dibenzoylbicyclo[1.1.1]pentane is a side product.

Scheme 67



A few alkyl iodides have been shown to react thermally with [1.1.1]propellanes,^{47,207} and a larger number of iodides and also activated bromides (e.g., methyl bromoacetate) react under UV irradiation^{6,20,91,138} to give the first member of the oligomeric series when the reaction is performed in diethyl ether. Oligomeric series of [*n*]staffanes are obtained²⁰ if concentrated pentane solutions of [1.1.1]propellanes are used. Bridgehead 1,4-diiodobicyclo[2.2.2]octane and 1,4-diiodocubane react with **2** in a benzene solution to give 1:1 and 1:2 adducts **218** and **219** (Scheme 67) in a ratio that can be controlled by reaction conditions.⁴⁴ 1,2-Dibromotetrafluoroethane gives two types of 1:2 adducts with **2**: **220** and **221**.²⁶⁴ Reaction of **2** with 1,2-dibromotetrachloroethane in the presence of PPh₃ yields the dibromides [**1**]18b and [**2**]18b in 31% and 21% yields, respectively (Scheme 68), and no products containing the tetrachloroethylene moiety have been reported.¹³⁸

Scheme 68



Reaction of **2** with 1,2-dibromotetrachloroethane in the presence of PPh₃ yields the dibromides [**1**]18b and [**2**]18b in 31% and 21% yields, respectively (Scheme 68), and no products containing the tetrachloroethylene moiety have been reported.¹³⁸

Addition of [1.1.1]propellane (**2**) to 1-iodocarboranes is accomplished upon irradiation with an incandescent lamp, while use of a mercury lamp decreases

Table 33. Other Radical-Mediated Additions to [1.1.1]Propellanes (Scheme 66)

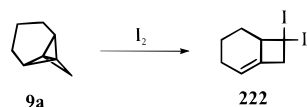
reagent	X	Y	solv	yield (%)	ref
MeCHO	COMe	CH(OH)Me	neat	52	180
<i>n</i> -PrCHO	CO(<i>n</i> -Pr)	CH(OH)(<i>n</i> -Pr)	neat	50	180
	CO(<i>n</i> -Pr)	H		19	
Me ₂ CHCHO	CMe ₂ CHO	H	neat	5	180
	COCHMe ₂	H		16	
	CH(OH)CMe ₂	CHMe ₂		9	
	CH(OH)CMe ₂	CMe ₂ CHO		13	
	CH(OH)CMe ₂	COCHMe ₂		13	
<i>t</i> -BuCHO	<i>t</i> -Bu	H	neat	<i>a</i>	180
	<i>t</i> -Bu	CHO		<i>a</i>	
PhCHO	COPh	CH(OH)Ph	neat	49	180
PhCHO	COPh	CH(OH)Ph	Et ₂ O	<i>a</i>	20
	Me(EtO)CH ^b	CH(OH)Ph ^b		<i>a</i>	
MeCOCO ₂ Me	Me(EtO)CH ^b	CMe(OH)CO ₂ Me ^b	Et ₂ O	48 ^c	20
C ₂ Br ₂ Cl ₄ , PPh ₃	Br	Br	Et ₂ O	31, 21 ^d	138, 142
CH ₂ =CHCH ₂ Br	Br	Br	Et ₂ O	<i>a</i> , 11	6
BrCH(CO ₂ Me) ₂	Br	Br	Et ₂ O	6 ^e	209
CBBr ₄	Br	Br	C ₆ H ₁₄	26 ^e	209
BrCN	Br	Br	C ₅ H ₁₂	8 ^e	180
CH ₂ =CHCH ₂ I	I	I	Et ₂ O	11	20
PhICl ₂ , CHCl ₃	I	CCl ₃	PhH	23	262
P(OEt) ₃	Et	P(O)(OEt) ₂	C ₆ D ₆	6	270
PhCH ₂ OP(OMe) ₂	PhCH ₂	P(O)(OMe) ₂	C ₆ D ₆	45 ^f	270
NO ₂ , Et ₂ O	NO ₂	H	Et ₂ O	8.7 ^e	94
NO, CS ₂	NO ₂	SCN	CS ₂	90	180
2 ArNO	ArNO	ArNO	PhH	<i>a</i>	273
ArNO, I ₂	ArNO	I	PhH	<i>a</i>	273
ArNO, PhSH	ArNO	PhS	PhH	<i>a</i>	273
ArNO, PhICl ₂	ArNO	Cl	PhH	<i>a</i>	273

^a Not reported. ^b The product is formed as a result of reaction with a solvent. ^c A mixture of diastereoisomers. ^d Yields of [*n*]staffanes based on [1.1.1]propellane are given in the sequence *n* = 1, 2. ^e Yield of the side product. For the major product see Table 32. ^f Conditions are optimized for this pathway of the reaction. For the alternative product see Table 32.

the yield of the desired bicyclo[1.1.1]pentanes substantially.^{249,265} 1,3-Diodobicyclo[1.1.1]pentane (**11**) reacts with an excess of **2** in pentane upon irradiation exclusively to [**2**]**13** in a high yield,^{20,266} while 3-butyl- and 3-phenyl-1-iodobicyclo[1.1.1]pentane give oligomeric series.²⁰ Iodobenzene oligomerizes with **2** in pentane under irradiation, but other aromatic iodides react with **2** under the same conditions only to a small degree if at all.^{20,267} Allyl iodide²⁰ and bromide⁶ do not give the usual adducts, and only the dihalides **13** and [**2**]**18b** have been isolated in about 10% yield. Benzyl bromide^{20,21,207} and cyanogen bromide^{4,180} react with **2** giving mostly the expected adducts, but small quantities of the dibromide [**2**]-**18b** have been also observed in the former reaction.

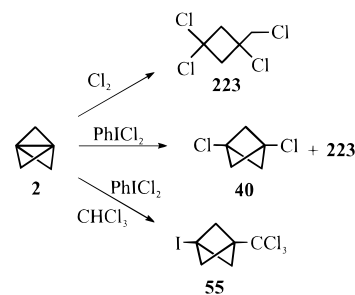
Most alkyl chlorides are not active enough to react with [1.1.1]propellanes. However, compounds containing the trichloromethyl group,²⁶¹ carbon tetrachloride,^{180,260} and sulfonyl chlorides^{20,163,268} easily gave the first few oligomeric derivatives of [*n*]-staffanes.

Iodine¹⁸⁰ and bromine²⁰ themselves react with **2** to give 1,3-dihalobicyclo[1.1.1]pentanes **13** and **18b**. However, the reaction of 2,4-trimethylene[1.1.1]propellane (**9a**) with iodine yielded only the ring-opened product **222** (Scheme 69).²⁰⁷ Addition of

Scheme 69

chlorine to [1.1.1]propellane (**2**) gave only the rear-

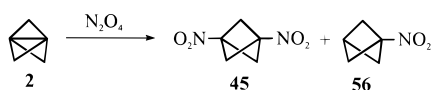
ranged product **223** (Scheme 70).²⁶² 1,3-Dichlorobi-

Scheme 70

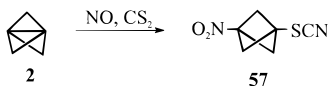
cyclo[1.1.1]pentane (**40**) was obtained along with the tetrachloride **223** upon reaction of **2** with PhICl₂.²⁶² In the presence of chloroform, the reaction of **2** with PhICl₂ yielded 1-iodo-3-trichloromethylbicyclo[1.1.1]pentane (**55**).³⁷

Dual mechanisms, proceeding via transient radicals or cations, have been considered²⁰⁷ for the reactions of **2** with halogens. Evidence for the involvement of cationic intermediates is discussed in section IV.B.3.

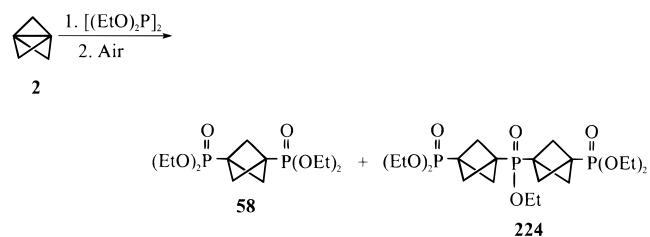
Organic disulfides,^{4,20,21,23,41,163,180,269} diphenyldiselenide,^{4,180} tetraethyl hypophosphite^{20,163} and dinitrogen tetroxide^{78,180} add successfully to [1.1.1]propellane (**2**). When the reaction of **2** with N₂O₄ is carried out in ether, in addition to 1,3-dinitrobicyclo[1.1.1]pentane (**45**), 1-nitrobicyclo[1.1.1]pentane (**56**) is isolated as the major side product (Scheme 71), presumably formed by abstraction of a hydrogen atom from the solvent by a transient radical.⁷⁸

Scheme 71

However, the intermediacy of 3-nitrobicyclo[1.1.1]pent-1-yl cation (**204**, Chart 10) cannot be ruled out. The reaction of NO with **2** in CS₂ yields a mixed product **57** (Scheme 72).¹⁸⁰ However, the more hin-

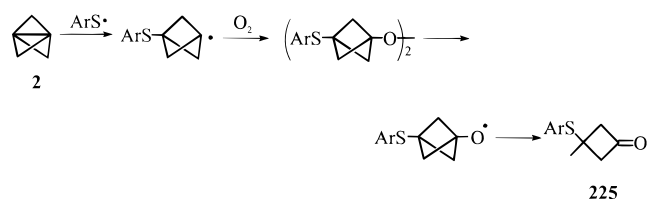
Scheme 72

dered di-*tert*-butyl and dipivaloyl disulfides did not react with **2** in diethyl ether.²⁶⁹ Reaction of the hypophosphite with **2** gave the diphosphonate **58**, but it also gave a significant amount of the more complex structure **224** (Scheme 73, see section IV.C.5 for

Scheme 73

further discussion).²⁰ Addition of bicyclo[1.1.1]pent-1-yl radicals, generated in situ from **2**, to molecules containing tricoordinate phosphorus has been studied in detail.^{270,271} The bicyclo[1.1.1]pent-1-yl radical attaches to tricoordinate phosphorus more eagerly than primary alkyl radicals and comparably to the phenyl radical.²⁷⁰ Both Arbuzov-type and radical substitution reactions may occur depending on the substitution pattern of the bicyclo[1.1.1]pentyl radical and the phosphine and depending on the reaction conditions.²⁷⁰

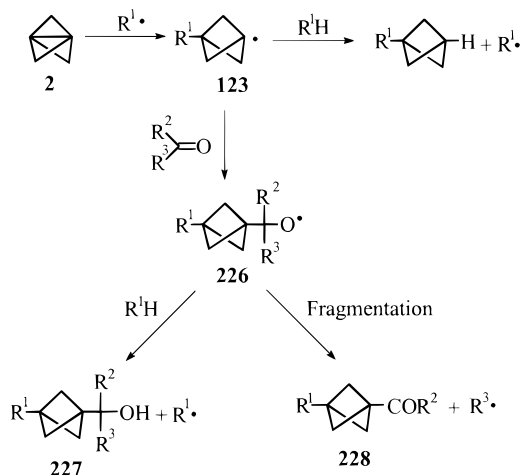
The reaction of the weakly electrophilic 2-nitrophenylsulfenyl chloride with **2** produces a complex mixture of products, and the cyclobutanone **225** has been isolated in 10% yield (Scheme 74). The forma-

Scheme 74

tion of the product has been explained by the presence of oxygen in the reaction mixture.²⁷² Tribromonitrosobenzene adds to **2** to yield a paramagnetic compound. The structures **205a-d** (Chart 10) have been proposed for the 2:1 adduct and some complex products of original radical interception with I₂, PhSH, and PhICl₂.²⁷³

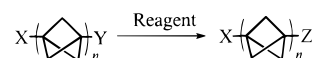
Bicyclo[1.1.1]pent-1-yl radicals are more nucleo-

philic than alkyl radicals, presumably because of the high electronegativity of the bridgehead carbon. Thus, [1.1.1]propellane (**2**) reacts easily in ethereal solution with compounds containing an electron deficient carbonyl group, such as biacetyl^{185,274} and benzil.²⁰ Less electrophilic aliphatic aldehydes react with neat **2**, yielding mixtures of products.¹⁸⁰ Unactivated carbonyl compounds such as amides, esters (including oxalates), thioesters, carbonates, and ketones, do not yield carbonyl adducts.^{20,180} Mechanistic schemes purporting to explain the observed addition products^{20,163,180} are summarized in Scheme 75. It has

Scheme 75

been proposed that the bicyclo[1.1.1]pent-1-yl radical **123** may abstract a hydrogen atom or add to the carbonyl group. The resulting oxy radical **226** may abstract a hydrogen atom, forming an alcohol **227**, or it can fragment with the formation of a ketone **228**. The radical R¹ may be formed by initial abstraction of hydrogen from an aldehyde, by cleavage of a dicarbonyl compound, by fragmentation of an initially formed carbonyl radical, or by abstraction of a hydrogen atom from the solvent. Depending on which pathway is favorable in particular reaction conditions, the products and their ratio may vary (Table 33). If reactions of the radical **123** with both hydrogen donors and carbonyl compounds are slow, formation of [*n*]staffane derivatives is possible, and the radicals R¹ will be bicyclo[1.1.1]pent-1-yl or [*n*]staff-3-yl radicals themselves.

The bridgehead radicals generated thermally, photochemically, or electrochemically from the carboxylic acids, *tert*-butyl peroxyesters **49**, or Barton esters **202**, react with a number of hydrogen,^{168,173,256} carbon,^{6,239} halogen,^{94,109,112,121,236,239,248,257,261,275-278} phosphorus,⁶ sulfur,^{6,278} and other^{236,278} radical traps (Scheme 76 and Table 34).

Scheme 76

Decomposition of the peroxyester **49** in neat chlorobenzene, 1,4-dichlorobenzene, benzonitrile, and

Table 34. Synthesis of Bridgehead Substituted Bicyclo[1.1.1]pentanes by Decarboxylation Bicyclo[1.1.1]pentane Carboxylic Acid Derivatives (Scheme 76)

X	reagent	solvent	Z	yield (%)	ref
Decarboxylation of Barton Esters 202 , Y = CO ₂ NC ₅ H ₄ S ^a					
H	Bu ₃ SnH	neat	H	73	168
H	CFCl ₃	neat	Cl	87	236
H	CF ₃ CCl ₃	neat	Cl	47	257
H	(PhSe) ₂	PhH	SePh	74	236
H	CF ₃ CHBrCl	neat	Br	68	275
D	CF ₃ CHBrCl	neat	Br	60	121
H ^b	CF ₃ CHBrCl	neat	Br ^b	42	109
H ^c	CF ₃ CHBrCl	neat	Br ^c	60	109
H	CF ₃ CH ₂ I	CH ₂ Cl ₂	I	87	236
H	CF ₃ CH ₂ I	neat	I	62	94
Me	(PhS) ₂	PhH	SPh	32	278
¹³ CH ₃	(PhS) ₂	PhH	SPh	<i>d</i>	278
Me	CFCl ₃	CH ₂ Cl ₂	Cl	17	261
¹³ CH ₃	CFCl ₃	CH ₂ Cl ₂	Cl	<i>d</i>	278
Me	(PhSe) ₂	PhH	SePh	71	278
¹³ CH ₃	(PhSe) ₂	PhH	SePh	<i>d</i>	278
Me	CF ₃ CHBrCl	neat	Br	81	239
¹³ CH ₃	CF ₃ CHBrCl	neat	Br	25	261
<i>t</i> -Bu	CF ₃ CHBrCl	neat	Br	89	239
Ph	C(CH ₂ OCO(CH ₂) ₂ SH) ₄	PhH	H	52	173
Ph	PhSD	neat	D	57	173
Ph	CF ₃ CHBrCl	neat	Br	89	239
Ph	CF ₃ CHBrCl	neat	Br	88	248
Ph	CF ₃ CH ₂ I	neat	I	92	94
<i>p</i> -C ₆ H ₄ Me	CF ₃ CH ₂ I	neat	I	96	94
<i>p</i> -C ₆ H ₄ NO ₂	CF ₃ CHBrCl	neat	Br	85	239
<i>p</i> -C ₆ H ₄ NO ₂	CF ₃ CH ₂ I	neat	I	96	94
<i>p</i> -C ₆ H ₄ OMe	CF ₃ CHBrCl	neat	Br	81	239
<i>p</i> -C ₆ H ₄ OMe	CF ₃ CH ₂ I	neat	I	87	94
<i>p</i> -C ₆ H ₄ Cl	CF ₃ CH ₂ I	neat	I	96	94
CN	CF ₃ CHBrCl	neat	Br	83	239
COMe	CF ₃ CHBrCl	neat	Br	94	239
CO ₂ Me	<i>t</i> -BuS	PhH	H	74	256
¹³ CO ₂ Me	<i>t</i> -BuS	PhH	H	74	248
CO ₂ Me	PhH	PhH	Ph	2, 10	6
CO ₂ Me	acridine	PhH	α-SC ₅ H ₄ N	53, 70	
CO ₂ Me	(MeCO) ₂	PhH	5-acridino	20	6
CO ₂ Me	(MeCO) ₂	CH ₂ Cl ₂	COMe	70	6
CO ₂ Me	XeF ₂ ^e	CH ₂ Cl ₂	COMe	84	239
CO ₂ Me	(SiMe ₃) ₂	PhH	COF ^e	95	239
CO ₂ Me	P(OEt) ₃	PhH	SiMe ₃	0	239
CO ₂ Me	(MeCOS) ₂	PhH	PO(OEt) ₂	28	6
CO ₂ Me	CFCl ₃	neat	SCOMe	85	6
CO ₂ Me	(PhSe) ₂	CH ₂ Cl ₂	Cl	82	239
CO ₂ Me	CF ₃ CHBrCl	neat	SePh	77	239
CO ₂ Me	CF ₃ CHBrCl	neat	Br	95	239
CO ₂ Me	(Me ₃ Sn) ₂	PhH	SnMe ₃	40	239
CO ₂ Me	CF ₃ CH ₂ I	PhH	I	81	276
F ^f	CF ₃ CHBrCl	neat	Br ^f	83	112
Me ₃ Si	CF ₃ CHBrCl	neat	Br	0	239
Cl	CF ₃ CHBrCl	neat	Br	80	239
Cl	CF ₃ CH ₂ I	PhH	I	89	277
PhSe	CF ₃ CHBrCl	neat	Br	0	239
Br	BrC ₅ H ₆ CO ₂ R ^g	CF ₃ CCl ₃	Br	45	239
Br	CF ₃ CH ₂ I	neat	I	45	239
Me ₃ Sn	CF ₃ CHBrCl	neat	Br	10	
I	CF ₃ CHBrCl	neat	Br	0	239
I	CF ₃ CH ₂ I	neat	I	0	277
Decarboxylation of <i>tert</i> -Butyl Peroxyesters 49 , Y = CO ₂ O- <i>t</i> -Bu					
CO ₂ Me		neat	H	26	6
			O- <i>t</i> -Bu	8	
CO ₂ Me	PhCN	neat	C ₆ H ₄ CN	<i>d</i>	6
CO ₂ Me	PhCO ₂ Me	neat	C ₆ H ₄ CO ₂ Me	<i>d</i>	6
CO ₂ Me	PhCl	neat	C ₆ H ₄ Cl	<i>d</i>	6
CO ₂ Me	<i>p</i> -C ₆ H ₄ Cl ₂	neat	2,5-C ₆ H ₃ Cl ₂	13	6
			O- <i>t</i> -Bu	7	

