C_4H_9 – CO), 119 (37, $M^+ - C_4H_9 - CO - H_2O$), 109 (10), 91 (20), 79 (19), 67 (19), 57 (46), 55 (30), 41 (35).

Fraction 6: 2^e-*tert*-butyl-4-oxoadamantan-2^a-ol[32] **30** (245.4 mg, 1.10 mmol); yield 17%; colorless solid; mp 108–110 °C; IR 3605 (m, OH), 3410 (s, br, OH), 1710 (s, C=O), 1365 (m, $C(CH_3)_3$), 1075 (s, C–O); MS 222 (1, M^+), 165 (100, $M^+ - C_4H_9$), 137 (31, $M^+ - C_4H_9 - CO$), 119 (26, $M^+ - C_4H_9 - CO - H_2O$), 95 (13), 79 (12), 67 (16), 57 (31), 55 (22), 40 (29); HRMS found m/z = 222.1620, calcd for $C_{14}H_{22}O_2$ 222.1620.

Fraction 7: **21** (435.7 mg, 1.94 mmol); yield 29%.

Reaction of 4-Methyleneadamantan-2-one (16) with *tert*-Butyllithium. **16** (340 mg, 2.10 mmol); in 100 mL of Et_2O, 4 mL of *t*-BuLi; CC, PE.

Fraction 1: 2^e-*tert*-butyl-4-methyleneadamantan-2^a-ol[32] (**31**, 74.9 mg, 0.34 mmol); yield 16%; colorless viscous oil; IR 3600 (w, OH), 3080 (w, C=CH_2), 1365 (m, $C(CH_3)_3$); MS 220 (2, M^+), 163 (100, $M^+ - C_4H_9$), 135 (85), 107 (21), 93 (36), 79 (26), 67 (12), 57 (34), 41 (30).

Fraction 2: 2^a-*tert*-butyl-4-methyleneadamantan-2^e-ol[32] (**39**, 145 mg, 0.66 mmol); yield 31%; colorless viscous oil; IR 3600 (w, OH), 1365 (m, $C(CH_3)_3$); MS 220 (6, M^+), 163 (100, $M^+ - C_4H_9$), 135 (99), 121 (12), 107 (28), 93 (48), 79 (36), 57 (43), 41 (42).

Fraction 3: **16** (9 mg, 28%).

Reaction of 4,4-Dimethyladamantan-2-one (17) with *tert*-Butyllithium. **17** (600 mg, 3.37 mmol); in 120 mL of Et_2O; 6 mL of *t*-BuLi; CC, PE.

Fraction 1: 2^e-*tert*-butyl-4,4-dimethyladamantan-2^a-ol[32] (**32**, 597.3 mg, 2.53 mmol); yield 75%; colorless viscous oil; IR 3625 (m, OH), 1365 (m, $C(CH_3)_3$), 1090 (m, C–OH); MS 218 (3, $M^+ - H_2O$), 179 (100, $M^+ - C_4H_9$), 161 (18, $M^+ - C_4H_9 - H_2O$), 151 (12), 119 (16), 95 (38), 81 (18), 57 (24), 41 (30); HRMS found m/z 218.2034, calcd for $C_{16}H_{26}$ 218.2034.

Fraction 2: **17** (61 mg, 10%).

Reaction of Adamantane-2,4-dione 4-(Ethylene acetal) (18) with *tert*-Butyllithium. **18** (641.3 mg, 3.08 mmol); in 100 mL of Et_2O; 7 mL of *t*-BuLi; CC, PE/AC (15:1).

Fraction 1: 2^e-*tert*-Butyl-4-oxoadamantan-2^a-ol 4-(ethylene acetal)[32] (**33**, 420 mg, 1.58 mmol); yield: 51%; colorless viscous oil; IR 3600 (m, OH), 3460 (w, br, OH), 1395 (w, $C(CH_3)_3$), 1365 (m, $C(CH_3)_3$); MS 266 (1, M^+), 209 (57, $M^+ - C_4H_9$), 165 (100, $M^+ - C_4H_9 - C_2H_4O$), 137 (30), 119 (35), 91 (14), 79 (12), 60 (38, $C_2H_4O_2^+$), 57 (40), 43 (46).

Fraction 2: **18** (162 mg, 25%).

Acknowledgment. The authors are deeply grateful to Prof. M. A. McKervey (Belfast, Northern Ireland) for helpful discussions and valuable suggestions. This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.

Supplementary Material Available: Tables of ^1H and ^{13}C NMR chemical shifts and positional assignments for compounds **1–40** and **42–53** (^1H NMR) and compounds **7, 8, 14–40,** and **42–53** (^{13}C NMR) and ^1H and ^{13}C NMR spectra for compounds **20–40** and **42–53** (75 pages). Ordering information is given on any current masthead page.

Reactions of Substituted 2-*tert*-Butyladamantan-2-ols

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The reaction of substituted 2-*tert*-butyladamantan-2-ols with triethylsilane and/or hydriodic acid is described. In addition to the expected hydrocarbons, interesting rearrangement products were observed in many cases. Reaction mechanisms are presented to rationalize the experimental results.

Introduction

In the preceding paper[1] we described the synthesis of a number of substituted 2-*tert*-butyladamantan-2-ols.[2] In order to synthesize a series of adamantane compounds carrying *tert*-butyl groups in secondary positions without a geminal substituent we wanted to reduce these carbinols to the corresponding hydrocarbons. To our surprise, however, we found many interesting products of other types of reaction.

Results

We employed two different reaction procedures to obtain substituted 2-*tert*-butyladamantanes. The first involved the exposure of the carbinols to triethylsilane in trifluoroacetic acid and methylene chloride (reaction type I),[2] a procedure suitable for removal of the hydroxy group to obtain the corresponding alkanes. The results were quite surprising and differed in part from our expectations. The molecular structures of the products and reaction details are listed in Chart I and in Table I (reaction type I), respectively. For comparison, some of the carbinols were treated with hydriodic acid (reaction type II, Table I) which is also a reducing reagent.

In general, the overall yields of the reactions were between 60 and 80%, only in a few cases were they lower. These values refer to isolated compounds after chromatographic separation and/or purification. The isolation procedure involving reduced-pressure distillation of the solvent on a rotary evaporator frequently caused losses of material due to the volatility of many of the adamantanes not containing polar groups.

It should be noted that Saba and Fry[2] used tri-*n*-hexylsilane for their alcohol reduction reactions. We found, however, that there is no significant difference in employing triethylsilane, apart from the fact that the reaction product triethylsilane—presumably hexaethyldisiloxane—could be removed more easily due to its lower boiling point.

The structural elucidation of the reaction products was again a crucial factor in this work and is the basis of all discussions of reaction mechanisms. For the methods employed see the preceding paper.[1]

The NMR data obtained are collected in the Tables II (^{13}C) and II (^1H) in the supplementary material.

(1) Duddeck, H.; Rosenbaum, D. *J. Org. Chem.*, preceding paper in this issue.

