(liquid, ν 1780, 1480, 1180, 1080 cm^{-1}; τ^{CCl_4} 9.05 (3 H, s), 9.25 (3 H, d)) while the epimeric acid **15a** yielded γ-lactone **17** (mp 99.5–100.5°; ν 1780, 1460, 1125 cm^{-1}; τ 9.10 (3 H, s), 9.18 (3 H, d)). In both examples, migration of the methine carbon prevails over methylene migration[9] even when this latter group has a high axial preference. More vigorous treatment of γ-lactone **16** with refluxing formic acid resulted in the recovery of only starting material and a trace of as yet unidentified δ-lactone. Further formic acid treatment of γ-lactone **17** produced quantitatively the same equilibrium mixture of γ-lactone **18** and δ-lactone **19** obtained by Heathcock[3c] from lactone **20**. Besides defining the rearrangement this route provides a simple and efficient synthetic entry to the eudesmane-type sesquiterpenes.

These pathways involving two discrete spiro intermediates may be involved in the interconversion of eudesmane and certain eremophilane sesquiterpenes.[10] Such a sequence not only leads to the correct relative and absolute configurational relationships but also provides a further link between the recognized associations in sesquiterpene chemistry (eudesmol → hinesol).[11] Appropriate ^{14}C labeling studies in this model system and on synthetic eudesmol (*in vivo*) are anticipated.

(9) The sequence parallels the situation with spirodienone rearrangements. See ref 2b, p 1028.

(10) The mechanistic sequence **7** → **5** → **6** → **11** → **12** is illustrative. Replacing the 6-CO_2R function with an isopropyl group and attaching a 4-methyl group demonstrates the natural product interrelationships. In the model system all compounds are enantiomeric mixtures and only one enantiomer is shown.

(11) See N. H. Anderson, M. S. Falcone, and D. D. Syidal, *Tetrahedron Lett.*, 1759 (1970); D. F. MacSweeney, R. Ramage, and A. Sattar, *ibid.*, 557 (1970).

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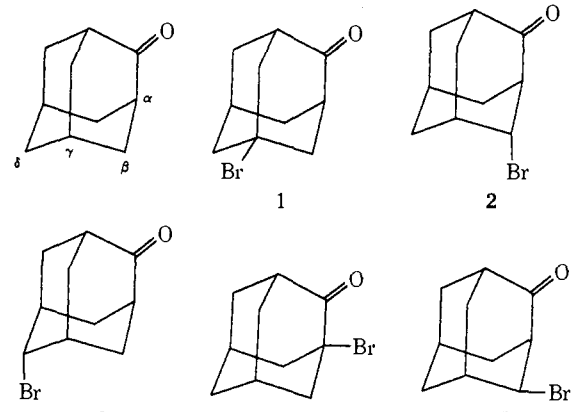
Substituent Effect of the Carbonyl Group on Free-Radical Substitution. Bromination of Adamantanone

Sir:

Despite a number of studies concerning the free-radical substitution of adamantanes,[1] the nature of the effects of 1 substituents is not, at present, fully understood.[2] The effect of 2 substituents of adamantanes on the reactivity problem, on the other hand, has never been investigated.

Now we wish to report the free-radical bromination of adamantanone, the first study of the free-radical substitution of polycyclic ketones as well as of 2-substituted adamantanes. Considerable deactivation of the hydrogens α to the carbonyl is an important conclusion of the present study. Stereoselective equatorial substitution on the C_β radical is another interesting point. Spectra of isomeric monobromoadamantanones are also described.

Five initial products, separated by means of preparative glpc (silicone SE 30 and poly(ethylene glycol) column), of the reaction of adamantanone and a brominating reagent (bromotrichloromethane, *N*-bromosuccinimide (NBS), or dibromomethane) in the presence of di-*tert*-butyl peroxide under nitrogen at 100–110° were determined to be isomeric monobromoadamantanones (**1**, **2**, **3**, **4**, and **5**, in the order of glpc elution from a poly(ethylene glycol) column). Melting points and spectra of the five bromo ketones are shown in Table I.



A high-frequency shift in $\nu_{C=O}$ and a small hypsochromic shift in λ_{max} of **4**, which has not been reported in the literature,[3] are in good agreement with the reported ir and uv spectra of α(e)-bromocyclohexanone derivatives.[5]

Favorskii rearrangement was also useful for distinguishing between isomeric bromo ketones. On treatment with alkaline solution (potassium hydroxide in aqueous ethanol) only **2** and **4** were converted, as expected, to known bicyclo[3.3.1]non-2-ene-7-carboxylic acid[4] and 1-noradamantanecarboxylic acid,[6] respectively.

