bromide **25** (1.80 g, 3.80 mmol) in boiling benzene (80 mL) was added under argon over 8 h a solution of tributyltinhydride (1.40 g 4.80 mmol) and azoisobutyronitrile (80 mg) in benzene (20 mL). After the solvent was distilled off, crystallization (*tert*-butyl methyl ether–hexane, 1:1) gave the 2-deoxyglucose **26** (1.17 g, 76%) with ^{18}O exclusively at the alkoxy group of the benzoate. Mp: 115.5 °C. ^1H NMR ($CDCl_3$): δ 2.06 (s, 3 H, OAc), 2.07 (s, 6 H, OAc), 2.10 (ddd, 1 H, $J_{1,2a}$ = 3.7, $J_{2a,3}$ = 11.6, $J_{2a,2e}$ = 13.6 Hz, H_{2a}), 2.45 (ddd, 1 H, $J_{1,2e}$ = 1.2, $J_{2e,3}$ = 5.3, $J_{2a,2e}$ = 13.6 Hz, H_{2e}), 4.06 (dd, 1 H, $J_{5,6}$ = 2.2, $J_{6,6}$ = 5.3 Hz, H_6), 4.17 (ddd, 1 H, $J_{2e,3}$ = 5.3, $J_{2a,3}$ = 11.6 Hz), 4.35 (dd, 1 H, $J_{5,6}$ = 4.0, $J_{6,6}$ = 12.4 Hz, H_6), 5.16 (dd, 1 H, $J_{3,4}$ = 9.6, $J_{4,5}$ = 10.1 Hz, H_4), 5.47 (ddd, 1 H, $J_{2e,3}$ = 5.3, $J_{3,4}$ = 9.6, $J_{2a,3}$ = 11.6 Hz, H_3), 6.53 (dd, 1 H, $J_{1,2e}$ = 1.2, $J_{1,2a}$ = 3.7 Hz, H_1), 7.48 (t, 2 H, aromat), 7.63 (t, 1 H, aromat), 8.09 (d, 2 H, aromat). ^{13}C NMR ($CDCl_3$): δ 20.64, 20.87, 34.09, 61.90, 68.62, 68.79, 70.50, 91.465 (C-1), 91.495 (C-1), 128.64, 129.33, 129.86, 133.67, 164.26 (C=O, benzoyl, no splitting of the signal), 165.63, 170.14, 170.51. Anal. Calcd for $C_{19}H_{22}O_{8.5}{}^{18}O_{0.5}$ (395.3): C, 57.73; H, 5.61. Found: C, 57.61; H, 5.68.

ESR Measurements. Radicals were generated by UV irradiation of solutions in sealed suprasil quartz tubes (outer diameter 4.0 mm) with the filtered light of a Hanovia 977-B1 1-kW Hg–Xe high-pressure lamp. The ESR solutions were composed of the sugar derivative (ca. 50 mg), dry benzene (0.2 mL), and hexamethylditin (0.2 mL). The addition of di-*tert*-butyl peroxide (0.02 mL) in some cases gave increased signal intensities. Oxygen was removed from the solutions by purging with dry nitrogen for 30 min. ESR spectra were recorded on a Bruker ER-420 spectrometer with use of a double cavity. ESR hyperfine coupling constants were refined by simulation of the manually evaluated ESR spectra on a PDP-11/34 computer. *G* values were determined with the aid of a microprocessor-controlled device, using the digital output of a microwave frequency counter and a NMR field measuring unit.

The ESR kinetic experiments with the rotating sector method were carried out as described elsewehre.[11] Radical concentrations were determined by numerical double integration of simulated spectra, best fitted to the experimental spectra, and comparison with the signals of a calibrated standard.[21]

Acknowledgment. This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.

(21) Korth, H.-G.; Trill, H.; Sustmann, R. *J. Am. Chem. Soc.* **1981**, *103*, 4483. Sustmann, R. *Kinetische-(KESR) und Modulations-(MESR) Spektroskopie*; Forschungsberichte des Landes Nordrhein-Westfalen, Nr. 3087, Westdeutscher Verlag, Opladen, 1981.

Photoacetylation of 2-Substituted Adamantanes. Stereochemistry and Substituent Effects

Koushi Fukunishi,*[†] Atsuya Kohno,[†] and Shosuke Kojo[‡]

Department of Chemistry, Kyoto Institute of Technology, Matsugasaki, Sakyo-ku, Kyoto 606, Japan, and Department of Public Health, Faculty of Medicine, Kyoto University, Kyoto 606, Japan

Received January 25, 1988

Photoacetylation of 2-substituted adamantanes with biacetyl gave regiospecifically syn- and anti-4-substituted 1-acetyladamantanes. Competitive reactions for two syn and anti δ-hydrogen abstractions by triplet biacetyl showed that the ρ^* values were −0.50 and −0.79, respectively. The carbon-13 NMR was studied in order to assign stereoisomers. The observed magnitude of the field-effect transmission for two series of substituent effects was understandable on the basis of the geometrical relationships (bond length and angle) between the reaction center and a substituent.

Introduction

Rigid and symmetrical adamantanes have a wide applicability for mechanistic and preparative studies for free-radical reactions as well as ionic reactions. It has been possible at least qualitatively to partition a substituent effect into the electronic (a direct or field effect and an inductive effect)[1,2] and steric effects[3] in free-radical reactions generally, by evaluating the substituent effect of hydrogen abstraction on the 1.2, 1.3, or 1.4 adamantane systems. From a synthetic viewpoint, it is very important to be able to introduce a substituent selectively into adamantanes. The direct functionalizations of adamantanes are most often achieved by ionic substitution[4] which affords bridgehead products exclusively, whereas a free-radical process generally yields both the bridgehead and bridge products.[5]

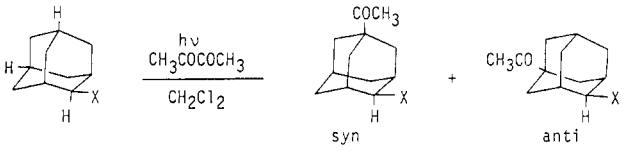
It has been found that the direct regiospecific functionalizations of adamantanes have been successfully carried out via free-radical routes.[2,6] Among them, photoacetylation for the regiospecific bridgehead substitution is one of the most excellent procedures.[2,7] The elegant photoacetylation is interesting and noteworthy because of bridgehead hydrogen abstraction from adamantanes by the excited state of biacetyl.[2] When δ-hydrogen abstraction (two remote bridgehead hydrogens) for 2-substituted adamantane proceeds exclusively, the photoacetylation can yield only two stereoisomers.[7] The knowledge on the relative reactivity for the abstraction of two hydrogens, which are not equivalent in the length and angle from substituent X, may be useful to investigate the effect of substituents on direct or indirect interaction between the

[†] Kyoto Institute of Technology.
[‡] Kyoto University.