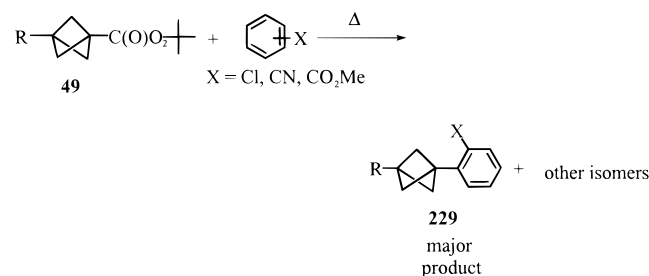
Table 34. (Continued)

X	reagent	solvent	Z	yield (%)	ref
Hunsdiecker Bromination, Y = CO ₂ H					
CO ₂ H	HgO, Br ₂	CH ₂ Cl ₂	Br	68	2
CO ₂ H ^h	HgO, Br ₂	(CF ₂ Br) ₂	Br ^h	68	48
CO ₂ Me	HgO, Br ₂	(CH ₂ Br) ₂	Br	68	218
CO ₂ Me ^h	HgO, Br ₂	(CF ₂ Br) ₂	Br ^h	78	97
Decarboxylation with XeF ₂ , Y = CO ₂ H					
H ^f	XeF ₂	CD ₂ Cl ₂	<i>i</i>		96
F ^f	XeF ₂	CD ₂ Cl ₂	no reaction		96
F ^f	XeF ₂	CDCl ₃	no reaction		96
Cl	XeF ₂	CD ₂ Cl ₂	F	trace ^j	96
			Cl	23 ^k	
			D	11 ^k	
			Cl ^l	3 ^k	
Cl	XeF ₂	CDCl ₃	Cl	20 ^k	96
			D	27 ^k	
			Cl ^l	4 ^k	
Br	XeF ₂	CD ₂ Cl ₂	<i>i</i>		96
CF ₃	XeF ₂	CD ₂ Cl ₂	F	4 ^k	96
			Cl	19 ^k	
			D	7 ^k	
			CF ₃ ^m	5 ^k	
CF ₃	XeF ₂	CDCl ₃	F	trace ^j	96
			Cl	10 ^k	
			D	36 ^k	
			CF ₃ ^m	4 ^k	
CO ₂ Me	XeF ₂	CD ₂ Cl ₂	F	27 ^k	96
			D	27 ^k	
			CO ₂ Me ⁿ	5 ^k	
CO ₂ Me	XeF ₂	CDCl ₃	D	80 ^k	279
Ph	XeF ₂	CDCl ₃	D ^o	35	5, 6, 279
Decarboxylation with Pb(OAc) ₄ , Y = CO ₂ H					
Me	Pb(OAc) ₄	PhH	Ph	<i>d</i>	278
CO ₂ Me	Pb(OAc) ₄	PhH	Ph	69	239
CO ₂ Me	Pb(OAc) ₄ , I ₂	PhH	I	91	276
Silver(I) Salt/Ammonium Persulfate Oxidation, Y = CO ₂ H					
CO ₂ Me	AgNO ₃ , (NH ₄) ₂ S ₂ O ₈ , benzoquinone	H ₂ O	C ₆ H ₃ O ₂ ^p	8	6
F ^f	Ag ⁺ /S ₂ O ₈ ²⁻	H ₂ O/ <i>c</i> -C ₆ H ₁₂	no reaction		96
Anodic Oxidation, Y = CO ₂ ⁻					
CO ₂ Me	e ⁻	H ₂ O	CO ₂ Me ⁿ	4	6

^a *N*-Carboxy-2-thiopyridone. ^b [2]Staffane derivatives. ^c [3]Staffane derivatives. ^d Not reported. ^e Attempted decarboxylation. The reaction proceeded as a nucleophilic displacement rather than a radical process. ^f Mixtures of 3-fluoro and 3-hydrobicyclo[1.1.1]pentane derivatives. ^g R = 2-thione-*N*-pyridyl. ^h Hexafluorobicyclo[1.1.1]pentane derivatives. ⁱ Reaction goes to completion with disintegration of the bicyclo[1.1.1]pentane cage. No individual products were identified. ^j Detected by ¹⁹F NMR. ^k Not an isolated yield. Relative proportion to other bicyclo[1.1.1]pentane derivatives in the product mixture determined by ¹H NMR. ^l 3,3'-Dichloro[2]staffane. ^m 3,3'-Bis(trifluoromethyl)[2]staffane. ⁿ Formation of 3,3'-diphenyl[2]staffane was claimed in ref 3. ^o Dimethyl [2]staffane-3,3'-dicarboxylate. ^p 1,4-Benzoquinonyl.

[1.1.1]pentane derivatives, if any (Scheme 78, Table 34).⁹⁶ 3-Fluorobicyclo[1.1.1]pentane-1-carboxylic acid (**20a**) is inert toward XeF₂, presumably due to an enhanced stability of the radical **230a** toward scission of the C(1)–COO bond. It seems that this radical is formed rather fast from the corresponding xenon

Scheme 77



ester **231** since the latter eluded detection by ¹²⁹Xe NMR.⁹⁶ Although the reactivity of 3-chloro and 3-trifluoromethyl substituted acids (**20b,c**) is also reduced, they do yield a set of products with the bicyclo[1.1.1]pentane cage retained. The composition of the product mixture depends on the reaction conditions, but in all cases the corresponding 3-substituted bicyclo[1.1.1]pent-1-yl radical can be readily envisioned as an intermediate.⁹⁶ These radicals are not only capable of abstracting hydrogen atoms from CD₂Cl₂ and CDCl₃, but chlorine atoms as well.⁹⁶ This is unusual because the abstraction of chlorine produces the less stable radical product, and is regarded⁹⁶ as another manifestation of a kinetic polar factor characteristic of reactions of 3-substituted bicyclo[1.1.1]pent-1-yl radicals (see also section IV.B.2.a.ii).

Scheme 78

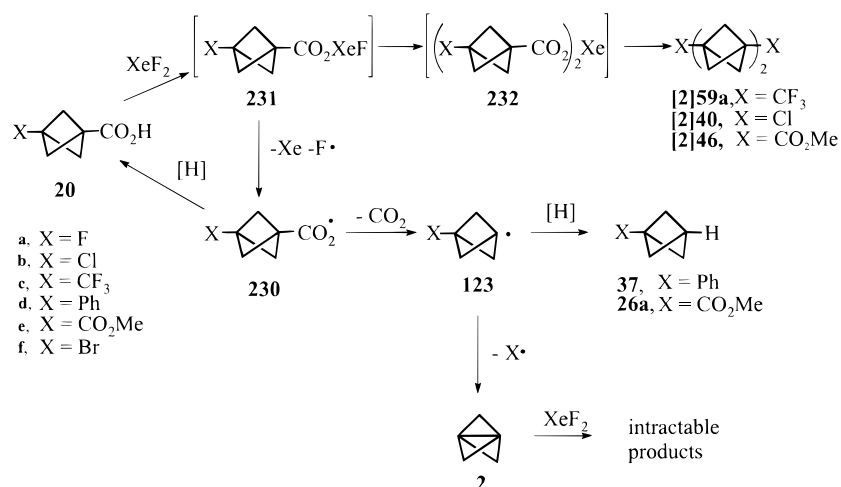


Table 35. Conversion of 1-Bromo-3-substituted- and 1-Iodo-3-substituted Bicyclo[1.1.1]pentanes into Other Derivatives by Homolytic Abstraction of the Halogen and Subsequent Radical Trapping (Scheme 79)

Y	X	n	reagent	solvent	Z	yield (%)	ref
Br	Br	2	Bu ₃ SnH	neat	H ^a	83	6
Br	CBr ₃	2	Bu ₃ SnH	neat	H ^b		266
Br	CH(CO ₂ Et) ₂	1	Bu ₃ SnH	PhH	H	46 ^c	6
Br	CH ₂ CO ₂ Me	1	Bu ₃ SnH	PhH	H	42 ^c	6
Br	CH ₂ CO ₂ Et	d	Bu ₃ SnH	PhH	H	2.7, 4.4, 1.6 ^c	20
I	Me	1	Bu ₃ SnD	neat	D	50	173
I	<i>n</i> -Bu	d	(MeCO) ₂	PhH	COMe	27, 12, 5, 5, 1 ^c	20
I	<i>n</i> -C ₅ H ₁₁	1	CH ₂ =CCl ₂	PhH	CH ₂ CHCl ₂	36 ^c	6
					H	traces	
					(CH ₂ CCl ₂) ₂ H	traces	
I	<i>n</i> -C ₅ H ₁₁	1	(MeCO) ₂	PhH	COMe	43 ^c	6
I	<i>n</i> -C ₅ H ₁₁	1	MeCOCN	PhH	COMe	35 ^c	6
I	Ph	1	(MeCO) ₂	PhH	COMe	0	20
I	glucosyl ^e	1	MeCOCO ₂ Me	PhH	CMe(OH)CO ₂ Me	49 ^c	6
I	CH ₂ COPh	1	MeCOCF ₃	PhH	CMe(OH)CF ₃	39 ^c	6
I	CH ₂ CO ₂ Et	1	<i>p</i> -ClC ₆ H ₄ CH=CH ₂	PhH	<i>p</i> -(CH ₂) ₂ C ₆ H ₄ Cl	24 ^c	6
					H	21 ^c	
I	butyrolacton-2-yl	1	CH ₂ =CHCO ₂ Me	PhH	(CH ₂) ₂ CO ₂ Me	39 ^c	6
I	CO ₂ Me	1	Bu ₃ SnH	neat	H	<i>f</i>	173
I	OMe	1	Bu ₃ SnD	neat	D	<i>f</i>	173
I	I	1	Bu ₃ SnH	neat	Bu ₃ Sn ^g	traces	6
I	I	1	CH ₂ =CHCN	<i>f</i>	(CH ₂) ₂ CN	0	6
I	I	2	Bu ₃ SnH	neat	H ^a	60	266
I	I	2	CH ₂ =CHCN	PhH	(CH ₂) ₂ CN ^a	83	6
I	I	2	(MeCO) ₂	PhH	COMe ^a	65	20
Hexafluorobicyclo[1.1.1]pentane Derivatives							
Br	CO ₂ Me	1	HSi(SiMe ₃) ₃	neat	H	83	97
Br	Br	1	HSi(SiMe ₃) ₃	neat	H ^a	69	97
Br	Br	1	SmI ₂	THF	I ^a	31	48

^a The same substituents in both 3 and 1 (or 3') positions. ^b The CBr₃ group is reduced to CH₃. ^c Yields are based on **174**, the precursor for **2**, which is in turn converted into crude starting material for the reaction discussed. ^d A mixture of starting oligomers is used for the reaction, and the oligomer products have been separated. ^e 6-Deoxytetra-*O*-acetyl- β -D-glucopyranos-6-yl. ^f Not reported. ^g Substituent in position 1 is H.

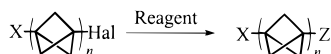
3-Phenyl- and 3-carbomethoxy-substituted acids (**20d,e**) give the corresponding reduced products **37** and **26a** in good yield,^{6,279} but formation of other products has been reported as well, at least in the case of **20e**.⁹⁶ Quite remarkable is the formation of the dimers [2]40, [2]46, and [2]59a in the reactions of the acids **20b**, **20e**, and **20c**, respectively, and the xenon diesters **232** were suggested as intermediates. The formation of 3,3'-diphenyl[2]staffane ([2]59b) in the decarboxylation of the acid **20d** has been claimed⁵ but disproven.⁶ The parent acid **14** and the 3-bromo acid **20f** undergo a facile reaction with disintegration

of the cage, most probably via cationic intermediates.⁹⁶ A possible mechanism involves the formation of the 3-bromobicyclo[1.1.1]pent-1-yl radical (**123c**), which rapidly loses a bromine atom to produce [1.1.1]-propellane (**2**), and the latter reacts with nucleophiles present in the reaction mixture.⁹⁶ Another possible route to bridgehead cations is electron transfer oxidation of the intermediate bridgehead radical by any species containing a Xe–F bond.

Radical transformations of bridgehead iodides induced by tin hydride are an attractive method of functionalization of the bridgehead position (Scheme

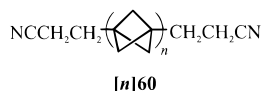
79 and Table 35).⁶ To a large extent this reaction,

Scheme 79



involving neutral and mild intermediates, is an alternative to preparative methods involving generation of bridgehead anion intermediates. Reactions of the bridgehead iodides with activated ketones in the presence of tin hydride once again showed the high propensity of the bridgehead radical toward additions to a carbonyl group and a low propensity toward hydrogen abstraction (see discussion above). In a competition between reactions of (a) bridgehead radical and carbonyl group, (b) bridgehead radical and tin hydride, and (c) tin hydride and the carbonyl compound, the first named path dominates, and an oxy radical **226** is formed. The radical either fragments to give a ketone or abstracts hydrogen from the tin hydride to form an alcohol (Scheme 75).⁶

Formation of [1.1.1]propellanes from transient 3-substituted bicyclo[1.1.1]pent-1-yl radicals may compete with addition reactions. Thus, 1,3-diiodobicyclo[1.1.1]pentane (**[1]13**) is not a useful starting material for preparation of symmetrically substituted bicyclo[1.1.1]pentanes by this method. 3,3'-Diiodo[2]-staffane (**[2]13**), however, gives the expected substituted [2]staffanes. The reaction of **[1]13** with acrylonitrile in the presence of tri-(*n*-butyl)tin hydride gives no dinitrile **[1]60**, while **[2]13** is converted into dinitrile **[2]60** under the same conditions in 83% yield.⁶ The acetylation reaction of the iodobicyclo[1.1.1]pentanes is one of the most useful synthetically. It has been successfully extended to the oligomeric iodides **[*n*]206** (Chart 10) and the diiodide **[2]13**.²⁰ The latter process is the key step on the optimal path for the preparation of [2]staffane-3,3'-dicarboxylic acid (**[2]42**).

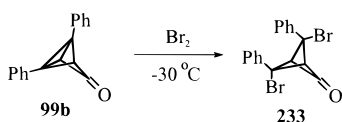


Attempts at fluoriodination of various substrates with XeF₂ [e.g., 1,3-diiodobicyclo[1.1.1]pentane (**13**),^{96,98} 1-iodobicyclo[1.1.1]pentane (**17h**),⁹⁶ 1-iodo-3-fluorobicyclo[1.1.1]pentane (**18a**),⁹⁶ and 1-iodo-3-phenylbicyclo[1.1.1]pentane (**61**)²⁷⁶] invariably lead to intractable mixtures of cage-opened products. The reaction presumably proceeds via cationic intermediates.



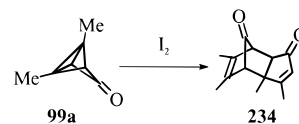
Only very few radical additions to tricyclo[2.1.0.0^{2,5}]pentanes have been described. Addition of bromine to the ketone **99b** at -35 °C produced an unstable dibromide **233** (Scheme 80), observed by low temper-

Scheme 80



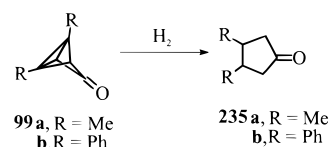
ature NMR.³¹² The addition of iodine to ketone **99a** under a variety of conditions led only to 3,4-dimethylcyclopentadienone dimer **234** (Scheme 81).²⁰⁴ A

Scheme 81



similar result was obtained upon a catalytic hydrogenation of the ketones **99a**⁷ and **99b**,⁸ where only 3,4-dimethyl and 3,4-diphenylcyclopentanone (**235a,b**) were isolated (Scheme 82).

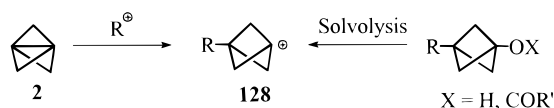
Scheme 82



3. Reactions Involving Bicyclo[1.1.1]pentyl Cations and Related Intermediates

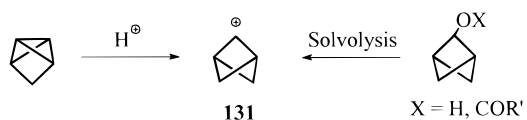
a. Electrophilic Attack (see section II.B.3.c for discussion of structure and stability of the bicyclo[1.1.1]pentyl cations). Bicyclo[1.1.1]pentyl cations may be formed either upon solvolysis of bromo- and iodobicyclo[1.1.1]pentanes, bicyclo[1.1.1]pentanols and their esters, or upon addition of an electrophile to [1.1.1]propellanes or tricyclo[2.1.0.0^{2,5}]pentanes (Schemes 83 and 84). Solvolysis can yield either

Scheme 83



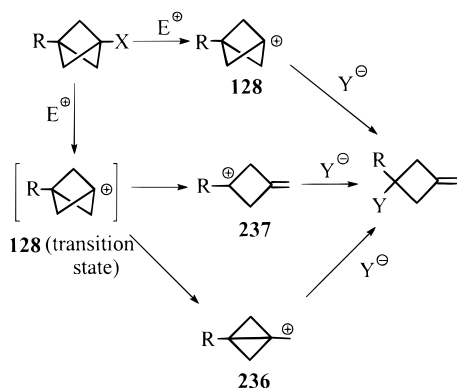
bicyclo[1.1.1]pent-1-yl (**126** or **128**, Chart 7) or bicyclo[1.1.1]pent-2-yl (**131**) cations depending on the precursor bicyclo[1.1.1]pentane derivatives. Addition to [1.1.1]propellanes yields only bicyclo[1.1.1]pent-1-yl cations, while addition to tricyclo[2.1.0.0^{2,5}]pentanes provides access to bicyclo[1.1.1]pent-2-yl cations.