(2) (a) Fry, J. L.; Engler, E. M.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1972**, *94*, 4628. (b) Saba, J. L.; Fry, J. L. *Ibid.* **1983**, *105*, 533.

0022-3263/91/1956-1707$02.50/0

Table I. Results from Reactions of Type I (Carbinols + Et_3SiH) and Type II (Carbinols + HI)[a] [Yields after Chromatographic Purification in Parentheses]

reactant	reaction type	reduction [1]	tetracyclic compds [2]	spirocyclopropanes [3]	other rearrangements [4]	protoadamantanes [5]
1	I	**20** (82)	–	–	–	–
	II	**20** (75)	–	–	**37** (5)	–
2	I	**21** (49)	–	–	–	–
3	I	–	**27** (81)	–	–	–
	II	–	**27** (81)	–	–	–
4	I	–	**27** (8)	–	**38** (53)	–
	II	–	**27** (55)	–	–	–
5	I	–	**30** (78)	–	–	–
6	I	–	**31** (83)	–	–	–
7[b]	I	{**22** (31)	–	–	–	**41** (38)}
	II	–	–	–	**39** (26)	**42** (28)
8	I	–	**27** (79)	–	–	–
{**9**/**16**}[b] (1:1)	I	{**23** + **25**} 3:2 (73)	–	–	–	–
10	I	**22** (80)	–	–	–	–
	II	–	–	–	–	**42** (60)
11	I	–	**27** (79)	–	–	–
12[b]	I	{**26** (22) 2:	–	**35** + **36**} 2:3 (50)	–	–
	II	–	–	{**35** + **36**} 3:4 (41)	**40** (12)	–
13	I	–	**27** (37) **32** (26) **33** (15)	–	–	–
	II	–	**34** (75)	–	–	–
14	I	–	**27** (8)	–	**38** (56)	–
	II	–	**27** (60)	–	–	–
15	I	–	**27** (78)	–	–	–
17	I	–	**27** (77)	–	–	–
18	I	–	**28** (78)	–	–	–
19	I	–	**29** (81)	–	–	–

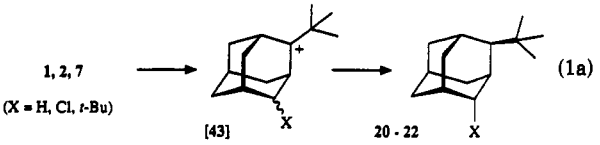
[a] The numbers in brackets refer to the reaction pathways described in the respective equations 1–4 and the scheme. [b] Compounds in braces could not be isolated and were investigated as mixtures; ratios determined by NMR.

The structure of **42** was confirmed by X-ray crystallography.[3]

Discussion

Equations 1–4 collect all reactions. As in the preceding paper,[1] the compound numbers in brackets indicate that these compounds have not been isolated or are assumed intermediates. In the following, all 2-adamantyl cations are represented as open ions. They may equally formulated as bridged cation;[4] the stereochemical consequences, however, are not affected.

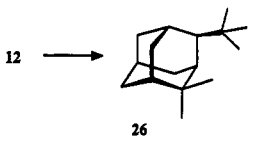
The reaction of **1** using method I (triethylsilane) gave 2-*tert*-butyladamantane (**20**) in good yield (eq 1a). Ac-



(1a)

cording to earlier reports[2] we expect that after protonation and water elimination the cation [**43**] is formed which then reacts, at least formally, with a hydride from the silane. Similarly, some 4-substituted 2-*tert*-butyladamantan-2-ols gave corresponding alkanes. These compounds contain two chirality centers (C-2 and C-4) so that diastereomers may be formed.

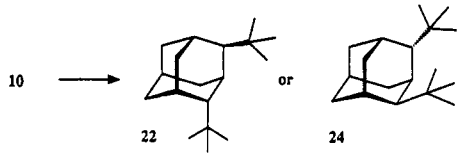
The compounds **2** and **12** (giving **21** and **26**, respectively, eqs 1a and 1b) allow the conclusion that the carbinol reduction took place with inversion of the *tert*-butyl position at C-2 since due to steric hindrance the silane/hydride can approach the cation only from the back side. Interest-



(1b)

ingly, the stereochemical position of the chlorine atom at C-4 was also inverted when **2** was converted to **21**. A chloride epimerization has been encountered before (eq 4a of the preceding paper).[1]

Both di-*tert*-butyl carbinols **7** and **10** (eqs 1a and 1c, respectively) gave the same product **22**. No stereochemical



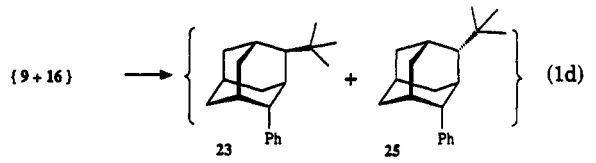
(1c)

statement can be made for the reaction of **7**, because **22** may have been formed either by double inversion (by analogy with **2** → **21**) or by double retention which forms **24**, the enantiomer of **22**; both cannot be discriminated. On the other hand, it is obvious that there is one inversion in the reaction **10** → **22**/**24**, probably at C-2.

Finally, the 1:1 mixture of the two epimers **9** and **16**, both with an equatorial phenyl group, afforded a 3:2 mixture of the corresponding hydrocarbons **23** and **25** (eq 1d), and no stereochemical assignment of the reaction mechanism can be made here, since the educts and the products cannot be correlated in the mixtures.

All other carbinols **3**–**6**, **8**, **11**, **13**–**15**, and **17**–**19** did not give any of the desired products on reduction using the

(3) Kojic-Prodic, B., unpublished results.
(4) (a) Lenoir, D.; Hall, R. E.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1974**, *96*, 2138. (b) Lenoir, D.; Raber, D. J.; Schleyer, P. v. R. *Ibid.* **1974**, *96*, 2149. (c) Dutler, R.; Rauk, A.; Sorensen, T. S.; Whitworth, S. M. *Ibid.* **1989**, *111*, 9024.

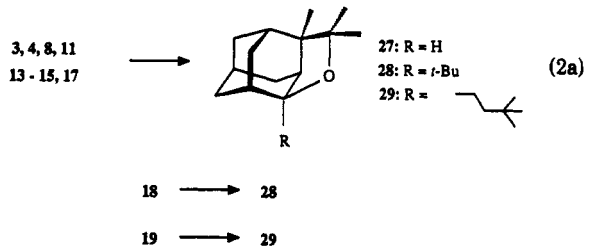


(1d)

triethylsilane method but reacted in different ways (see below).

It should be noted that except for the unsubstituted carbinol **1** (→ **20**), for **7** (→ **39**, see below), and for **12** (→ **40**, see below) the HI reaction failed in producing 2-*tert*-butyladamantanes.

