

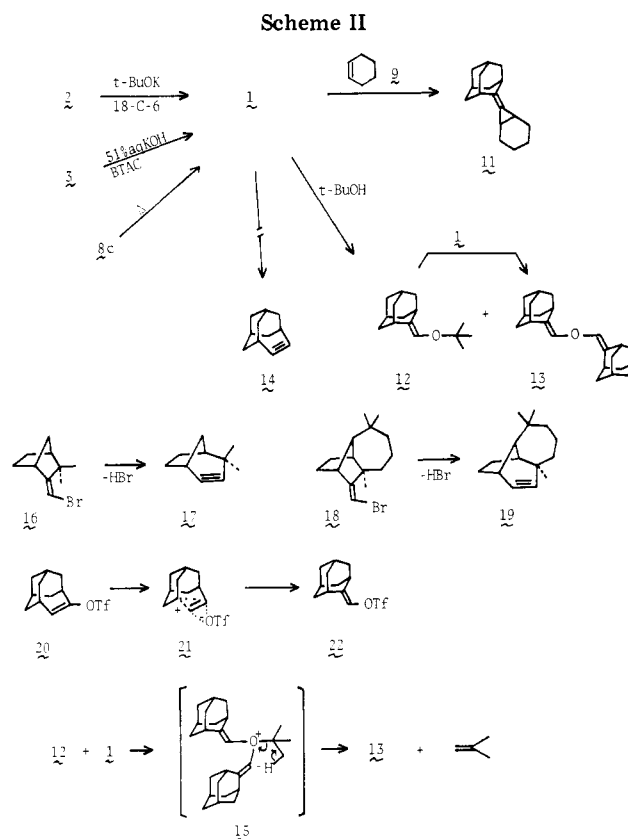
Table I. Generation of 1 under Various Conditions^a

| expt | pre-cursor | base ^b (mol) | catalyst ^c (mol %) | cyclohexene, mol | solvent | reaction temp, °C | time, h | product ^d (yield, %) |
|------|------------|-------------------------|-------------------------------|------------------|---|-------------------|---------|--|
| 1 | 2 | <i>t</i> -BuOK (2.0) | none | 68 | none | refl | 36 | 11 (7.2) ^e |
| 2 | 2 | <i>t</i> -BuOK (2.0) | 18-C-6 (8.0) | 68 | none | refl | 31 | 11 (97.1) ^e |
| 3 | 2 | <i>t</i> -BuOK (2.2) | 18-C-6 (8.0) | 73 | none | refl | 50 | 11 (57.8) ^f |
| 4 | 2 | <i>t</i> -BuOK (2.0) | 18-C-6 (11.0) | 20 | C ₆ H ₅ CH ₃ | 100 ^g | 40 | 11 (70.0) ^f |
| 5 | 3 | 51% KOH ⁱ | BTAC (7.3) | 82 | CH ₂ Cl ₂ | -10-25 | 1.5 | 11 (44.2) ^e |
| 6 | 8c | none | none | 82 | none | 20-25 | 12 | 11 (10.1) ^e |
| 7 | 2 | <i>t</i> -BuOK (2.0) | 18-C-6 (59.0) | 30 | none | 20-25 | 48 | 11 (45.0), ^e 12 (18.0) ^e |
| 8 | 2 | <i>t</i> -BuOK (2.0) | 18-C-6 ^h (50.0) | 30 | C ₆ H ₆ | 25-40 | 3.5 | 11 (90.0), ^e 12 (5.0) ^e |
| 9 | 2 | KOH (2.5) | 18-C-6 ^h (50.0) | 45 | C ₆ H ₆ | 25-30 | 7 | 11 (63.0) ^e |
| 10 | 2 | <i>t</i> -BuOK (3.0) | 18-C-6 (38.0) | 0 | C ₆ H ₅ CH ₃ | refl | 7 | 12 (99.3), ^e 13 (0.4) ^e |
| 11 | 2 | <i>t</i> -BuOK (3.3) | 18-C-6 (15.0) | 0 | C ₆ H ₅ CH ₃ | 150 ^g | 8 | 12 (86.0), ^f 13 (10.2) ^f |

