The Reaction of Chlorosulfonyl Isocyanate with Bridged Bi- and Tricyclic Olefins[1-3]

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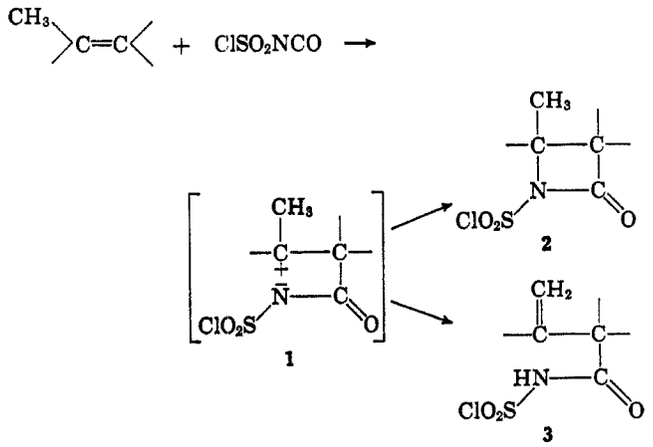
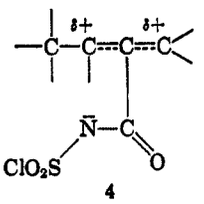
The addition of chlorosulfonyl isocyanate (CSI) to norbornene (**5**), norbornadiene (**24**), 7-benzoyloxy- (**28**) and 7-*t*-butoxynorbornadiene (**30**), *endo*- (**32**) and *exo*-dicyclopentadiene (**37**), and bicyclo[2.2.2]octene (**40**) led, in each case, to a single, unrearranged cycloadduct, the N-chlorosulfonyl-β-lactam. A nonconcerted cycloaddition mechanism is proposed. Attempts to form the bis adduct from norbornadiene were unsuccessful. Assignment of the *exo* configuration to the azetidinone ring in these N-chlorosulfonyl-β-lactams is based predominantly on nmr evidence. Benzenethiol–pyridine reduction of the N-chlorosulfonyl cycloadducts led to the corresponding unsubstituted β-lactams. The infrared spectrum of *exo*-2-*p*-toluenesulfonamido-3-carboxybicyclo[2.2.1]heptane (**14**), ultimately prepared from the norbornene cycloadduct, expectedly differed from that of the *endo* isomer (**18**) prepared by a stereospecific Lossen rearrangement on N-phenylsulfonyloxynorbornane-*endo*-2,3-dicarboximide (**16**). Treatment of N-phenylsulfonyloxynorbornane-*exo*-2,3-dicarboximide (**21**) under Lossen conditions failed to yield rearrangement product, as did the Hofmann reaction on norbornane-*exo*-2,3-dicarboximide (**22**) and *exo*-2-carbomethoxy-3-carboxamidonorbornane (**23**). A Lossen rearrangement, however, successfully converted N-sulfonyloxybicyclo[2.2.2]octane-2,3-dicarboximide (**46**) into 2-amino-3-carboxybicyclo[2.2.2]octane hydrochloride (**43**), identical with the acid hydrolysis product of the β-lactam cycloadduct from **40**.

The discovery of the reagent chlorosulfonylisocyanate (CSI),[4] and the exceptional ease with which it undergoes, predominantly, cycloaddition reactions with olefins and allenes[5-8] has provided a simple means of introducing an azetidinone (β-lactam) moiety into such substrates. In Graf's brilliant pioneering work on the cycloaddition of CSI to olefins, he envisioned a two-step mechanism involving the initial formation of a "dipolar adduct" **1** which could stabilize itself through closure of the four-membered ring to **2** and/or *via* proton shift to **3**.



The recently developed Woodward–Hoffman theoretical selection rules[9] and the experimental results of the reaction between CSI and allenes[8] prompted us also to suggest a stepwise, 1,2-dipolar cycloaddition to produce, in the transition state, an allyl-type stabilized carbonium ion (**4**).



In an effort to determine the extent of participation of the open-chain carbonium ion (**1**, **4**) in the formation of β-lactams, we have examined the cycloaddition reaction[10] between CSI and the rearrangement-prone[11] bridged bicyclic [norbornene (**5**), norbornadiene (**24**), bornylene (**27**), 7-benzoyloxy- (**28**) and 7-*t*-butoxynorbornadiene (**30**), and bicyclo[2.2.2]octene (**40**)] and tricyclic [*endo*- (**32**) and *exo*-dicyclopentadiene (**37**)] olefins.

Results

The addition of CSI to **5** (Chart I), **24** (Chart II), **32** and **37** (Chart III), and **40** (Chart IV) led in each case to a single adduct, the N-chlorosulfonyl-*exo*-β-lactam, **6** (86%), **25** (94%), **33** (78%), **38** (71%), and **41** (63%), respectively. With the hindered 7-substituted norbornadienes, **28** and **30** (Chart V), the *exo* adducts were also obtained, albeit in lower yields [**29** (11%) and **31** (35%), respectively], accompanied by large amounts of intractable tars and very small amounts of possibly rearranged but unidentified products. All the N-chlorosulfonyl-*exo*-β-lactams were moderately stable; **6**, however, could not be purified by either distillation or chromatographic treatment. It would not crystallize, even after prolonged standing at −20°, although it appeared to be stable at this temperature; it decomposed slowly at room temperature. Two crystalline, ring-cleaved derivatives of **6** were prepared by reaction with nucleophiles[5] *p*-chloro-

(1) This research was supported by the Directorate of Chemical Sciences, Air Force Office of Scientific Research, under Grant AF-AFOSR-488-64 and by the Department of the Army, Walter Reed Army Institute of Research, under Contract DA-49-193-MD-2992.

(2) Presented at the First International Congress of Heterocyclic Chemistry, the University of New Mexico, Albuquerque, N. M., June 12–15, 1967, paper no. 76.

(3) Taken entirely from the Ph.D. Thesis of W. C. Crawford, Fordham University, New York, N. Y., 1968.

(4) R. Graf, *Ber.*, **89**, 1071 (1956); *Org. Syn.*, **46**, 23 (1966).

(5) R. Graf, *Ann.*, **661**, 111 (1963); *Org. Syn.*, **46**, 51 (1966).

(6) H. Ulrich [*Chem. Rev.*, **65**, 369 (1965)] summarizes the chemistry of CSI to July 1964 and lists all the references (at least 13 patents and five articles) on the reactions of CSI with olefins (including enol ethers, vinyl amides, and conjugated dienes), carbocyclic and heterocyclic aromatics, alcohols, phenols, and carbonyl compounds (aldehydes, ketene, amides, and carboxylic acids). See also H. Ulrich, "Cycloaddition Reactions of Heterocumulenes," Academic Press Inc., New York, N. Y., 1967, pp 135–141.

(7) E. J. Moriconi and P. Mazzocchi, *J. Org. Chem.*, **31**, 1372 (1966).

(8) E. J. Moriconi and J. F. Kelly, *J. Am. Chem. Soc.*, **88**, 3657 (1966).

(9) R. Hoffman and R. B. Woodward, *ibid.*, **87**, 395, 2046 (1965).

(10) R. Huisgen, R. Grashey, and J. Sauer in "The Chemistry of Alkenes," S. Patai, Ed., Interscience Publishers, Inc., New York, N. Y., 1964, p 739.

(11) J. A. Berson in "Molecular Rearrangements," Vol. I, P. de Mayo, Ed., Interscience Publishers, Inc., New York, N. Y., 1963, p 111.

CHART I

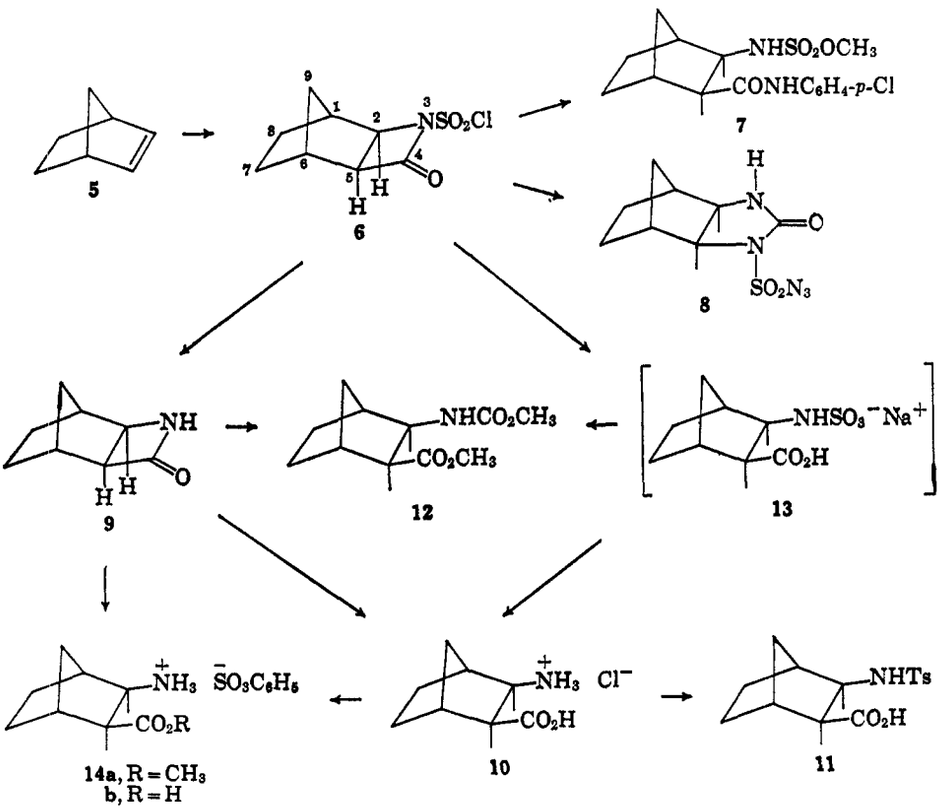
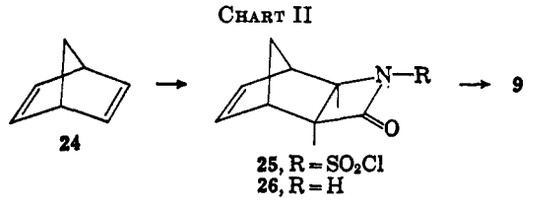