In Table II are summarized the relative amounts of the five products, which were ascertained to correspond to the kinetically controlled product distribution.[7]

As shown in Table II, the reaction took place preferentially at the C_γ position. An important observation was that the other bridgehead position, C_α, α to the carbonyl, had considerably reduced reactivity

(1) (a) P. H. Owens, G. J. Gleicher, and L. M. Smith, Jr., *J. Amer. Chem. Soc.*, **90**, 4122 (1968); (b) G. J. Gleicher, J. L. Jackson, P. H. Owens, and J. D. Unruh, *Tetrahedron Lett.*, 833 (1969); (c) I. Tabushi, T. Okada, Y. Aoyama, and R. Oda, *ibid.*, 4069 (1969).

(2) It has been reported that the relative rates of the bridgehead hydrogen abstraction from 1-substituted adamantanes by trichloromethyl[1a] or atomic bromine[1b] were correlated with use of the Taft equation. The bridgehead-to-bridge product ratio, a measure of the effect of 1 substituents on the bridge positions, can be correlated with σ^* when the trichloromethyl is an abstracting species. On the contrary, no such correlation is possible in the case of bromine as an attacking species. In chlorocarbonylation, the bridgehead-to-bridge product ratio may best be understood on steric grounds.[1c]

(3) All other monobromoadamantanones were reported elsewhere: **1**, Table I, footnotes *d* and *i*; **3**, Table I, footnote *i*; **5**, Table I, footnote *g*; **2**, Table I, footnotes *f* and *g* and ref 4.

(4) A. C. Udding, H. Wynberg, and J. Strating, *Tetrahedron Lett.*, 5719 (1968).

(5) (a) R. C. Cookson, *J. Chem. Soc.*, 282 (1954); (b) N. J. Leonard and F. H. Owens, *J. Amer. Chem. Soc.*, **80**, 6039 (1958).

(6) B. R. Vogt and R. E. Hoover, *Tetrahedron Lett.*, 2841 (1967).

(7) The reverse reaction of the intermediate radicals with hydrogen bromide[8] was negligible, for the product ratio showed no appreciable change in the course of the reaction. The authors also found that hydrogen bromide had little effect on the bridgehead-to-bridge product ratio of the free-radical bromination of adamantane.[9]

(8) D. D. Tanner, D. Darwish, M. W. Mosher, and N. J. Bunce, *J. Amer. Chem. Soc.*, **91**, 7398 (1969), and references therein.

(9) I. Tabushi, S. Kojo, Y. Aoyama, and Z. Yoshida, unpublished results.

Table I. Melting Points and Spectra[a] of Monobromoadamantanones

Compd	Mp,[b] °C (lit.)	$\nu_{C=O}$, cm^{-1} (KBr)	λ_{max}, mμ (ε)[c] ($CHCl_3$)	Nmr, τ ($CDCl_3$, TMS)
1	153.5–156 (150–154[d])	1730[e]	294 (16.6)	7.40 (8 H), 7.71 (1 H), 7.92 (4 H)[e]
2	159.5–161 (156–159[f])	1731[g] 1709[h]	298 (75.0)	5.45 (1 H), 7.18 (1 H), 7.37 (2 H) 7.68 7.93 8.25 (9 H)[g]
3	186.5–188.5 (187–189[i])	1727 1704[h]	292 (17.4)	5.24 (1 H), 7.17 (1 H), 7.39 (3 H) 7.78, 7.98, 8.23 (8 H)
4	124–125	1749[h] 1734	288 (13.5)	7.03 (1 H), 7.40 (4 H), 7.95 (8 H)
5	156.5–159.5	1733[g]	292 (28.5)	5.20 (1 H),[j] 7.08 (1 H), 7.40 (2 H) 7.70, 7.85, 8.11 (9 H)[g]

[a] Every bromo ketone showed the molecular peak at *m/e* 228 and 230 in its mass spectrum. [b] From hexane, sealed tube, uncorrected. [c] Adamantanone, 291 (24.2). [d] H. W. Geluk and J. L. M. A. Schlatmann, *Tetrahedron*, **24**, 5369 (1968). [e] Similar spectrum was obtained.[d] [f] A. C. Udding, J. Strating, and H. Wynberg, *Tetrahedron Lett.*, 1345 (1968). [g] Similar spectrum was obtained: G. Snatzke and G. Eckhardt, *Chem. Ber.*, **101**, 2010 (1968). [h] Shoulder. [i] M. A. McKervey, D. Faulkner, and H. Hamill, *Tetrahedron Lett.*, 1971 (1970). [j] Quartet.