Scheme 84



b. Bicyclo[1.1.1]pent-1-yl Cations: Intermediates or Transition States in Solvolysis of 1-Substituted Bicyclo[1.1.1]pentanes. The role of the parent bicyclo[1.1.1]pent-1-yl cation **126** and its substituted analogues **128** (Chart 7) in solvolysis and the mechanism of their rearrangement have been investigated in detail.^{94,121,280,281} Three cationic structures are considered as possible transition states and intermediates on the way from a 1-halobicyclo[1.1.1]pentane to the corresponding 3-methylenecyclobutane derivative, the usual product of solvolysis. Calculations (MP2/6-31G*) suggested that the parent bicyclo[1.1.1]pent-1-yl cation **126** can only be a tran-

Scheme 85

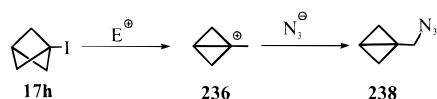


sition state, and it opens to the bicyclo[1.1.0]but-1-ylcarbanyl cation (**236**) which is believed to be the real intermediate (Scheme 85).⁹⁴ It has been suggested that substitution stabilizes the initial cation, and that 3-(trifluoromethyl)-, 3-phosphino-, 3-methyl-, and 3-silylbicyclo[1.1.1]pent-1-yl (**128e–h**) cationic structures are local minima on the corresponding potential energy surfaces. 3-Fluoro-, 3-chloro-, 3-hydroxy-, and 3-aminobicyclo[1.1.1]pent-1-yl (**128a–d**) cations are calculated to be unstable, and the corresponding 3-methylenecyclobutyl cations (**237**) are believed to be the solvolytic intermediates.⁹⁴ Analysis of the optimized geometries suggests that cations with an interbridgehead distance in the range 1.530–1.541 Å (**128a–d**) are stable enough to be intermediates themselves. The cations with a distance larger than 1.546 Å (**128e–h**) are transition states, and the rearranged cations **237** are the intermediates.⁹⁴

Substitution effects on the rates of solvolysis of 1-halobicyclo[1.1.1]pentanes in protic solvents have been studied on a series of bromo¹²¹ and iodo⁹⁴ derivatives. In both cases the rate of solvolysis decreased significantly with increasing inductive/field electron-withdrawing effect of the substituent on the other bridgehead carbon. This fact confirms the presence of a strong transannular interaction. An additional confirmation is provided by a large secondary H/D γ -isotope effect (1.3–1.37) on the solvolysis of 1-bromobicyclo[1.1.1]pentane (**17i**).¹²¹ Unfortunately, it is not possible to study the substitution and solvent effects on the behavior of **128** to determine whether it is an intermediate or a transition state.⁹⁴ Thus, explicit experimental evidence against or in favor of the intermediacy of **128** still remains to be found.

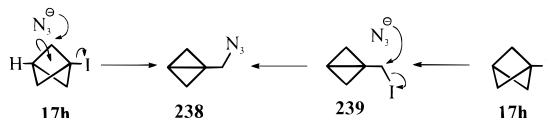
Experimentally, the intermediate cation **236** is trapped in the form of the azide **238** during the solvolysis of 1-iodobicyclo[1.1.1]pentane (**17h**) in aprotic solvents (Scheme 86) and it has been studied by ¹H and ¹³C NMR spectroscopy in SO₂ClF solution.⁹⁴ The cation **236** is also prepared in solution by a reaction of SbF₅ with 1-bromobicyclo[1.1.1]pentane (**17i**) and was studied by ¹³C NMR at –120 °C.⁹⁴

Scheme 86



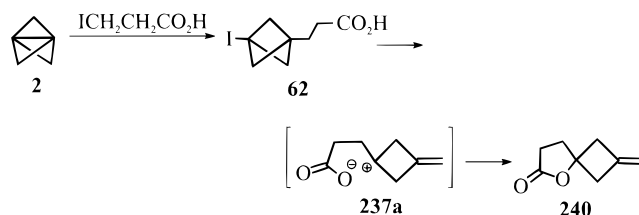
Alternative possible mechanisms for the formation of **238** in the trapping experiment, avoiding the formation of **236**, have been offered.¹²¹ One possibility may be that in an aprotic solvent that only weakly supports S_N1 substitution, the highly reactive **17h** slowly rearranges to the 1-iodomethylbicyclo[1.1.0]butane (**239**), and the latter yields **238** by an S_N2 mechanism upon treatment with an azide (Scheme 87). Another possible scenario is that the azide anion attacks the bridge carbon of the bicyclo[1.1.1]pentane cage and causes a C–C bond cleavage and concomitant iodine elimination.

Scheme 87



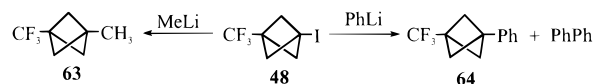
An interesting example of trapping of a cation of type **237** is an intramolecular nucleophilic attack in **237a**, formed upon solvolysis of 3-iodobicyclo[1.1.1]pentane-1-propionic acid (**62**, Scheme 88). The spirocyclic product **240** is obtained in a high yield.⁶

Scheme 88



Possible stabilization of the bicyclo[1.1.1]pent-1-yl cations **128** by an electronegative substituent in the other bridgehead position has been tested by attempted nucleophilic substitution of iodine in 1-(trifluoromethyl)-3-iodobicyclo[1.1.1]pentane (**48**).²⁵⁰ Reactions of **48** with MeLi and PhLi indeed gave the desired substitution products **63** and **64** (Scheme 89),

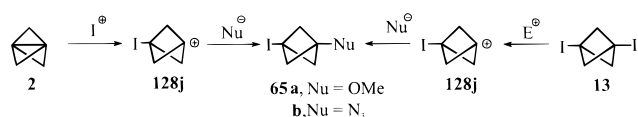
Scheme 89



but no mechanistic evidence in favor of intermediacy of the 3-trifluoromethylbicyclo[1.1.1]pent-1-yl cation (**128e**) was obtained. In the case of PhLi, a concomitant formation of biphenyl and color changes of the reaction mixture indicated the presence of radical intermediates.²⁵⁰ The iodide **48** is unreactive under solvolysis conditions even in the presence of silver acetate in 95% ethanol at 65 °C.⁹⁴ Bromination of **48** at –20 °C in CH₂Cl₂ with Br₂ gave a mixture of polybrominated compounds, and no bicyclo[1.1.1]pentane derivatives. This result has been interpreted as an evidence of low stability of the cation **128e**, which could not be captured by bromine under these conditions.⁹⁴

Iodine atom in position 3 significantly stabilizes the bicyclo[1.1.1]pent-1-yl cation. Basic solvolysis of 1,3-diiodobicyclo[1.1.1]pentane (**13**) in the presence of azide anion yielded the azide **65b** as the major

Scheme 90



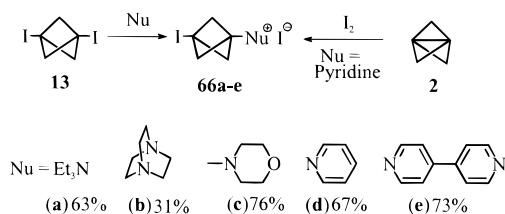
product, while addition of MeOI to [1.1.1]propellane (**2**) yields 1-iodo-3-methoxybicyclo[1.1.1]pentane (**65a**, Scheme 90).⁹⁴ Reaction of **13** with Br₂ in CCl₄ at 0 °C yielded 1-bromo-3-iodobicyclo[1.1.1]pentane (**18d**) in 14% yield.⁹⁴ These reactions are presumed to involve 3-iodobicyclo[1.1.1]pent-1-yl cation (**128j**) as an intermediate.

Addition of halogens to [1.1.1]propellane (**2**) may proceed via cationic intermediates, as we have mentioned in section IV.B.2 (Scheme 69). The isolated yield of symmetric 1,3-dihalobicyclo[1.1.1]pentanes, obtained in two steps starting with the [1.1.1]propellane precursor **174a** (Table 24), drops from 67% for the diiodide **13**²⁸² to 31% for the dibromide **18b**²⁸² and to 0% for the dichloride,²⁶² conceivably due to the decreased stability of the corresponding 3-bromo- and 3-chloro cations **128i** and **128b**, respectively, compared to the 3-iodo cation **128j**. The yield of the dibromide **18b** can be substantially increased when the reaction of **2** with Br₂ is carried out in the presence of 10 equiv of LiBr, presumably favoring trapping of the intermediate cation **128i** over a rearrangement.²⁸² Mixed 1,3-dihalobicyclo[1.1.1]pentanes **18d–f** were obtained in cross-trapping reactions upon addition of a halogen to **2** in the presence of a lithium salt of a different halogen, but this method is of preparative value only for the synthesis of **18d**, since the other 1,3-dihalobicyclo[1.1.1]pentanes are formed only in modest yields in mixtures that are difficult to separate.²⁸²

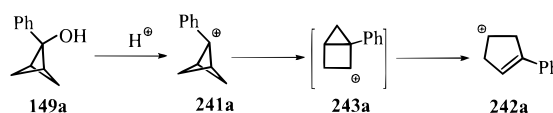
Aliphatic and aromatic amines react with **13** to give 3-iodobicyclo[1.1.1]pent-1-ylammonium salts **66a–e** (Scheme 91). The same products are obtained in lower yields upon the addition of I₂ to **2** in the presence of pyridine.^{47,250,283} 3-Iodobicyclo[1.1.1]pent-1-yl cation (**128j**) stabilized by amines can be an intermediate in these reactions as well.²⁸⁴ The reactions proceeded well in polar solvents, especially in acetone. A large (10-fold) excess of nucleophiles is used, and only 1:1 adducts are obtained even in the case of bidentate amines, such as 1,4-diazabicyclo[2.2.2]octane and 4,4'-bipyridyl. Attempts to substitute the remaining iodine on the bicyclo[1.1.1]pentane cage with a nucleophile invariably failed, and **2** or methylenecyclobutane derivatives were obtained as the main products.^{47,250}

c. Solvolysis of Bridge-Substituted Bicyclo[1.1.1]pentanes. The 2-phenylbicyclo[1.1.1]pent-2-yl cation (**241a**) has been observed spectroscopi-

Scheme 91

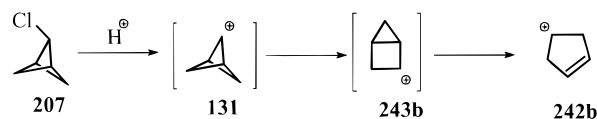


Scheme 92



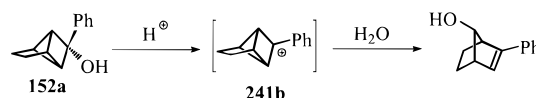
cally²⁸⁵ when the alcohol **149a** is ionized with FSO₃H/SO₂ClF or SbF₅/SO₂ClF at –140 °C to produce a mixture of cations **241a** and **242a** (Scheme 92). The former species rearranged quantitatively to the latter upon heating to –30 °C. In the hope of generating the parent cation **131**, 2-chlorobicyclo[1.1.1]pentane (**207**) was subjected to the same conditions, but only the cation **242b** was observed (Scheme 93).²⁸⁵ The

Scheme 93



alcohol **152a** rearranges in the presence of Brønsted and Lewis acids, presumably via a similar mechanism via the cation **241b** (Scheme 94).^{194,286}

Scheme 94



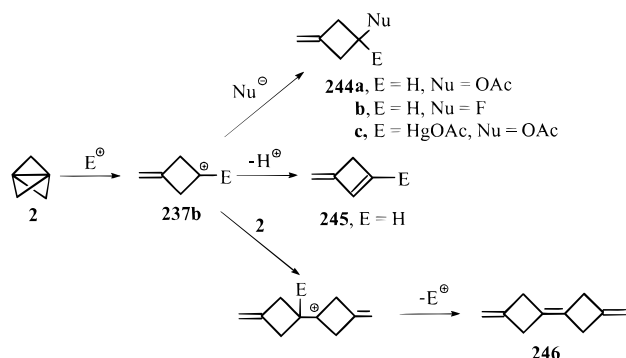
A solvolytic study of derivatives of bicyclo[1.1.1]pentan-2-ols has shown that the ionization of the bridge derivatives is much slower than that of the bridgehead ones, and it may proceed with participation of the one-carbon bridge adjacent to the departing group (Schemes 92, 93, and 94).^{286,287} It has been postulated that the solvolysis occurs in two steps through a bicyclo[2.1.0]pentyl cation (**243**), although the intermediate has not been observed.^{194,286,287,288}

d. Electrophilic Attack on [1.1.1]Propellanes. Electrophilic attack on the [1.1.1]propellane cage is another example of a reaction in which the cations **128** may be involved.

Addition of MeOI to [1.1.1]propellane (**2**) yielded the unrearranged product **65a** (see section IV.B.3.b, Scheme 90).⁹⁴ The same product is formed upon solvolysis of 1,3-diiodobicyclo[1.1.1]pentane (**13**) in methanol.⁹⁴ The latter reaction has been shown to produce **2** and MeOI in its initial stage, thus, the addition of MeOI to **2** is believed to be the second step of the methanolysis of **13**. The proposed mechanism for the addition of MeOI included an initial attack of iodonium cation on **2** with formation of a stabilized cation **128j**, which is trapped with methanol before rearrangement (Scheme 90).⁹⁴

If a bicyclo[1.1.1]pent-1-yl cation **128** is not stabilized, the cation **237b** is an intermediate in reactions which start with an electrophilic attack on **2** (Scheme 95). Methylenecyclobutane derivatives **244** are the usual products of these reactions. Protonation of **2** with acetic acid yielded 3-methylenecyclobutyl acetate (**244a**).^{2,58} The formation of 1-fluoro-3-methylenecyclobutane (**244b**) from **2** in the presence of XeF₂ in ether has been attributed to a protonation of the former with traces of HF present in the solution.²⁵⁰

Scheme 95

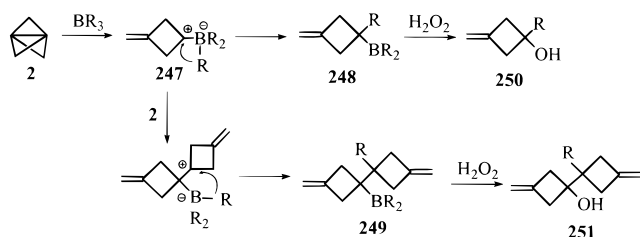


Reaction of **2** with $\text{Hg}(\text{OAc})_2$ yields a methylenecyclobutane derivative containing mercury (**244c**).

In the absence of a good nucleophile trap, an intermediate cation **237b** may eject the electrophile to give 3-methylenecyclobutane (**245**)¹⁷⁰ or add **2** with a concomitant rearrangement of the bicyclo[1.1.1]pentane cage (Scheme 95). Compound **246** is obtained along with more complex olefins in reactions of **2** with AgBF_4 , $[\text{Rh}(\text{CO})_2\text{Cl}]_2$, complexes of Pt(0), Pt(II), Pd(II), and Ir(I).¹⁸⁰ Third row transition metal complexes react with **2** more slowly, and the ratio of **245** and **246** in the product mixture strongly depends on the metal used. Intervention of metallocarbene intermediates in these reactions cannot be ruled out.

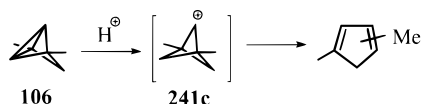
Trialkylboranes add to [1.1.1]propellane (**2**), but only rearranged products are formed.^{209,289} The suggested explanation involves formation of a zwitterionic intermediate **247** (Scheme 96), which undergoes an intramolecular alkyl transfer to give **248**. Such a 1,2-shift may be preceded by an addition of another molecule of **2**, and **249** is formed. Both organoboron compounds were oxidized and isolated as the corresponding alcohols **250** and **251**.

Scheme 96



e. Electrophilic Addition to Tricyclo[2.1.0.0^{2,5}]pentanes. 2,4-Dimethyltricyclo[2.1.0.0^{2,5}]pentane (**106**) rearranges readily to a mixture of dimethylcyclopentadienes upon mild acid catalysis,⁹⁰ presumably via the bridge 1,3-dimethylbicyclo[1.1.1]pent-2-yl cation (**241c**, Scheme 97). It has been noted that even such mild acids as methanol and water catalyze the rearrangement.

Scheme 97

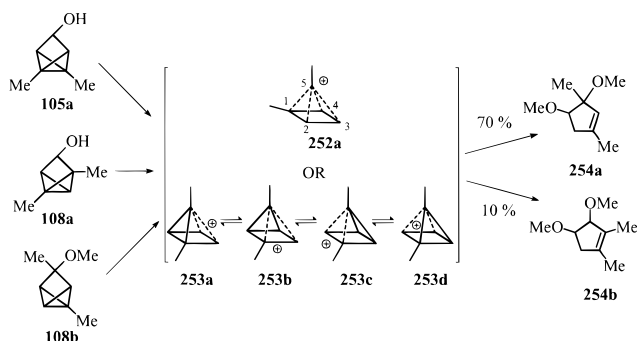


f. Solvolysis of Tricyclo[2.1.0.0^{2,5}]pentan-3-ol Esters: The $(\text{CH})_5^+$ Species. Quantum mechanical

calculations predict that a highly delocalized square pyramidal cation **134** is a minimum on the potential surface of $(\text{CH})_5^+$ species (see section II.B.3.c).¹²⁶ Earlier studies have shown that 1,5-diphenyltricyclo[2.1.0.0^{2,5}]pentan-3-ol ester **101c** solvolyzes 3 times faster than 1-chlorobicyclo[1.1.1]pentane (**17b**) under similar conditions.²⁹⁰ No structure has been assigned to the products of the solvolysis.