(1) (a) Owens, P. H.; Gleicher, G. J.; Smith, L. H., Jr. *J. Am. Chem. Soc.* **1968**, *90*, 4122. (b) Gleicher, G. J.; Jackson, J. L.; Owens, P. H.; Unruh, J. D. *Tetrahedron Lett.* **1969**, 833.
(2) (a) Tabushi, I.; Kojo, S.; Yoshida, Z. *Tetrahedron Lett.* **1973**, 2329. (b) Tabushi, I.; Kojo, S.; Fukunishi, K. *J. Org. Chem.* **1978**, *43*, 2370.
(3) Aoyama, Y. Doctor's Thesis, Kyoto University, 1974, p 116.
(4) (a) Stetter, H.; Schwarz, M.; Hirschborn, A. *Chem. Ber.* **1959**, *92*, 1629. (b) Koch, H.; Haaf, W. *Org. Synth.* **1964**, *44*, 1. (c) Kovacic, P.; Roskos, P. D. *J. Am. Chem. Soc.* **1969**, *91*, 6457. (d) Olah, G. A.; Chi-hung Lin, H. *Ibid.* **1971**, *93*, 1259.
(5) Smith, G. W.; Williams, H. D. *J. Org. Chem.* **1961**, *26*, 2207. (b) Tabushi, I.; Yoshida, Z.; Takahashi, N. *J. Am. Chem. Soc.* **1970**, *92*, 6670. (c) Tabushi, I.; Hamuro, J.; Oda, R. *Ibid.* **1967**, *89*, 7127. (d) Tabushi, I.; Hamuro, J.; Oda, R. *J. Org. Chem.* **1968**, *33*, 2108. (e) Breslow, D. S.; Edwards, E. I.; Leone, R.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1968**, *90*, 7097. (f) Perkins, R. R.; Pincock, R. E. *Can. J. Chem.* **1978**, *56*, 1269.
(6) Tabushi, I.; Fukunishi, K. *J. Org. Chem.* **1974**, *39*, 3748.
(7) Tabushi, I.; Aoyama, Y. *J. Org. Chem.* **1973**, *38*, 3447.

0022-3263/88/1953-4369$01.50/0

Scheme I



1	X = H		11
2	CH_3	12s	12a
3	OCH_3	13s	13a
4	$COOCH_3$	14s	14a
5	$OCOCH_3$	15s	15a
6	Cl	16s	16a
7	Br	17s	17a
8	F	18s	18a
9	CN	19s	19a

substituent and the radical. In this paper, synthetic and mechanistic studies are made on the photoacetylation of 2-substituted adamantanes and the regiospecific syntheses of syn- and anti-4-substituted 1-acetyladamantanes are described. The relative reactivities of 2-substituted adamantanes and the stereochemistry of their products are also discussed.

Results and Discussion

Products. According to the same procedure as the photoacetylation of adamantane and 1-substituted adamantanes,[2] a methylene chloride solution of 2-substituted adamantane and biacetyl was irradiated in a Pyrex vessel with a high-pressure 100-W (or 450W) mercury lamp (Scheme I). The acetylated products were isolated by column chromatography in 30–80% yield based on the adamantanes consumed (4–10% yield based on the adamantanes used). The structures of products obtained, **11–19**, were determined on the basis of chemical conversion to known compounds (or different acetylated compounds) and from interpretation of spectral data. Thus, acetylacetoxyadamantane **15** (two samples with isomer ratios of 74:26 and 5:95 were used, expressed in order of the GLC retention time) was hydrolyzed to the known hydroxyacetyladamantane **10**[7] (30:70 and 95:5, respectively), which was converted to 4-methoxy-1-acetyladamantane (**13**) (28:72 and 94:6, respectively) from a diazomethane–ether solution. Refluxing of a methanol–water solution of the bromide **17** in the presence of potassium carbonate gave **10**; the bromide **17** (58:42) was then converted to the fluoride **18** (28:72) by silver fluoride and to the cyanide **19** (75:25) by cuprous cyanide in low yield. Acidic hydrolysis of **19** (75:25), followed by esterification with diazomethane, gave the methyl ester **14** (73:27). The Baeyer–Villiger oxidation of **15** (79:21) gave the diacetate **20** (86:14), which was hydrolyzed to the diol **21** in agreement with the product derived from reduction of 1-hydroxy-4-adamantanone.[8] The diol **21** was converted to **20** with acetic anhydride, with retention of the original isomer ratio (85:15). The pathways are summarized in Scheme II.

The structures of these acetylated products were also determined by the following NMR spectroscopic observations: (i) lack of the methine proton α to acetyl; (ii) presence of the doublet corresponding to the 4-methyl of **12**; (iii) observed chemical shift was what is predicted for a methine proton α to the subsequent X; (iv) observed carbon-13 chemical shift was what is predicted from the additivity relationship (Table IV) (see paragraph at end of paper regarding supplementary material). The proton

(8) Geluk, H. W.; Schilatmann, J. L. M. A. *Tetrahedron* **1968**, *24*, 5369.