CHART II



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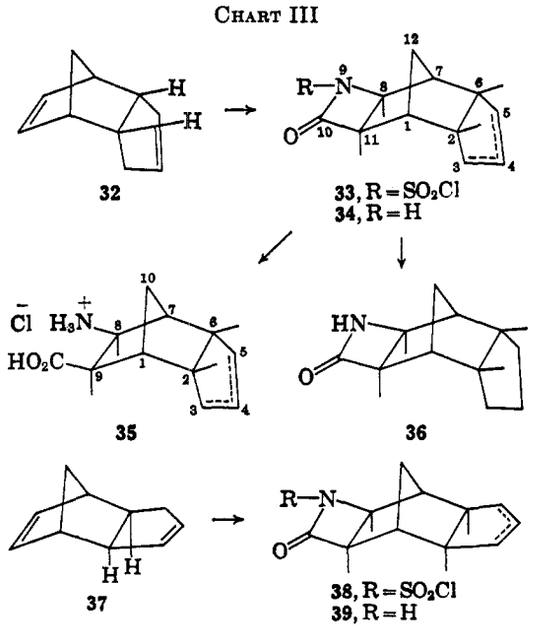

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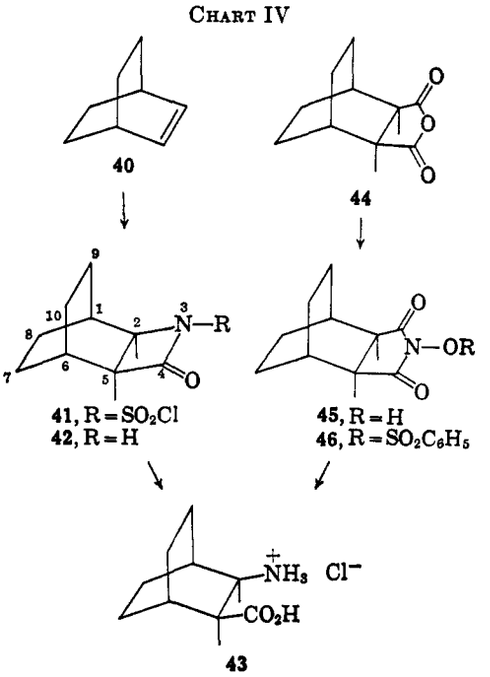


aniline in methanol and sodium azide to produce, respectively, *exo*-2-amino-(N-methylsulfonyloxy)-3-carboxamido-(N′-*p*-chloroanilino)norbornane (**7**) and N-sulfonylazido-*exo*-3,5-diaza-4-ketotricyclo[5.2.1.$0^{2,6}$]-decane (**8**). In the case of *endo*- (**32**) and *exo*- dicyclopentadiene (**37**), CSI added solely to the more strained norbornene double bond. Melting point behavior and tlc of the respective products, **33** and **38**, indicate each to be homogeneous; precedent,[12] however, suggests both to be inseparable mixtures of double-bond isomers (as formulated) since there is no compelling reason why CSI should add stereoselectively to **32** and **37** to form a single product. The decreased reaction rate between bicyclo[2.2.2]octene (**40**) and

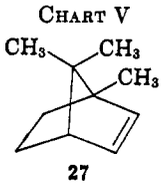
(12) R. Huisgen, M. Seidel, G. Wallbillich, and H. Knupfer, *Tetrahedron*, **17**, 3 (1962).

TABLE I
INFRARED AND NMR SPECTRAL DATA OF *exo*-β-LACTAMS

N-Chlorosulfonyl-β-lactams	Infrared, λmax, μ: Matrix/solvent	N—H: Free	N—H: Bonded	C=O	−SO2−	Nmr: Solvent	Chemical shift, δ	Area	Multiplicity	Coupling constant	Proton assignment
6	Neat			5.51	7.09, 8.46	CCl_4	4.14, 3.28	2	AB quartet[f]	J = 4 cps	C-2, -5 *endo*
							2.62, 2.15	2	Broad singlets[f]		C-1, -6 bridgehead
25	CCl_4			5.49	7.09, 8.40	CCl_4	4.20, 3.20	2	AB quartet[f]	J = 4 cps	C-2, -5 *endo*
							3.42	2	Broad singlet[f]		C-1, -6 bridgehead
29	KBr			5.53,[c] 5.85[d]	7.14, 8.46	$CDCl_3$	4.38	1	Doublet[f]	J = 5 cps	C-2 *endo*
							3.90–3.35	3	Multiplet[f]		C-1, -5, -6
31	KBr			5.55	7.22, 8.46	$CDCl_3$	4.26, 3.49	2	AB quartet[f]	J = 5 cps	C-2, -5 *endo*
							3.2–3.0	2	Multiplet[f]		C-1, -6 bridgehead
33	KBr			5.49	7.09, 8.49	$CDCl_3$	4.20, 3.38	2	AB quartet[f]	J = 5 cps	C-8, -11 *endo*
							3.10–2.10	6	Multiplet[f]		Methine and allyl
38	KBr			5.50	7.15, 8.40	$CDCl_3$	4.28, 3.28	2	AB quartet[f]	J = 4 cps	C-8, -11 *endo*
							2.90–1.60	6	Multiplet		Methine and allyl
41	CCl_4			5.49	7.07, 8.42	$CDCl_3$	4.36, 3.46	2	AB quartet[f]	J = 7 cps	C-2, -5
							2.39–1.92	2	Multiplet[f]		C-1, -6 bridgehead
β-Lactams											
9	CCl_4	2.92[a]	3.11[b]	5.71[e]		CCl_4	3.38, 2.95	2	AB quartet[f]	J = 4 cps	C-2, -5 *endo*
							2.39	2	Broad singlet[f]		C-1, -6 bridgehead
26	CCl_4	2.93[a]	3.12[b]	5.68[e]		$CDCl_3$	3.50	1	Doublet[f]		C-2 *endo*
							2.92	3	Center of overlapping bands[f]		C-1, -5, -6
34	CCl_4	2.94[a]	3.11[b]	5.69[e]		$CDCl_3$	3.46, 3.18	2	AB quartet[f]	$J \simeq 4$ cps	C-8, -11 *endo*
							2.90–2.00	6	Multiplet		Methine and allyl
36	CCl_4	2.94[a]	3.12[b]	5.69[e]		$CDCl_3$	3.62, 3.21	2	AB quartet[f]	$J \simeq 3.5$ cps	C-8, -11 *endo*
							2.48	4	Doublet		C-1, -2 ,-6, -7
39	CCl_4	2.94[a]	3.12[b]	5.66[e]		$CDCl_3$	3.48, 3.05	2	AB quartet[f]	J = 4 cps	C-8, -11 *endo*
							2.80–1.70	6	Multiplet		Methine and allyl
42	CCl_4	2.93[a]	3.13[b]	5.70[e]		$CDCl_3$	3.62, 3.12	2	Quartets[f,g]		C-2, -5
							2.18–1.28	10	Multiplet		C-1, -6, -7, -8, -9, -10

[a] Sharp band. [b] Broad band. [c] Amide carbonyl. [d] Ester carbonyl. [e] Center of doublet. [f] With fine splitting. [g] Partially resolved.

CHART V



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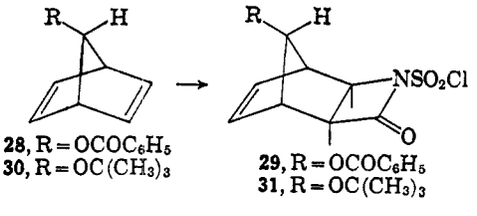


28, R = $OCOC_6H_5$
30, R = $OC(CH_3)_3$

29, R = $OCOC_6H_5$
31, R = $OC(CH_3)_3$

CSI clearly reflects the less strained nature of the double bond in such an ethano-bridged cyclohexene when compared to **5**.[13] In the infrared, the low wavelength carbonyl band (5.49–5.53 μ, Table I) in **6**, **25**, **29**, **31**, **33**, **38**, and **41** provide spectral support for the combined effect of a strained, four-membered ring and the presence of the powerful electronegative $ClSO_2$ group on the lactam nitrogen. All these N-chlorosulfonyl-*exo*-β-lactams displayed the expected two sulfone absorptions in the 7.07–7.22 and 8.40–8.49 μ regions.[14,15]

Benzenethiol–pyridine reduction[5] of **6**, **25**, **33**, **38**, and **41** led to the unsubstituted *exo*-β-lactams **9** (77%),[16,17] **26** (72%), **34** (44%), **39** (34%), and **42** (78%), respectively. The carbonyl bands in these azetidinones now show the effect of removal of the $ClSO_2$ group by a red shift to doublets centered in the 5.66–5.71-μ region (Table I).[18] Further, in solution, all displayed the characteristic sharp (free) N–H peak at 2.92–2.94 μ and broad (bonded) N–H peak at 3.11–3.13 μ[18] (Table I).

Assignment of the *exo* configuration to the fused azetidinone ring in the N-chlorosulfonyl-β-lactams **6**, **25**, **29**, **31**, **33**, and **38** is based largely on nmr evidence. Thus, **6**, **25**, **31**, **33**, and **38** show the fused-ring *endo* protons as an AB quartet, J = 4–5 cps (Table I). The *endo* proton adjacent to the N–SO_2Cl group (C-2 in **6**, **25**, and **31**; C-8 in **33** and **38**) is the more deshielded and is assigned the low-field signal of the quartet; the high-field resonance correspondingly is assigned to the *endo* proton (C-5 in **6**, **25**, **31**; C-11 in **33** and **38**) on the carbonyl side. The magnitude of J_{2-5} (in **6**, **25**, and **31**) and J_{8-11} (in **33** and **38**) is indicative of their *endo* nature.[19] Each member of the quartet exhibits fine splitting ($J \cong 1$ cps) due to virtual coupling with the bridge *anti* proton, expected only if the protons at the site of β-lactam fusion are configurationally *endo*.[19] Finally, noteworthy is the absence of appreciable coupling of the bridgehead protons (C-1, -6 in **6**, **25**, and **31**; C-1, -7 in **33** and **38**) with their respective, vicinal *endo* protons. This feature is also

(13) P. von R. Schleyer, *J. Am. Chem. Soc.*, **80**, 1700 (1958).