^a For detailed procedures, see Experimental Section. ^b Commercial samples were used without further purification as *t*-BuOK (95%, Merck) and KOH (85%, Tokyo Kasei). ^c 18-C-6 = 18-crown-6 ether and BTAC = benzyltriethylammonium chloride. ^d Even in the presence of an excess amount of cyclohexene, compound 12 was also formed in trace-5% yields (expt 1-5). ^e Relative yields of 11 (and/or 12 and 13) to 2 on GLC analysis. ^f Isolated yields. ^g In a sealed tube. ^h Under ultrasonic irradiation. ⁱ Aqueous solution.

5 to 6 followed by dehydrobromination with 51% aqueous KOH in the presence of Aliquat 336 as the phase-transfer catalyst¹³ was examined as the third route, which provided the most convenient and efficient route to 2, affording 91-100% yields from 5 (Scheme I). Compound 3 was prepared by nitrosation of acetylamino alcohol 7c, which was obtained from 4 via the known 7a¹⁴ and 7b.^{14a} Compound 8c was very unstable and was used quickly after generation from 8a via 8b by the known method.¹⁰

Generation of Adamantylidenecarbene (1). The compounds 2 and 3 were treated with base under several conditions, and the results are summarized in Scheme II and Table I. The dehydrobromination of 2 with *t*-BuOK in cyclohexene was very slow in the absence of 18-crown-6 ether (experiment 1), however, the same reaction in the presence of a catalytic amount of 18-crown-6 proceeded more rapidly to afford adamantylidenecyclopropane 11 in much better conversion (experiment 2). The adduct 11 was isolated in 57.8% yield after usual workup and distillation (experiment 3). The reaction in toluene at 100 °C gave a better yield (70.0%) (experiment 4). The decomposition of the nitroso progenitor 3 in cyclohexene with 51% aqueous KOH under the phase-transfer catalyzed conditions^{9b} gave also the adduct 11 but only in 44.2% yield. Thermal decomposition of 8c in cyclohexene afforded also 11 but in a very lower yield (experiment 6). Above results indicated that 1 can be generated from 2, 3, and 8c and can be trapped with cyclohexene to afford 11. The vinyl bromide 2 was concluded to be the most useful precursor because 2 is stable and easy to prepare and gives the best yield of 11. Therefore, the dehydrobromination of 2 was examined under other several conditions. The dehydrobromination with *t*-BuOK in the absence of cyclohexene yielded vinyl ether derivatives 12 and 13 in 99.3:0.4 ratio (experiment 10). These products were isolated and characterized (see Experimental Section). The vinyl ether 12 is the insertion product of 1 into the OH bond of *t*-BuOH rather than the nucleophilic addition-elimination (Ad_N-E) product as demonstrated recently by Stang and co-workers^{6a} in the reactions of unsaturated carbenes generated from vinyl triflates and *t*-BuOK. However, the formation of divinyl ether 13 might deserve brief comment. When the same reaction was



carried out at 150 °C, 13 was produced in an increased yield (experiment 11). Furthermore, an equimolar reaction of 12 with 1 at 100 °C afforded 13 in 20.3% yield. These results can be explained reasonably by an initial attack of 1 upon the oxygen atom of 12 to form an ylide intermediate,¹⁵ which decomposes thermally to give 13 and isobutylene as shown in 15. It should also be noted that no trace of homoadamantylene (14) or derivatives thereof were produced in the dehydrobromination of 2 with *t*-BuOK, because the formation of bicyclo[3.2.1]octylene derivatives 17 and 19 has been postulated in the dehydrobrominations of ω -bromocamphene (16)¹⁶ and -longifolene (19),^{12b} respectively, with *t*-BuOK (the so-called Fritsch-Buttenberg-Wiechell rearrangement).¹⁷ The observed nonrear-

(13) For recent reviews, see: (a) Starks, C. M.; Liotta, C. "Phase Transfer Catalysis"; Academic Press: New York, 1978; p 330. (b) Dehmlow, E.; Dehmlow, S. S. "Phase Transfer Catalysis"; Verlag Chemie: Weinheim, West Germany, 1980; p 149.