Scheme II

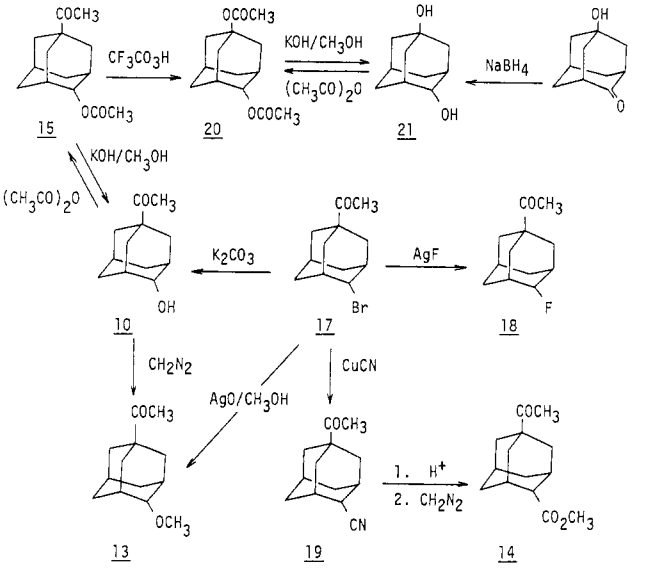


Table I. Product Ratios in the Photoacetylation of 2-Substituted Adamantanes

X	product composition,[a] % 1st peak	2nd peak	syn/anti[b]
CH_3, **12**	48	52	0.93
OCH_3, **13**	34	66	1.9
$COOCH_3$, **14**	56	44	1.3
$OCOCH_3$, **15**	63	37	1.7
Cl,[c] **16**			1.3
Br, **17**	59	41	1.4
F, **18**	30	70	2.3
CN, **19**	49	51	0.95

[a] Product composition was determined by GLC analysis except in the case of **16**. [b] The assignment of syn and anti isomers was made by carbon-13 NMR analysis and the chemical conversion. [c] The composition of **16** was determined from the intensity ratio of two acetyl methyl signals of H NMR because of the unsuccessful separation of GLC analysis.

NMR chemical shifts of the bridgehead polysubstituted adamantanes,[9] 2,4-disubstituted adamantanes,[10] and 1,4-disubstituted adamantanes[7] were predicted with excellent accuracy on the basis of the additivity relationship. The signals of the α methine protons for 4-substituted 1-acetyladamantanes are also in excellent agreement with the calculated signals from the additivity rule.

Thus, the photoacetylation of 2-substituted adamantanes gave the corresponding 4-substituted 1-acetyladamantanes **12–19** (a mixture of syn and anti stereoisomers). This exclusive δ-substitution of 2-substituted adamantanes is considered to originate from the higher reactivity of δ-hydrogen abstraction than the α, β, and γ-abstraction because of significant nonbonding repulsion between a hydrogen-abstracting species (the bulky photoexcited biacetyl) and γ-axial hydrogens and/or a substituent X,[2,7] although the electronic effect may not be ignored for the α, β, or γ-hydrogen abstraction.

Contrary to the above-described high regiospecificity for the δ-hydrogen abstraction, a moderate selectivity was observed between δ-syn and δ-anti hydrogen abstractions, which resulted in formation of syn- and anti-4-substituted 1-acetyladamantanes (Table I). The structural assignments of two stereoisomers were made by using carbon-13 NMR analysis.

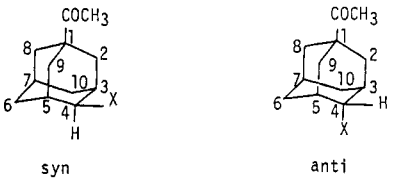
(9) Fort, R. C., Jr.; Schleyer, P. v. R. *J. Org. Chem.* **1965**, *30*, 789.
(10) (a) Deursen, F. W. V.; Korver, P. K. *Tetrahedron Lett.* **1967**, 3923. (b) Deursen, F. W. V.; Bakker, J. *Tetrahedron* **1971**, *27*, 4593.

Table II. Relative Rates of Syn and Anti Bridgehead Hydrogen Abstraction from 2-Substituted Adamantanes by Triplet Biacetyl

X	σ^* [a] (for XCH_2-)	$k_{syn\text{-}X}/k_H$	$k_{anti\text{-}X}/k_H$
CH_3	-0.10	1.15 ± 0.02	1.24 ± 0.04
H	0	1.00	1.00
OCH_3	0.52	0.574 ± 0.012	0.302 ± 0.009
$COOCH_3$	0.71	0.519 ± 0.018	0.393 ± 0.008
$OCOCH_3$	0.87[b]	0.392 ± 0.015	0.228 ± 0.009
Br	1.00	0.227 ± 0.012	0.161 ± 0.007
F	1.10	0.352 ± 0.010	1.152 ± 0.003
CN	1.30	0.0914 ± 0.0049	0.0962 ± 0.0034

[a] Taken from the following: *Steric Effects in Organic Chemistry*; Newman, M. S., Ed.; Wiley: Asian Edition (Tokyo), 1956; p 595. [b] The σ^* value estimated as $\sigma_I \times 1/0.45$, using the σ_I (=0.39) value taken from the following: Gordon, A. J.; Ford, R. A. *The Chemist's Companion*; Wiley: New York, 1972; p 153.

Carbon-13 NMR Analysis. Additivity relationships for carbon-13 NMR chemical shifts have played an important role in making peak assignments. The assignments of the carbon-13 chemical shifts for the present syn- and anti-4-substituted 1-acetyladamantane derivatives were made on the basis of the premise that the effects of substituents are additive.[11] The analysis of the carbon-13 NMR spectra for a number of 1- and 2-substituted adamantanes makes the determination of carbon chemical shifts of the present products possible,[12] although some ambiguity remains with respect to assignments of δ-anti and δ-syn carbon chemical shifts of 2-substituted adamantanes.[13] The carbon chemical shifts for adamantane, 1-acetyladamantane, and 2-substituted adamantanes were used for the additivity calculations of syn- and anti-4-substituted 1-acetyladamantanes. The carbon-13 NMR spectra were taken for a series of mixtures of syn- and anti-substituted acetyladamantanes after the isomer ratios were previously determined. On the basis of the observed signal intensities, ^{13}C–H coupling, and peak positions predicted by the additivity rule, the signals were assigned and divided into two groups. The chemical shifts, observed and predicted, are listed in Table IV (see paragraph at end of paper regarding supplementary material). The chemical shifts of acetyl methyl ($COCH_3$), carbonyl ($COCH_3$), and substituent carbon were readily distinguished from the others. Other carbon absorptions were also clearly separated. Observed and predicted values are in good agreement, with deviations less than ±1.0 ppm. An example of the additivity relationship can be seen for C-2 (or C-9) and C-6 (or C-10) where C-2 was more shielded than C-6 in a syn isomer (observed shielding was 6.20, 5.06, 3.89,



2.37, and 1.65 ppm for **12s**, **17s**, **10s**, **18s**, and **19s**, respectively) as expected from the γ-gauche shielding effect[12,14] (estimated to be 6.39, 5.27, 3.87, 2.62, and 2.13 ppm for **12s**, **17s**, **10s**, **18s**, and **19s**, respectively). The substituent effects on these upfield shifts between syn- and anti-substituted acetyladamantanes range from 3.4 to 8.0 ppm, depending on the nature of the substituent.