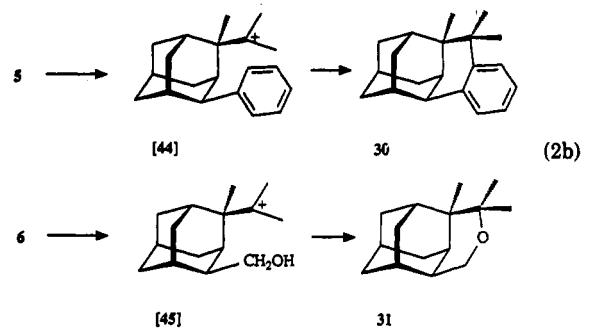
Some of the *tert*-butyl carbinols displayed a *tert*-butyl rearrangment and formed condensed tetracyclic compounds, a reaction reminiscent of those encountered before. The carbinols **3**, **4**, **8**, **11**, **13**–**15**, and **17** (eq 2a), all having



(2a)

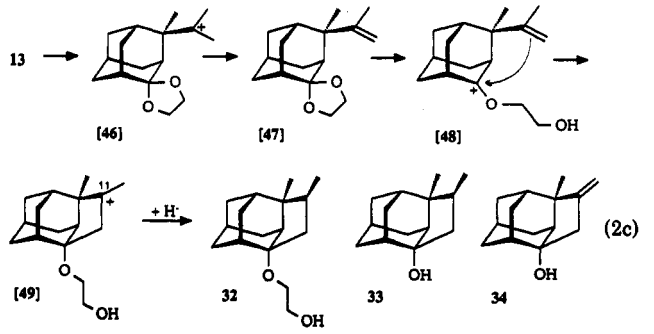
one or two oxygen atoms at C-4, produced the tetrahydrofuran derivative **27** as the sole product; only the dioxolane **13** afforded additional products (**32** and **33**, see below). The diols **18** and **19** gave the analogues **28** and **29**, respectively (eq 2a), again exclusively. We assume that the same mechanisms are operating as described before (eqs 4a and 4b of the preceding paper).[1] It should be noted that **11**, **13**, and **17** have been reduced, probably by the silane.

Compounds **5** and **6** formed tetracyclic compounds with six-membered rings condensed to the adamantane framework exclusively, namely **30** and **31**, respectively (eq 2b). Again isopropyl cations ([**44**] and [**45**], respectively) can be expected as intermediates.



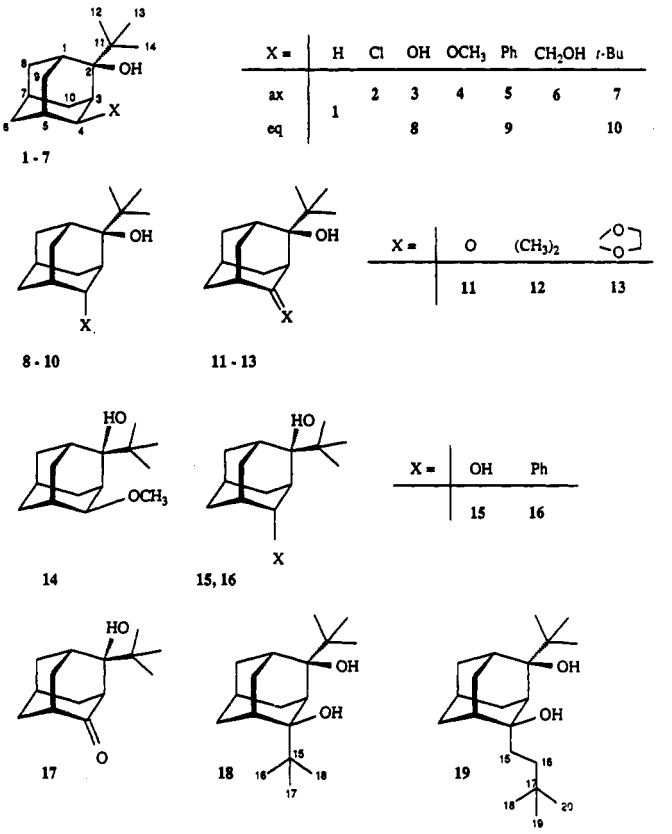
(2b)

The dioxolane **13** gave the cyclopentano derivatives **32** and **33** along with **27**. A multistep mechanism is proposed in eq 2c involving the cationic intermediates [**46**]–[**49**]. C-11 of the ion [**49**] is approached by the silane/hydride



(2c)

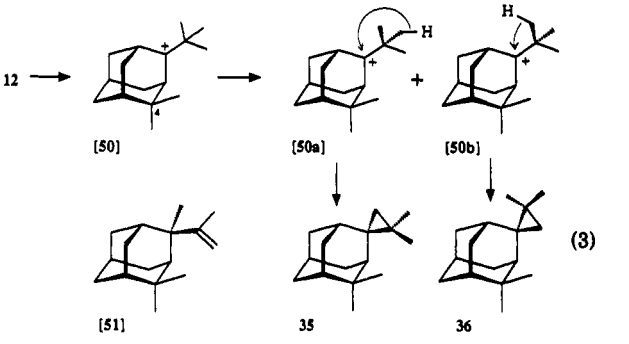
Chart I. Structures of Reactants[a]



[a] The numbering of the adamantane carbons is not necessarily in accordance with the IUPAC nomenclature. For better comparison, however, we employed a numbering which is consistent throughout irregardless of the substituents. The term "axial" (a) and "equatorial" (e) denote the stereochemical position of the substituent with respect to the six-membered ring bearing the highest number of substituents. In case of doubt (e.g. **39**) the ring of reference is that where the carbon with the other substituent has the lower number.

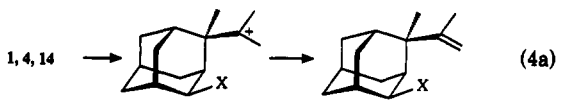
from the less hindered back side to produce **32**. Apparently, **32** or the ions [**48**] or [**49**] are precursors of the alcohol **33**. This mechanism is corroborated by the fact that in the hydriodic acid reaction (type II) of **13** the sole product (75% yield) with the olefin **34** which was formed by deprotonation either of [**49**] (followed by ether cleavage) or of the cationic precursor of **33**, which is analogous to [**49**].