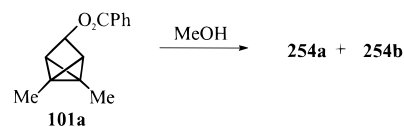
Treatment of tricyclo[2.1.0.0^{2,5}]pentan-3-ol derivatives **105a**, **108a**, and **108b** with 3:2 mixture of SO_2 -ClF and FSO_3H yields solutions with identical ¹H and ¹³C NMR spectra, which have been assigned to either the square pyramidal cation **252a** or equilibrating cations **253a–d** (Scheme 98).¹²⁹ A striking feature of

Scheme 98



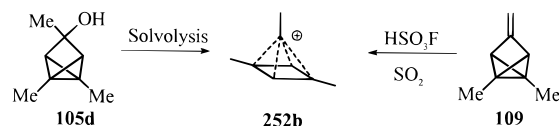
the ¹³C NMR spectrum is a signal at $\delta -23$ ppm assigned to C(5).¹²⁹ The same cyclopentene derivatives **254a,b** are obtained upon rearrangement and subsequent methanolysis of the benzoate **101a**, but no definite mechanism has been assigned to this reaction (Scheme 99).¹²⁸ Solvolysis of 1,3,5-tri-

Scheme 99



methyltricyclo[2.1.0.0^{2,5}]pentan-3-ol (**105d**) and protonation of 1,5-dimethyl-3-methylenetricyclo[2.1.0.0^{2,5}]pentane (**109**) with FSO_3H in liquid SO_2 at -75°C yielded a solution of a stable species with the NMR spectra very similar to those of **252a** or a mixture of **253a–d**, and it has been assigned to the cation **252b** (Scheme 100).¹³⁰

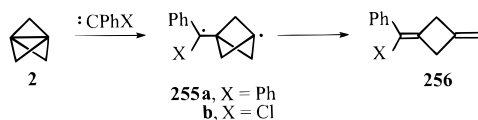
Scheme 100



4. Reactions Involving Biradicals

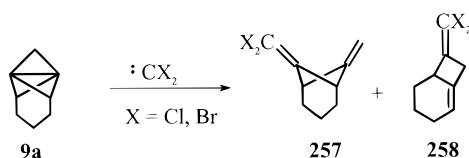
A flash photolysis investigation showed that the triplet 1,4-diradical **255a** ($\text{X} = \text{Ph}$, $\lambda_{\text{max}} = 330$ nm), formed by the addition of diphenylcarbene to [1.1.1]propellane (**2**), rearranges to the diene **256** with an

Scheme 101



unusually long lifetime of 9.7 μs (Scheme 101).²⁵¹ It has been suggested that the mutual orthogonality of the singly occupied orbitals is responsible for the slow intersystem crossing and the long lifetime for **255a** (theory²⁹¹ suggests that in such a case spin-orbit coupling is weak unless the energies of the two orbitals differ sufficiently). The diradical **255b** ($X = \text{Cl}$) is much less stable, and its lifetime is 30 ns.²⁵³ Dichloro- and dibromocarbenes similarly react with the [1.1.1]propellane **9a**, yielding a mixture of dimethylenecyclobutanes **257** and **258** (Scheme 102).²⁰⁷

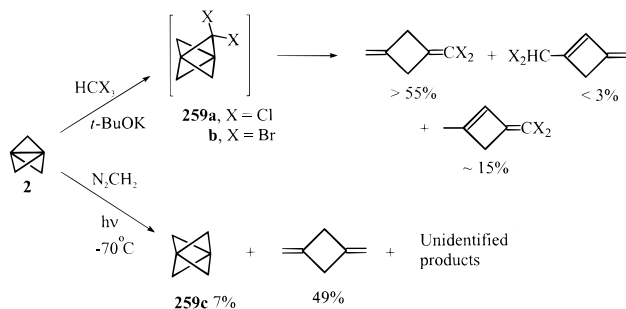
Scheme 102



The rates of reactions of triplet carbenes with [1.1.1]propellane **2** ($6.7 \pm 0.8 \times 10^6 \text{ M}^{-1} \text{ s}^{-1}$ for diphenylcarbene²⁵¹ and $6.7 \times 10^7 \text{ M}^{-1} \text{ s}^{-1}$ for chlorophenylcarbene reactions with **2**²⁵³) are comparable with those of radical additions to **2**.

Singlet dichloro- and dibromocarbenes also add to **2** readily. [1.1.1]Paddlane derivatives (**259a,b**) have been proposed as intermediates in these reactions (Scheme 103).²⁹² The parent [1.1.1]paddlane (**259c**)

Scheme 103

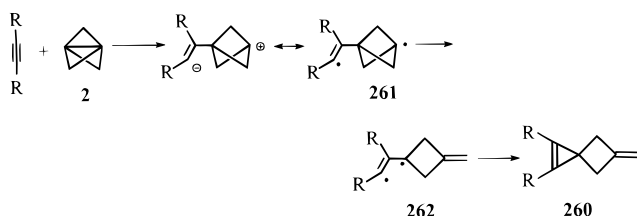


has been very recently claimed to form as a moderately stable minor product upon irradiation of a solution of **2** with diazomethane at -70°C . It was not isolated, but GC-MS and ^1H , ^{13}C , DEPT, and HMBC NMR spectra were considered compatible with the proposed structure.²⁹³ A confirmation of these initial results is eagerly awaited. The major products in all these reactions are dimethylenecyclobutanes.

Reactions of electron-deficient olefins and acetylenes (dicyanoacetylene, dimethyl acetylenedicarboxylate, tetracyanoethylene, and dichlorodicyanoquinone) with [1.1.1]propellane produce several ring-opened products, e.g., **260**.^{91,180,294} It has been proposed that the initially formed 1,5-biradical **261** opens up to 1,3-biradical **262** which collapses to the product,

although a zwitterionic mechanism is also possible (Scheme 104).^{180,294}

Scheme 104

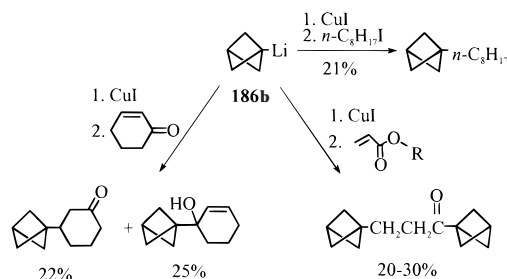


5. Transition-Metal-Catalyzed Coupling Reactions

Transition-metal-catalyzed carbon-carbon coupling reactions offer a potentially very powerful route to terminally substituted bicyclo[1.1.1]pentanes and [n]staffanes by bridgehead-to-arene and similar types of coupling, and to longer [n]staffanes by bridgehead-to-bridgehead coupling. Although both types of reactions have been reported in recent years, they have so far always used species carrying the electropositive substituent on the bridgehead, and it appears that oxidative addition of a metal center across a bridgehead-halogen bond in a bicyclo[1.1.1]pentane or a [n]staffane has not been accomplished. E.g., attempts to cross-couple bicyclo[1.1.1]pent-1-ylzinc chloride with 1-iodo-3-phenylbicyclo[1.1.1]pentane (**61**) were unsuccessful.²⁴⁹ Thus, the bridgehead-to-bridgehead cross-coupling of two different bicyclo[1.1.1]pentanes or [n]staffanes is an unsolved problem and remains as a synthetic challenge for the future.

Bridgehead lithium compounds may be converted into the corresponding organocuprates and reacted with alkyl iodides and enones.¹⁸⁰ Bicyclo[1.1.1]pent-1-yl cuprates give mostly 1,4-addition products while the organolithium derivatives yield mostly 1,2-adducts (Scheme 105).^{180,243} Coupling of the cuprates

Scheme 105



with acid chlorides yielded complex mixtures of products. Single addition products are the major components of the mixtures, but double addition products are also found in significant quantities.¹⁸⁰

Cross-coupling between bicyclo[1.1.1]pent-1-ylzinc chloride or bicyclo[1.1.1]pent-1-ylmagnesium bromide derivatives and haloarenes proceeds in the presence of Pd or Ni catalysts with yields ranging from good to excellent.^{49,241} The best yields for the Grignard reagents were achieved with dppeNiCl_2 and espe-

Scheme 106

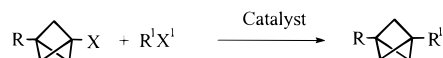
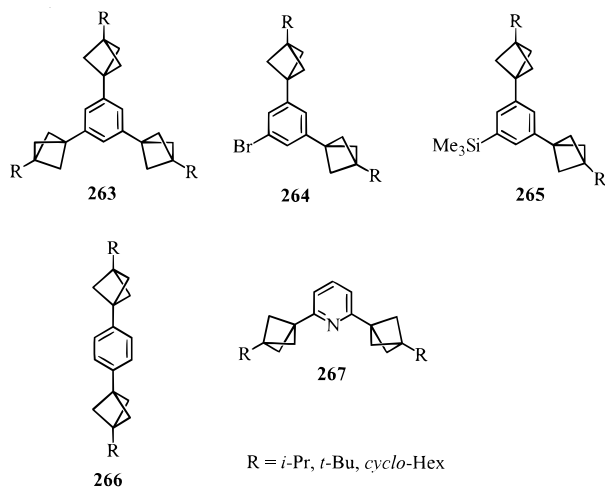


Table 36. Cross-Coupling Reactions of Bicyclo[1.1.1]pent-1-ylzinc Chloride and Bicyclo[1.1.1]pent-1-ylmagnesium Bromide Derivatives with Haloarenes (Scheme 106)

R	X	R ¹	X ¹	catalyst	yield (%)	ref
<i>i</i> -Pr	MgCl	4-Me ₃ SiC ₆ H ₄	Br	dppfPdCl ₂	91	49
<i>t</i> -Bu	MgCl	Ph	Br	dppfPdCl ₂	88	49
<i>t</i> -Bu	MgCl	3-furanyl	Br	dppfPdCl ₂	56	49
<i>t</i> -Bu	MgCl	2-pyridyl	Br	dppfPdCl ₂	48	49
<i>t</i> -Bu	MgCl	4-ClC ₆ H ₄	Br	dppfPdCl ₂	90	49
<i>t</i> -Bu	MgCl	4-CF ₃ C ₆ H ₄	Br	dppfPdCl ₂	98	49
<i>t</i> -Bu	MgCl	3-MeOC ₆ H ₄	Br	dppfPdCl ₂	87	49
<i>t</i> -Bu	MgCl	4-MeOC ₆ H ₄	Br	dppfPdCl ₂	97	49
<i>t</i> -Bu	MgCl	4-PhC ₆ H ₄	Br	dppfPdCl ₂	96	49
<i>t</i> -Bu	MgCl	2-naphthyl	Br	dppfPdCl ₂	93	49
<i>c</i> -Hex	MgCl	4-ClC ₆ H ₄	Br	dppfPdCl ₂	89	49
<i>c</i> -Hex	MgCl	4-Me ₃ SiC ₆ H ₄	Br	dppfPdCl ₂	96	49
Ph	MgBr	Ph	Br	dppfPdCl ₂	82	49
Ph	MgBr	4-ClC ₆ H ₄	Br	dppfPdCl ₂	87	49
Ph	MgBr	4-CF ₃ C ₆ H ₄	Br	dppfPdCl ₂	73	49
Ph	MgBr	3-pyridyl	I	dppfPdCl ₂	traces	241
Ph	MgBr	2-pyrimidyl	Br	dppfPdCl ₂	61	241
Ph	MgBr	1- <i>c</i> -octenyl	Br	dppfPdCl ₂	50	241
Ph	MgBr	<i>trans</i> -styryl	Br	dppfPdCl ₂	76	241
Ph	MgBr	5-pyrimidyl	I	dppfPdCl ₂	18	241
Ph	MgBr	Ph	I	dppeNiCl ₂	23	241
Ph	MgBr	4-FC ₆ H ₄	Br	dppeNiCl ₂	38	241
Ph	MgBr	4-MeC ₆ H ₄	I	dppeNiCl ₂	21	241
Ph	MgBr	3-pyridyl	I	dppeNiCl ₂	4	241
Ph	MgBr	2-pyrimidyl	Br	dppeNiCl ₂	35	241
Ph	MgBr	1- <i>c</i> -octenyl	Br	dppeNiCl ₂	11	241
4- <i>n</i> -PrC ₆ H ₄	MgBr	4-FC ₆ H ₄	Br	NiCl ₂ (PPh ₃) ₂	9	241
4- <i>n</i> -PrC ₆ H ₄	MgBr	4-CF ₃ C ₆ H ₄	Br	NiCl ₂ (PPh ₃) ₂	6	241
<i>n</i> -Pr	ZnCl	4-MeC ₆ H ₄	I	dppfPdCl ₂	86	241
<i>n</i> -Pr	ZnCl	Ph	I	dppfPdCl ₂	79	241
<i>n</i> -Pr	ZnCl	2-pyrimidyl	Br	dppfPdCl ₂	75	241
<i>n</i> -Pr	ZnCl	Ph	I	Pd(PPh ₃) ₄	14	241
<i>n</i> -Pr	ZnCl	4-CH ₃ C ₆ H ₄	I	Pd(PPh ₃) ₄	28	241
<i>n</i> -Pr	ZnCl	4-BrC ₆ H ₄	Br	dppfPdCl ₂	43	241
<i>n</i> -Bu	ZnCl	4-BrC ₆ H ₄	Br	dppfPdCl ₂	14	241
<i>n</i> -Bu	ZnCl	4-(4'-BrC ₆ H ₄)C ₆ H ₄	Br	dppfPdCl ₂	87 ^a	241
<i>n</i> -Bu	ZnCl	4-Me ₃ SiC ₆ H ₄	Br	dppfPdCl ₂	72	241
<i>n</i> -C ₈ H ₁₇	ZnCl	4-FC ₆ H ₄	Br	dppfPdCl ₂	43	241
<i>n</i> -C ₈ H ₁₇	ZnCl	4-CF ₃ C ₆ H ₄	Br	dppfPdCl ₂	68	241
<i>n</i> -C ₈ H ₁₇	ZnCl	4-NCC ₆ H ₄	Br	dppfPdCl ₂	75	241
<i>n</i> -C ₈ H ₁₇	ZnCl	4-[4'-(<i>n</i> -C ₈ H ₁₇)C ₆ H ₄]C ₆ H ₄	Br	dppfPdCl ₂	80	241
<i>n</i> -C ₈ H ₁₇	ZnCl	4-[5'-(<i>n</i> -C ₈ H ₁₇)C ₄ N ₂ H ₂]C ₆ H ₄ ^b	OTf	dppfPdCl ₂	63	241
<i>n</i> -C ₈ H ₁₇	ZnCl	4-[5'-(<i>n</i> -C ₈ H ₁₇ O)C ₄ N ₂ H ₂]C ₆ H ₄ ^b	OTf	dppfPdCl ₂	70	241
<i>n</i> -C ₈ H ₁₇	ZnCl	4-[2'-(<i>n</i> -C ₈ H ₁₇ O)C ₄ N ₂ H ₂]C ₆ H ₄ ^b	OTf	dppfPdCl ₂	79	241
<i>n</i> -C ₈ H ₁₇	ZnCl	4-BrC ₆ H ₄	Br	dppfPdCl ₂	61	241
THP-O(CH ₂) ₂ ^c	ZnCl	4-(4'-EtC ₆ H ₄)C ₆ H ₄	Br	dppfPdCl ₂	10	241
THP-O(CH ₂) ₃ ^c	ZnCl	4-(4'-EtC ₆ H ₄)C ₆ H ₄	Br	dppfPdCl ₂	61	241
THP-O(CH ₂) ₄ ^c	ZnCl	4-[4'- <i>cis</i> -(<i>trans</i> -2''-OEt- <i>c</i> -Pr)CH=CHC ₆ H ₄]C ₆ H ₄	Br	dppfPdCl ₂	48	241
Et-C≡C(CH ₂) ₂	ZnCl	4-BrC ₆ H ₄	Br	dppfPdCl ₂	39 ^d	241

^a Excess 3-*n*-butylbicyclo[1.1.1]pent-1-ylzinc chloride was used. ^b C₄N₂H₂ is pyrimidyl. ^c THP is 2-tetrahydropyranyl. ^d 4,4'-Bis(3-substituted bicyclo[1.1.1]pent-1-yl)biphenyl was obtained in 50% yield when excess 3-substituted bicyclo[1.1.1]pent-1-ylzinc chloride was used.

Chart 11

cially dppfPdCl₂ complexes (Scheme 106 and Table 36). The latter complex also proved to be an excellent

catalyst for the cross-coupling of the zinc-containing bicyclo[1.1.1]pentanes with bromo- and iodoarenes.²⁴¹ This methodology was used to prepare bis- and tris-bicyclo[1.1.1]pentane-substituted arenes **263–267** (Chart 11) from the corresponding di- and tribromoarene starting materials.⁴⁹

1-(Tri-*n*-butylstannyl)bicyclo[1.1.1]pentane was coupled with various benzoyl halides in the presence of Pd catalysts in modest yields (30–50%).²⁹⁵ Aryl iodides may also be used, but they produce even lower yields.

Bicyclo[1.1.1]pent-1-yl cuprates can be oxidatively coupled to give symmetrically substituted [*n*]staffanes in good yields (Scheme 107 and Table 37).²⁴⁹

Scheme 107

Table 37. Oxidative Coupling of Bicyclo[1.1.1]pent-1-yl Organometallic Reagents (Scheme 107)

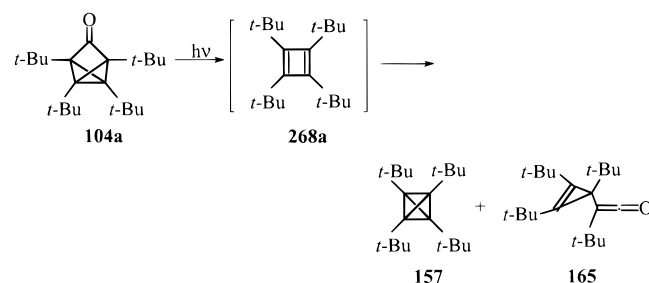
X	R	n	reagent	yield (%)	ref
I	Ph	1	NiCl ₂ (PPh ₃) ₂ or PdCl ₂ [P(<i>n</i> -Bu) ₃] ₂	20–40	249
I	Ph	1	1. CuI(PPh ₃) ₂ ; 2. <i>p</i> -C ₆ H ₄ (NO ₂) ₂	66	249
I	Hex ₃ SiC ₂ B ₁₀ ^a	1	1. CuI(PPh ₃) ₂ ; 2. <i>p</i> -C ₆ H ₄ (NO ₂) ₂	65	249
Br	SiMe ₃	2	1. CuI(PPh ₃) ₂ ; 2. <i>p</i> -C ₆ H ₄ (NO ₂) ₂	28	249
I ^b	CH ₂ Cl ^b	1	1. CuI(PPh ₃) ₂ ; 2. <i>p</i> -C ₆ H ₄ (NO ₂) ₂	70	249

^a 12-(Tri-*n*-hexylsilyl)-1,12-dicarba-*clos*o-dodecaboran-1-yl.
^b 2,4-Ethanobicyclo[1.1.1]pentane derivative.