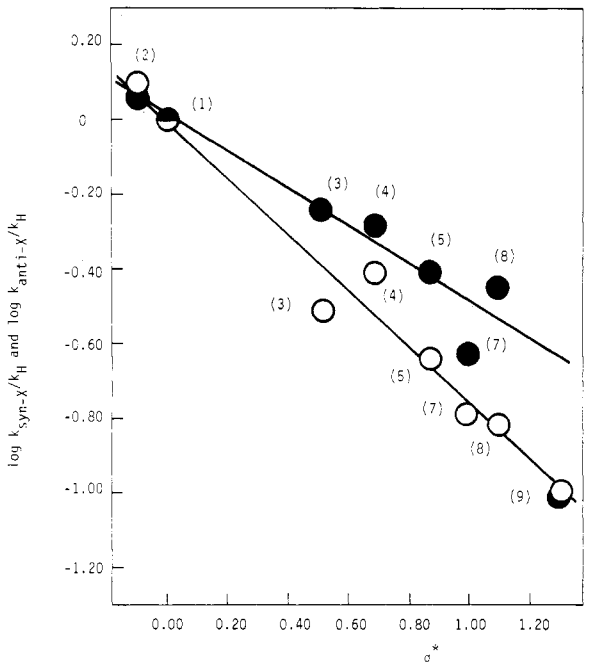


Figure 1. Correlation of log $k_{syn\text{-}X}/k_H$ and log $k_{anti\text{-}X}/k_H$ with σ^* for syn (●) and anti (○) bridgehead hydrogen abstraction from 2-substituted adamantanes by triplet biacetyl: X = H (**1**), CH_3 (**2**), OCH_3 (**3**), $COOCH_3$ (**4**), $OCOCH_3$ (**5**), Br (**7**), F (**8**), and CN (**9**).

Substituent Effects. Competitive reactions between one of the 2-substituted adamantanes and adamantane demonstrated two different series of relative reactivities, which corresponded to the reactivities of two δ bridgehead hydrogens as shown in Table II. A plot of the logs of the relative rates vs σ^* is given in Figure 1. Polar effects of substituents correlated well with σ^*, where the ρ^*'s for syn and anti hydrogen abstraction were calculated to be -0.50 (n = 7, r = 0.952, except for cyano) and -0.79 (n = 8, r = 0.985), respectively. As might be expected,[2] electron-donating substituents more or less facilitate the reaction.[15] The especially interesting points to note are that the ρ^* value for anti hydrogen abstraction (-0.79) is comparable in magnitude with the ρ^* (-0.71) observed for the 3-photoacetylation on the 1-substituted adamantanes[2] and is more negative than the ρ^* value for the corresponding syn hydrogen (-0.50). Thus, the conclusion may be drawn that the substituent effect on the reactivity is dependent on the angle between the substituent dipole and C–H to be reacted; in other words, it is incompatible with the simple inductive model because the number of C–C linkages inserted between the reaction center and the substituent is the same for the syn and anti isomers.

The successful approaches to the field model for adamantanes[1,16] and other rigid molecules[17] have been based

(11) Simeral, L.; Maciel, G. E. *J. Phys. Chem.* **1973**, *77*, 1590.
(12) Maciel, G. E.; Dorn, H. C.; Green, R. L.; Kleschick, W. A.; Peterson, M. R., Jr.; Wahl, G. M., Jr. *Org. Magn. Reson.* **1974**, *6*, 178.
(13) The ambiguity for the assignment of δ-anti and δ-syn carbon chemical shifts was resolved by Duddeck and Dietrich, who concluded that the greater shielding was assigned to the δ anti carbon. Duddeck, H.; Dietrich, W. *Tetrahedron Lett.* **1975**, 2925.
(14) Cheney, B. V.; Grant, D. M. *J. Am. Chem. Soc.* **1967**, *89*, 5319.
(15) The more electron donating methyl than hydrogen was in contrast to the cases in which it decreases the solvolysis of 1-bromoadamantane[15a] and increases the strength of 1-adamantanecarboxylic acid.[15b] (a) Grob, G. A.; Schwarz, W.; Fisher, H. P. *Helv. Chim. Acta* **1964**, *47*, 1385 and ref 16b. (b) Fort, R. C., Jr.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1964**, *86*, 4194.
(16) Stetter, H.; Mayer, J. *Chem. Ber.* **1962**, *95*, 667. (b) Schleyer, P. v. R.; Woodworth, C. W. *J. Am. Chem. Soc.* **1968**, *90*, 6528. (c) Bogal, M. L.; Lantvoev, V. I. *J. Org. Chem. USSR (Engl. Transl.)* **1973**, 290; *Zh. Org. Khim.* **1973**, 291.
(17) For example, for the pK_a of rigid carboxylic acids: (a) Baker, F. W.; Parish, R. C.; Stock, L. M. *J. Am. Chem. Soc.* **1967**, *89*, 5677. (b) Wilcox, C. W.; Leung, C. *Ibid.* **1968**, *90*, 336. (c) Liotta, C. L.; Fisher, W. F.; Greene, G. H., Jr.; Joyner, B. L. *Ibid.* **1972**, *94*, 4891.

Table III. Parameters for Angular Dependency Calculation

X	μ,[a] D	R,[b] Å		cos θ		$\mu \cos \theta/R^2 \times 10^2$	
		syn	anti	syn	anti	syn	anti
CH_3	0.13	4.03	4.98	0.5600	0.9478	0.0045	0.0050
OCH_3	1.52	3.68	4.30	−0.4153	−0.9302	−0.0466	−0.0765
$COOCH_3$	1.79	4.18	5.22	−0.5993	−0.9540	−0.0614	−0.0627
Br	2.51	3.67	4.27	−0.3942	−0.9297	−0.0735	−0.1280
F	2.11	3.51	3.98	−0.3267	−0.8844	−0.0560	−0.1178
CN	3.89	4.22	5.28	−0.6088	−0.9545	−0.1330	−0.1332

[a] Taken from the following: Deady, L. W.; Kendall, M.; Tonison, R. D.; Jones, R. A. Y. *J. Chem. Soc., Perkin Trans. 2* **1973**, 416. [b] Obtained from the ground-state geometry with tetrahedral carbons.