(14) Normal sulfones absorb in the 7.41–7.69- and 8.62–8.93-μ regions.[15a] Substitution of chlorine directly on the S-atom of the sulfone would be expected to cause the observed blue shift in both bands[15b] which is in accord with those previously reported.[6,7,8]

(15) (a) L. J. Bellamy, "The Infra-red Spectra of Complex Molecules," John Wiley and Sons, Inc., New York, N. Y., 1958, p 360; (b) p 363; (c) p 208.

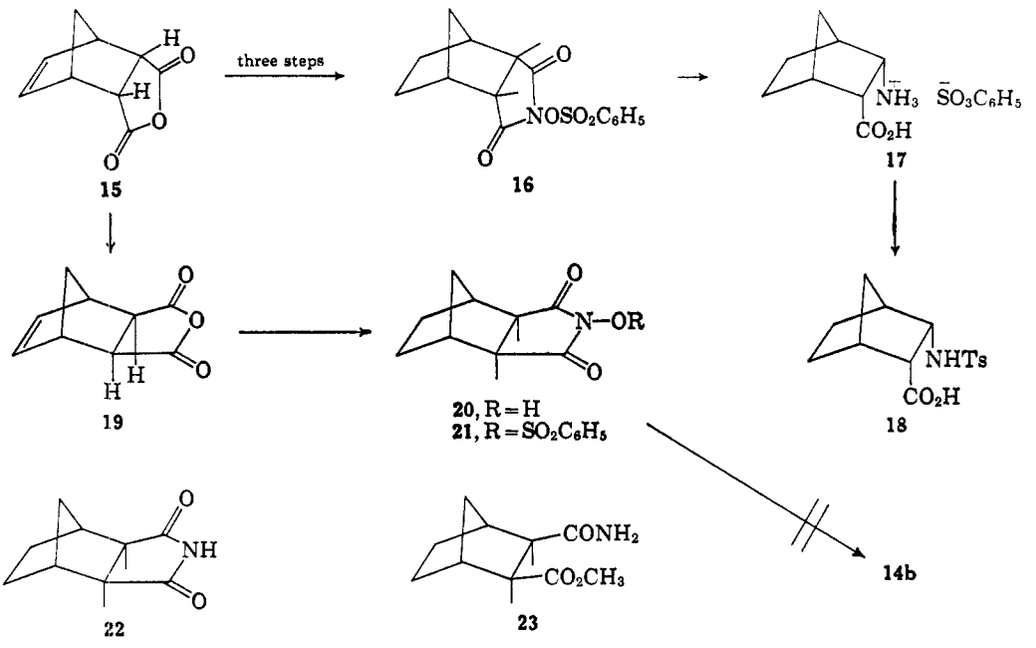
(16) Compound **6** was also reduced to **9** by redox–hydrolysis using potassium iodide in aqueous sodium hydroxide[5] and Raney nickel in ethanol[17] in yields of 41% and 17%, respectively (see Experimental Section). Each method has experimental advantages, but the thiophenol–pyridine procedure invariably gave the highest yields of β-lactam product. In this procedure, however, it is difficult to remove the last traces of diphenyl disulfide from the β-lactam in large-scale runs, and the redox–hydrolysis technique seems preferred.

(17) Suggested by Professor G. L. Buchanan, The University, Glasgow.

(18) The concentration-dependent, marked, and reversible changes characteristically observed in azetidinone solutions are suggestive of monomer ⇌ dimer ⇌ polymer equilibrium and have been ascribed to intermolecular hydrogen bonding between N—H and O=C bonds.[8,15c]

(19) In norbornenes and norbornanes, coupling constants $J_{endo,endo}$ are smaller than their $J_{exo,exo}$ counterparts. Further, there is a difference between coupling of *endo* ($J \cong 0$ cps) and of *exo* (J = 3.0–5.0 cps) protons with the adjacent bridgehead hydrogen: P. Laszlo and P. von R. Schleyer, *J. Am. Chem. Soc.*, **86**, 1171 (1964), and references cited therein.

CHART VI



expected only if the fused-ring protons are *endo*.[19,20] In **29**, the C-2 *endo* proton appeared as a low-field doublet (δ 4.38, J = 5 cps) while the C-5 *endo* proton and the C-1, -6 bridgehead proton resonances overlap to give a multiplet (δ 3.90–3.35) of area 3.

The symmetrical and unsymmetrical vinyl multiplets observed in **26**, **29**, and **31**, respectively, also exhibit virtual coupling of about 0.5 cps.[21–23] This has been ascribed to the interaction of the π electrons of the double bond and the orbital system of the C-9 *anti* proton.[23]

The long-range deshielding effect of a β-lactam ring on the vinyl protons of the norbornene system is worthy of note. Thus, the vinyl resonance in **5** appears as a singlet at δ 5.93. These same protons in β-lactams **25** and **26**, show up as multiplets centered at δ 6.29 and 6.25, respectively.[24] Finally the C-1, -7 bridgehead, C-2, -6 ring-fused, and C-5, -3 allyl protons appear in **33** and **38** as a 6 H multiplet in the δ 3.10–2.10 and 2.90–1.60 regions (Table I).

The nmr spectra of the reduced azetidinones also display the characteristic features of a *cis,exo* fusion of the β-lactam ring, *viz.*, an AB quartet for the *endo* protons (C-2, -5 in **9** and **26**; C-8, -11 in **34**, **36**, and **39**), J = 3.5–4 cps, which in turn show virtual coupling ($J \simeq 1$ cps) with the *anti*-methano bridge proton. In **26**, the more deshielded portion of the AB quartet (δ 3.50) is assigned to the C-2 *endo* proton. The resonances for the allylic, bridgehead protons (C-1, -6) and the high-field portion of the AB quartet (C-5 proton) overlap and appear as a 3 H multiplet of overlapping bands (δ 2.92). The expected upfield shift for the C-1, -6 bridgehead protons is observed in going from an allylic proton (in **26**, δ 2.92) to such protons in the saturated derivative (**9**, δ 2.39).[25] Conversely the C-8 *endo* proton in **34** must be shielded (δ 3.46) relative to its hydrogenated derivative **36**, where this portion of the AB quartet is shifted downfield to δ 3.62.[26] In all unsubstituted β-lactams (Table I), the N–H resonance disappeared on addition of D_2O.

Considerable chemical effort was expended in determining the stereochemistry of adducts **6** and **9**, and therefrom, **25** and **26**. Thus, **9** was rapidly and quantitatively hydrolyzed with hydrochloric acid to the hydrochloride of *exo*-2-amino-3-carboxybicyclo[2.2.1]-heptane (**10**) (Chart I). Alkaline hydrolysis of **6** led to ring-opened **13** which on treatment with hydrochloric acid converted it to **10**. Concomitant esterification of the carboxyl group and hydrolysis of the N-sulfonate salt in **13** was effected in refluxing methanol saturated with hydrogen chloride. Since the free amino ester product could not be made to crystallize, it was converted to the carbamate ester **12** with methyl chloroformate and pyridine at −80°. The same sequence of reactions (methanolysis followed by treatment with methyl chloroformate and pyridine at −80°) also converted **9** to **12**. Methanolysis of **9** in the presence of benzenesulfonic acid led to the crystalline *exo*-2-amino-3-carbomethoxybicyclo-[2.2.1]heptane benzenesulfonate salt **14a**. The C-2, -3 *endo* protons in **10**, **12**, **13**, and **14a** showed identical coupling constants (J = 8 cps) and virtual coupling (J = 1 cps) with the C-7 *anti* proton.[19] Since **10** could be converted to **14a**, all the chemical and spectral evidence clearly indicated that the stereochemical integrity of the C-2, -5 *endo* protons in **6** and **9** had been maintained in the ring-open hydrolysis products, **10**, **12**, **13**, and **14a**.

Bauer and Miarka[27] had successfully converted *endo*-norborn-5-ene-2,3-dicarboxylic anhydride (**15**) to ring-opened *endo*-2-amino-3-carboxynorbornane ben-

(20) The dihedral angle between vicinal bridged and *endo* protons is about 80°; between vicinal bridged and *exo* protons, it is about 45°.

(21) Indicating the C-9 substituent to be *syn* to the double bond.

(22) This and the low wavelength carbonyl absorption eliminate the possibility of the isomeric γ-lactam fused to a nortricyclene structure.

(23) E. I. Snyder and B. Franzus, *J. Am. Chem. Soc.*, **86**, 1166 (1964).

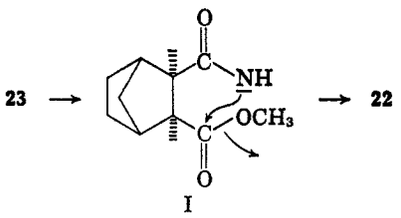
(24) The introduction of a second double bond into the bicyclo[2.2.1]heptyl system deshields all vinyl protons since in **24** these now appear as a 4 H triplet centered at δ 6.75: NMR Spectra Catalog, Vol. 2, Varian Associates, Palo Alto, Calif., 1963, Spectrum 487.

(25) *Cf.* also **25** and **6**.

(26) Dreiding models suggest that the C-8 proton in **34** must be in the π cloud of the cyclopentene double bond, and this suggests a *single isomer* for **34**. Melting point behavior, tlc, and vpc also indicate homogeneity.