Obviously, the 4,4-dimethyl compound **12** is unable to form tetracyclic adamantanes like those in the eqs 2a, 2b, and 2c so that the cation [**50**] was forced to stabilize itself by forming the isomeric spirodimethylcyclopropanoadamantanes **35** and **36** via the isopropyl cations [**50a**] and [**50b**], respectively, in a ratio of 2:3 (eq 3); the stereochemistry of the respective product, **35** or **36**, depends on



(3)

which methyl group a proton is abstracted. The two spiro isomers **35** and **36** could not be separated, but they were identified unequivocally by NMR. This kind of reaction had been reported by Saba and Fry[2] for alcohol **1** as starting material. In our case, however, the yield was higher and their reaction[2] was conducted at 100 °C, a temperature at which they showed the products were rather unstable. The question arises why spirocyclopropanes were formed at all and not the methylisopropene derivative [**51**] (eq 3); in other cases, 2-isopropenyl-2-methyladamantanes **37** (from **1** in the HI reaction) and its 4[a]-methoxy derivative **38** (from **4** and **14** in the triethylsilane reaction) were observed, indeed, [**52**] being a possible intermediate (eq 4a). Apparently, the intermediate ion(s)

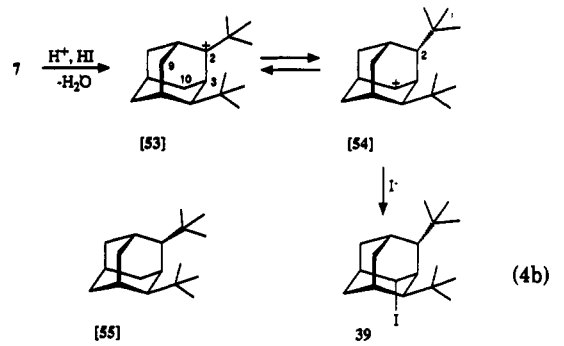


(4a)

[52] **37**: X = H; **38**: X = OCH_3

[**50**] (eq 3) is/are deprotonated in the way indicated as a consequence of the bulky axial methyl group at C-4 which forces the intermediate [**50**] to produce the dimethylcyclopropane because this is less space-demanding than the methyl/isopropenyl grouping (eq 3). In the production of **37** and **38**, however, the corresponding atoms at C-4 at hydrogen and the oxygen atom of a methoxy group, respectively, which are much smaller than methyl. In addition, this argument explains why **35** and **36** are much more stable than Saba and Fry's unsubstituted compounds.[2]

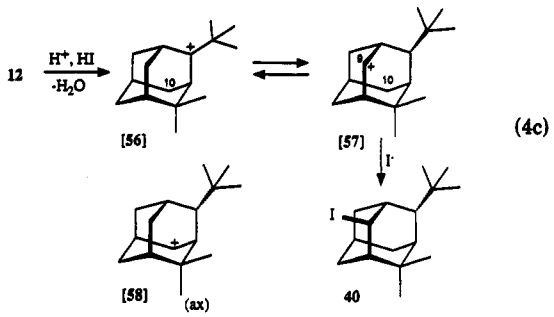
The hydiodic acid reaction (type II) of the di-*tert*-butyl carbinol **7** produced the 2,4-di-*tert*-butyl-10-iodoadamantane **39** in a regio- and stereoselective way (eq 4b).



[53] [54] [55] **39** (4b)

This can be explained by the formation of cation [**53**] which may isomerize to ion [**54**] by a series of three consecutive 1,3-hydride shifts (C-9 → C-2, C-8 → C-9, C-10 → C-8; intermediates not shown). Attack of iodide on [**54**] occurs exclusively from below due to steric hindrance of the *tert*-butyl group at C-2. A one-step 1,3-hydride shift (H-10 migrates directly to C-2) is principally possible. Here, however, such a shift would lead to an iodo derivative of the diaxially substituted 2,4-di-*tert*-butyladamantane [**55**]. It is apparent, however, that this would be too much of steric congestion. (On the other hand, such a compound with two 1,3-diaxial *tert*-butyl groups would be highly desirable from a theoretical point of view.) The alcohol **10** did not produce an iodide corresponding to **39**, apparently, because C-10 in the repective di-*tert*-butyl cation is blocked by axially positioned *tert*-butyl groups.

The dimethyl derivative **12** afforded iodide **40** (eq 4c). In this example, a possible C-10 cation ([**58**] formed by a series of 1,3-hydride shifts similar to the formation of [**54**] from [**53**]) cannot be approached by an iodide atom from



[56] [57] [58] (ax) **40** (4c)

either side due to the presence of the 2-*tert*-butyl and the axial 4-methyl group (ax). Thus, [**57**] may be formed from [**56**] by a 1,3-hydride shift and the iodide could approach from the least hindered side of the molecule to form **40**.

Presumably, the cations displayed in the eqs 4b and 4c are in an equilibrium; a C-9-cation may have been present as well in the reaction **7** → **39** and a C-10 cation in the reaction **12** → **40**.

The last type of reaction products obtained were protoadamantanes (Scheme I) which were produced from the di-*tert*-butyl carbinols **7** and **10**. The triethylsilane reaction (type I) with **7** gave the di-*tert*-butylprotoadamantane **41**. Interestingly, the configuration at C-4 has been inverted. This can be rationalized by an equilibrium of several isomeric di-*tert*-butylprotoadamantane cations [**59**]–[**65**]. This series includes ion [**62**], the key compound for the above mentioned configuration inversion. In these molecules the six-membered ring carrying both *tert*-butyl groups (C-1 to C-5 and C-9) adopts a boat conformation, and molecular models suggest that an ion with an endo-oriented *tert*-butyl group at C-4 (e.g., [**63**] and [**64**]) is sterically less hindered than that with an exo-oriented one (e.g. [**59**]–[**61**]). Thus, a hydride from triethylsilane is small enough to allow the reaction to form **41** from [**63**] and/or [**64**].[5]

As mentioned above, additionally, the di-*tert*-butyladamantane **22** (or its enantiomer **24**) was formed from **7** and **10** (cf. eqs 1a and 1c). The same reaction (type I) with **10**, however, did not product the di-*tert*-butylprotoadamantane **41**. Apparently, the hydride addition to the di-*tert*-butyladamantane cation [**65**] is too fast so that **22** is formed exclusively.[7] The difference in the reactivities of the two reactions (**7** → **22** or **24**) and (**10** → **22**) explains why both reactions gave different products: whereas the hydride can approach [**65**] easily, this is much more difficult to [**53**] due to the axial position of the *tert*-butyl group at C-4 in the latter ion. Thus, this steric crowding allows [**53**] to rearrange into the protoadamantyl series. This interpretation favors **24** (double retention, i.e. front-side attack of the hydride to C-2) as the reduction product of **7** rather than **22**.

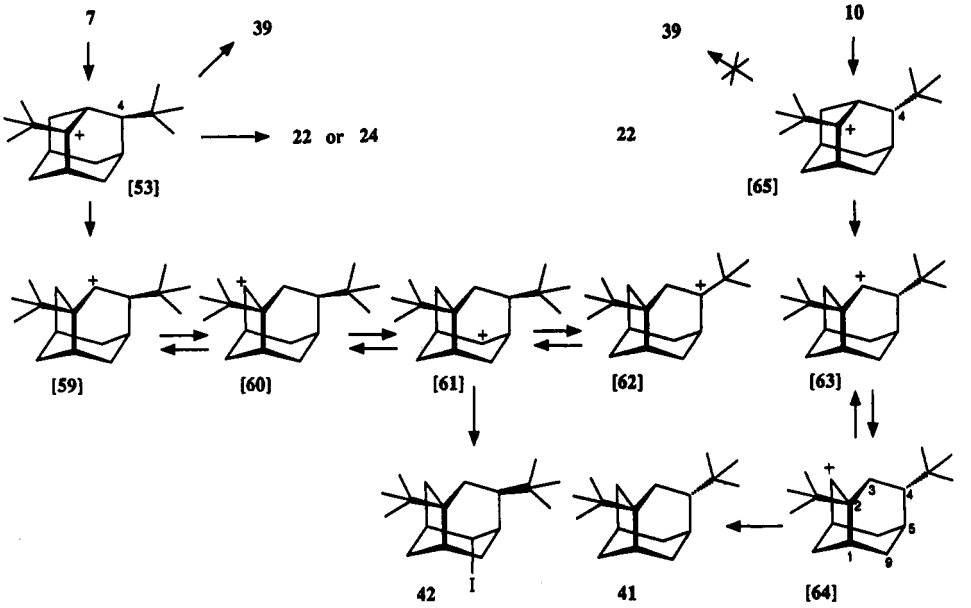
The HI reaction (type II) afforded the iododi-*tert*-butylprotoadamantane **42** from both **7** and **10**. Here the configuration inversion at C-4 took place for **10**, a fact which supports the existence of the equilibrium of the cations [**59**]–[**64**]. The formation of **42** is achieved by stereoselective iodide addition to [**61**] which apparently