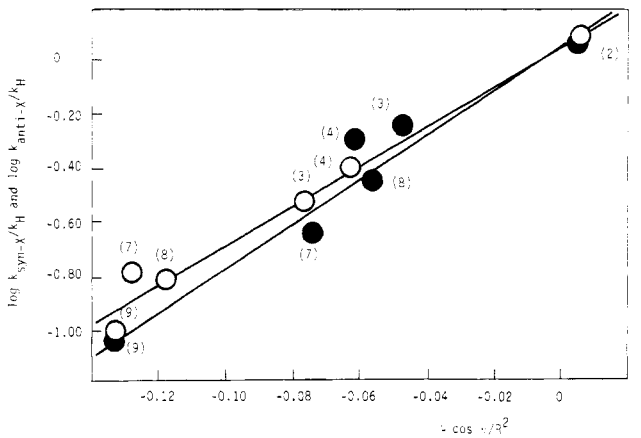


Figure 2. Correlation of log $k_{syn\text{-}X}/k_H$ and log $k_{anti\text{-}X}/k_H$ with $\mu \cos \theta/R^2$ for syn (●) and anti (○) bridgehead hydrogen abstraction from 2-substituted adamantanes by triplet biacetyl: X = CH_3 (**2**), OCH_3 (**3**), $COOCH_3$ (**4**), Br (**7**), F (**8**), and CN (**9**).

on the electrostatic interaction of a substituent dipole with the reaction center. The present relative rates were estimated by means of the more simplified formula[18]

$$\log k_X/k_H = A\mu \cos \theta/R^2 + B$$

where μ is the substituent dipole, R the distance between the center of the substituent dipole and the center of the carbon–hydrogen bond to be cleaved, and θ the angle between the extension of the carbon–substituent bond and the direction of the dipole, and A and B are constants. Table III presents the values of $\mu \cos \theta/R^2$. The linear relationships between log k_X/k_H and $\mu \cos \theta/R^2$ are shown in Figure 2. This field model is also supported by the linear relation observed for the similar angular dependence of dissociation constants, pK_a's, of rigid carboxylic acids.[17a,c] The present results are consistent with the angular dependence of the transmission of the polar effect through space.

Experimental Section

Apparatus. GLC analysis was carried out with a Shimazu gas chromatography 6 APTF equipped with a capillary column (FFAP 4%, 0.25 mm × 60 m). Mass spectra were obtained with Hitachi mass spectra RMU-6E and M80-B. Unless otherwise indicated, NMR spectra were taken in carbon tetrachloride and recorded with a Varian T-60 spectrometer. For carbon-13 NMR measurements, a Varian CFT-20 was used. Elemental analyses were performed at the Microanalysis Center of Kyoto University.

Materials. Adamantane (**1**), 2-bromoadamantane (**7**), and 2-chloroadamantane (**6**) were purchased and purified by sublimation. Reagent grade biacetyl was distilled under reduced pressure before use.

2-Methyladamantane (**2**) was prepared by catalytic hydrogenation of methyleneadamantane, generated by dehydration of the alcohol, mp 144–145 °C (lit.[19] mp 143.8–146.0 °C).

2-Methoxyadamantane (**3**) was obtained by a procedure similar to that for the preparation of 1-methoxyadamantane,[20] n^{25} 1.4988 (lit.[20] n^{25} 1.498).

2-Acetoxyadamantane (**5**) was prepared from 2-adamantanol with acetic anhydride in the presence of sodium acetate,[21] n^{25} 1.4942.

2-Carbomethoxyadamantane (**4**) was prepared by the diazomethane esterification of 2-adamantanecarboxylic acid, which was obtained from the epoxidation of adamantanone, followed by the opening of the epoxide and oxidation of the resulting aldehyde,[22] n^{25} 1.4992.

2-Fluoroadamantane (**8**) was obtained by treating the bromide **7** with silver fluoride, according to the procedure described for the preparation of 1-fluoroadamantane,[9] mp 220–225 °C.

2-Cyanoadamantane (**9**) was prepared by treating adamantanone with tosylmethyl isocyanate, according to the method of Oldenziel and Leusen,[23] mp 183–185 °C (lit.[23] mp 181–182 °C, sealed).

General Procedure for Photoacetylation of 2-Substituted Adamantanes with Biacetyl.[2] A mixture of 2-substituted adamantane (0.037 mol) and 30 mL of biacetyl in 500 mL of methylene chloride was irradiated by a 450-W high-pressure mercury lamp for 20 h in an ice bath under nitrogen. The reaction mixture was washed with 5% sodium hydrogen carbonate aqueous solution and dried over sodium sulfate, and methylene chloride was distilled off. The residue was chromatographed on a silica gel column using benzene as an eluent. Products eluted (a mixture of syn and anti stereoisomers) were purified by distillation under reduced pressure, using a Kugelrohr apparatus.

The isomer ratios of products obtained, except in the case of 4-chloro-1-acetyladamantane (**16**) (not separated), were determined by GLC analyses of the reaction mixtures and are listed in Table I.

Two isomeric acetyl derivatives (syn and anti) formed in each run described below, where methyl absorption of acetyl in H NMR showed two sharp singlets corresponding to each isomer (except for **12** and **18**). The ratio of these two sharp singlets was approximately equal to the ratio determined by GLC (see Table I).

4-Methyl-1-acetyladamantane (12s and 12a): yield, 4% (based on the adamantane used) or 30% (based on the adamantane consumed); IR (neat) ν 2900, 1692, 1446, 1354, 1215, 1075 cm^{-1}; NMR δ 1.01 and 1.08 (2 d, 2 CH_3), 1.99 (sharp s, 3 H, $COCH_3$, not separated), 1.5–2.1 (m, 14 H, the remaining adamantyl protons); mass spectrum, m/z (relative intensity) 192 (M^+, 7), 149 (100); HRMS calcd for $C_{13}H_{20}O$ m/z 192.1514, found 192.1505.