(14) (a) Schlatmann, J. L. M. A.; Korsloot, J. G.; Schut, J. *Tetrahedron* 1970, 26, 949. (b) Stetter, H.; Tillmanns, V. *Chem. Ber.* 1972, 105, 735.

(15) For reactions of carbenes with alcohols and ethers, see: Kirmse, W. "Carbene Chemistry", 2nd ed.; Academic Press: New York, 1971; Chapter 11-IV.

(16) Erickson, K. L.; Wolinsky, J. *J. Am. Chem. Soc.* 1965, 87, 1142.

rangement aptitude of **2** with *t*-BuOK is presumably ascribable to a considerable strain increase expected in the ring enlargement of **1** to **14** due to the rigidity of molecular framework. Also, the exclusive ring contraction of 4-homoadamanten-4-yl triflate (**20**) to adamantylidene-methyl triflate (**22**) via **21** as well as no ring expansion of **22** to the homoadamantenyl system have been reported recently.^{6b}

The above-described generation of **1** from **2** with *t*-BuOK required relatively higher temperatures in order to obtain reasonable yields, but interestingly the reaction even at room temperature was accelerated considerably by ultrasonic irradiation (experiment 8).¹⁸ Under these conditions, potassium hydroxide was also a useful base (experiment 9).

Adamantylidenecyclopropanations of Various Olefins.

The above-described method of adamantylidenecyclopropanation of cyclohexene with **2** and *t*-BuOK was applied to various olefinic substrates as summarized in Table II. The reactions of acyclic and cyclic alkenes **23**–**27** afforded the corresponding adamantylidenecyclopropane derivatives in 19–92% yields, depending on the substrate structures and reaction conditions. The structures of products **38**–**54** were supported by analytical and spectral data (Table III). All of these adamantylidenecyclopropanes exhibited a characteristic IR absorption at 1765–1790 cm⁻¹ due to a methylene-cyclopropane C=C moiety¹⁹ and characteristic ¹H NMR signals at δ 2.9–2.3 (broad s or m for 2 H) due to allylic bridgehead protons. The lower yields of adamantylidenecyclopropanation of **26**, **30**, and **32** are apparently ascribable to steric hindrance. Such considerable steric retardations are also well-known in other alkylidenecarbene-olefin additions,^{2,9c,20} and in fact, relative reactivity studies described below indicated a considerable steric hindrance operating between **1** and polyalkyl-substituted olefins. In the reactions with homoconjugated (**34**) or conjugated olefins (**35**), the initial adducts rearranged to the corresponding isomeric cyclopropanes. Norbornadiene (**34**) afforded exclusively rearranged product **50** at a higher temperature (B),²¹ but unrearranged adduct **49** was obtained at a lower reaction temperature (C) as the major product. The reaction of 2,5-dimethyl-2,4-hexadiene (**35**) at 100 °C gave almost exclusively spirocyclopropane derivative **52**, probably via the corresponding trimethylenemethane intermediate.²² The unrearranged product **51** was obtained at a lower temperature