(5) One referee suggested that the occurrence of 1,2-hydride shifts[6] connecting [**59**], [**62**], and [**63**] may be a more appropriate explanation. The authors do not want to give priority to one of these alternative interpretations.

(6) Fărcasiu, D.; Seppo, E.; Kizirian, M.; Ledlie, D. B.; Sevin, A. *J. Am. Chem. Soc.* **1989**, *111*, 8466.

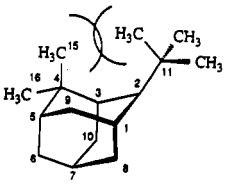
(7) One referee remarked that it is conceivable that the hydride reduction of **65** is concerted with loss of water from O-protonated **10** to give **22**, whereas **7** has to form a carbocation, because concerted attack by hydride would place both *tert*-butyl groups in axial positions.

Scheme I. HI Reactions



is the least hindered ion. Details about the dynamic behavior of **42** have been published before.[8]

NMR Spectra. Compound **26** with 1,3-diaxial methyl and *tert*-butyl groups is the most suitable candidate for an inspection of the effects of intramolecular strain on ^{13}C chemical shifts. To that end we calculated the ^{13}C chemical shifts of **26** by using substituent effects taken from 2-*tert*-butyladamantane (**20**) and 2,2-dimethyladamantane[9] and compared this set of data with the experimental ^{13}C chemical shifts. For C-4 bearing the geminal dimethyl grouping we could not obtain a calculated value because the respective chemical shift of 2,2-dimethyladamantane was not reported.[9] Differences are regarded as nonadditivity effects (NAE); for details see preceding paper.[1]



26

We found noticeable NAE only at C-2 carrying the *tert*-butyl group. Apparently no significant distortion of the adamantane skeleton is introduced by the steric interference between the two 1,3-diaxial alkyl groups beyond that already present in **20** and 2,2-dimethyladamantane. This interpretation is supported by MM2 calculations for **20**, **26**, and 2,2-dimethyladamantane. The only geometrical parameters which are significantly altered in **26**, as compared to **20** and 2,2-dimethyladamantane, are the torsional angles C-8/C-1/C-2/C-11 (149.1°) and C-10/C-3/C-2/C-11 (−152.2°); the corresponding angles in **20** are ca. 157.5°, i.e., the *tert*-butyl group in **20** is considerably bent outward so that the through-space interaction with the 1,3-diaxial methyl group is less severe than expected from Dreiding models and leads only to a relatively small additional distorsion; the geometrical situation next to the methyl groups remains more or less unchanged (see **26**).

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Experimental Section

For general information see the preceding paper.[1]

Syntheses. The syntheses of the starting materials **1**–**19** are described in the preceding paper.[1]

Procedure I: Reactions of 2-*tert*-Butyladamantan-2-ols with Trifluoroacetic Acid (TFA) and Triethylsilane (TES) (General Procedure). Under stirring TFA is added slowly to a solution of the respective 2-*tert*-butyladamantan-2-ol in methylene chloride (CH_2Cl_2) at room temperature. Then TES is added, and the mixture is stirred overnight at the same temperature. After addition of water, the organic layer is washed with aqueous sodium bicarbonate ($NaHCO_3$) and water, dried over $MgSO_4$, and evaporated. If possible, the obtained raw material was separated into the pure compounds by column chromatography (CC).

Reaction of 2-*tert*-Butyladamantan-2-ol (1) with TFA/TES. 1 (250 mg, 1.20 mmol) in 20 mL of CH_2Cl_2, 2.5 mL of TFA, and 1 mL of TES; CC: PE.

2-*tert*-Butyladamantane (**20**): 188.2 mg, 0.98 mmol); yield 82% colorless viscous oil; IR 1390 (w, $C(CH_3)_3$), 1360 (m, $C(CH_3)_3$); MS 192 (2, M^+), 149 (18, $M^+ - C_3H_7$), 135 (100, $M^+ - C_4H_9$), 107 (10), 93 (23), 79 (21), 67 (23), 57 (15), 56 (14), 41 (22).

Reaction of 2^e-*tert*-Butyl-4^a-chloroadamantan-2^a-ol[10] (2) with TFA/TES. 2 (45 mg, 0.19 mmol) in 10 mL of CH_2Cl_2, 0.5 mL of TFA, and 0.2 mL of TES; CC: PE.

2^a-*tert*-Butyl-4^e-chloroadamantane[10] (**21**, 21 mg, 0.09 mmol): yield 49%; colorless viscous oil; IR 1365 (m, $C(CH_3)_3$), 1075 (m, C–Cl); MS 228/226 (0.7/2.2, M^+), 190 (12, $M^+ - HCl$), 171/169 (32/100, $M^+ - C_4H_9$), 133 (32, $M^+ - HCl - C_4H_9$), 119 (21), 105 (37), 91 (77), 79 (42), 57 (36), 41 (44).

Reaction of 2^e-*tert*-Butyladamantane-2^a,4^a-diol[10] (3) with TFA/TES. 3 (200 mg, 0.89 mmol) in 20 mL of CH_2Cl_2, 2 mL of TFA, and 0.8 mL of TES; CC: PE/AC (50:1).

2,11,11-Trimethyl-15-oxa-2,4-ethanoadamantane[10] (**27**, 148.3 mg, 0.72 mmol); yield 81%; spectroscopic data in the preceding paper,[1] compound **45**.

Reaction of 2^e-*tert*-Butyl-4^a-methoxyadamantan-2^a-ol[10] (4) with TFA/TES. 4 (109 mg, 0.46 mmol) in 1 mL of CH_2Cl_2; 1 mL of TFA, and 0.4 mL of TES; CC: PE/AC (100:1).