6. Photochemical Rearrangements

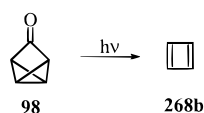
Photochemistry of tricyclo[2.1.0.0^{2,5}]pentan-3-ones has been studied in detail since these compounds are precursors for cyclobutadiene and tetrahedrane derivatives.^{200,296} Photochemical extrusion of CO from 1,2,4,5-tetra-*tert*-butyltricyclo[2.1.0.0^{2,5}]pentan-3-one (**104a**) yields tetra-*tert*-butyltetrahedrane (**157**) and the ketene **165** (Scheme 108).^{200,206} Tetra-*tert*-

Scheme 108

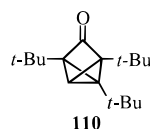


butylcyclobutadiene **268a** is an intermediate in this reaction.²⁰⁶ 1,2,4-Tri-*tert*-butyltricyclo[2.1.0.0^{2,5}]pentan-3-one (**110**) is photochemically stable, while tricyclo-

Scheme 109

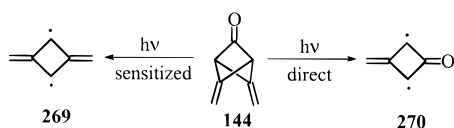


[2.1.0.0^{2,5}]pentan-3-one (**98**) gives only cyclobutadiene (**268b**) upon irradiation (Scheme 109).²⁰⁰



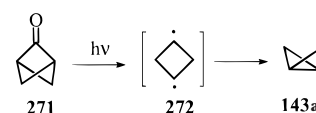
4,5-Dimethylenebicyclo[1.1.1]pentan-2-one (**144**) yields two types of 1,3-cyclobutanediyl radicals upon irradiation at 10 K in a matrix: **269** and **270** (Scheme 110).²⁹⁷ Irradiation of bicyclo[1.1.1]pentan-2-one (**271**)

Scheme 110



leads to bicyclo[1.1.0]butane (**143a**) as the principal product in either gas or condensed phase (Scheme 111).¹⁹¹ The reaction probably proceeds via a 1,3-cyclobutanediyl diradical (**272**). Even at low temper-

Scheme 111

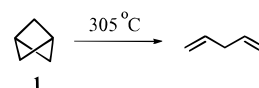


ature no EPR signal attributable to this diradical could be observed, but this is not surprising, as only substituted biradicals of this type have ever been observed in matrix isolation, but not the parent itself.²⁹⁸

7. Thermal Rearrangements

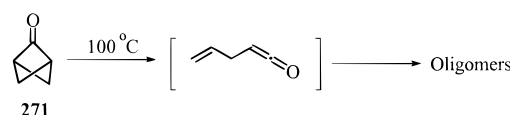
a. Bicyclo[1.1.1]pentanes. Heating of the vapor of **1** at 305 ± 2 °C for 9 h resulted in 50% conversion into 1,4-pentadiene (Scheme 112).¹⁶⁰ Bicyclo[1.1.1]-

Scheme 112



pentan-2-one (**271**) is significantly less stable and decomposes readily at 100 °C (Scheme 113).¹⁹¹ The

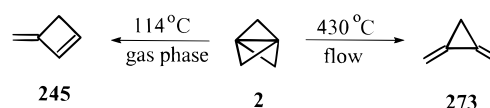
Scheme 113



activation energies for rearrangement of **1** and **271** are 49.0²³⁰ and 28.6¹⁹¹ kcal/mol, respectively.

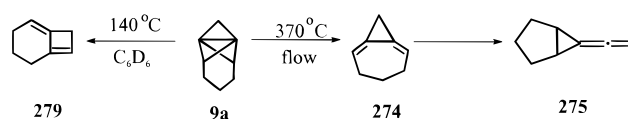
b. [1.1.1]Propellanes. Thermal decomposition of [1.1.1]propellanes has given different products depending on the conditions. In a static gas system at 114 °C, [1.1.1]propellane (**2**) rearranged to 3-methylenecyclobutene **245** (Scheme 114) with a half-life

Scheme 114



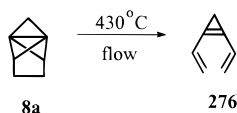
time of 5 min.² In a flow system, gas-phase pyrolysis of the [1.1.1]propellanes **2**, **8a,b**, and **9a,b** yielded the products **273–278**, all of which retain the [1.1.1]-propellane central bond (Schemes 114–118).^{22,23} Not surprisingly, the temperature required is much higher than in a static system or in solution and varies from 370 to 430 °C.²² In a sealed tube at 140 °C, 2,4-trimethylene[1.1.1]propellane (**9a**) decomposes completely in 30 min in benzene-*d*₆ to yield bicyclo[4.2.0]octa-1,6-diene (**279**, Scheme 115), and in 9 h in

Scheme 115

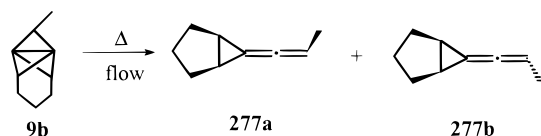


pyridine-*d*₅ to yield polymeric products only.²² It appears that the products containing the methylenecyclobutene motif are formed by an electrophile-catalyzed rearrangement.

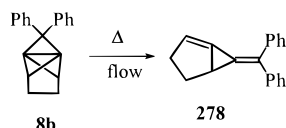
Scheme 116



Scheme 117

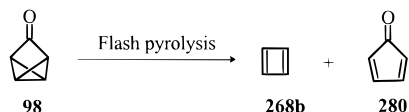


Scheme 118



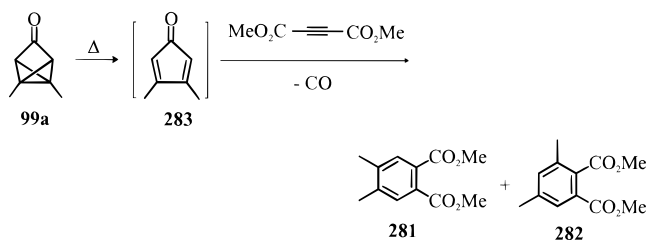
c. Tricyclo[2.1.0.0^{2,5}]pentanes. Flash pyrolysis of tricyclo[2.1.0.0^{2,5}]pentan-3-one (**98**) in a supersonic jet expansion nozzle yields the parent cyclobutadiene (**268b**) along with some amount of cyclopentadienone (**280**, Scheme 119).²⁶

Scheme 119



Pyrolysis of 1,5-dimethyltricyclo[2.1.0.0^{2,5}]pentan-3-one (**99a**) in the presence of dimethyl acetylenedicarboxylate yields the substituted phthalic esters **281** and **282**, and it has been proposed that they result from the trapping of transient cyclopentadienone **283** with concomitant CO extrusion (Scheme 120).²⁹⁹ A

Scheme 120

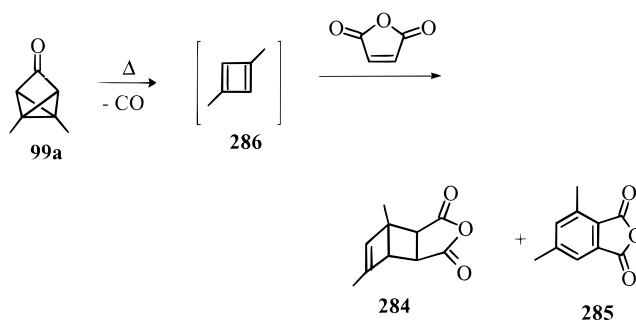


similar reaction with maleic anhydride yields a mixture of **284** and **285**, and it has been proposed to proceed via the cyclobutadiene intermediate **286** (Scheme 121).³⁰⁰ It now appears likely that the product **282** results from a similar process.

C. Transformations Involving an Adjacent Reactive Center

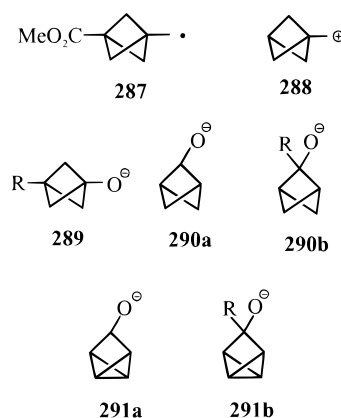
Upon moving the reaction center to a carbon or a heteroatom separated from the bicyclo[1.1.1]pentane cage by one bond, reactivity is changed dramatically, as the properties of reactive intermediates with an adjacent reactive center are no longer affected so significantly by bridgehead-bridgehead interactions. The adjacent reactive center interacts primarily with the two or three proximate endocyclic bonds, and the

Scheme 121



properties of the reactive intermediates are similar to those of the corresponding cyclobutylmethyl reactive intermediates. Reactive intermediates **287**–**291** are shown in Chart 12.

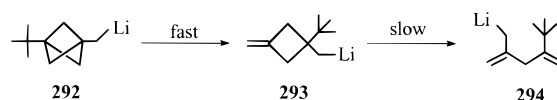
Chart 12



1. Reactions Involving A Reactive Center on Carbon

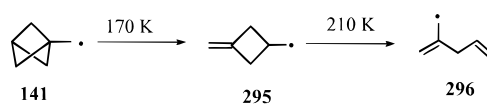
Like the cyclobutylcarbinyl anion and in contrast to bicyclo[1.1.1]pentyl anions, the bicyclo[1.1.1]pent-1-ylcarbinyl anion is not stable.^{301,302} The half-life time of [(3-*tert*-butylbicyclo[1.1.1]pent-1-yl)methyl]lithium (**292**) in pentane/diethyl ether solution is less than 15 min at -131 °C.³⁰³ The initially formed cyclobutylcarbinyl anion **293** undergoes further, somewhat slower, rearrangement to the 1,4-pentadiene derivative **294** (Scheme 122).³⁰³

Scheme 122



Bicyclo[1.1.1]pent-1-ylcarbinyl radical (**141**) rearranges readily in a similar way via β -scission even at low temperatures (>170 K, Scheme 123). Two

Scheme 123

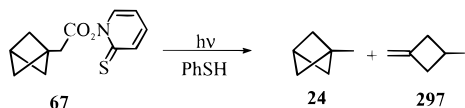


measurements of activation energy for the rearrangement, by EPR³⁰⁴ and in trapping experiments,³⁰⁵ gave very similar values: 7.1 ± 1.2 and 7.79 ± 0.35 kcal/mol, respectively. This is in a reasonably good agreement with the value of 11.2 kcal/mol

calculated at the UHF/6-31G* level of theory.³⁰⁴ For the 3-carboxymethyl-substituted radical **287** (Chart 12) the experimental activation energy for the rearrangement is less than 5 kcal/mol.³⁰⁶ At a higher temperature (>210 K), the primary 3-methylenecyclobutylmethyl radical (**295**) product rearranges further into the 2-allylallyl radical (**296**).^{304,305}

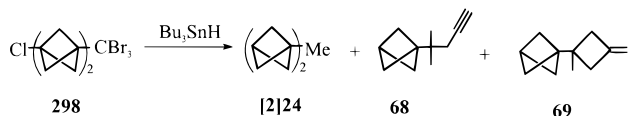
Photochemical decomposition of the Barton ester **67** in the presence of thiophenol as a hydrogen donor produced a mixture of 1-methylbicyclo[1.1.1]pentane (**24**) and the ring-opened 3-methylmethylenecyclobutane **297** in a ratio about 3:1 (Scheme 124).³⁰⁵

Scheme 124



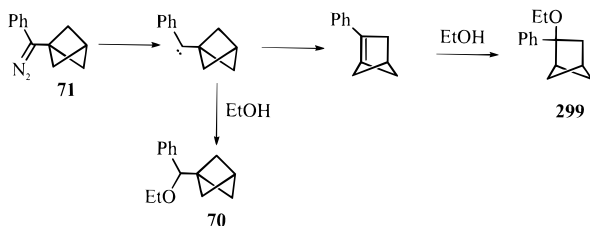
Reduction of 3-chloro-3'-(tribromomethyl)[2]staffane (**298**) with *n*-Bu₃SnH only afforded a moderate yield of 3-methyl[2]staffane (**24**) along with much higher yields of two rearranged products **68** and **69** (Scheme 125).²⁶⁶

Scheme 125



A string of rearrangements is initiated by generating a carbene next to the bridgehead carbon.^{180,307} Both rearranged (**299**) and unrearranged (**70**) products are trapped by ethanol after the carbene is generated from phenylbicyclo[1.1.1]pentyl diazoalkane (**71**, Scheme 126).¹⁸⁰

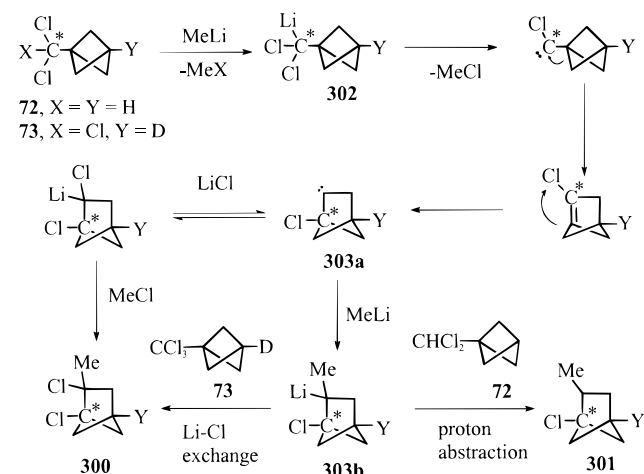
Scheme 126



1-(Dichloromethyl)bicyclo[1.1.1]pentane (**72**) has been converted into mixtures of bicyclo[2.1.1]hexanes (**300** and **301**) upon treatment with MeLi. Under similar conditions, 1-(trichloromethyl)bicyclo[1.1.1]pentane (**73**) yields primarily the bicyclo[2.1.1]hexane **300**. A mechanism involving two bond-breaking and two bond-forming steps has been proposed for the conversion of the isotopically labeled **73** into **300** (Scheme 127).³⁰⁷

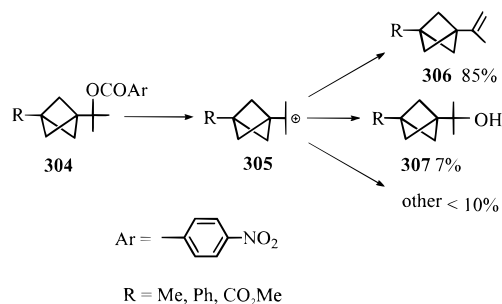
Metalation of the bicyclo[1.1.1]pentane **72** with MeLi presumably would lead to the unlabeled carbenoid **302**, which would rearrange into the carbene **303a**. The latter may add MeLi with formation of **303b**, which abstracts the acidic proton from bicyclo[1.1.1]pentane **72** to form **301** instead of exchanging Li for Cl to yield **300**.³⁰⁷

Scheme 127



We have found no reports of studies of the unsubstituted bicyclo[1.1.1]pent-1-ylmethyl cation (**288**, Chart 12). The first-order rate constants for the solvolysis of the *p*-nitrobenzoates **304** in 80% acetone have been measured.²¹⁸ The esters solvolyze much faster than the corresponding methyl ester but more slowly than a typical tertiary ester. The difference is attributed to the influence of the hybridization of the bridgehead carbon one bond away on the stability of the transient cation **305**. The solvolysis of the esters produced the olefins **306** as the major product, the alcohols **307**, and only about 10% of rearranged products (Scheme 128). All the evidence suggests that the alkyl-oxygen (S_N1) solvolysis mechanism is operative.

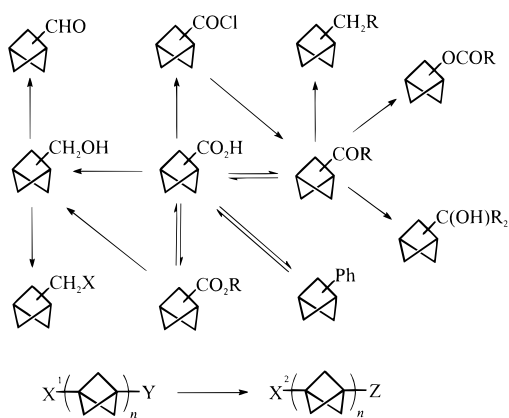
Scheme 128



Synthetically useful functional group transformations of bicyclo[1.1.1]pentanes involving a reactive center on a carbon one bond away from the cage usually involve oxygen-substituted starting materials and intermediates. The bicyclo[1.1.1]pentane cage is preserved in these reactions. Interconversion of different carbon-containing functional groups bound to the bicyclo[1.1.1]pentane skeleton is shown in Table 38 and Scheme 129.

Almost all of those transformations involve carboxylic acids and their derivatives, either as a starting material or as a product, and anionic intermediates. The carboxylic acids can be obtained by oxidation of arylbicyclo[1.1.1]pentanes with RuO₂/NaIO₄ or RuO₂/NaOCl, or with ozone,^{20,58,173,218,239} and by haloform reaction of acetylbicyclo[1.1.1]pentanes.^{20,185,274} Esters of the acids can be hydrolyzed under relatively mild conditions into acids, and in the case of 1,3-

Scheme 129



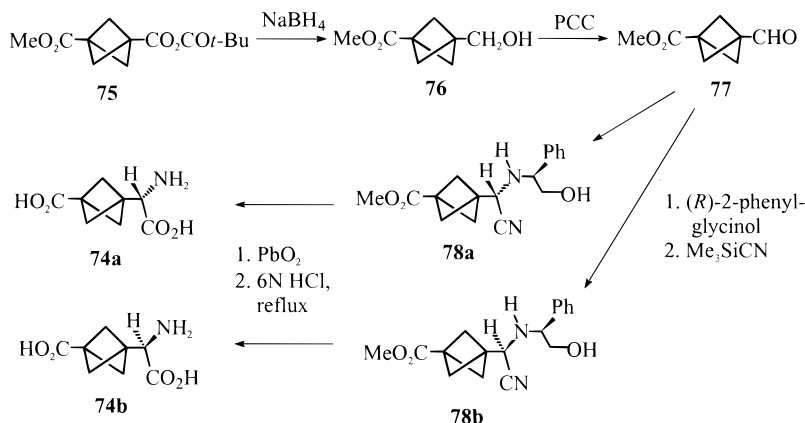
diesters protocols for a selective partial hydrolysis on one side of the cage have been developed.^{97,185} The resulting monoacid monoesters are valuable precursors for the synthesis of unsymmetrically 1,3-disubstituted bicyclo[1.1.1]pentanes.