(27) L. Bauer and S. Miarka, *J. Org. Chem.*, **24**, 1293 (1959).

zenesulfonate salt **17** in a four-step procedure, the key reaction of which was the stereospecific Lossen rearrangement on N-phenylsulfonyloxynorbornane-*endo*-2,3-dicarboximide (**16**) (Chart VI). Since the *exo* isomer of **15** (*i.e.*, **19**), was available by thermal rearrangement of **15** at 190°,[28] a similar reaction sequence on **19** should then lead to *exo*-2-amino-3-carboxynorbornane benzenesulfonate salt **14b**. Thus, catalytic hydrogenation of **19** produced a saturated anhydride which was converted to the N-hydroxynorbornane-*exo*-2,3-dicarboximide (**20**) with hydroxylamine. The N-phenylsulfonyloxy derivative (**21**) was obtained by treatment of **20** with benzenesulfonyl chloride and triethylamine. Application of the Lossen reaction to **21**, however, led to the isolation of no identifiable rearrangement products. Equally unsuccessful was the Hofmann rearrangement reaction upon the independently prepared norbornane-*exo*-2,3-dicarboximide (**22**) and *exo*-2-carbomethoxy-3-carboxamidonorbornane (**23**). Under Hofmann conditions, **22** was recovered unchanged, while **23** led only to **22**, presumably *via* the anion I.[29]



I

Finally, the analytically pure *endo*-N-tosylate **18**, mp 138–40°, and our *exo*-N-tosylate **11**, mp 198–200°, prepared, respectively, from **17** and **11**, were clearly dissimilar in the infrared.[30]

Catalytic hydrogenation of **26** led to **9**, relating their stereochemistry and that of their precursors, **25** and **6**, and, of course, the similar mode of addition of CSI to **24** and **5**. Formation of the monoadduct **25** must decrease the reactivity of the second double bond toward CSI since all attempts to form the bis adduct from **24** were unsuccessful.[31] When the *exo* approach by CSI is sterically hindered, as in bornylene (**27**), no β-lactam adduct could be detected. At 0°, room temperature, and reflux conditions, a slow reaction did ensue, but infrared analyses never showed the presence of a β-lactam carbonyl band. Substituents in the 7 position of norbornadiene [7-benzoyloxy (**28**) and 7-*t*-butoxy (**30**)] also seemed to influence the reaction course, as evidenced by the lower yield of N-chlorosulfonyl-β-lactam products, **29** and **31**. In both instances, however, very low yields of unidentified non-β-lactam and/or nonamidic products were also obtained.[32]

Our conclusion as to the *exo* stereochemistry of the adducts between CSI and **32** and **37** is based on nmr evidence already discussed (Table I) and the precedented, preferred pathway for additions with such electrophiles as benzenesulfonyl azide,[33] aqueous solutions of mercuric acetate,[34] and acidified alcohols.[35] In all cases, the reaction occurred exclusively at the more strained norbornene double bond.[36]

Finally, the reaction between CSI and **40** was examined to determine the effect of a less strained double bond in a bicyclic system on the ease of cycloaddition. Although the reaction clearly proceeded more slowly in ether/methylene chloride and at room/reflux temperatures, the *cis*-N-chlorosulfonyl-β-lactam (**41**)[37] was isolated as the sole product from the organic phase after the usual aqueous work-up. The benzenethiol–pyridine reduction product **42** was quantitatively hydrolyzed with concentrated hydrochloric acid to *cis*-2-amino-3-carboxybicyclo[2.2.2]octane hydrochloride (**43**). The Lossen rearrangement on N-phenylsulfonyloxybicyclo[2.2.2]octane-2,3-dicarboximide (**46**) also led to **43** (confirming its *cis* stereochemistry).

Conclusions

In general, the mechanism of addition of CSI to strained and/or "activated"[38] olefinic double bonds seems to depend on the substrate. In the bridged bi- and tricyclic olefinic systems studied, the highly strained **24** was the most reactive to CSI, followed by **5**, **32** and **37**, **40**, and **28** and **30**. The decreased reactivity of the latter two may be a reflection of the inductive electron withdrawal by the 7-benzoyloxy- and 7-*t*-butoxy substituents. In all, CSI attack at the more accessible *exo* face is the preferred route. The Woodward–Hoffman rules[9] do not allow a simple 2 + 2 concerted cycloaddition although such a mechanism could simply account for the complete absence of any skeletal rearrangement usually observed in additions to bicycloheptenes, bicyclooctenes, and tricyclodecenes.[11] Our view is based simply on the premise that the concerted closure of the two new σ bonds does not necessarily mean that the bonds are formed at the same rate, and is summarized in Chart VII using norbornene[39,40] as a substrate: (i) initial attack by the electrophilic CSI at the *exo* face with the equilibrium formation of a π complex **47**,[41,42] (ii) rearrangement of **47** to the 1,4-dipole (**48**) where the charged species are aligned for bonding,[43a] (iii) col-

(28) D. Craig, *J. Am. Chem. Soc.*, **73**, 4889 (1951).

(29) The presence of bromine was irrelevant since the cyclization could be effected with sodium methoxide in methanol or concentrated hydrochloric acid. Thus, at least under alkaline conditions, anion formation and ring closure successfully competes with the Hofmann rearrangement. Dreiding models indicate that the distance between the lone pair on nitrogen and the carbonyl carbon in I can approach 1 A.

(30) These compounds unfortunately were too insoluble for nmr comparison.

(31) Variables studied included concentration, solvents, and temperature.

(32) See Experimental Section for details.

(33) A. C. Oehlschlager and L. H. Zalkow, *J. Org. Chem.*, **30**, 4205 (1965).

(34) J. K. Stille and S. C. Stinson, *Tetrahedron*, **20**, 1387 (1964).

(35) S. J. Cristol, W. K. Seifert, D. W. Johnson, and J. B. Jurale, *J. Am. Chem. Soc.*, **84**, 3918 (1962).

(36) We have determined, however, that CSI will add to cyclopentene itself (24-hr reflux in methylene chloride) to form an unstable N-chlorosulfonyl-β-lactam (43%) which must be immediately reduced at −50° to the only slightly more stable β-lactam (48%) [J. M. McCrae and E. J. Moriconi, unpublished information]. However, when excess CSI and **32** were refluxed in methylene chloride, extensive decomposition ensued and only **33** was isolated.

(37) Which is *exo* to one ethano bridge but *endo* to the other.

(38) By inductive and/or resonance effects.

(39) Viewed from the side to show the approximately 20° dihedral angle determined by H—C_3–C_4—H.[40]

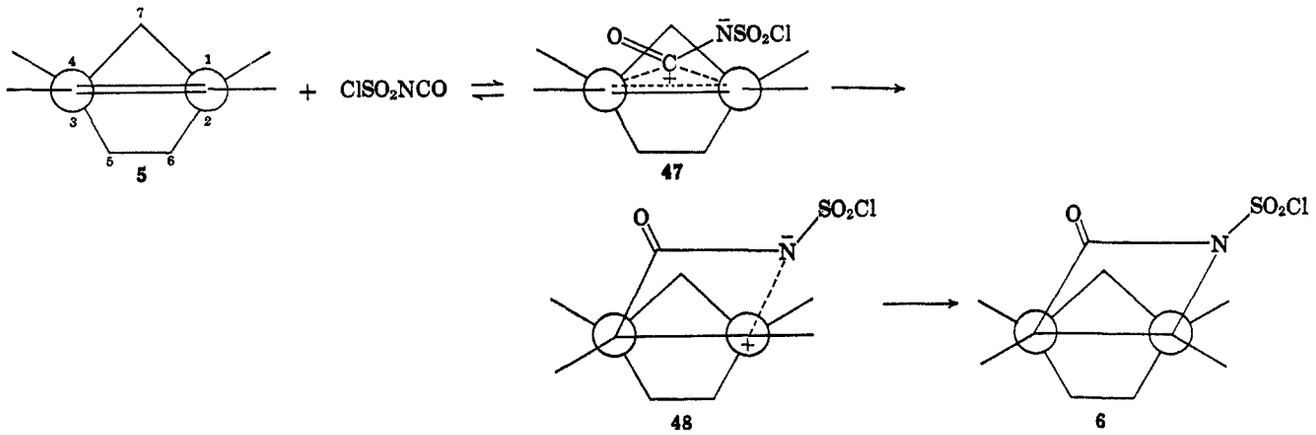
(40) P. von R. Schleyer, *J. Am. Chem. Soc.*, **89**, 701 (1967).

(41) T. G. Traylor and A. W. Baker, *ibid.*, **85**, 2746 (1963).

(42) As the rate-determining step, the formation of **47** would account for the electronic influence of substituents on the ease of addition of CSI to olefins in general.

(43) (a) The increased H—C_3–C_4—H dihedral angle resulting from *exo* attack has decreased torsional strain.[40] Although the α carbon must have some carbonium ion character, the electronegative nitrogen is situated in a favorable position for frontal attack. *Cf.* S. Proskow, H. E. Simmons, and T. L. Cairns, *J. Am. Chem. Soc.*, **88**, 5254 (1966). (b) Similar cycloadducts have been obtained from the addition of benzenesulfonyl isocyanate to norbornene and norbornadiene: H. R. Davis, U. S. Patent 3,185,677 (1965).

CHART VII



lapse of **48** to the β-lactam **6**[43b] (only a small change in atomic positions is necessary for this transformation since the two reactive centers are juxtaposed for bonding). That rearrangement does not occur implies that the collapse of **48** must be more rapid. Finally, relief of torsional strain in going from **5** to **6** provides the impetus for greater reactivity of the norbornene system.