Fraction 1: 4^a-methoxy-2^e-methyl-2^a-isopropylideneadamantane[10] (**38**, 53.8 mg, 0.24 mmol); yield 53%; colorless viscous oil; IR 3080 (w, C=CH_2), 1100 (m, C—O); MS 188 (18, $M^+ - CH_3OH$), 105 (12), 91 (38), 79 (52), 67 (31), 55 (47), 41 (100); HRMS found m/z 188.1562, calcd for $C_{14}H_{20}$ 188.1565.

Fraction 2: **27** (7.5 mg, 0.04 mmol); yield 8%.

Reaction of 2^e-*tert*-Butyl-4^a-phenyladamantan-2^a-ol[10] (5) with TFA/TES. 5 (112 mg, 0.39 mmol) in 10 mL of CH_2Cl_2,

(10) See caption Chart I.

1 mL of TFA, and 0.4 mL of TES; CC: PE/AC (250:1).

2,11,11-Trimethyl-1′,2′-benzo-4,2-propenoadamantane[10] (**30**, 81.3 mg, 0.31 mmol); yield 78%; colorless viscous oil; IR 3010, 1365 (m, $C(CH_3)_3$); MS 266 (17, M^+), 251 (100, $M^+ - CH_3$), 169 (14), 155 (32), 141 (30), 129 (13), 91 (15), 79 (12), 67 (10), 41 (14); HRMS found m/z 266.2035, calcd for $C_{20}H_{26}$ 266.2035.

Reaction of 2^e-*tert*-Butyl-4^a-(hydroxymethyl)-adamantan-2^a-ol[10] (6) with TFA/TES. **6** (80.3 mg, 0.34 mmol) in 10 mL of CH_2Cl_2, 0.7 mL of TFA, and 0.3 mL TES; CC: PE/AC (50:1).

2,11,11-Trimethyl-16-oxa-2,4-propanoadamantane[10] (**31**, 61.9 mg, 0.28 mmol); yield 83%; colorless viscous oil; IR 1370 (m, $C(CH_3)_3$), 1115 (s, C–O); MS 220 (3, M^+), 205 (31, $M^+ - CH_3$), 162 (100, $M^+ - (CH_3)_2CO$), 147 (21, $M^+ - (CH_3)_2CO - CH_3$), 133 (23, $M^+ - (CH_3)_2CO - CH_3 - CH_2$), 119 (24), 93 (60), 79 (42), 67 (15), 55 (18), 41 (36).

Reaction of 2^e,4^a-Di-*tert*-butyladamantan-2^a-ol[10] (7) with TFA/TES. **7** (50 mg, 0.19 mmol) in 10 mL of CH_2Cl_2, 0.5 mL of TFA, and 0.2 mL of TES; CC: PE.

Mixture of 2^a,4^e-di-*tert*-butyladamantane[10] (**22**; or the enantiomer 2^e,4^a-di-*tert*-butyladamantane[8] (**24**)) and 2,4-*endo*-di-*tert*-butylprotoadamantane (**41**) (1.2:1, from NMR) (32.5 mg, 0.13 mmol); total yield 69%; IR 1395 (m, $C(CH_3)_3$); MS 248 (1, M^+), 191 (100, $M^+ - C_4H_9$), 135 (69, $M^+ - C_4H_9 - C_4H_8$), 121 (39), 109 (13), 107 (15), 95 (22), 93 (22), 81 (18), 79 (24), 57 (68), 41 (21); HRMS found m/z 248.2509, calcd for $C_{18}H_{32}$ 248.2504.

Reaction of 2^e-*tert*-Butyladamantane-2^a,4^e-diol[10] (8) with TFA/TES. **8** (100 mg, 0.4 mmol) in 10 mL of CH_2Cl_2, 1 mL of TFA, and 0.4 mL of TES; CC: PE/AC (50:1).

27 (73 mg, 0.3 mmol): yield 79%.

Reaction of 2^e-*tert*-Butyl-4^e-phenyladamantan-2^a-ol[10] (9) and 2^a-*tert*-butyl-4^e-phenyladamantan-2^e-ol[8] (16) with TFA/TES. Mixture of **9** and **16** (30 mg, 1.07 mmol) in 30 mL of CH_2Cl_2, 2.3 mL of TFA, and 0.9 mL of TES; CC: PE.

2^a-*tert*-Butyl-4^e-phenyladamantane[8] (**23**) and 2^e-*tert*-butyl-4^e-phenyladamantane[10] (**25**) (3:2, from NMR) (210 mg, 0.78 mmol): yield 73%; colorless viscous oil; IR 1365 (m, $C(CH_3)_3$); MS 268 (24, M^+), 212 (100, $M^+ - C_4H_8$), 211 (92, $M^+ - C_4H_9$), 129 (28), 117 (18), 91 (85), 79 (32), 57 (25), 41 (27); HRMS found m/z 268.2181, calcd for $C_{20}H_{28}$ 268.2191.

Reaction of 2^e,4^e-Di-*tert*-butyladamantan-2^a-ol[10] (10) with TFA/TES. **10** (50.5 mg, 0.19 mmol) in 10 mL of CH_2Cl_2, 0.5 mL of TFA, and 0.2 mL of TES; CC: PE.

22 (**24**) (23.8 mg, 0.10 mmol): yield 80%; colorless viscous oil; IR 1365 (m, $C(CH_3)_3$); MS 248 (2, M^+), 191 (100, $M^+ - C_4H_0$), 135 (73, $M^+ - C_4H_9 - C_4H_8$), 121 (43), 109 (14), 107 (17), 95 (24), 93 (24), 79 (30), 57 (72), 41 (30).

Reaction of 2^e-*tert*-Butyl-2^a-hydroxyadamantan-4-one[10] (11) with TFA/TES. **11** (51.4 mg, 0.23 mmol) in 10 mL of CH_2Cl_2, 0.5 mL of TFA, and 0.2 mL of TES; CC: PE/AC (50:1).

27 (37.3 mg, 0.18 mmol): yield 79%.

Reaction of 2^e-*tert*-Butyl-4,4-dimethyladamantan-2^a-ol[10] (12) with TFA/TES. **12** (166 mg, 0.70 mmol) in 2 mL of CH_2Cl_2, 1.5 mL of TFA, and 0.6 mL of TES; CC: PE.

Mixture of 2^a-*tert*-4,4-dimethyladamantane[10] (**26**), 4,4,11,11-tetramethylcyclopropane-2′-spiro-4-adamantane[10] (**35**), and 4,4,12,12-tetramethylcyclopropane-2′-spiro-4-adamantane[10] (**36**) (2:2:3, from NMR) (110.8 mg) corresponding to **26** (33.8 mg, 0.1 mmol; yield: 22%) and **35** plus **36** (77.0 mg, 0.3 mmol; yield 50%). Spectroscopic data of **26**: IR 1365 (m, $C(CH_3)_3$); MS 220 (3, M^+), 163 (100, $M^+ - C_4H_9$), 149 (20), 135 (13), 121 (15), 107 (19), 91 (26), 79 (40), 57 (59), 41 (43).