Bicyclo[1.1.1]pentanecarboxylic acids can be esterified through conversion into acid chlorides with thionyl chloride or under milder conditions upon treatment with DCC/DMAP. Methyl esters and acid chlorides are successfully converted into amides with aqueous solutions of ammonia^{46,239} and ammonium chloride.¹⁶¹

Bicyclo[1.1.1]pentanecarboxylic acids,³⁰⁴ their esters,¹⁸⁶ and mixed anhydrides with pivalic acid³⁰⁸ are reduced to methyl alcohols with lithium aluminum hydride^{186,294} or sodium borohydride.³⁰⁷ *tert*-Butyl esters are less reactive toward reduction, and only the methoxycarbonyl group is reduced in a mixed methyl *tert*-butyl bicyclo[1.1.1]pentane-1,3-dicarboxylate.¹⁸⁶ A reaction of bicyclo[1.1.1]pentane-1-carboxylic acid (**14**) with MeLi and PhLi yielded corresponding methyl and phenyl ketones, while acid chlorides are successfully converted into ketones with diethylzinc.

Optically active amino acids **74a** and **74b** containing the bicyclo[1.1.1]pentane moiety were obtained starting with the mixed anhydride **75** (Scheme 130). The anhydride was reduced to the alcohol **76**, which was selectively oxidized to the aldehyde **77**. The

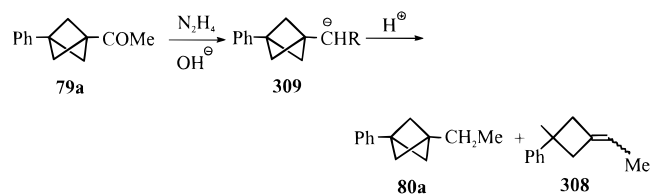
Scheme 130



aldehyde was converted into the α -aminonitrile diastereomers **78a** and **78b**. The latter were separated and converted separately into the α -amino acids **74a** and **74b**.³⁰⁸

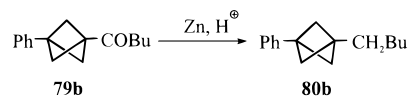
Wolff–Kishner reduction of the ketone **79a** yields the desired product **80a** (53%) and the olefin **308** (8%, Scheme 131).³⁰⁹ The olefin is formed as a result of a

Scheme 131



rearrangement of the transient carbanion **309**. In contrast, Clemmensen reduction of the ketone **79b** gave a much better yield (84%) of the desired hydrocarbon **80b** (Scheme 132).³¹⁰

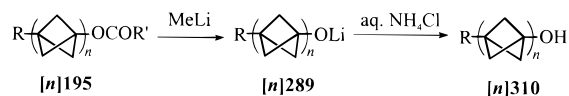
Scheme 132



2. Reactions Involving a Reactive Center on Oxygen

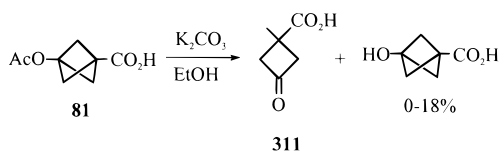
Bicyclo[1.1.1]pent-1-yloxy (**289**, Chart 12), bicyclo[1.1.1]pent-2-yloxy (**290a,b**), and tricyclo[2.1.0.0]pent-3-yloxy (**291a,b**) anions are involved in a number of reactions. Basic cleavage of the esters [**n**]195, involving the bridgehead oxyanions [**n**]289, is a convenient way to prepare the bicyclo[1.1.1]pentan-1-ols [**n**]310 (Scheme 133).^{77,91,267} However, the reaction must be

Scheme 133

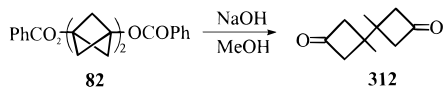


performed under aprotic conditions, and MeLi should be used.⁷⁷ The alcohols are isolated by quenching of [**n**]289 with aqueous ammonium chloride.

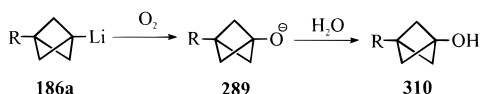
Basic hydrolysis of the bridgehead esters **81**²¹⁸ and

Scheme 134

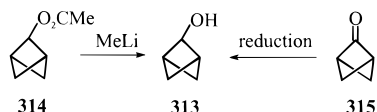
82⁹¹ in protic solvents produces the ring-opened products **311** and **312** (Schemes 134 and 135).

Scheme 135

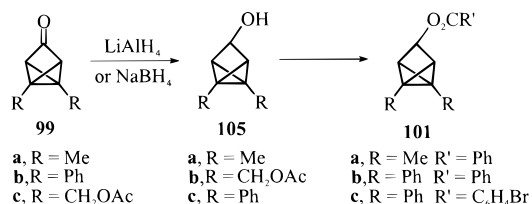
Oxidation of bicyclo[1.1.1]pent-1-yllithium derivatives (**186a**) is another convenient way to bicyclo[1.1.1]pentan-1-ols **310** via the oxyanion **289** (Scheme 136).^{180,243} The relevant reactions are listed in Table 30 (see section IV.B.1).

Scheme 136

Bicyclo[1.1.1]pentan-2-ol (**313**) is generated via the corresponding O-anion by methyllithium cleavage of bicyclo[1.1.1]pentan-2-ol acetate (**314**)⁷⁷ and by reduction of bicyclo[1.1.1]pentan-2-one (**315**, Scheme 137).¹⁹¹ Tricyclo[2.1.0.0^{2,5}]pentan-3-ones **99a–c** are

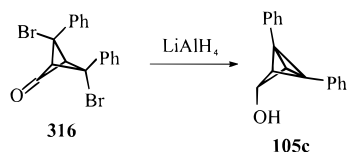
Scheme 137

smoothly reduced^{128,290,311,312} to the corresponding tricyclo[2.1.0.0^{2,5}]pentan-3-ols (**105a–c**, Scheme 138).

Scheme 138

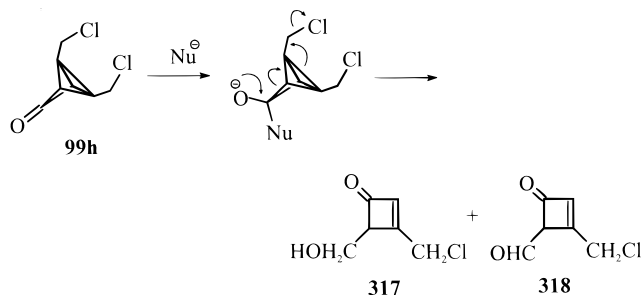
The latter may be converted into the esters **101**.^{290,312}

The reduction of the dibromoketone **316** is complicated by an elimination–cyclization process leading to the tricyclic alcohol **105c** (Scheme 139).³¹² These

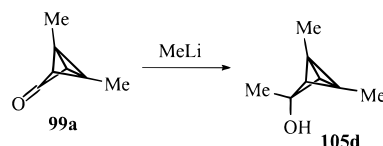
Scheme 139

reactions provide evidence that the anions **290a** and **291a** are rather stable.

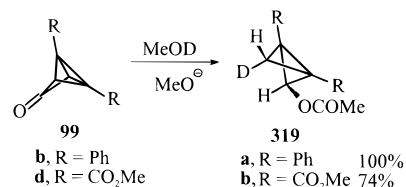
Thus, only the cyclobutenones **317** and **318** were isolated upon attempted reduction of the bis(chloromethyl)ketone **99h**, and their formation was rationalized as due to Grob fragmentation (Scheme 140).³¹¹

Scheme 140

Nevertheless, the reaction of the ketone **99a** with MeLi yields the alcohol **105d** (Scheme 141).¹³⁰

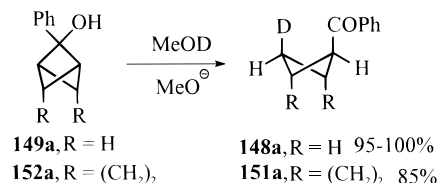
Scheme 141

In contrast to the relatively straightforward reduction of tricyclo[2.1.0.0^{2,5}]pentan-3-ones **99** by the addition of a hydride anion, an attack of a methoxide anion on these compounds causes only ring cleavage and produces the methyl bicyclo[1.1.0]butane-2-carboxylates **319** (Scheme 142).^{311,312} Experiments per-

Scheme 142

formed in deuterated solvents have shown 100% incorporation of deuterium syn to the ester group and, thus, full retention of configuration.^{311,312}

Like the ketones **99**, the 2-phenylbicyclo[1.1.1]pentan-2-ols **149a** and **152a** are also very sensitive to base. A catalytic amount of sodium methoxide in methanol completely cleaves the alcohols within 30 min to 3 h at room temperature to form exclusively the phenyl cyclobutyl ketones **148a** and **151a** (Scheme 143).^{194,286,313} Thus the methanolysis represents a

Scheme 143

synthetic reversal of the photochemical ring closure.

Table 38. Interconversion of Functional Groups Involving a Reactive Center One Carbon Away from the Bicyclo[1.1.1]pentane Cage (Scheme 129)

X ¹	Y	reagent	X ²	Z	yield	ref
Oxidation of Carbon-Containing Substituents, Ru Catalyzed						
H	CHMe(OEt) ^a	RuO ₂ , NaOCl	H	CO ₂ H	16, 11, 5, 3, 2 ^b	20
			H	CHMe(OAc)	<i>c, d</i>	
			H	COMe	<i>c, d</i>	
COPh	COPh ^a	RuO ₂ , NaOCl	CO ₂ Me ^e	CO ₂ Me ^e	4.5, 2.7, 0.7, 0.1 ^b	20
			COPh	CO ₂ Me ^e	<i>c, d</i>	
CN	Ph	RuO ₂ , NaOCl	CN	CO ₂ H	56	218
CO ₂ Me	Ph	RuO ₂ , NaOCl	CO ₂ Me	CO ₂ H	62	218
CO ₂ Me ^f	Ph ^f	RuO ₂ , NaOCl	CO ₂ Me ^f	CO ₂ H ^f	<i>d, g</i>	20
CO ₂ Me ^h	Ph ^h	RuO ₂ , NaOCl	CO ₂ Me ^h	CO ₂ H ^h	0 ^g	20
¹³ CO ₂ Me	Ph	RuCl ₃ , KIO ₄	¹³ CO ₂ Me	CO ₂ H	83	248
NO ₂	Ph	RuO ₂ , NaOCl	NO ₂	CO ₂ H	44	218
OCOMe	Ph	RuO ₂ , NaOCl	OCOMe	CO ₂ H	52	218
			OH	CO ₂ H	0–18	
SiMe ₃	Ph	RuCl ₃ , NaIO ₄	SiMe ₃	CO ₂ H	74	239
SnMe ₃	Ph	RuCl ₃ , NaIO ₄	Cl	CO ₂ H	<i>d</i>	239
Haloform Oxidation of Methyl Ketones						
<i>n</i> -Bu ⁱ	COMe ⁱ	NaOBr	<i>n</i> -Bu ⁱ	CO ₂ H ⁱ	80 ⁱ	20
Ph	COMe ^a	NaOBr	Ph	CO ₂ Me ^e	3.9, 1.8, 0.8, 0.7 ^b	20
COMe	COMe	NaOBr	CO ₂ H	CO ₂ H	68	185, 274
COMe ^f	COMe ^f	NaOBr	CO ₂ H ^f	CO ₂ H ^f	88	20
<i>n</i> -C ₅ H ₁₁	COMe	NaOBr	<i>n</i> -C ₅ H ₁₁	CO ₂ H	88	355
<i>j</i>	COMe	NaOBr	<i>j</i>	CO ₂ H	30 ^k	91
Other Oxidations						
CO ₂ H	Ph	O ₃	CO ₂ H	CO ₂ H	62	58
CO ₂ Me	CH ₂ OH	PCC	CO ₂ Me	CHO	16 ^k	308
Reactions of Carboxylic Acid Derivatives with Organometallic Reagents						
H	CO ₂ H	MeLi	H	COMe	<i>d</i>	173
D	CO ₂ H	MeLi	D	COMe	<i>d</i>	173
Me	CO ₂ H	MeLi	Me	COMe	51	218
Ph	CO ₂ H	MeLi	Ph	COMe	89	218
CO ₂ H	CO ₂ Me	MeMgBr	CO ₂ Me ^f	C(OH)Me ₂	33	218
H	COCl	Et ₂ Zn	H	COEt	55	77
Addition of Methylolithium to Carbonyl Derivatives						
Me	COMe	MeLi	Me	C(OH)Me ₂	69	218
Ph	COMe	MeLi	Ph	C(OH)Me ₂	88	218
Reduction of Carboxylic Acid Derivatives						
H	CO ₂ H	LiAlH ₄	H	CH ₂ OH	98	304
H ^f	CO ₂ H ^f	LiAlH ₄	H ^f	CH ₂ OH ^f	<i>d</i>	159
H	CO ₂ H	LiAlD ₄	H	CD ₂ OH	37	173
CO ₂ Me	CO ₂ CO- <i>t</i> -Bu	NaBH ₄	CO ₂ Me	CH ₂ OH	16 ^l	308
Reduction of Ketones ^m						
Ph	COMe	N ₂ H ₄ , OH ⁻	Ph	CH ₂ Me	53	309
Ph	COBu	Zn, H ⁺	Ph	CH ₂ Bu	84	310
Nucleophilic Substitution						
H	CH ₂ OTs	LiBr	H	CH ₂ Br	75	304
H	CH ₂ OTs	LiBr	H	CH ₂ Br	<i>d</i>	159

^a A crude mixture of oligomers has been used. ^b Yields of [*n*]staffanes are given in the sequence *n* = 1, 2, Yields are based on **174**, a precursor to [1.1.1]propellane. ^c Isolated intermediate products. ^d Not reported. ^e Products have been separated and characterized as methyl esters, which have been obtained upon subsequent treatment of the mixture of primary products with diazomethane. ^f [2]Staffane derivatives. ^g Very slow conversion. ^h [3]Staffane derivatives. ⁱ The reaction has been performed separately for [1]-, [2]-, and [3]staffane derivatives. The average yield for different oligomers is listed. ^j 3-[2-(3-*n*-pentylbicyclo[1.1.1]pent-1-yl)ethyl]bicyclo[1.1.1]pent-1-yl. ^k The yield is based on a precursor to the starting material listed. ^l The yield of a subsequent product is based on a precursor to the starting material listed. ^m For a discussion of a proposed mechanism see section IV.C.1.

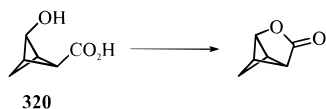
A reaction run in methanol-*d* revealed a competition between two mechanisms for the formation of the product, involving the protonation of the intermediate carbanion either by the solvent or intramolecularly by a 1,3-H shift. The distribution of deuterium has shown that both mechanisms contribute to the course of the highly stereospecific reaction almost equally.²⁸⁶

Attempts to alkylate the O-anion by metalation of the alcohol **149a** with alkyllithiums in hexanes at -78 °C followed by methylation with methyl iodide or dimethyl sulfate were unsuccessful, and only

phenylcyclobutyl ketone was isolated.²⁸⁶ Apparently, the base-induced cleavage of the bicyclo[1.1.1]pentane system is much faster than O-methylation. It may be noted that in contrast to the lithium salts of **149a** and **152a**, the lithium salt of the parent bicyclo[1.1.1]pentan-2-ol is stable in aprotic solvents.⁷⁷ The reaction appears to be similar to the ring opening of other strained alcohols,³¹⁴ and the driving force probably is the relief of strain in the transition state for ring opening.

Formation of esters^{91,195,218,267,286,290} and an urethane³³ from alcohols represents another set of clas-

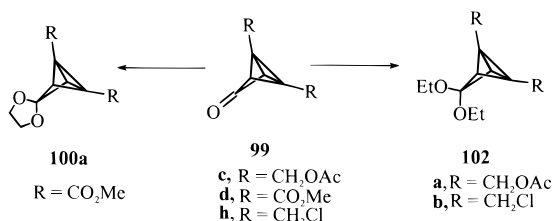
Scheme 144



sical nucleophilic reaction of the alcoholate oxygen. The reactions of these rather hindered and presumably not very nucleophilic alcohols are slow, and reactivity enhancement by conversion to the O-anions is required.⁹¹ However, a theoretical consideration^{315,316} of an acid-catalyzed lactonization process in *syn*-2-hydroxybicyclo[1.1.1]pentane-4-carboxylic acid (**320**, Scheme 144) led to the prediction of relatively high rate constant (95 M⁻¹ min⁻¹) for the reaction.