Experimental Section[44]

Reaction of CSI with Norbornene (5).—A solution of 20.0 g (0.21 mole) of **5** in 100 ml of anhydrous ether[45] was cooled to 0° (ice bath). A solution of 30.0 g (0.21 mole) of CSI in 40 ml of anhydrous ether was then added dropwise with stirring. Stirring was continued while the reaction mixture was allowed to attain room temperature. The reaction was considered to be complete when an aliquot no longer gave a violent reaction with water (6 hr). The flask was then recooled to 0° and 50 ml of distilled water was added dropwise with stirring. After addition was complete, the layers were separated. The ether layer was washed with two successive 50-ml portions of water and with 50 ml of brine, and then dried over sodium sulfate. The ether layer was decanted from the sodium sulfate and the solvent removed *in vacuo*. The residual oil, after washing with pentane to remove unreacted norbornene, yielded 40.0 g (86%) of **N-chlorosulfonyl-*exo*-3-aza-4-ketotricyclo[4.2.1.0^{3,5}]nonane (6)**. The oil could not be induced to crystallize, nor was it stable to distillation. Tlc on silica gel G (petroleum ether or benzene eluents), however, showed the presence of only one compound: nmr (CCl_4) δ 4.14 and 3.28 (2 H AB quartet, J = 4 cps, C-2, -5 protons, respectively), 2.62 and 2.15 (2 H broad singlet, C-1, -6 protons, respectively), 2.0–1.0 (6 H multiplet, C-7, -8, -9 protons). Work-up of the aqueous layer yielded no organic products.

Preparation of Two Crystalline, Ring-Opened Derivatives of 6. A. *exo*-2-Amino(N-methylsulfonyloxy)-3-carboxamido-(N′-*p*-chloroanilino)norbornane (7).—A solution of 17.5 g of triethylamine and 22.0 g of *p*-chloroaniline in 50 ml of methanol was added dropwise with stirring to **6**, prepared from 20.0 g (0.21 mole) of **5** and 29.6 g (0.21 mole) of CSI. The white solid which precipitated during the course of the addition was filtered and dried in air to give 45.0 g (62% based on **5**) of **7**. This crude material showed only one spot on tlc; two crystallizations from methanol led to an analytical pure sample, mp 198–200° dec, infrared (KBr) 6.00 μ (C=O).

Anal. Calcd for $C_{15}H_{19}N_2SO_4Cl$: C, 50.40; H, 5.34; N, 7.81. Found: C, 50.48; H, 5.40; N, 7.60.

B. N-Sulfonylazido-*exo*-3,5-diaza-4-ketotricyclo[5.2.1.0^{2,6}]decane (8).—A solution of 16.4 g (0.07 mole) of **6** in 30 ml of ether was added dropwise to a stirred solution of 9.14 g (0.14 mole) of sodium azide in 35 ml of water. The two phase system was vigorously stirred for 2 hr. The ether layer was separated, dried over anhydrous sodium sulfate and filtered. The filtrate was diluted with an equal volume of methanol, and the whole reduced in volume on a steam bath to *ca.* 15 ml. Complete solvent removal *in vacuo* led to a white solid which was recrystallized thrice from 95% ethanol to give 5.1 g (57%) of **8**: mp 142–143°; infrared (KBr) 3.12 (N–H), 4.20 ($-N_3$), 5.88 (C=O), 7.20 and 8.50 μ (SO_2).

Anal. Calcd for $C_8H_{11}N_5SO_3$: C, 37.35; H, 4.31; N, 27.22. Found: C, 37.60; H, 4.31; N, 27.46.

Reduction of N-Chlorosulfonyl-β-lactam (6). A. With Benzenethiol and Pyridine in Acetone.—A solution of 18.2 g (0.077 mole) of **6** and 16.5 g (0.15 mole) of benzenethiol in 60 ml of acetone (Purified, Fisher) was cooled in a Dry Ice–ethanol–water bath to −50°. A solution of 11.0 g (0.12 mole) of pyridine in 40 ml of purified acetone was then added dropwise. During the addition, diphenyl disulfide precipitated out. Stirring at −40° to −50° was continued for 2 hr after the addition was complete. Water (100 ml) was then added, dropwise, with stirring at −50°; the whole was stirred for 0.5 hr and filtered while still cold; the filtrate was extracted five times with 100-ml portions of ether; the extracts were dried over anhydrous sodium sulfate and filtered; and the solvent was removed *in vacuo* to give 8.2 g (77%) of ***exo*-3-aza-4-ketotricyclo[4.2.1.0^{3,5}]nonane (9)** as a yellow oil, slightly contaminated with phenyl disulfide.

The oil was extracted on the steam bath with portions of petroleum ether. The extracts were combined and cooled to −20° to give **9** as white plates: mp 60–61°; nmr (CCl_4) δ 3.38 and 2.95 (2 H AB quartet, J = 4 cps, C-2, -5 protons, respectively), 2.39 (2 H broad singlet, C-1, -6 protons), 1.90–0.90 (6 H multiplet, C-7, -8, -9 protons).

Anal. Calcd for $C_8H_{11}NO$: C, 70.04; H, 8.08; N, 10.21. Found: C, 70.09; H, 8.14; N, 10.24.

Vpc of **9** (FFAP suspended on Chromosorb W; 200°; He flow 50 cc/min) showed a single product with a retention time of 3.25 min.

Redox–hydrolysis of a methanolic solution of **6** with KI and 12 *N* NaOH (pH 3–7) led to a 41% yield of **9**.

With Raney Nickel.—To a stirred suspension of 32.0 g of freshly prepared Raney Ni catalyst in absolute ethanol at 0° was added, dropwise, a solution of 20.0 g (0.086 mole) of **6** in absolute ethanol. The resulting green solution was filtered through Filter-Cel and the solvent removed *in vacuo* to give a green oil. The oil was triturated with water and extracted with petroleum ether to give 2.0 g of **9** (17%).

Hydrolysis of 9 with Concentrated HCl.—To 3.0 g (0.022 mole) of **9** was added sufficient concentrated HCl to just cover the β-lactam. After a short induction period, an exothermic reaction occurred and the contents of the beaker set to a white,

(44) All melting points and boiling points are uncorrected. Infrared spectra were obtained on a Perkin-Elmer, Model 337, grating spectrophotometer. Nmr spectra were determined at 60 Mc with a Varian Model A-60 spectrometer; chemical shifts are expressed as δ values in ppm relative to a tetramethylsilane internal standard. Microanalyses were determined by the Schwarzkopf Microanalytical Laboratory.

CSI was obtained from the American Hoechst Corp.; norbornene (**5**), norbornadiene (**24**), and *endo*-dicyclopentadiene (**32**) were purchased from Aldrich. 7-Benzoyloxy- (**28**) and 7-*t*-butoxynorbornadiene (**30**), bicyclo-[2.2.2]octene (**40**), and bicyclo[2.2.2]octane-2,3-dicarboxylic anhydride (**44**) were obtained from Frinton. Solvent petroleum ether used throughout refers to the 60–70° mixture.

(45) A marked increase in reaction rate was observed when polar solvents acetyl chloride or acetonitrile were used. Yields of **6** dropped, however, to 50 and 70%, respectively.

pasty mass. This was dried *in vacuo* over concentrated H_2SO_4, and then recrystallized from methanol–ether to yield 3.8g (98%) of the **hydrochloride** of ***exo*-2-amino-3-carboxybicyclo-[2.2.1]heptane** (**10**) as white, microcrystals: mp 240–245° dec; infrared (KBr) 5.81 μ (C=O); nmr (D_2O) δ 3.58 and 2.91 (2 H AB quartet, J = 8 cps), 2.72 and 2.50 (2 H broad singlets, C-1, -4 protons), 2.01–1.01 (6 H multiplet, C-5, -6, -7 protons).

Anal. Calcd for $C_8H_{14}NO_2 \cdot HCl$: C, 50.13; H, 7.36; N, 7.31. Found: C, 50.09; H, 7.47; N, 7.34.

Preparation of N-Tosyl Derivative (11) of 10.—A solution of 0.350 g (0.0018 mole) of **10** in 5.8 ml of 1 *N* NaOH and an ethereal solution of 0.364 g (0.0018 mole) of *p*-toluenesulfonyl chloride was mechanically shaken for 4 hr. The layers were separated and the ether layer was discarded. The aqueous layer was acidified with concentrated HCl to yield an amorphous precipitate. Four recrystallizations from 60% ethanol–water afforded 0.26 g (41%) of ***exo*-2-*p*-toluenesulfonamide-3-carboxybicyclo[2.2.1]heptane** (**11**): mp 198–200°; infrared (KBr) 3.08 μ (N–H), 5.88 (C=O).

Anal. Calcd for $C_{15}H_{19}NO_4S$: C, 58.23; H, 6.19; N, 4.52. Found: C, 58.04; H, 6.08; N, 4.74.

Hydrolysis of 9 with Benzenesulfonic Acid.—To 3.0 g (0.022 mole) of **9** dissolved in 50 ml of anhydrous methanol was added excess benzenesulfonic acid monohydrate (Eastman). The solution was evaporated on the steam bath to a volume of 10 ml, and ether was added. After cooling, the precipitated salt was filtered and dried to yield 5.0 g (75%) of ***exo*-2-amino-3-carbomethoxybicyclo[2.2.1]heptane benzenesulfonate** (**14a**): mp 139–140° (recrystallization from methanol–ether did not raise the melting point): infrared (KBr) 5.78 μ (C=O); nmr (D_2O) δ 3.62 (3 H singlet, OCH_3), 3.36 and 2.72 (2 H AB quartet, J = 8 cps, C-2, -3 protons), 1.90–1.00 (6 H multiplet, C-5, -6, -7 protons).

Anal. Calcd for $C_9H_{15}NO_2 \cdot C_6H_5SO_3H$: C, 54.97; H, 6.47; N, 4.28. Found: C, 55.23; H, 6.61; N, 4.54.