Reaction of 2^e-*tert*-Butyl-2^a-hydroxyadamantan-4-one 4-(Ethylene acetal)[10] (13) with TFA/TES. **13** (240.2 mg, 0.90 mmol) in 2 mL of CH_2Cl_2, 2 mL of TFA, and 0.8 mL of TES; CC: PE/AC (50:1).

Fraction 1: **27** (68.3 mg, 0.33 mmol); yield 37%.

Fraction 2: 4-hydroxy-2,11-*endo*-dimethyl-2,4-ethanoadamantane[10] (**33**, 27.8 mg, 0.13 mmol); yield 15%; colorless glassy solid; IR 3595 (m, OH), 3440 (w, br, OH), 1050 (m, C–OH); MS 206 (91, M^+), 191 (17, $M^+ - CH_3$), 188 (100, $M^+ - H_2O$), 173 (11, $M^+ - H_2O - CH_3$), 164 (24, $M^+ - C_3H_6$), 149 (15, $M^+ - C_3H_6 - CH_3$), 135 (19), 121 (33), 107 (19), 93 (29), 79 (31), 67 (18), 55 (28), 41 (46); HRMS found m/z 206.1667, calcd for $C_{14}H_{22}O$ 206.1671.

Fraction 3: 4-(2′-hydroxyethoxy)-2,11-*endo*-dimethyl-2,4-ethanoadamantane[10] (**32**, 59.3 mg, 0.24 mmol); yield 26%; colorless viscous oil; IR 3595 (m, OH), 3430 (m, br, OH); MS 250 (9, M^+), 206 (57, $M^+ - C_2H_4O$), 189 (92, $M^+ - O(CH_2)_2OH$), 188 (100, $M^+ - (CH_2OH)_2$), 173 (12, $M^+ - (CH_2OH)_2 - CH_3$), 164 (20), 145 (19), 135 (24), 121 (36), 107 (28), 95 (43), 93 (48), 79 (43), 67 (23), 55 (35), 43 (63), 41 (53).

Reaction of 2^a-*tert*-Butyl-4^a-methoxyadamantan-2^e-ol[10] (14) with TFA/TES. **14** (20.3 mg, 0.09 mmol) in 5 mL of CH_2Cl_2, 0.3 mL of TFA, and 0.15 mL of TES; CC: PE/AC (100:1).

Fraction 1: **38** (11.1 mg, 0.05 mmol); yield 56%.

Fraction 2: **27** (1.5 mg, 0.007 mmol); yield 8%.

Reaction of 2^a-*tert*-Butyladamantane-2^e,4^e-diol[10] (15) with TFA/TES. **15** (100.3 mg, 0.4 mmol) in 10 mL of CH_2Cl_2, 1 mL of TFA, and 0.4 mL of TES; CC: PE/AC (50:1).

27 (72.1 mg, 0.3 mmol): yield 78%.

Reaction of 2^a-*tert*-Butyl-2^e-hydroxyadamantan-4-one[10] (17) with TFA/TES. **17** (60.5 mg, 0.27 mmol) in 10 mL of CH_2Cl_2, 0.6 mL of TFA, and 0.25 mL of TES; CC: PE/AC (50:1).

27 (42.8 mg, 0.21 mmol): yield 77%.

Reaction of 2^e,4^e-Di-*tert*-butyladamantane-2^a,4^a-diol[10] (18) with TFA/TES. **18** (40.5 mg, 0.14 mmol) in 10 mL of CH_2Cl_2, 0.5 mL of TFA, and 0.2 mL of TES; CC: PE/AC (50:1).

4-*tert*-Butyl-2,11,11-trimethyl-15-oxa-2,4-ethanoadamantane[8] (**28**, 28.6 mg, 0.11 mmol): yield 78%; for spectroscopic data see the preceding paper,[1] compound **46**.

Reaction of 2^e-*tert*-Butyl-4^e-(3,3-dimethylbutyl)-adamantane-2^a,4^a-diol[10] (19) with TFA/TES. **19** (20.2 mg, 0.07 mmol) in 5 mL of CH_2Cl_2, 0.3 mL of TFA, and 0.15 mL of TES; CC: PE/AC (50:1).

4-(3,3-Dimethylbutyl)-2,11,11-trimethyl-15-oxa-2,4-ethanoadamantane[10] (**29**, 16.5 mg, 0.06 mmol); yield 81%; colorless viscous oil; IR 1365 (m, $C(CH_3)_3$), 1175 (m, C–O); MS 275 (39, $M^+ - CH_3$), 232 (100, $M^+ - 2CH_3 - CO$), 175 (29, $M^+ - 2CH_3 - CO - C_4H_9$), 161 (10), 147 (38, $M^+ - 2CH_3 - CO - (CH_2)_2C(CH_3)_3$), 105 (28), 91 (23), 79 (18), 69 (10), 57 (44), 41 (31).

Procedure II: Reactions of 2-*tert*-Butyladamantan-2-ols with Gaseous Hydrogen Iodide (HI) (General Procedure). Gaseous hydrogen iodide is passed into a solution of the respective 2-*tert*-butyladamantan-2-ol in carbon tetrachloride (CCl_4) under stirring at room temperature until saturation. After 15 h of stirring at room temperature the solution is washed, evaporated, and chromatographed as described for procedure I.

Reaction of 2-*tert*-Butyladamantan-2-ol (1) with HI. **1** (100 mg, 0.48 mmol) in 10 mL of CCl_4/HI(g); CC: PE.

Fraction 1: **20** (69.1 mg, 0.36 mmol); yield 75%.

Fraction 2: 2-methyl-2-isopropenyladamantane (**37**, 4.2 mg, 0.02 mmol); yield 5%; for spectroscopic data see the preceding paper,[1] compound **47**.

Reaction of 2^e-*tert*-Butyladamantane-2^a,4^a-diol[10] (3) with HI. **3** (102 mg, 0.4 mmol) in 10 mL of CCl_4/HI(g); CC: PE/AC (50:1).

27 (74.9 mg, 0.36 mmol): yield 81%.

Reaction of 2^e-*tert*-Butyl-4^a-methoxyadamantan-2^a-ol[10] (4) with HI. **4** (55.4 mg, 0.23 mmol) in 6 mL of CCl_4/HI(g); CC: PE/AC (50:1).

27 (26.2 mg, 0.13 mmol): yield 55%.

Reaction of 2^e,4^a-Di-*tert*-butyladamantan-2^a-ol[10] (7) with HI. **7** (30 mg, 0.11 mmol) in 10 mL of CCl_4/HI(g); CC: PE.

Fraction 1: 2^e,4^a-di-*tert*-butyl-10^e-iodoadamantane[10] (**39**, 10.5 mg, 0.03 mmol); yield 26%; colorless viscous oil; IR 1365 (m, $C(CH_3)_3$); MS 247 (31, $M^+ - I$), 191 (12, $M^+ - I - C_4H_8$), 177 (23), 135 (12), 121 (11), 109 (11), 95 (13), 91 (12), 79 (13), 57 (100, $C_4H_9^+$), 41 (26).