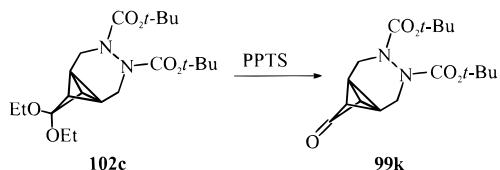
The ketones **99** are converted into the ketals **100a** and **102a,b** under acidic conditions (Scheme 145).^{36,72,171} The tetracyclic ketone **99k** is recovered

Scheme 145



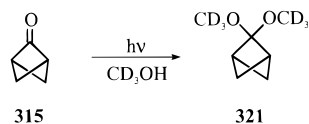
from the ketal **102c** by reaction with acetone in the presence of pyridinium *p*-toluenesulfonate (Scheme 146).¹⁷¹ Transformation of ketones into ketals has a

Scheme 146



pronounced effect on molecular geometry of the tricyclic cage.⁶⁵ The ketal **321** is formed upon irradiation of the ketone **315** in the absence of base (Scheme 147).¹⁹¹

Scheme 147

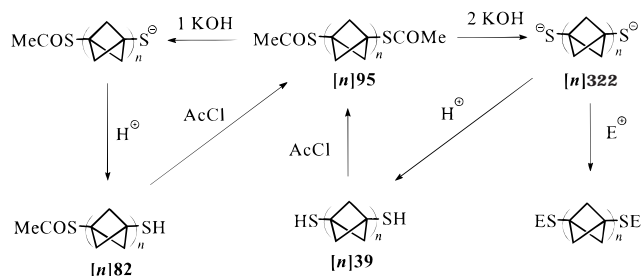


The unstable 3-arylthiobicyclo[1.1.1]pent-1-yloxy radical is presumed to be an intermediate in the formation of a rearranged product by addition of the weakly nucleophilic 2-nitrophenylsulfenyl chloride to [1.1.1]propellane (**2**) in the presence of air (see section IV.B.2.b.iii).²⁷²

3. Reactions Involving A Reactive Center on Sulfur

Bridgehead *n*]staffanedithiols (**[n]39**) have been generated via the corresponding thiolate dianions **[n]-322** by lithium/diethylamine cleavage of 3,3'-bis-methylthio[*n*]staffanes (**[n]30b**, see section IV.B.1.a)⁴¹

Scheme 148



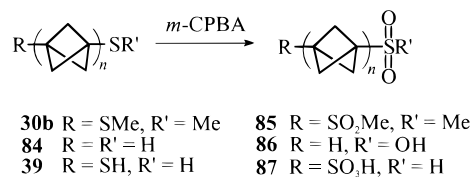
and, more conveniently, by the basic hydrolysis of the readily accessible 3,3'-bis(acetylthio)[*n*]staffanes (**[n]-95**, Scheme 148).^{6,20,269} Partial hydrolysis on one thioester group can be carried out selectively on the monomer **[n]95**.^{20,317} Partial hydrolysis of higher oligomers with a controlled amount of base yields statistical mixtures of dithiols **[n]39**, monothio-monothioesters **[n]83**, and unhydrolyzed **[n]95**, which can be separated by sublimation.^{20,317} The thiols **[n]-39** and **[n]83** may be converted back into the bithioacetate **[n]95** with acetyl chloride.

Unlike the corresponding alcoholates, thiolates did not show any tendency to rearrange. The difference between behavior of alcoholates and thiolates in protic solvents is presumably related to the differences in the strength of the C=O and C=S bonds, whose formation provides the thermodynamic driving force for the former reaction.

The anions **322** react with electrophiles (butyl iodide, the diphenylchloronium cation, and benzoquinone), giving the expected products in good yields.^{6,20,163,269}

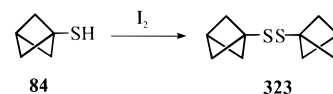
The bridgehead bicyclo[1.1.1]pentyl sulfides **30b**, thiols **84**, and *n*]staffanedithiols **[n]39** with *n* = 1–4 are oxidized to corresponding sulfone **85**¹⁷⁹ and sulfonic acids **86** and **87** (Scheme 149).³¹⁸ Bicyclo[1.1.1]-

Scheme 149



pent-1-ylthiol (**84**) is oxidized to the corresponding disulfide **323** with iodine in good yield (Scheme 150).¹¹⁴

Scheme 150



4. Reactions Involving a Reactive Center on Nitrogen

Bicyclo[1.1.1]pent-1-ylamines and bicyclo[1.1.1]pent-2-ylamines (**324**) may be oxidized to nitro compounds with *m*-chloroperbenzoic acid (Scheme 151 and Table 39). Amine **88** is oxidized to the azodioxide

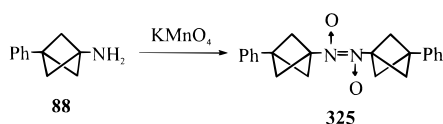
Table 39. Oxidation of Bicyclo[1.1.1]pentylamines into Nitrobicyclo[1.1.1]pentanes (Scheme 151)

position ^a	R	reagent	yield (%)	ref
1	H	<i>m</i> -ClC ₆ H ₄ CO ₂ H	<i>b</i>	77
2	H	<i>m</i> -ClC ₆ H ₄ CO ₂ H	24	78
1	Me	<i>m</i> -ClC ₆ H ₄ CO ₂ H	<i>b</i>	278
1	¹³ CH ₃	<i>m</i> -ClC ₆ H ₄ CO ₂ H	<i>b</i>	278
1	Ph	<i>m</i> -ClC ₆ H ₄ CO ₂ H	72	218

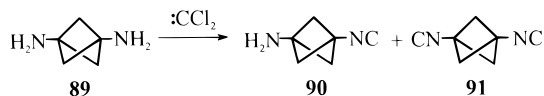
^a Position on the bicyclo[1.1.1]pentane cage of the NH₂ group in the substrate and that of the NO₂ group in the product.
^b Yield was not reported.

Scheme 151

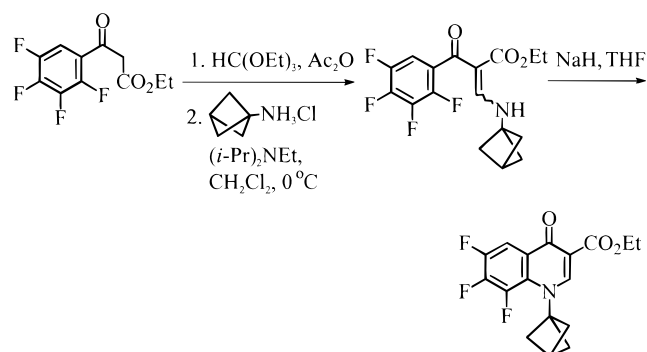
325 (Scheme 152).³¹⁹ Reaction of 1,3-bicyclo[1.1.1]-

Scheme 152

pentanediamine (**89**) with dichlorocarbene under phase transfer conditions yielded the isonitriles **90** and **91** (Scheme 153).⁴⁶

Scheme 153

Amines **15** and **324** are weakly nucleophilic, presumably due to an enhanced electronegativity of the cage carbons (see section II.B.1.d). To the best of our knowledge only one example of successful arylation of bicyclo[1.1.1]pentylamine has been reported (Scheme 154).³²⁰

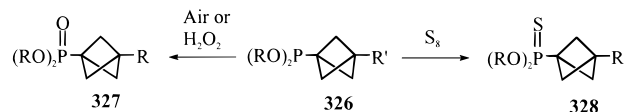
Scheme 154

5. Reactions Involving a Reactive Center on Phosphorus

Only two types of reactions have been reported so far for 1-phosphitobicyclo[1.1.1]pentanes, Arbuzov-type addition^{20,270} and oxidation.^{20,180,270} The former is observed in the course of [1.1.1]propellane insertion

into the P–P bond of tetraethyl hypophosphite as the initially formed 1:1 adduct **58** is partially converted into an alternating co-oligomer **224** after oxidation with air (see section IV.B.2.b.iii).²⁰

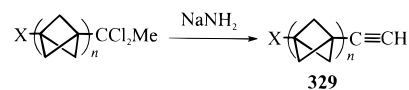
Oxidation of 1-phosphitobicyclo[1.1.1]pentanes **326** into phosphonates **327** occurs very easily with air^{20,180} or with hydrogen peroxide²⁷⁰ (Scheme 155), and

Scheme 155

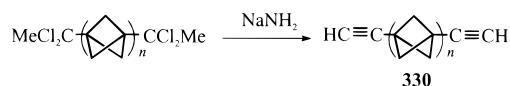
special precautions should be taken to avoid it if the unoxidized product is desired.²⁷⁰ Treatment with S₈ yielded thiophosphonate derivatives **328**.²⁷⁰

D. Transformation Involving a Remote Reaction Center

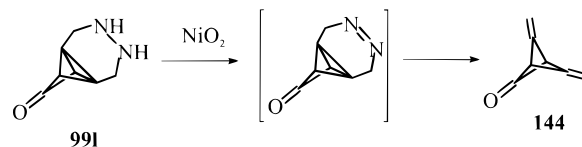
The influence of the bicyclo[1.1.1]pentane cage on a remote reactive center diminishes very fast with the increasing number of intervening bonds, and the reactive intermediates then behave as if they were not attached to the cage. Several examples of reactions in which an initial attack occurs on a remote center but the reaction site moves closer to the

Scheme 156

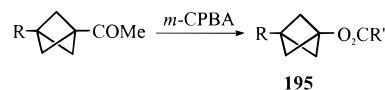
bicyclo[1.1.1]pentane cage include the synthesis of bridgehead acetylenes **329** and **330** (Schemes 156 and 157).^{138,244,261} and oxidation of the hydrazine **991** into

Scheme 157

a 4,5-dimethylenebicyclo[1.1.1]pentan-2-one (**144**, Scheme 158).¹⁷¹ Baeyer–Villiger oxidation of bicyclo-

Scheme 158

[1.1.1]pent-1-yl ketones with *m*-chloroperbenzoic acid,^{91,173,218,239,267,278} trifluoroperacetic acid,¹⁸⁰ or hydrogen peroxide in acetic acid^{20,91,267} gives esters of corresponding bicyclo[1.1.1]pentan-1-ols (**195**) almost exclusively and in good to excellent yields (Scheme 159 and Table 40). Curtius,⁴⁶ Schmidt,^{77,78,218,278} and

Scheme 159

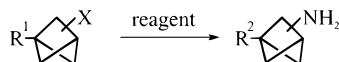
Hofmann¹⁸¹ rearrangements of bridgehead and bridge carboxylic acid derivatives yield the corresponding

Table 40. Baeyer–Villiger Oxidation of Bicyclo[1.1.1]pentyl Ketones (Scheme 159)

X ¹	Y	reagent	X ²	Z	yield	ref
H	COMe	MCPBA	H	OCOMe	<i>a</i>	173
H	CO- <i>t</i> -Bu	CF ₃ CO ₂ OH	H	OCO- <i>t</i> -Bu	<i>a, b</i>	180
			H	CO ₂ - <i>t</i> -Bu	<i>a, b</i>	
Me	COMe	MCPBA	Me	OCOMe	<i>a</i>	278
Ph	COMe	MCPBA	Ph	OCOMe	82	218
COPh ^c	COPh ^c	H ₂ O ₂ , AcOH	OCOPh ^c	OCOPh ^c	98	20
Br	COMe	MCPBA	Br	OCOMe	72	239
<i>n</i> -C ₅ H ₁₁	COMe	MCPBA	<i>n</i> -C ₅ H ₁₁	OCOMe	90	91
<i>n</i> -C ₄ H ₉ ^c	COMe	MCPBA	<i>n</i> -C ₄ H ₉ ^c	OCOMe	90	91

^a Not reported. ^b The ratio of the products *tert*-butylcarboxylate:pivalate is 2.3:1. ^c [2]Staffane derivatives.

amines (Scheme 160 and Table 41). Decarboxylation

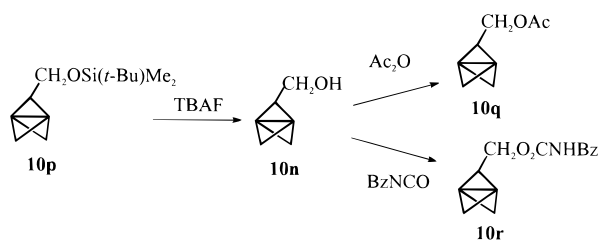
Scheme 160**Table 41. Rearrangements of Bicyclo[1.1.1]pentylcarboxylic Acid Derivatives into Amines (Scheme 160)**

X	position ^a	R ¹	reagent	R ²	yield (%)	ref
CO ₂ H	1	H	HN ₃	H	77	77
	2	H	HN ₃	H	83 ^b	78
	1	Me	HN ₃	Me	<i>c</i>	278
	1	¹³ CH ₃	HN ₃	¹³ CH ₃	<i>c</i>	278
	1	Ph	HN ₃	Ph	51 ^b	218
CONH ₂	1	H	PhIO	H	60 ^b	181
COCl	1	COCl	HN ₃	NH ₂	77	46
COCl ^d	1	COCl ^d	HN ₃	NH ₂ ^d	72	46

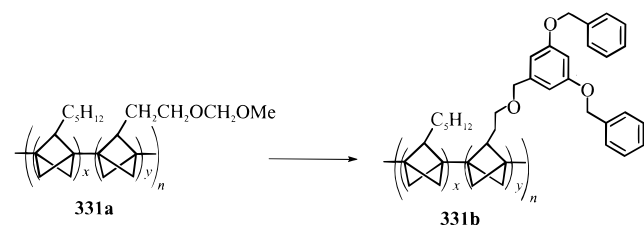
^a Position of the X group in the substrate and that of the NH₂ group in the product. ^b Yield of amine hydrochlorides. ^c Not reported. ^d [2]Staffane derivatives.

reactions of bridgehead carboxylic acids and its derivatives were described in section IV.B.2.

A series of transformations of ([1.1.1]propellanyl)-methanol derivatives **10n**, **p–r** (Scheme 161)³²¹ and

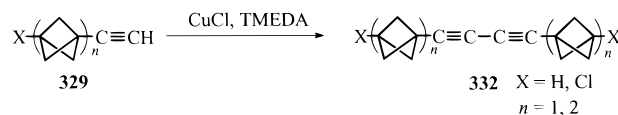
Scheme 161

bicyclo[1.1.1]pent-2-ylethanol groups in polymer **331**³²² (Scheme 162) did not affect the cage of the corre-

Scheme 162

sponding [1.1.1]propellanes and bicyclo[1.1.1]pentanes, respectively.

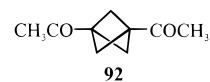
Building up complicated structures containing bicyclo[1.1.1]pentane units as an integral part would often require connections through a reactive group remote from the cage or a modification of such a group (see also section V). An example of such reactions is the oxidative coupling of the bicyclo[1.1.1]pent-1-ylacetylenes **329** into longer rodlike molecules **332** (Scheme 163).²⁶¹

Scheme 163**E. Summary**

A wide variety of synthetic approaches and methods is applicable to compounds with bicyclo[1.1.1]pentane framework. The most general, efficient, and versatile methods for the preparation of bicyclo[1.1.1]pentanes are the following: (i) addition across the central bond of [1.1.1]propellanes and (ii) functional group transformations starting with other bicyclo[1.1.1]pentanes. Radical addition is the most versatile tool of conversion of the parent [1.1.1]propellane (**2**) into 1- and/or 1,3-substituted bicyclo[1.1.1]pentanes. Anionic addition is useful in some cases, whereas cationic reactions usually lead to destruction of the cage.

A significant recent development in the synthetic chemistry of **2** is the preparation of solvent-free **2** starting from 1,3-diiodobicyclo[1.1.1]pentane (**13**, see section IV.B.1.b.i). It provided several very important advantages over prior methods: (i) flexibility in the choice of solvent and concentration of **2** for carrying out further reactions,³²³ (ii) high purity of **2**,³²⁴ and (iii) long-term storage of the relatively unstable **2** (see section II.A) in the form of the virtually indefinitely stable **13**, from which **2** can be synthesized as needed for immediate use. The diiodide **13** is synthesized from an ethereal solution of **2**.²⁴ With the procedures available now, the estimated yield of pure **2** based on the tetrahalocyclopropane **174a** is 64%. This is almost twice the yield of the previous procedure for preparation of ether-free **2** (solution in pentane).²⁰

Two of the most valuable precursors for functional group transformations are bicyclo[1.1.1]pentane-1,3-dicarboxylic acid (**42**) and dimethyl bicyclo[1.1.1]pentane-1,3-dicarboxylate (**46**). The diacid **42** is prepared from an ethereal solution of **2** in three steps via 1,3-diacetylbicyclo[1.1.1]pentane (**92**) in good



yield. It may be converted into symmetrically substituted derivatives of bicyclo[1.1.1]pentane (**1**) via radical decarboxylation–addition reactions or by nucleophilic reactions on the carboxyl group. Unsymmetrically bridgehead disubstituted bicyclo[1.1.1]pentanes are accessible from **46** via partial hydrolysis to 1-methoxycarbonylbicyclo[1.1.1]pentane-3-carbox-

ylic acid (**50**) and subsequent selective transformations of the carboxyl and/or methoxycarbonyl groups. An alternative general method of synthesis of unsymmetrically 1,3-disubstituted bicyclo[1.1.1]pentane is the addition of **2** across a C–I bond of a reagent and subsequent radical transformation of the bridge-head iodide into another bicyclo[1.1.1]pentane derivative.

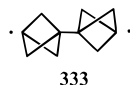
[*n*]Staffanes have been prepared by radical- or anion-initiated oligomerization of [1.1.1]propellanes or by reductive coupling of certain bicyclo[1.1.1]pentanes. Radical oligomerization yields mixtures of [*n*]staffanes with a distribution of *n* dependent on the kinetics of the initiation, propagation, and termination steps of the oligomerization. Yields of individual oligomers are usually low. Separation of the first several homologous staffanes is normally relatively easy. Pure individual [*n*]staffanes have usually been isolated up to *n* = 4 or 5. Only recently an efficient symmetric coupling of 1-halobicyclo[1.1.1]pentanes and [*n*]staffanes has been achieved via copper derivatives (see section IV.B.5),²⁴⁹ and it permits a doubling of the rod length.

Tricyclo[2.1.0.0^{2,5}]pentanes are useful, and sometimes unique, precursors for other strained cyclic structures, such as tetrahydranes (**157**) and cyclobutadienes (**268**).

V. Applications of Bicyclo[1.1.1]pentanes and [*n*]Staffanes

The symmetry of the bicyclo[1.1.1]pentane cage makes it a valuable unit in the construction of oligomers with predetermined shapes and polymers and dendrimers with unprecedented properties. Early achievements in poly[1.1.1]propellane chemistry have been reviewed.³²⁵

Polymers. A propensity of the parent [1.1.1]-propellane (**2**) toward spontaneous polymerization, slow in solution and fast in pure form, was noticed as soon as significant quantities of it had been prepared. A mechanism for this process has been studied computationally at SINDO/1 level. The triplet diradical **333** is a minimum on the T₁ surface. Thus, it has been suggested that it may form upon reaction of two molecules of the monomer **2** to a singlet biradical followed by intersystem crossing to the triplet.³²⁶ Once formed, it would initiate radical polymerization.