Preparation of N-Carbomethoxy-*exo*-2-amino-3-carbomethoxynorbornane (**12**).—Gaseous HCl was bubbled through a solution of 7.9 g (0.06 mole) of **9** in 150 ml of anhydrous methanol until refluxing commenced. The solvent was then removed *in vacuo;* the residual oil was made basic with cold NaOH solution and extracted with ether. The ether extracts were dried over anhydrous Na_2SO_4, and, after filtration, the solvent was removed *in vacuo*. The crude amino ester was converted to the carbamate **12** using excess methyl chloroformate and pyridine at −70°. An analytical sample was prepared by chromatography on silica gel using benzene–ether (2:1) as the eluent. This fraction was recrystallized from benzene–pentane to give **12**: mp 124–126°; infrared (KBr) 3.05 μ (N–H), 5.78 and 5.93 (C=O's); nmr ($CDCl_3$) δ 4.70 (6 H singlet, OCH_3), 3.96 and 2.70 (2 H AB quartet, J = 8 cps, C-2, -3 protons), 2.48 and 2.20 (2 H broad singlets, C-1, -4 protons), 2.00–1.00 (6 H, multiplet, C-5, -6, -7 protons).

Anal. Calcd for $C_{11}H_{17}NO_4$: C, 58.13; H, 7.54; N, 6.16. Found: C, 58.28; H, 7.37; N, 6.44.

Alternatively **12** was prepared from **6** *via* **13**. N-Chlorosulfonyl-β-lactam **6** (21.1 g, 0.09 mole) was added dropwise (3 hr) with stirring to 60 ml of 6 *N* NaOH solution maintained at 40–50°. After addition was complete, the yellow solution was cooled to 0° and carefully acidified with concentrated HCl to pH 4. The white crystalline precipitate was filtered, quickly washed with ice water, and then dissolved in warm water (50°). The addition of methanol to saturation followed by cooling to 0° led to 6.5 g (26%) of slightly impure **13**, mp 200° dec.

Anal. Calcd for $C_8H_{12}NSO_5Na$: C, 37.35; H, 4.70; N, 5.45. Found: C, 38.29; H, 4.73; N, 5.54.

Gaseous HCl was bubbled into a refluxing suspension of 3.1 g (0.01 mole) of **13** in 100 ml of anhydrous methanol. Solution was soon effected; when a white solid began to precipitate, the HCl source was removed and refluxing continued for 30 min. The solvent was removed *in vacuo*, and the residual oil, cooled in an ice bath, was made strongly basic with 12 *N* NaOH. The basic solution was extracted four times with 50-ml portions of ether, and the extracts were dried over anhydrous Na_2SO_4. Filtration followed by treatment of the ethereal solution with methyl chloroformate and pyridine at −70° led to the carbamate **12** (mp 117–119°) after recrystallization from benzene–pentane. That this product was polymorphic with the carbamate obtained from **9** was shown by indistinguishable (i) infrared spectra, (ii) tlc behavior (*e.g.*, silica gel G and eluents benzene–pentane, ether, and ethyl acetate could effect no separation of a mixture of the two); and (iii) vpc (identical retention time of 2.7 min on a QF-1 column maintained at 70° with a He flow of 60 cc/min).

Finally, **13** (2.0 g, 0.008 mole) was converted to **10** by refluxing (45 min) in 10 ml of concentrated HCl. After cooling to 0°, the precipitated NaCl was removed by filtration, and the filtrate was evaporated to dryness *in vacuo*. Recrystallization of the residue from methanol–ether gave 0.8 g (53%) of **10**, identical with that obtained from **9**.

Preparation of N-Tosyl Derivative (18) of 17.—From 1.8 g (0.006 mole) of ***endo*-2-amino-3-carboxynorbornane benzenesulfonate** (**17**), mp 228–232°, prepared by the Bauer and Miarka procedure,[27] 1.1 g of *p*-toluenesulfonyl chloride, and 15 ml of 1 *N* NaOH was obtained 0.6 g (32%) of ***endo*-2-*p*-toluenesulfonamido-3-carboxybicyclo[2.2.1]heptane** (**18**), mp 138–140°, employing the same procedure used to prepare **11**: infrared (KBr) 3.03 (N–H) and 5.91 μ (C=O).

Anal. Calcd for $C_{15}H_{19}NO_4S$: C, 58.23; H, 6.19; N, 4.52. Found: C, 58.33; H, 6.15; N, 4.35.

Preparation of *exo*-Norbornane-2,3-dicarboxylic Anhydride.—***exo*-Norborn-5-ene-2,3-dicarboxylic anhydride** (**19**), mp 141–143°, was prepared from the *endo* anhydride by Craig's procedure[28] with only minor modification.[46] Hydrogenation of **11** over 5% Pd-C in a Parr apparatus led to ***exo*-norbornane-2,3-dicarboxylic anhydride,** mp 78–79°.

Preparation of N-Hydroxynorbornane-*exo*-2,3-dicarboximide (**20**).—The procedure used to prepare the *endo* isomer was used.[27] Thus, from 3.0 g (0.018 mole) of ***exo*-norbornane-2,3-dicarboxylic anhydride,** 1.6 g of $NH_2OH \cdot HCl$, and 1.4 g of Na_2CO_3 in 30 ml of H_2O was obtained 3.1 g (95%) of **20** as white needles: mp 123–124° (from benzene–pentane); infrared (KBr) 2.94 (OH), 5.70 and 5.98 μ (C=O's); nmr (DMSO-d_6) δ 10.20 (1 H broad mound, OH), 2.65 (2 H singlet, C-2, -3 protons), 2.48 (2 H doublet, C-1, -4 protons), 1.7–1.0 (6 H multiplet, C-5, -6, -7 protons).

Anal. Calcd for $C_9H_{11}NO_3$: C, 59.66; H, 6.12; N, 7.73. Found: C, 59.85; H, 6.37; N, 7.71.

Preparation of N-Phenylsulfonyloxynorbornane-*exo*-2,3-dicarboximide (**21**).—The procedure used to prepare the *endo* isomer was used.[27] Thus from 3.1 g (0.017 mole) of **20**, 8.2 ml of triethylamine and 2.5 ml of benzenesulfonyl chloride in 25 ml of chloroform was obtained 3.2 g (57%) of **21**. Three recrystallizations from 95% ethanol gave pure **21**: mp 120–121°; infrared (KBr) 5.56 and 5.75 (C=O's), 7.25 and 8.42 μ (SO_2); nmr ($CDCl_3$) δ 8.18–7.50 (5 H aromatic multiplet), 2.68 (4 H broad singlet, C-1, -2, -3, -4 protons), 1.9–1.1 (6 H multiplet, C-5, -6, -7 protons).

Anal. Calcd for $C_{15}H_{15}NO_5S$: C, 56.06; H, 4.71; N, 4.36. Found: C, 56.25; H, 4.75; N, 4.38.

Treatment of **21** under Lossen rearrangement conditions led to no identifiable products.

Preparation of Norbornane-*exo*-2,3-dicarboximide (**22**).—A suspension of ***exo*-norbornane-2,3-dicarboxylic anhydride** (5.7 g, 0.34 mole) was refluxed in 75 ml of concentrated ammonium hydroxide until the anhydride dissolved completely. The solution was evaporated to dryness and the solid residue heated at 210° (oil bath) for 15 min after which it was permitted to cool, protected from moisture. The solidified melt was recrystallized from benzene–pentane to give 3.4 g (61%) of **22**: mp 149–150°; infrared (KBr) 3.14 (N-H), 5.64 and 5.94 μ (C=O's); nmr ($CDCl_3$) δ 9.30 (1 H, broad mount, N–H), 2.66 (4 H, two overlapping singlets, low field absorption shows fine splitting, C-1, -2, -3, -4 protons), 1.90–1.20 (6 H multiplet, C-5, -6, -7 protons).

Anal. Calcd for $C_9H_{11}NO_2$: C, 65.43; H, 6.71; N, 8.48. Found: C, 65.22; H, 6.52; N, 8.56.

A sample of the solid residue before pyrolysis (presumably the diammonium salt) was dissolved in a minimum amount of water and acidified. The resulting white precipitate was filtered, dried, and recrystallized from acetonitrile to give **norbornane-*exo*-2,3-dicarboxylic acid,** mp 150–151° dec (lit.[47] mp 153°).

Treatment of **22** under Hofmann rearrangement conditions led only to an 80% recovery of starting material and no detectable rearrangement products.

(46) A private communication from Velsicol Chem. Co. suggested the use of toluene to be added after pyrolysis was completed and the flask contents had cooled to 100°. This technique gave a manageable precipitate rich in the *exo* isomer.

(47) K. Alder and G. Stein, *Ann.*, **504**, 216 (1933).

Preparation of *exo*-2-Carbomethoxy-3-carboxamidonorbornane (23).—***exo*-2-Carbomethoxy-3-carboxynorbornane** (mp 96°, lit.[47] mp 95°; 2.0 g, 0.01 mole) was treated with 20.0 g of oxalyl chloride. After stirring at room temp for 5 days, the excess oxalyl chloride was removed *in vacuo* (HOOD) at 30°. The crude acid chloride, obtained as an oil, was dissolved in 250 ml of anhydrous ether and cooled to Dry Ice–acetone bath temperature. Gaseous ammonia was bubbled into the solution for 30 min and the whole stirred for an additional hour. After the excess ammonia and ether were allowed to evaporate, the resulting white residue was extracted (Soxhlet) with $CHCl_3$ for 8 hr. Removal of the chloroform *in vacuo* followed by recrystallization from benzene–pentane gave 2.09 g (95%) of **23**: mp 131–133°; infrared (KBr) 5.75 (ester C=O), 5.95 (shoulder) and 5.99 μ (amide C=O); nmr ($CDCl_3$) δ 6.12 (2 H broad singlet, NH_2), 3.63 (3 H singlet, CH_3), 2.65 (2 H doublet, C-2, -3 protons), 2.28 (2 H multiplet, partially overlapping the 2.65 signal, C-1, -4 protons), 1.90–1.10 (6 H multiplet, C-5, -6, -7 protons).

Anal. Calcd for $C_{10}H_{15}NO_3$: C, 60.93; H, 7.67; N, 7.00. Found: C, 60.82; H, 7.58; N, 6.92.

Treatment of **23** under Hofmann rearrangement conditions (CH_3OH, CH_3ONa, Br_2) led only to a 48% yield of imide **13**.