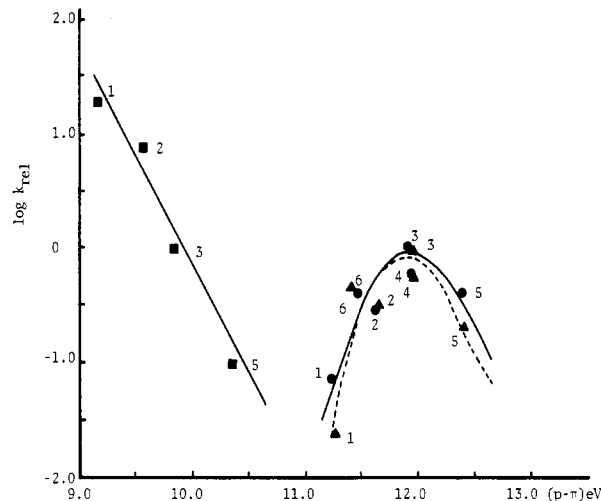


Figure 1. Plots of $\log k_{rel}$ against $p-\pi$ for **1**: (●) $\text{Me}_2\text{C}=\text{C}$; (▲) ref **20**, and $\text{Me}_2\text{C}=\text{C}=\text{C}$: (■) ($\text{Me}_2\text{C}=\text{CHBr}/t\text{-BuOK}/18\text{-crown-6}$, 0–5 °C: Patrick, T. B.; Schmidt, D. J. *J. Org. Chem.* 1977, 42, 3354). For ($p-\pi$) values, see Table IV (the orbital energies of $\text{Me}_2\text{C}=\text{C}=\text{C}$: were calculated by the INDO method, our unpublished results). 2,3-Dimethyl-2-butene (**26**) = **1**, 2-methyl-2-butene (**25**) = **2**, cyclohexene (**9**) = **3**, norbornene = **4**, 1-hexene (**23**) = **5**, and styrene (**37**) = **6**, respectively.

reaction (C in Table II). The reactions of **36** and **37** gave the corresponding unrearranged adducts **53** and **54**, respectively, under the employed conditions.

Relative Reactivity and Theoretical Studies. Adamantylidenecarbene (**1**) was generated from **2** under the crown ether catalyzed basic conditions (*t*-BuOK) in the presence of a large excess of cyclohexene (10-fold excess to **2**) and a second olefin (10-fold excess). Analysis of the reaction mixtures by use of GLC and authentic samples for product identification furnished the product ratios from which the relative reactivities were calculated.²³ Identical runs were performed until at least three results within ±3% were obtained. Cross-checks were performed to ensure internal consistency: These results were within ±10% of the cyclohexene standard results. The results are given in Table IV and are compared with the data reported for isopropylidenecarbene by Stang and Newman and co-workers.^{9c,20} The data obtained for **1** are surprisingly very close to those reported for isopropylidenecarbene, in particular to the values obtained from the vinyl triflate precursor. Stang and co-workers have demonstrated clearly that the vinyl triflate derived alkylidenecarbenes are unencumbered electrophilic singlet carbenes, different from the species derived from Newman's oxazolidines and vinyl halides on the basis of reactivity studies and the Hammett ρ value.^{20,24} The same trend of reactivity of **1** from **2** (in the presence of crown ether)²⁵ with vinyl triflate derived isopropylidenecarbene is indicative of the electrophilic and unencumbered singlet nature of **1**, although the reactivity should depend on the reaction conditions.²⁶

(17) (a) For rearrangements of (bromomethylene)cycloalkenes, see also: Erickson, K. L.; Vanderwaart, B. E.; Wolinsky, J. *Chem. Commun.* 1968, 1031. Erickson, K. L.; Markstein, J.; Kim, K. *J. Org. Chem.* 1971, 36, 1024. Erickson, K. L. *Ibid.* 1971, 36, 1031. Erickson, K. L.; Gordon, S. B. *Ibid.* 1973, 38, 1431. (b) For rearrangements of acyclic alkylidenecarbenes, see: Wolinsky, J.; Clark, G. W.; Thorstenson, P. C. *Ibid.* 1976, 41, 745. (c) For rearrangements of free alkylidenecarbenes, see: Stang, P. J.; Fox, D. P.; Collins, C. J.; Watson, C. R., Jr. *Ibid.* 1978, 43, 364. See also ref 7. (d) For theoretical studies, see: Osamura, Y.; Schaefer, H. F., III; Gray, S. K.; Miller, W. H. *J. Am. Chem. Soc.* 1981, 103, 1904; also see ref 2e for a recent review.