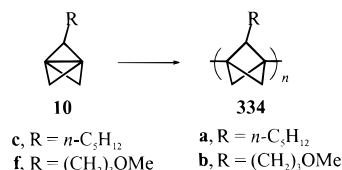
Radical-induced polymerization of **2** itself produces highly insoluble polymers of low molecular weight.^{21,327} For instance, with atomic hydrogen as the initiator,⁴² the parent [*n*]staffanes form; and after the lower members of the series are separated (up to *n* ≈ 6), the remaining insoluble material has an average degree of polymerization of only 10–20. Higher molecular weights for the parent poly[1.1.1]propellane can be achieved when precipitation is prevented by performing the polymerization inside the ZMS-5

zeolite. After dissolution of the zeolite, this procedure yields polymers with up to ~100 bicyclo[1.1.1]pentane units, judging by the intensity of the terminal group signals in ¹³C NMR spectra.³²⁸ The polymer is thermally stable up to ~290 °C, at which temperature it decomposes violently with a 85% weight loss and evolution of a complex mixture of vapors, primarily toluene, benzene, and the lower alkenes up to hexene.³²⁸

Nucleophile-induced polymerization may well proceed via a radical mechanism as well. Upon treatment with organolithium reagents, the parent [1.1.1]-propellane (**2**),^{21,327} 2,2-trimethylene[1.1.1]propellane (**11b**),^{237,238} and 2,2-dichloro[1.1.1]propellane (**11c**)¹⁹⁴ are all rapidly converted to insoluble polymers.

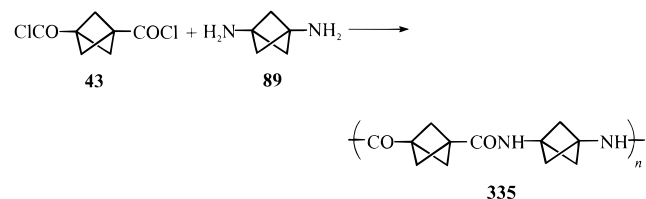
Soluble poly[1.1.1]propellanes of high molecular weight can be obtained in the presence of solubilizing substituents on the monomer.³²⁵ 2-*n*-Pentyl- and 2-[2'-(methoxymethoxy)ethyl][1.1.1]propellanes (**10c** and **10s**, respectively) copolymerized upon initiation with AIBN under UV irradiation to yield the polymer **331a**,³²² which was converted into a cylindrically shaped dendritic structure by transformation of the side chains (see section IV.D.).³²² Homopolymer of **10s** is also obtained with AIBN initiation.²¹² Benzophenone-sensitized homopolymerization of **10c** and 2-(5'-methoxy-*n*-pentyl)[1.1.1]propellane (**10f**) yielded polymers **334a** and **334b** (Scheme 164).³²⁵ Copolymer-

Scheme 164



ization of [1.1.1]propellanes **2**, **10c**, **10p**, and **11b** with a large number of olefins without addition of initiator has been studied,^{210,325,329–333} and plausible mechanisms for these copolymerizations have been discussed.³²⁵ Polycondensation of the diamine **89** with the diacid chloride **43** in *N*-methylpyrrolidone afforded the polyamide **335** (Scheme 165), soluble in

Scheme 165



concentrated sulfuric acid.³³⁴ A series of liquid-crystalline polymers **336** (Chart 13) containing bicyclo[1.1.1]pentane cages in the main chain was obtained starting with the diacid chloride **43**.

Liquid Crystals. About one hundred low molecular weight and polymeric³³⁵ compounds have been prepared to assess the effect of the bicyclo[1.1.1]pentane-1,3-diyl moiety (**1a**) on the liquid-crystalline properties of materials.³³⁶ The low molecular weight

Chart 13. Substituted Bicyclo[1.1.1]pentanes with Liquid-Crystalline Properties

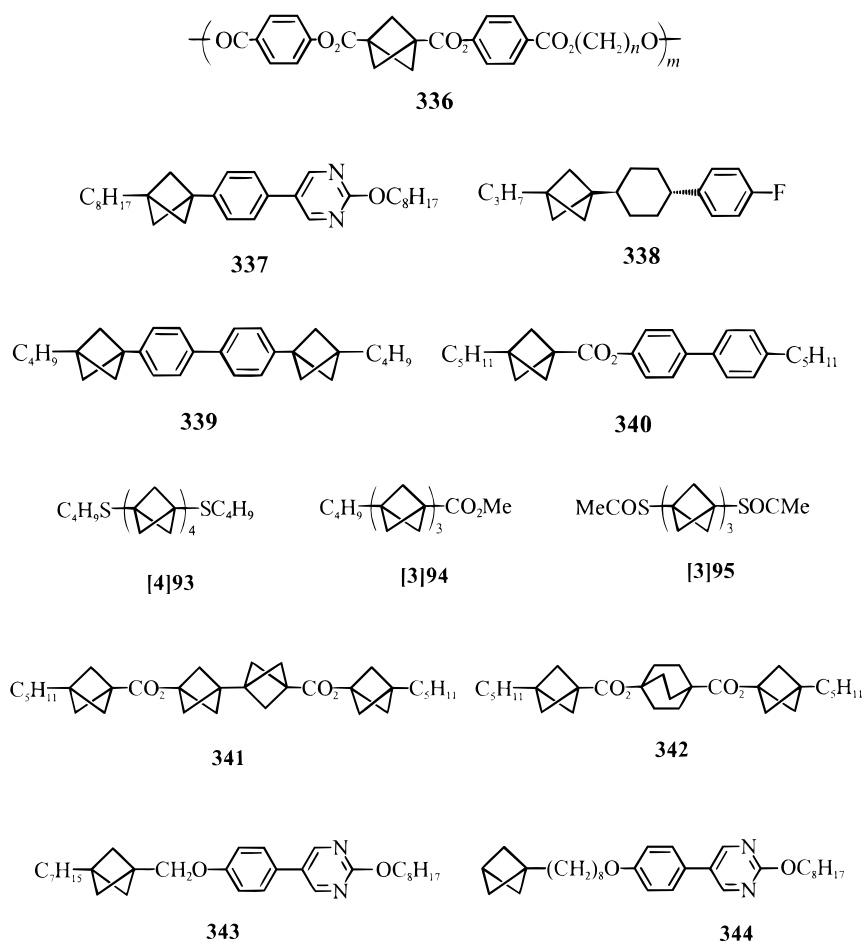
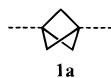


Table 42. Comparison of Calculated (HF/6-31G*) Molecular Parameters of Bicyclo[1.1.1]pentane, Bicyclo[2.2.2]octane, Cubane, *p*-Carborane, Cyclohexane, and Benzene and Their Effectiveness as Structural Elements in Liquid Crystals

cage or ring	geometry ^a			polarizability ^b		ring effectiveness ^c		
	L_{CC}	D_H	L/D	$\Delta\alpha$	$\Delta\alpha/L$	ΔT_N	ΔT_S	ΔT_{Cr}
bicyclo[1.1.1]pentane	1.87	4.10	0.46	-6.0	-3.2	0	0	0
bicyclo[2.2.2]octane	2.59	4.31	0.60	0.3	0.1	+97 (4)	+66 (1)	+31 (3)
cubane	2.70	4.58	0.59	0.0	0.0	+12 (2)	<i>d</i>	+27 (2)
1,12-dicarba- <i>closo</i> -dodecaborane	3.04	5.03	0.60	-7.1	-2.3	+7 (1)	<i>d</i>	+7 (1)
cyclohexane	2.96	3.45	0.86	2.2	0.7	+90 (4)	+87 (1)	+54 (7)
benzene	2.77	4.26	0.65	23.7	8.6	+70 (3)	<i>d</i>	+1 (5)

^a Distances are in Å. L_{CC} is the interbridgehead separation and D_H is the diameter of a hydrogen cylinder of rotation. ^b Polarizability anisotropy in Å³ is calculated as the difference between the polarizability components parallel and perpendicular to the C-C axis. ^c Mesophase (N = nematic, S = smectic) stability and melting points (T_{Cr}) relative to bicyclo[1.1.1]pentane derivatives for structurally analogous compounds. The number of pairs considered is given in parentheses. ^d No pair available.

molecules have been reported in journals,^{20,267,337,338} in Ph.D. dissertations,^{91,339} and in patents.^{340,341}



Industrial interest in this class of compounds stems from the expectation that incorporation of **1a** into a molecular structure will increase the thermal stability of the mesogen and improve its mechanical properties in a manner similar to that of some other small rings (e.g., cyclobutane).^{342,343} Inspection of molecular models for **1a** and other cylindrical moi-

eties such as bicyclo[2.2.2]octane-1,4-diyl, cubane-1,4-diyl, and 1,12-dicarba-*closo*-dodecaborane-1,12-diyl, as well as *trans*-cyclohexane-1,4-diyl and 1,4-phenylene, shows that bicyclo[1.1.1]pentane is the smallest among the rings considered. The unusually short interbridgehead distance of 1.87 Å is reflected in the lowest aspect ratio ($L/D = 0.46$) and negative polarizability anisotropy $\Delta\alpha$ (Table 42), which are the key parameters used in classical theories describing the nematic state.³⁴⁴

Liquid crystals containing the bicyclo[1.1.1]pentane ring exhibit both low order (N, S_A , S_C)^{267,338} and high-order (S_B , S_{G3})^{337,338} phases. The thermal stabilities

Table 43. Examples of Mesogens Containing Bicyclo[1.1.1]pentane

compd	transition temp ^a	ref
[4]93	Cr 81 S 233 I	337
[3]94	Cr 118 S 151 I	91
[3]95	Cr 137 S _C 167 N 192 I	337
337	Cr 85 S _B 113 S _A 115 I	338
338	Cr 57.0 N 63.7 I	338
339	Cr 128 S _B 142.6 N 170.2 I	338
340	Cr 80 S 82 N 113.5 I	91
341	Cr 144 S 197 I	91
342	Cr 67 S 207 I	91
343	Cr 69 S _C 95 S _A 100 N 103 I	338
344	Cr 32 S _C 74 S _A 90 I	338

^a Transition temperatures in °C. Cr = crystal; S, S_A, S_B, S_C, S_G = smectics; N = nematic; I = isotropic phases.

of the liquid-crystalline phases are generally lower than those found with analogous compounds containing other ring systems. Although there are too few data points for a meaningful statistical comparison,³⁴⁵ it appears that the effectiveness of the bicyclo[1.1.1]pentane cage in stabilizing nematic phases is similar to that of the cubane and 1,12-dicarba-*closo*-dodecaborane cages and much inferior to that of bicyclo[2.2.2]octane cage and cyclohexane and benzene rings (Table 42). This has been ascribed to low rotational barriers and consequently high conformational mobility of the bridgehead substituents.^{335,338}

Typically, bicyclo[1.1.1]pentane has been a part of the molecular rigid core connected to other rings directly (e.g., **337**, **338**, and **339**) or through an ester (e.g., **340**) or an ethylene link (Chart 13 and Table 43). When **1a** is attached directly to an aromatic ring, the mesogen exhibits the same phase behavior as the analogues containing the bicyclo[2.2.2]octane cage and cyclohexane and benzene rings, but markedly lower clearing points. A particularly detrimental effect of bicyclo[1.1.1]pentane on mesophase stability is observed when the ring is placed between two aromatic groups. Then, only very low transition temperatures are observed, consistent with the general trend.³⁴⁶ The 4,4-disubstituted biphenyl **339** displays S_B and N phases, unlike 4,4'-diheptylbiphenyl, which shows the S_B phase exclusively. This behavior is similar to that found for a dicyclohexyl derivative of biphenyl, which exhibits the N phase with a high clearing point. The mesogenic properties are slightly improved when **1a** is connected to the aromatic ring through an ester link.

Relatively high phase stabilities have been observed for mesogens with all aliphatic rings either connected directly (e.g., **[4]93**, **[3]94**, and **[3]95**, Chart 13)³³⁷ or through an ester link (e.g., **341** and **342**).^{91,337} These compounds exhibit highly ordered smectic phases, except that the dithiolester **[3]95** surprisingly displays a nematic phase following the S_G phase.³³⁷ [*n*]Staffanes exhibiting liquid-crystalline phases have a minimum of $n = 3$ bicyclo[1.1.1]pentane rings,^{91,337} while even single ring bicyclo[2.2.2]octanes exhibit nematic properties³⁴⁷ and the two-ring systems, bisbicyclo[2.2.2]octanes, are smectics with high clearing temperatures.³⁴⁸

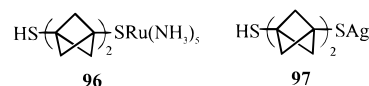
The effectiveness of bicyclo[1.1.1]pentane as a part of a flexible aliphatic substituent, e.g., **343** and **344**

(Chart 13) has also been tested.³³⁸ When a $-(CH_2)_3$ -fragment is replaced by **1a** close to the rigid core, as in **343**, a similar phase sequence and almost no effect on the clearing temperature are observed. A replacement of the terminal propyl group by bicyclo[1.1.1]pentane in **344** lowers both the melting and the clearing temperatures, presumably due to steric bulk.

A comparison of the main-chain liquid crystal polymer **336** with the analogous phenyl and cyclohexyl polymers shows a strong destabilization of smectic phases by the introduction of bicyclo[1.1.1]pentane and also shows much lower clearing temperatures in **336**.³³⁵

Supramolecular Structures. Much of the interest in bicyclo[1.1.1]pentanes and [*n*]staffanes is due to their attractiveness for applications as modules for simple axial rods in supramolecular structures.^{20,349} The bicyclo[1.1.1]pentane-1,3-diyl moiety (**1a**) yields rods that are relatively rigid compared to most other simple axial module available to date.³⁴⁹ Useful properties of these spacers are a small length increment of only about $3^{-1/3}$ Å, optical transparency, chemical inertness, and potential availability of numerous sites for lateral functionalization. The enhanced electronegativity of the bridgehead carbons and a strong transannular σ -electron interaction in the bicyclo[1.1.1]pentane cage may lead to interesting charge-transmission properties (see section II). The bicyclo[1.1.1]pentane and [*n*]staffane rods may be incorporated into larger molecules by covalent bonds using the chemistry discussed in section IV or by complexation of appropriately end-functionalized rods to metal atoms. Formation of linear complexes has been shown for bicyclo[1.1.1]pentane-1,3-diisonitrile with molybdenum pentacarbonyl⁴⁶ and bicyclo[1.1.1]pentane-1,3-dicarboxylate anions with the Rh₂⁴⁺ cation.³⁵⁰ A square grid constructed of [2]staffane rods was used as a support for molecular propellers in a computer simulation of their behavior in a stream of helium atoms.³⁵¹

Monolayers.³⁵² Single-side protected [*n*]staffane-3,3^(*n*-1)-dithiols **[n]83** and **96** formed highly ordered and electrically blocking self-assembled monolayers on polycrystalline gold electrodes. IR measurements showed that the rods were oriented perpendicular to the surface, with the methyl of the acetyl group rotated outward.³¹⁷ The protective acetyl groups in **[n]83** were then hydrolyzed from the surface, and subsequent derivatization with Ru(NH₃)₅ occurred without damage to the film, permitting a redox cycling of the ruthenium ion between oxidation states +2 and +3.³¹⁷ Au(111) surface derivatized with thiols **96** and **97** has been studied by scanning tunneling microscopy.³⁵³

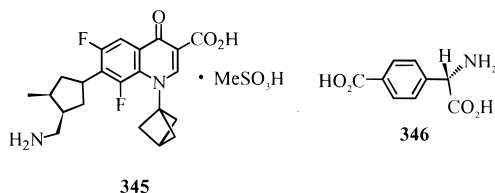


[*n*]Staffane-3-carboxylates (**[n]19e**) readily form Langmuir–Blodgett films on pure water when $n = 4$ and on concentrated aqueous solution of CaCl₂ when $n = 3$.³⁵⁴ The limiting area for both oligomers is 26.0 Å²/molecule, independent of the counterion. Grazing-incidence IR measurements demonstrated that in a

monolayer the staffane rods are oriented perpendicular to the surface when transferred onto a gold substrate. The very high degree of alignment was well apparent in the IR spectrum; e.g., the single terminal CH stretching vibration due to the terminal bridgehead was very clearly observed, whereas the peaks due to the stretching of the 24 CH bonds of the CH₂ bridges were essentially inobservably weak. According to ellipsometric, IR absorption, and grazing-incidence X-ray reflection results, in multilayers, the rods are tilted by about 20 ° away from the normal.³⁵⁴ This is nearly the same angle of tilt that is observed in crystals of low-molecular weight [n]-staffane oligomers, suggesting a similar tight packing of the rods.⁴²

Incorporation of 3-pentylbicyclo[1.1.1]pentane-1-carboxylic acid into a model stratum corneum lipid structure and its influence on the order in it have been studied by low-angle X-ray diffraction and deuterium NMR.³⁵⁵

Drug Design. Unique properties of the bicyclo[1.1.1]pentane moiety make it an interesting part of a palette of substituents in the rational design of small molecules in drug discovery. One can view a bicyclo[1.1.1]pentyl group as a substitute for a *tert*-butyl group when, in addition to lipophilicity, such properties as an enhanced electronegativity and relatively small size are required.³²⁰ Incorporation of bicyclo[1.1.1]pent-1-yl group into quinolone antibacterial agents afforded compounds with potent activity against aerobic Gram-positive and Gram-negative bacteria and also anaerobic organisms (one of them is U-87947E, **345**).³²⁰ Symmetry of the bicyclo[1.1.1]pentane cage is used in the design of new potent and selective antagonists to metabotropic glutamate receptors.³⁰⁸ Substitution of a phenylene spacer in a known antagonist (+)- α -methyl(4-carboxyphenyl)glycine (**346**) with the bicyclo[1.1.1]pentane-1,3-diyl moiety (**1a**) in the amino acids **74** allowed to elucidate the role of the spacer in specific ligand–receptor interactions.³⁰⁸



VI. Conclusion

In its 35 years of existence, the chemistry of compounds with bicyclo[1.1.1]pentane framework has provided numerous examples of fascinating reactions and unusual properties. The interest in [1.1.1]propellanes and bicyclo[1.1.1]pentanes is now gradually changing from purely academic to application-oriented. The high cost of these compounds prevents them from being considered for large-scale industrial applications, but as new properties and potential applications for these compounds are discovered and the methods of synthesis are becoming more efficient, applications in specialty materials appear possible.

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