Reaction of CSI with Norbornadiene (24).—A solution of 30.0 g (0.22 mole) of CSI in 50 ml of anhydrous ether was added dropwise to a magnetically stirred solution of 20.0 g (0.22 mole) of **24** in an equal volume of anhydrous ether maintained at −40°. After stirring for an additional 2 hr at this temperature, the mixture was allowed to warm slowly to ambient temperature. The reaction was considered complete when an aliquot no longer gave a violent reaction with water. The volume was reduced to *ca.* 20 ml under a N_2 stream with gentle warming, and pentane was then added. Cooling the solution to −20° for 24 hr gave 47.0 g (94%) of **N-chlorosulfonyl-*exo*-3-aza-4-keto-tricyclo[4.2.1.0^{2,5}]non-7-ene (25)**: mp 59–60° after one recrystallization from pentane; nmr (CCl_4) δ 6.50–6.18 (2 H vinyl multiplet), 4.20 and 3.20 (2 H AB quartet, J = 4 cps, C-2, -5 protons), 3.42 (2 H broad singlet, C-1, -6 protons), 1.88 (2 H singlet, C-9 protons).

Anal. Calcd for $C_8H_8NSO_3Cl$: C, 41.11; H, 3.45; N, 5.99. Found: C, 41.12; H, 3.59; N, 6.27.

Reduction of N-Chlorosulfonyl-β-lactam (25) with Benzenethiol and Pyridine in Acetone.—Using the same procedure as in the benzenethiol–pyridine reduction of **6**, a solution of 7.9 g (0.10 mole) of pyridine in 50 ml of acetone was added dropwise (2 hr) to a cooled (−50°) solution of 16.6 g (0.071 mole) of **25** and 15.4 g (0.14 mole) of benzenethiol in 50 ml of acetone. The usual work-up yielded an oil which was thrice recrystallized from benzene–pentane to give 6.9 g (72%) of ***exo*-3-aza-4-keto-tricyclo[4.2.1.0^{2,5}]non-7-ene (26)**: mp 116–117°; nmr ($CDCl_3$) δ 7.2–6.9 (1 H broad mound, N–H), 6.25 (2 H, center of vinyl septet), 3.50 (1 H doublet, C-2 proton), 2.92 (3 H, center of overlapping bands, C-1, -5, -6 protons), 1.70 (2 H, broad singlet, C-9 protons).[48]

Anal. Calcd for C_8H_9NO: C, 71.08; H, 6.71; N, 10.37. Found: C, 71.31; H, 6.81; N, 10.61.

Hydrogenation of 26 to 9.—A solution of **26** (1.0 g, 0.0074 mole) in 50 ml of ethyl acetate was hydrogenated in a Parr Apparatus over 5% Pd–C at an initial hydrogen pressure of 50 psi for 30 min. The catalyst was removed by filtration through Filter-Cel and the solvent removed *in vacuo*. The residual oil was recrystallized from petroleum ether to yield 0.84 g (82%) of **9**.

Reaction of CSI with 7-Benzoyloxynorbornadiene (28).—A solution of 6.5 g (0.03 mole) of **28** in 50 ml of ether was treated with 4.2 g (0.03 mole) of CSI in 50 ml of ether at −50° in the usual manner. After stirring for 20 hr at room temperature, 50 ml of water was added and the two-phase system was separated. Conventional work-up of the ether layer led to **N-chlorosulfonyl-*exo*-3-aza-4-keto-9-*syn*-benzoyloxytricyclo-[4.2.1.0^{2,5}]non-7-ene (29)** as a yellow oil which crystallized from methylene chloride–petroleum ether as white plates (1.2 g, 11%): mp 109° dec; nmr ($CDCl_3$) δ 8.18–7.20 (5 H aromatic multiplet), 6.50–6.15 (2 H vinyl multiplet), 5.15 (1 H broad singlet, C-9 proton), 4.38 (1 H doublet, J = 5 cps, C-2 proton), 3.90–3.25 (3 H multiplet, C-1, -5, -6 protons).

Anal. Calcd for $C_{15}H_{12}NO_5SCl$: C, 50.90; H, 3.42; N, 3.98. Found: C, 51.21; H, 3.47; N, 4.01.

Work-up of the aqueous layer led to 0.1 g of a white crystalline solid, mp 136°, of empirical formula $C_{15}H_{12}O_4$: infrared (KBr) 5.71 (C=O doublet) and 5.88 μ (ester C=O); nmr ($CDCl_3$) δ 8.20–7.30 (5 H aromatic multiplet), 5.32 (1 H singlet α to $OCOC_6H_5$), 4.86 (1 H narrow, partially resolved quartet), 3.28 (1 H doublet), 2.88 (2 H broad singlet), 2.50–1.68 (4 H multiplet).

Reaction of CSI with 7-*t*-Butoxynorbornadiene (30).—Using a procedure similar to that for the preparation of **29**, 16.0 g (0.10 mole) of **30** and 14.1 g (0.10 mole) of CSI ultimately led to 10.6 g (35%) of **N-chlorosulfonyl-*exo*-3-aza-4-keto-9-*syn*-*t*-butoxytricyclo[4.2.1.0^{2,5}]non-7-ene (31)** as white plates (from petroleum ether): mp 82–83° dec; nmr ($CDCl_3$) 6.28–6.00 (2 H vinyl multiplet), 4.26 and 3.49 (2 H AB quartet, J = 5 cps, C-2, -5 protons), 3.78 (1 H singlet with fine splitting, C-9 proton), 3.4–3.2 and 3.2–3.0 (2 H unresolved multiplets, C-1, -6 protons), 1.20 (9 H singlet, *t*-butyl).

Anal. Calcd for $C_{12}H_{16}O_4NSCl$: C, 47.13; H, 5.28; N, 4.58. Found: C, 47.40; H, 5.43; N, 4.86.

From the aqueous layer, an unidentified compound was isolated (*Anal.* Found: C, 31.18; H, 3.85; N, 7.14; S, 1628; mol wt 175): mp 71–72°; nmr ($CDCl_3$) δ 3.12 (2 H singlet) and 1.80 (7 H singlet).

Reaction of CSI with *endo*-Dicyclopentadiene (32).—A solution of 14.4 g (0.10 mole) of CSI in 50 ml of anhydrous ether was added at 0° to 13.2 g (0.10 mole) of **32** in 50 ml of anhydrous ether. The solution was stirred overnight as the temperature rose slowly to ambient temperature. Water (30 ml) at 0° was added and the two phases were separated. The ether layer was extracted twice with 25-ml portions of water, after which it was dried over anhydrous Na_2SO_4. Hexane (20 ml) was then added to the filtered ether solution, and the solution evaporated to cloudiness. Refrigeration at −20° gave 21.2 g (78%) of an inseparable mixture of **N-chlorosulfonyl-*endo*-*exo*-9-aza-10-ketotetracyclo[5.4.1.0^{2,6}0^{8,11}]dodec-3-** and **-4-enes (33)** which was obtained as white chunks: mp 59–61° (from benzene–pentane); infrared (KBr) 5.49 (C=O), 7.09 and 8.49 μ (SO_2); nmr ($CDCl_3$) δ 5.90–5.60 (2 H vinyl multiplet), 4.20 and 3.38 (2 H AB quartet, J = 5 cps, C-8, -11 protons), 3.10–2.10 (6 H multiplet, methine and allyl protons), 1.78 (2 H singlet, C-12 protons).

Anal. Calcd for $C_{11}H_{12}NSO_3Cl$: C 48.26; H, 4.42; N, 5.12 Found: C, 48.40; H, 4.63; N, 5.30.

Work-up of the aqueous layer led to no isolable organic products

Reduction of **33** (7.2 g, 0.027 mole) with 5.8 g of benzenethiol in 50 ml of acetone and 3.2 g of pyridine in 40 ml of acetone at −40° led to an inseparable mixture of ***endo*,*exo*-9-aza-10-ketotetracyclo[5.4.1.0^{2,6}0^{8,11}]dodec-3-** and **-4-enes (34)** (2.3 g, 44%): mp 112–114° (from benzene–pentane); nmr ($CDCl_3$) δ 6.48 (1 H broad singlet, N–H), 5.90–5.60 (2 H vinyl multiplet), 3.46 and 3.18 (2 H AB quartet, J = 4 cps, C-8, -11 protons), 2.90–2.00 (6 H multiplet, methine and allyl protons), 1.68 (2 H quartet, J = 10 cps, C-12 protons).

Anal. Calcd for $C_{11}H_{13}NO$: C, 75.40; H, 7.47; N, 7.99. Found: C, 75.14; H, 7.74; N, 8.17.

Hydrolysis of **34** with concentrated HCl quantitatively converted it to the **amino acid hydrochloride 35**: mp 200° dec (from methanol–ether); infrared (KBr) 5.88 μ (C=O); nmr (DMSO-d_6) δ 8.5–7.5 (3 H multiplet, $^+NH_3$), 5.80–5.48 (2 H vinyl multiplet), 3.3–1.9 (8 H multiplet), 1.42 (2 H doublet, C-10 protons).

Anal. Calcd for $C_{11}H_{16}NO_2Cl$: C, 57.51; H, 7.02; N, 6.10. Found: C, 57.35; H, 7.26; N, 5.81.

Hydrogenation of **34** (1.0 g) in ethyl acetate over 5% Pd–C at an initial pressure of 50 psi in a Parr apparatus quantitatively converted it to ***endo*,*exo*-9-aza-10-ketotetracyclo[5.4.1.0^{2,6}0^{8,11}]-dodecane (36)**: mp 108–110° (from benzene–pentane); nmr ($CDCl_3$) δ 6.62 (1 H broad mound, N–H), 3.62 and 3.21 (2 H AB quartet, J = 3.5 cps, C-8, -11 protons), 2.48 (4 H doublet, C-1, -2, -6, -7 protons), 1.90–1.20 (6 H multiplet, C-3, -4, -5 protons), 1.53 (2 H doublet, C-12 protons).