Anal. Calcd for $C_{13}H_{20}O$ (192.3): C, 81.20; H, 10.48. Found: C, 80.90; H, 10.51.

4-Methoxy-1-acetyladamantane (13s and 13a): yield, 4% (based on the adamantane used) or 62% (based on the ada-

(18) The simplified formula in this text was obtained by modifying the Kirkwood–Westheimer equation, used by Owens, Gleicher, and Smith.[1a] In the Kirkwood–Westheimer equation, the effective dielectronic constant D_E, which depends upon the charge in some interaction between the substituent and solvent, was taken as an invariant constant because of the steric inhibition of solvation to the bulky adamantane frame.

(19) Schleyer, P. v. R.; Nicholas, R. D. *J. Am. Chem. Soc.* **1961**, *83*, 182.
(20) Coffi-Nketsia, S.; Kergomard, A. *Bull. Soc. Chim. Fr.* **1973**, 2115.
(21) Boyd, J.; Overton, K. H. *J. Chem. Soc., Perkin Trans. 1* **1972**, 2533.
(22) Farcasiu, D. *Synthesis* **1972**, 615.
(23) Oldenziel, O. H.; Leusen, A. M. v. *Synth. Commun.* **1972**, *2*, 281; *Tetrahedron Lett.* **1973**, 1357.

mantane consumed); IR (neat) ν 2920, 1695, 1455, 1350, 1220, 1100 cm^{-1}; NMR δ 3.30 (sharp s, 3 H, OCH_3), 2.0 (2 sharp s, 3 H, combined, $COCH_3$, 0.02 ppm between 2 $COCH_3$ chemical shifts), 3.23 (br, 1 H, $CHOCH_3$), and 1.6–2.2 (m, 13 H, the remaining adamantyl protons); mass spectrum, m/z 208 (M^+, 10), 165 (100).

Anal. Calcd for $C_{13}H_{20}O_2$ (208.3): C, 74.96; H, 9.68. Found: C, 74.66; H, 9.52.

4-Carbomethoxy-1-acetyladamantane (14s and 14a): yield, 4% (based on the adamantane used) or 42% (based on the adamantane consumed); IR (neat) ν 2870, 1718, 1692, 1447, 1344, 1195, cm^{-1}; NMR δ 2.00 and 2.04 (sharp s, 3 H, combined, $COCH_3$), 3.66 (sharp s, 3 H, $COOCH_3$, not separated), 2.48 (br, 1 H, $CHCOOCH_3$), 1.5–2.2 (m, 13 H, the remaining adamantyl protons); mass spectrum, m/z 236 (M^+, 11), 193 (100); HRMS calcd for $C_{14}H_{20}O_3$ m/z 236.1412, found 236.1416.

Anal. Calcd for $C_{14}H_{20}O_3$ (236.3): C, 71.16; H, 8.53. Found: C, 70.91; H, 8.70.

4-Acetoxy-1-acetyladamantane (15s and 15a): yield, 22% (based on the adamantane used) or 84% (based on the adamantane consumed); IR (neat) ν 1740, 1705, 1260 cm^{-1}; NMR δ 2.00 (sharp s, 3 H × 2, $COCH_3$ and $OCOCH_3$), 4.75 (br, 1 H, $CHOCOCH_3$), 1.6–2.2 (m, 13 H, the remaining adamantyl protons); mass spectrum, m/z 236 (M^+, 5), 193 (86), 151 (100), 133 (100).

Anal. Calcd for $C_{14}H_{20}O_3$ (236.3): C, 71.16; H, 8.53. Found: C, 71.06; H, 8.39.

4-Chloro-1-acetyladamantane (16s and 16a): yield, 5% (based on the adamantane used) or 50% (based on the adamantane consumed); IR (neat) ν 2920, 1695, 1455, 1355, 1215, 790, 770 cm^{-1}; NMR δ 2.00 and 2.03 (2 sharp s, 3 H, combined, $COCH_3$), 4.27 (br, 1 H, CHCl), 1.4–2.6 (m, 13 H, the remaining adamantyl protons); mass spectrum, m/z 214 and 212 (M^+, 4 and 11, respectively), 171 and 169 (36 and 100, respectively), 133 (54).

Anal. Calcd for $C_{12}H_{17}OCl$ (212.7): C, 67.76; H, 8.06; Cl, 16.67. Found: C, 67.51; H, 8.05; Cl, 16.97.

4-Bromo-1-acetyladamantane (17s and 17a): yield, 4% (based on the adamantane used) or 60% (based on the adamantane consumed); IR (neat) ν 2910, 1690, 1450, 1352, 1194 cm^{-1}; NMR δ 2.01 and 2.06 (2 sharp s, 3 H, combined, $COCH_3$), 4.52 (br, 1 H, CHBr), 1.4–2.6 (m, 13 H, the remaining adamantyl protons); mass spectrum, m/z 256 and 258 (M^+, 9 and 9, respectively), 215 and 213 (100 and 94, respectively).

Anal. Calcd for $C_{12}H_{17}OBr$ (257.2): C, 56.04; H, 6.66; Br, 31.07. Found: C, 55.80; H, 6.60; Br, 31.39.

4-Fluoro-1-acetyladamantane (18s and 18a): yield, 6% (based on the adamantane used) or 30% (based on the adamantane consumed); IR (neat) ν 2890, 1692, 1449, 1351, 1064 cm^{-1}; NMR δ 2.03 (s, 3 H, $COCH_3$, not separated), 4.59 (br d, J_{HF} = 52 Hz, 1 H, CHF), 1.3–2.5 (m, 13 H, the remaining adamantyl protons); mass spectrum, m/z 196 (M^+, 6), 176 (50), 153 (50), 133 (59), 43 (100).

Anal. Calcd for $C_{12}H_{17}OF$ (196.3): C, 73.44; H, 8.73; F, 9.68. Found: C, 73.24; H, 8.86; F, 9.39.

4-Cyano-1-acetyladamantane (19s and 19a): yield, 1.4% (based on the adamantane used) or 22% (based on the adamantane consumed); IR (neat) ν 2890, 2227, 1695, 1449, 1351, 1220 cm^{-1}; NMR δ 2.07 and 2.13 (2 sharp s, 3 H, combined, $COCH_3$), 2.80 (br, 1 H, CHCN), 1.3–2.6 (m, 13 H, the remaining adamantyl protons); mass spectrum, m/z 203 (M^+, 8), 160 (100).