Fraction 2: 2,4-*exo*-di-*tert*-butyl-6-*exo*-iodoprotoadamantane[10] (**42**, 11.6 mg, 0.03 mmol); yield 28%; colorless solid; mp 90–91 °C; IR 1395 (w, $C(CH_3)_3$), 1365 (m, $C(CH_3)_3$); MS 247 (100, $M^+ - I$), 191 (33, $M^+ - I - C_4H_8$), 177 (83), 163 (18), 135 (14), 121 (20), 107 (21), 95 (16), 91 (20), 79 (19), 57 (97, $C_4H_9^+$), 41 (32).

Reaction of 2^e,4^e-Di-*tert*-butyladamantan-2^a-ol[10] (10) with HI. **10** (30 mg, 0.11 mmol) in 10 mL of CCl_4/HI(g); CC: PE.

42 (24.8 mg, 0.07 mmol); yield 60%.

Reaction of 2^e-*tert*-Butyl-4,4-dimethyladamantan-2^a-ol[10] (12) with HI. **12** (115 mg, 0.49 mmol) in 1 mL of CCl_4/HI(g); CC: PE.

Fraction 1: mixture of **35** and **36** (3:4, from NMR) (44.1 mg, 0.20 mmol); yield 41% IR 1375 (m, $C(CH_3)_2$); MS 218 (54, M^+), 203 (91, $M^+ - CH_3$), 191 (25, $M^+ - C_2H_3$), 163 (100, $M^+ - C_4H_7$),

149 (32), 135 (52), 121 (45), 107 (53), 93 (50), 79 (54), 69 (36), 57 (40), 41 (43).

Fraction 2: 2e-*tert*-butyl-9e-iodo-4,4-dimethyladamantane[10] (**40**, 20.5 mg, 0.06 mmol); yield 12%, colorless viscous oil; IR 1385 (m, CH_3), 1365 (s, $C(CH_3)_3$), 710; MS 331 (0.4, $M^+ - CH_3$), 219 (100, $M^+ - I$), 163 (26, $M^+ - I - C_4H_8$), 149 (22), 135 (12), 121 (13), 107 (17), 91 (24), 79 (36), 69 (24), 57 (84), 41 (43).

Reaction of 13 with HI. **13** (60 mg, 0.23 mmol) in 10 mL of CCl_4/HI(g); CC: PE/AC (50:1).

4-Hydroxy-2-methyl-11-methylene-2,4-ethanoadamantane[10] (**34**, 35.2 mg, 0.17 mmol): yield 75%; colorless viscous oil; IR 3595 (m, OH), 3440 (m, br, OH), 3075 (2, C=CH_2), 1375 (m, CH_3); MS 204 (100, M^+), 189, (62, $M^+ - CH_3$), 176 (15, $M^+ - C_2H_4$), 161 (30, $M^+ - C_2H_4 - CH_3$), 150 (16), 133 (15), 123 (52), 109 (46), 105 (24), 95 (28), 91 (36), 79 (41), 67 (18), 55 (20), 41 (33).

Reaction of 14 with HI. **14** (19.8 mg, 0.08 mmol) in 5 mL of CCl_4/HI(g); CC: PE/AC (50:1).

27 (9.8 mg, 0.05 mmol): yield 60%.

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Supplementary Material Available: Tables of ^{13}C and ^1H NMR chemical shifts and positional assignments as well as the ^1H and ^{13}C NMR spectra for compounds **20–26**, **29–36**, and **38–42** (43 pages). Ordering information is given on any current masthead page.

Transacetoacetylation with *tert*-Butyl Acetoacetate: Synthetic Applications

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Reaction of various nucleophiles with *tert*-butyl acetoacetate (*t*-BAA, **1a**) is shown to be a convenient method for the preparation of a wide variety of acetoacetic acid derivatives. This material can be used to prepare acetoacetates and acetoacetamides from a wide variety of alcohols and amines. Reaction of **1a** with an unhindered primary amine such as *n*-heptylamine under standard conditions gives unwanted byproducts due to the formation of the enamines **24** and **25**. Formation of these byproducts can be minimized by dilution and/or altering the mode of addition.

Introduction

Acetoacetylated materials (**1**) are of interest as chemical intermediates in the pharmaceutical, agrichemical, chemical, and polymer industries.[1,2] The lachrymatory properties of diketene along with concerns regarding its toxicity and shipping have predicated a need for alternative acetoacetylation technologies. One such "diketene-free" approach which has been described by Clemens, Hyatt,[3a,b] and Kato[3c,d] involves the thermal reaction of 2,2,6-trimethyl-4*H*-dioxin-4-one (**2**) with nucleophiles to produce acetoacetic acid derivatives in good yield (eq 1). Mechanistic studies have suggested that this reaction proceeds via the intermediacy of acetylketene (**3**).[3e] While the laboratory utility of dioxinone **2** has been well documented, it has yet to gain widespread use. Another "diketene-free" approach to the preparation of acetoacetates involves the transesterification of the corresponding nucleophile with an appropriate acetoacetate (transacetoacetylation). This approach appeared particularly worthy of attention since it should, in principle, be readily amenable to industrial application. While the use of this reaction has been demonstrated by the work of Bader,[4a,b] Taber,[4c] Gilbert,[4d] and

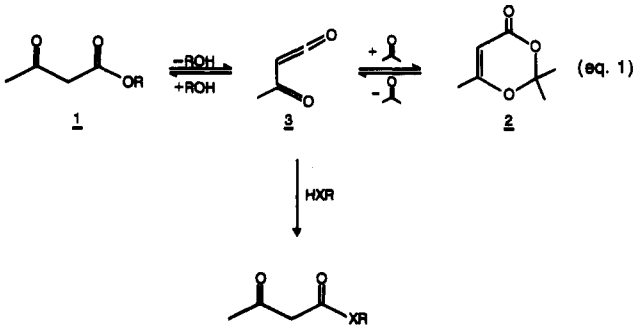

Table I. Rate Constants for Reaction of Various Acetoacetates (1a–g) and 2,2,6-Trimethyl-4*H*-dioxin-4-one (2) with *n*-Butyl Alcohol at Various Temperatures

entry	compound	R	T (°C)	$k \times 10^4$ [a]
1	**1a**	tBu	91.9	1.65
2	**1a**	tBu	98.7	2.50
3	**1a**	tBu	106.0	5.16
4	**1b**	Et	91.9	0.102
5	**1b**	Et	98.7	0.190
6	**1b**	Et	106.0	0.370
7	**1c**	Me	91.9	0.097
8	**1d**	iBu	91.9	0.138
9	**1e**	iPr	91.9	0.140
10	**1f**	$HC(iPr)_2$	91.9	0.083
11	**1g**	tAm	91.9	1.46
12	TKD (**2**)[b]		91.9	1.07
13	TKD (**2**)[b]		98.5	3.08
14	TKD (**2**)[b]		106.7	6.32

[a] First-order rate constant in s^{-1}. Data from ref 5a unless otherwise indicated. [b] See ref 3e for a complete listing of kinetic parameters for this compound.

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