Anal. Calcd for $C_{11}H_{15}NO$: C, 74.54; H, 8.53; N, 7.90. Found: C, 74.35; H, 8.46; N, 8.12.

Reaction of CSI and *exo*-Dicyclopentadiene (37).—Using the same experimental procedure as with the *endo* derivative, 13.2 g

(48) The nmr spectrum of **26** in benzene solvent shows the C-9 protons as a quartet centered at δ 1.6 with a geminal coupling constant of 10 cps. For the effect of solvent benzene on nmr spectra, *cf.* J. Ronayne and D. White, *Chem. Commun.*, 712 (1966); K. C. Ramey, D. C. Lini, R. M. Moriarty, H. Gopal, and H. G. Welsh, *J. Am. Chem. Soc.*, **89**, 2401 (1967).

(0.10 mole) of **37**[49] in 75 ml of ether and 14.1 g (0.10 mole) of CSI in 40 ml of ether ultimately gave 19.4 g (71%) of an inseparable mixture of **N-chlorosulfonyl-*exo*-*exo*-9-aza-10-ketotetracyclo[5.4.1.0^{2,6}0^{5,11}]dodec-3-** and **-4-enes (38)**: mp 88–90° (from benzene–pentane); nmr ($CDCl_3$) δ 5.90–5.60 (2 H symmetrical vinyl multiplet), 4.28 and 3.28 (2 H AB quartet, J = 4 cps, C-8, -11 protons), 2.90–1.60 (6 H multiplet, methine and allyl protons), 1.62 (2 H singlet, C-12 protons).

Anal. Calcd for $C_{11}H_{12}NSO_3Cl$: C, 48.26; H, 4.42; N, 5.12. Found: C, 48.45; H, 4.51; N, 5.32.

Reduction of **38** (7.6 g, 0.028 mole) with 5.8 g of benzenethiol in 50 ml of acetone and 3.2 g of pyridine in 40 ml of acetone at −40° led ultimately to an inseparable mixture of ***exo*,*exo*-9-aza-10-ketotetracyclo[5.4.1.0^{2,6}0^{5,11}]dodec-3-** and **-4-enes (39)** (34%): mp 129–131° (from benzene–pentane); nmr ($CDCl_3$) δ 6.92 (1 H broad mound, N–H), 5.90–5.40 (2 H vinyl multiplet), 3.48 and 3.05 (2 H AB quartet, J = 4 cps, C-8, -11 protons), 2.80–1.70 (6 H multiplet, methine and allyl protons), 1.42 (2 H singlet, C-12 protons).

Anal. Calcd for $C_{11}H_{13}NO$: C, 75.40; H, 7.47; N, 7.99. Found: C, 75.58; H, 7.60; N, 7.83.

Reaction of CSI with Bicyclo[2.2.2]octene (40).—A solution of 6.5 g (0.05 mole) of **40** in 50 ml of anhydrous ether[50] was added dropwise to a stirred solution of 7.8 g (0.05 mole) of CSI in 50 ml of anhydrous ether. The solution was then refluxed for 120 hr, cooled to 0° and treated with 30 ml of water; the unreacted CSI reacted vigorously. The ether layer was separated and washed three times in succession with 30-ml portions of water (wash water added to aqueous layer), followed by 30 ml of a saturated salt solution. The ethereal solution was dried and the solvent removed *in vacuo* to give 8.5 g (63%) of **N-chlorosulfonyl-3-aza-4-ketotricyclo[4.2.2.0^{2,5}]decane (41)** as a viscous oil. Tlc on silica gel G, using pentane and pentane–ether as eluents, showed the presence of only a single product. Recrystallization from petroleum ether gave **41** as a white solid: mp 60–62°; nmr ($CDCl_3$) δ 4.36 and 3.46 (2 H, AB quartet, J = 7 cps, C-2, -5 protons), 2.38–1.92 (2 H multiplet, C-1, -6 protons), 1.9–1.7 (8 H multiplet, $-CH_2-$).

Anal. Calcd for $C_9H_{12}NSO_3Cl$: C, 43.29; H, 4.84; N, 5.61. Found: C, 43.52; H, 5.09; N, 5.34.

Work-up of the aqueous layer led to no isolable organic products.

Reduction of **41** (5.0 g, 0.02 mole) with benzenethiol (4.4 g, 0.04 mole) in 100 ml of acetone and 2.4 g (0.03 mole) of pyridine in 30 ml of acetone led ultimately to a yellow oil which crystallized from petroleum ether to give 2.2 g (78%) of the β-lactam, **3-aza-4-ketotricyclo[4.2.2.0^{2,5}]decane (42)** as white needles: mp 207–210° dec; nmr ($CDCl_3$) δ 7.18 (1 H broad mound N–H), 3.62 and 3.12 (2 H, partially resolved quartets), 2.18–1.28 (10 H multiplet).

Anal. Calcd for $C_9H_{13}NO$: C, 71.49; H, 8.64; N, 9.26. Found: C, 71.48; H, 8.56; N, 9.23.

Hydrolysis of 42 with Hydrochloric Acid.—A 1.09-g (0.007 mole) sample of **42** was hydrolyzed with concentrated HCl at room temperature to give 1.5 g (78%) of ***cis*-2-amino-3-carboxybicyclo[2.2.2]octane hydrochloride (43)**: mp 232–235° dec (from methanol–ether); infrared (KBr) 5.88 μ (C=O); nmr (DMSO-d_6) δ 8.4–7.9 (3 H, broad mound, $^+NH_3$), 3.4 and 3.0 (2 H, centers of two broad doublets, C-2, -3 protons), 2.1–1.2 (10 H multiplet).

Anal. Calcd for $C_9H_{16}O_2NCl$: C, 52.55; H, 7.84; N, 6.81. Found: C, 52.76; H, 8.08; N, 6.76.

Preparation of N-Hydroxybicyclo[2.2.2]octane-2,3-dicarboximide (45).—A mixture of 3.0 g (0.017 mole) of **bicyclo[2.2.2]octane-2,3-dicarboxylic anhydride (44)**, 1.1 g (0.017 mole) of hydroxylamine hydrochloride, and 0.9 g (0.008 mole) of sodium carbonate in 45 ml of water was refluxed for 1 hr; the resulting solution was acidified with concentrated HCl while still hot and cooled to yield 2.7 g (81%) of **45**: mp 164° after one recrystallization from benzene; infrared (KBr) 2.91 (OH), 5.63 (weak) and 5.90 μ (C=O's); nmr (DMSO-d_6) δ 10.6 (1 H, broad mound, O–H), 2.88 (2 H broad singlet, C-2, -3 protons), 2.3–1.9 (2 H multiplet, C-1, -4 protons), 1.68 and 1.38 (8 H, two singlets, C-5, -6, -7, -8 protons).

Anal. Calcd for $C_{10}H_{13}O_3N$: C, 61.65; H, 6.71; N, 7.17. Found: C, 61.42; H, 6.51; N, 7.27.

Preparation of N-Phenylsulfonyloxybicyclo[2.2.2]octane-2,3-dicarboximide (46).—Benzenesulfonyl chloride (2.3 ml) was added to a cooled (0°), stirred solution of **45** and 7.8 ml of triethylamine. Stirring was continued 15 min at 0° and 45 min at ambient temperature. The volatile material was removed *in vacuo* and the white residue remaining was recrystallized from 95% ethanol to give 2.7 g (62%) of **46**. An analytical sample was obtained from ethyl acetate–benzene: mp 169–171°; infrared (KBr) 5.52 (shoulder) and 5.74 (C=O's), 7.28 and 8.35 μ (SO_2); nmr ($CDCl_3$) δ 8.20–7.60 (5 H aromatic multiplet), 2.95 (2 H singlet, C-2, -3 protons), 1.66 (8 H, center of doublet, C-5, -6, -7, -8 protons).

Anal. Calcd for $C_{16}H_{17}NO_5S$: C, 57.30; H, 5.11; N, 4.18. Found: C, 57.57; H, 5.29; N, 4.16.

Lossen Rearrangement on 46.—A suspension of 2.0 g (0.006 mole) of **46** in 30 ml of 15% NaOH solution was refluxed until solution was complete, whereupon the hot solution was acidified with concentrated HCl, cooled, and extracted with chloroform. The chloroform extracts ultimately led to 0.4 g (0.002 mole) of **45**. The aqueous solution was evaporated to dryness, and the residue extracted with absolute ethanol. The ethanol extracts ultimately yielded 0.5 g (0.002 mole, 42% based on **46** consumed) of **43**.

Registry No.—CSI, 1189-71-5; **6**, 14932-21-9; **7**, 14932-23-1; **8**, 14932-24-2; **9**, 14805-23-3; **10**, 14932-25-3; **11**, 14805-24-4; **12**, 14932-26-4; **13**, 14805-25-5; **14a**, 14805-26-6; **18**, 14932-27-5; **20**, 14805-27-7; **21**, 14805-28-8; **22**, 14805-29-9; **23**, 14932-28-6; **25**, 14805-30-2; **26**, 14805-31-3; **29**, 14932-29-7; **31**, 14951-94-1; **33** (3-ene), 14932-30-0; **33** (4-ene), 14805-35-7; **34** (3-ene), 14805-32-4; **34** (4-ene), 14805-33-5; **35** (3-ene), 14805-34-6; **35** (4-ene), 14805-36-8; **36**, 14805-37-9; **38** (3-ene), 14951-95-2; **38** (4-ene), 14932-22-0; **39** (3-ene), 14930-20-2; **39** (4-ene), 14930-21-3; **41**, 14932-31-1; **42**, 14932-32-2; **43**, 14932-33-3; **45**, 14795-80-3; **46**, 14795-81-4; *exo*-norbornane-2,3-dicarboxylic anhydride, 14166-28-0.

(49) H. A. Bruson and T. W. Riener, *J. Am. Chem. Soc.*, **67**, 1178 (1945).

(50) The use of refluxing dichloromethane led to **41** in 47% yield, but reaction time was reduced to 24 hr.