Anal. Calcd for $C_{13}H_{17}ON$ (203.3): C, 76.81; H, 8.43; N, 6.89. Found: C, 76.61; H, 8.35; N, 6.70.

1,4-Diacetoxyadamantane (20) from 15. The Baeyer–Villiger reaction was applied to **15** with trifluoroperoxyacetic acid. A solution of trifluoroperoxyacetic acid was prepared by dropwise addition of 1.2 g of trifluoroacetic acid to a suspension of 0.13 g of hydrogen peroxide (distilled in vacuo) in 3 mL of cold methylene chloride. This solution was then added dropwise to a stirred suspension of 1.4 g of dry finely ground disodium hydrogen phosphate in a mixture of 5 mL of methylene chloride and 224 mg of **15** (isomer ratio, 79:21). Then, the solution was heated under reflux for 30 min and then insoluble salt precipitated was filtered. The salt was washed with methylene chloride. The combined filtrate was then washed with sodium carbonate solution and dried over magnesium sulfate. The solvent was removed, and the residual liquid (158 mg, 66% yield) was obtained (the isomer ratio was determined to be 86:14 from GLC analysis) as a crude product. Chromatography (silica gel–benzene) followed by distillation gave a pure compound **20**: IR (CCl_4) ν 2860, 1733, 1368, 1235, 1060, 860 cm^{-1}; NMR δ 1.90 (s) and 2.0 (3 sharp s, $OCOCH_3$ and $COCH_3$), 4.80 (br, 1 H, $CHCOCH_3$), 1.6–2.5 (m, 13 H, the remaining adamantyl protons); mass spectrum, m/z (M^+, 0.1), 192 (46), 43 (100).

Anal. Calcd for $C_{14}H_{20}O_4$ (252.3): C, 66.65; H, 7.99. Found: C, 66.12; H, 8.10.

1,4-Adamantanediol (21) from 20. Hydrolysis of **20** (86:14) with ethanolic potassium hydroxide gave 1,4-adamantanediol (**21**) in 80% yield: IR (KBr) ν 3260, 2895, 1447, 1355, 1095, 1040 cm^{-1}; NMR ($CDCl_3$) δ 1.53 (s, 2 H, OH), 3.80 (br, 1 H, CHOH), 1.6–2.3 (m, 13 H, the remaining adamantyl protons); mass spectrum, m/z 168 (M^+, 32), 150 (21), 110 (59), 95 (100).

Anal. Calcd for $C_{10}H_{16}O_2$ (168.2): C, 71.39; H, 9.59. Found: C, 71.26; H, 9.65.

The compound **21** was identified with the authentic 1,4-diol, obtained from the sodium borohydride reduction of 1-hydroxyadamantan-4-one.[8] The diol was converted to **20** (80:15) with excess acetic anhydride in the presence of sodium acetate.

4-Hydroxy-1-acetyladamantane (10) from 15. Alkaline hydrolysis of **15** (74:26 and 5:95) in methyl alcohol gave **10** (30:70 and 95:5, respectively) in 77–80% yield. Pure **10** was obtained by distillation, using a Kugelrohr apparatus: IR (CCl_4) ν 3460, 1700, 1452, 1335, 1217, 1068, 1037 cm^{-1}; NMR ($CDCl_3$) δ 2.10 (s, 3 H, $COCH_3$, not separated), 3.87 (br, 1 H, CHOH), 1.4–2.8 (m, 14 H, hydroxy proton and the remaining adamantyl protons); mass spectrum, m/z 194 (M^+, 15), 151 (100), 133 (48); HRMS calcd for $C_{12}H_{18}O_2$ m/z 194.1307, found 194.1306.

Anal. Calcd for $C_{12}H_{18}O_2$ (194.3): C, 74.19; H, 9.34. Found: C, 73.90; H, 9.40.

The reaction of **17** in a methanol–water solution of potassium carbonate also gave **10** in 50% yield.

4-Methoxy-1-acetyladamantane (13) from 10 or 17. The boron trifluoride catalyzed reaction of **10** (30:70 and 95:5) with diazomethane in ether solution gave **13** (28:72 and 94:6) in 35% yield.

The reaction of 200 mg of **17** with 10 mL of absolute methyl alcohol in the presence of silver oxide (3 g) was carried out under reflux for the preparation of **13**, and the yield was 120 mg (58%).

4-Fluoro-1-acetyladamantane (18) from 17. A solution of 50 mg of **17** (58:42) in dry chlorobenzene (5 mL) was refluxed in the presence of excess silver fluoride (100 mg) overnight. GLC analysis showed that the yield of **18** was quantitative and the isomer ratio was 27:73, isolated yield, 55%.

4-Cyano-1-acetyladamantane (19) from 17. According to the procedure for the preparation of 1-cyanoadamantane,[1a] 540 mg of **17** (58:42) was added to a mixture of copper(I) cyanide and pyridine and the solid complex formed was slowly heated to 230 °C. After cooling, the residue was refluxed with 50 mL of benzene overnight to extract **19**. The benzene solution was filtered and concentrated. The product **19** was obtained in 28% (isomer ratio, 75:25) yield.

4-Carbomethoxy-1-acetyladamantane (14) from 19. To 65 mg of **19** (75:25) was added a mixture of sulfuric acid (2 mL), acetic acid (2 mL), and water (2 mL). The solution was refluxed for 2 h, and after cooling, the mixture was extracted with benzene. The extract was dried over magnesium sulfate and evaporated. The residue was esterified by the usual procedure with diazomethane. The GLC analysis of a reaction mixture showed that **14** was formed in 65% yield (isomer ratio, 73:27).