Table II. Product Ratio and Reactivity Ratio of Bromination of Adamantanone

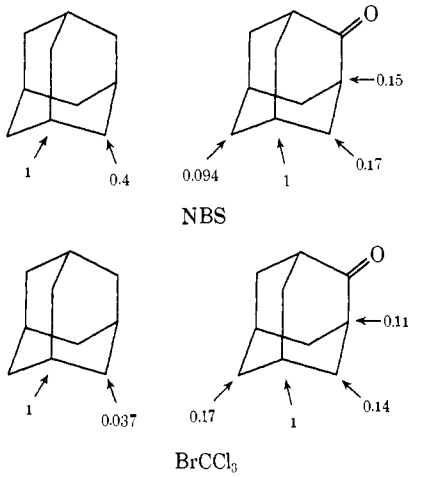
Reagent	Solvent	Product ratio[a] 1	2	3	4	5[b]	Reactivity ratio C_γ to C_α	C_β to C_δ[c]
$BrCCl_3$[d]	$BrCCl_3$	9.8	4.3	1.7	1.1	1.0	9.0	0.78
NBS	C_6H_5Cl	5.0	2.4	0.47	0.75	1.0	6.7	1.8
CH_2Br_2[e]	CH_2Br_2	5.3	2.3	0.72	0.67	1.0	7.9	1.2

[a] Determination was made by glpc peak area method and the values listed are averages of more than one run. [b] Taken as a standard. [c] There were some unidentified byproducts (presumably chloroadamantanones by glpc analysis, although their identification was not complete), the total amount of which was about 3% of the total amount of brominated products. Our reinvestigation revealed that the reaction of adamantane with bromotrichloromethane gave bromoadamantanes together with a small amount (*ca.* 5%) of 1-chloroadamantane. [d] In the case of dibromomethane, the chain length was short, so that prolonged reaction time with a large amount of initiator was necessary. [e] The product ratio of the β-substituted isomers **2** and **5** to the δ-substituted isomer **3** was converted to the statistically corrected reactivity ratio.

toward hydrogen abstraction. The deactivation is presumably due to the rigid bridgehead structure, which prevents resonance stabilization[10] by fixing the carbonyl π orbital perpendicular to the orbital of the odd electron, leaving only the operation of the inductive effect of the carbonyl. Geometrical inhibition of resonance stabilization by an adjacent perpendicular (pseudo) π system, as elucidated directly in the solvolyses of spiro[cyclopropane-1,2′-adamantyl] chloride[10a] or tosylate[10b] and 2-methyleneadamantyl tosylate,[10b] thus became evident also in the case of free radicals. On the other hand, two bridge positions (C_β and C_δ) had comparable reactivities. It is interesting to note that the selectivity between two bridge positions (C_β to C_δ) was appreciably reagent dependent.

As for the radical-transfer step, the preference of equatorial attack (equatorial to the cyclohexane ring containing the carbonyl, leading to **2**) to axial attack (leading to **5**) to the C_β radical[11] may be interpreted in terms of a dipolar effect.[12] However, the dependence of stereoselectivity on the brominating reagent, coupled with the published result[13] that the Hunsdiecker reaction of 4(e)-carboxyadamantanone afforded **2** and **5** in a ratio of 1.7:1, may show that a steric factor is, in part, responsible for the stereoselectivity.

Another interesting feature of the present reaction is that the effect of the carbonyl was different for two brominating reagents (NBS and bromotrichloromethane), as indicated by relative reactivities (per hydrogen) shown below.[14] For NBS bromination, the deactivation, as evidenced by competitive experiments of adamantanone with adamantane, was more important in the bridge positions than in C_γ. On the contrary, C_γ was deactivated to a greater extent than the bridge positions in the case of bromotrichloromethane.[15] Detailed discussion of this point will be deferred until additional experiments are completed.



(10) (a) P. v. R. Schleyer and V. Buss, *J. Amer. Chem. Soc.*, **91**, 5880 (1969); (b) B. R. Ree and J. C. Martin, *ibid.*, **92**, 1660 (1970).

(11) Moderate stereoselective radical substitution at the homoallylic position has also been observed in the case of the 7-norbornenyl radical: G. A. Russell and D. W. Lamson, *ibid.*, **91**, 3968 (1969); S. J. Cristol and A. L. Noreen, *ibid.*, **91**, 3969, (1969).

(12) (a) G. A. Russell and A. Ito, *ibid.*, **85**, 2983 (1963); (b) C. C. Price, C. D. Beard, and K. Akune, *ibid.*, **92**, 5916 (1970).

(13) Footnote *g* of Table I.

(14) Substitution on adamantane was carried out at 95° in the presence of benzoyl peroxide.

(15) Hydrogen abstraction by the radicals from the initiator (*tert*-butoxy and methyl) was not very important, for neither a change of initiator (from di-*tert*-butyl peroxide to benzoyl peroxide) nor a change in the amount of an initiator brought about significant change in the product distribution.

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