Competitive Reactions. Competitive reactions between adamantane and substituted adamantanes were carried out for the kinetic experiments. A methylene chloride (9 mL) solution of adamantane (1 mmol), 2-substituted adamantane (4 mmol), and biacetyl (1 mL) was prepared. Approximately 3 mL of the mixture was placed in each of several Pyrex ampules. The ampules were bubbled with dry nitrogen and stoppered. Ampules placed 5 cm away from a 100-W mercury lamp cooled by water were rotated with a merry-go-round apparatus. Reaction times were from 20 to 40 h, until adamantanes were consumed by ca. 20%, as determined by GLC from the amount of adamantanes remaining. Analysis of products, 1-acetyladamantane, syn and anti 4-substituted 1-acetyladamantanes was carried out by GLC. For **13** and **18**, the anti isomers were eluted faster than the syn isomers, while for **12**, **14**, **15**, **17**, and **19**, the syn isomers were eluted faster. Mole amounts of syn and anti isomers relative to 1-acetyl-

adamantane were obtained from the calibration curve. The relative rate constants, $k_{syn\text{-}X}/k_H$ and $k_{anti\text{-}X}/k_H$, were determined on the basis of the relative amounts of products found and were corrected statistically. These results are shown in Table II.

Supplementary Material Available: Table IV showing the carbon-13 chemical shifts of syn- and anti-4-substituted 1-acetyladamantanes (1 page). Ordering information is given on any current masthead page.

Relative Rates of the Reaction of (Ethoxycarbonyl)carbene with Several Aromatic and Heteroaromatic Compounds. Selectivity and Mechanism

Martin Pomerantz* and Peter Rooney

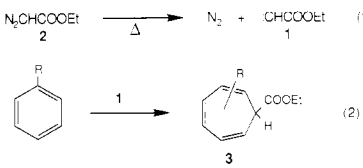
Department of Chemistry, The University of Texas at Arlington, Arlington, Texas 76019-0065

Received June 14, 1988

The relative rates of reaction of (ethoxycarbonyl)carbene (1), formed by the thermal decomposition of ethyl diazoacetate (2), with toluene, anisole, phenanthrene, pyridine, quinoline, acridine, furan, benzofuran, dibenzofuran, thiophene, benzothiophene, dibenzothiophene, pyrrole, indole, carbazole, fluorene, 1,2-dimethoxybenzene, 1,4-dimethoxybenzene, 1,2,4-trimethoxybenzene, 1-methoxynaphthalene, 2-methoxynaphthalene, 2,6-dimethoxynaphthalene, and 2,7-dimethoxynaphthalene versus naphthalene at 150 °C were measured. The relative rate data for the four series toluene, naphthalene, and phenanthrene, the furans, the thiophenes, and the pyrroles are consistent with direct addition of 1 to the aromatic ring systems. Significantly, the more nucleophilic ring systems show a selectivity of up to a factor of about 100 relative to the simple benzene derivative toluene. The pyridine, quinoline, acridine series appears to react with 1 by an ylide mechanism, and in these cases, the selectivities are even larger, up to about 150 relative to toluene. Thus, unlike the reaction of 1 with a series of substituted benzenes, where the selectivity is fairly modest, the heteroaromatic systems studied here show selectivities that are quite large. Methoxy substitution on benzene and naphthalene gives rise to only limited increases in selectivity with one or two groups on the ring system; however, 1,2,4-trimethoxybenzene shows a significantly increased selectivity. Experiments using isooctane as the solvent showed a small selectivity decrease, which is consistent with either a complex of 1 with hexafluorobenzene acting as the reactive intermediate or, perhaps more likely, a possible solvent effect involving a polar transition state. Kinetic measurements were consistent with carbene formation being the rate-determining step in these reactions.

Introduction

The reaction of carbenes, especially (ethoxycarbonyl)-carbene (1), formed by the thermal, photochemical, or catalytic decomposition of ethyl diazoacetate (2; eq 1) with a large variety of organic compounds is quite well-known.[1] The thermal decomposition of 2 in the presence of a series of monosubstituted benzenes to form 7-carbethoxycyclohepta-1,3,5-trienes (3; eq 2) was shown to proceed selec-



tively with a Hammett ρ value of −0.38 relative to benzene, which demonstrates somewhat preferential addition of the electrophilic carbene to the more electron rich aromatic molecules.[2] The relative rates of this series of aromatic molecules were measured competitively relative to benzene as the standard. The Rh(II)-catalyzed decomposition of 2 in the presence of several substituted benzenes also showed preference for addition to the more electron rich molecules.[3] Table I shows the comparison of the relative reactivity of 1, produced thermally or catalytically, toward several substituted benzenes, all relative to benzene as the standard.[2,3]

Table I. Relative Reactivities of Substituted Aromatic Compounds with 1

substrate	Rh(II)[a]	thermal[b]
(trifluoromethyl)benzene		0.55
chlorobenzene	0.1	0.84
fluorobenzene	0.46	0.80
benzene	1.0	1.0
toluene	1.10	1.06
anisole	1.16	1.15
o-xylene	1.6	
m-xylene	1.20	
p-xylene	1.0	

[a] Rhodium(II) trifluoroacetate catalyzed, ref 3. [b] Temperature 129.6 °C, ref 2.

It appears that carbene 1 is somewhat selective and that the carbene species produced in the catalyzed reaction is a little more selective than that produced in the thermal reaction.

For the thermal decomposition of 2 in the presence of 2,6-dimethylnaphthalene in competition with naphthalene, it was found that the partial rate factor for the addition of 1 was 1.4 for the 1,2-bond and 4.2 for the 3,4-bond relative to the 1,2-bond of naphthalene (eq 3).[4] Thus, once again, one can conclude that carbene 1 is somewhat selective, and in this case there is also a positional selectivity.

A search of the literature reveals no study of the selectivity of carbene 1 toward fused aromatics, heteroaromatics, and benzo-fused aromatics. In this paper we

(1) For reviews, see: (a) Kirmse, W. *Carbene Chemistry*, 2nd ed.; Academic: New York, 1971. (b) Marchand, A. P.; MacBrockway, N. *Chem. Rev.* **1974**, *74*, 431. (c) Dave, V.; Warnhoff, E. W. *Org. React. (N.Y.)* **1970**, *18*, 217.

(2) Baldwin, J. E.; Smith, R. A. *J. Am. Chem. Soc.* **1967**, *89*, 1886.

(3) Anciaux, A. J.; Demonceau, A.; Noels, A. F.; Hubert, A. J.; Warin, R.; Teyssie, P. *J. Org. Chem.* **1981**, *46*, 873.

(4) Huisgen, R.; Juppe, G. *Tetrahedron* **1961**, *15*, 7.

0022-3263/88/1953-4374$01.50/0