(18) For application of ultrasonic irradiation to generation of dichlorocarbene, see: Regen, S. L.; Singh, A. *J. Org. Chem.* 1982, 47, 1587.

(19) Silverstein, R. M.; Bassler, G. C.; Morrill, T. C. "Spectrometric Identification of Organic Compounds", 4th ed.; Wiley: New York, 1981; p 174.

(20) Stang, P. J.; Madsen, J. R.; Mangum, M. G.; Fox, D. P. *J. Org. Chem.* 1977, 42, 1802.

(21) Such thermal isomerization of alkylidene-tricyclo[3.2.1.0^{2,4}]oct-6-ene system to 3-alkylidene-tetracyclo[3.3.0.0^{4,6}.0^{2,8}]octane system is well-known: (a) Bloch, R.; Leyendecker, F.; Toshima, N. *Tetrahedron Lett.* 1973, 1025. (b) Newman, M. S.; Zwan, M. C. V. *J. Org. Chem.* 1974, 39, 761. (c) Bloch, R.; Bortolussi, M. *Tetrahedron Lett.* 1976, 309.

(22) (a) For a recent review, see: Berson, J. A. *Acc. Chem. Res.* 1978, 11, 446. (b) For theoretical studies, see: Feller, D.; Tanaka, K.; Davidson, E. R.; Borden, W. T. *J. Am. Chem. Soc.* 1982, 104, 967 and references cited therein.

(23) (a) Skell, P. S.; Garner, A. Y. *J. Am. Chem. Soc.* 1956, 78, 5430. (b) Doering, W. von E.; Henderson, A., Jr. *Ibid.* 1958, 80, 5274.

(24) Stang, P. J.; Mangum, M. G. *J. Am. Chem. Soc.* 1975, 97, 6478.

(25) Moss and co-workers have shown crown ethers to be an effective means of generating unencumbered carbenes, identical in their selectivities with the species derived from thermal or photochemical decompositions of diazo precursors and greatly differing from the carbenoid selectivities: Moss, R. A.; Pilkievicz, F. G. *J. Am. Chem. Soc.* 1974, 96, 5632. Moss, R. A.; Joyce, M. A.; Pilkievicz, F. G. *Tetrahedron Lett.* 1975, 2725.

(26) For excellent reviews on carbene selectivity, see: (a) Moss, R. A. "Carbenes"; Jones, M., Jr., Moss, R. A., Eds.; Wiley-Interscience: New York, 1973; Vol. 1, Chapter 2. (b) Moss, R. A. *Acc. Chem. Res.* 1980, 13, 58.

Table II. Adamantylidene-cyclopropanation of Olefins

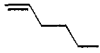
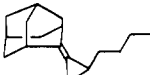

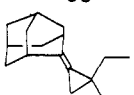

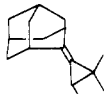

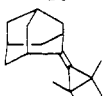

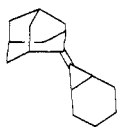

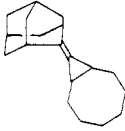

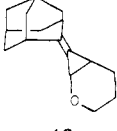

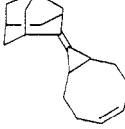

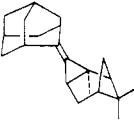

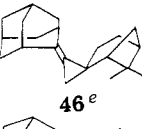

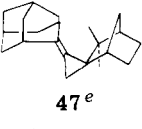

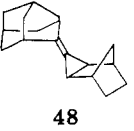

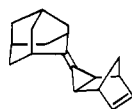

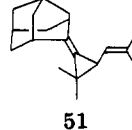

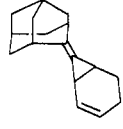

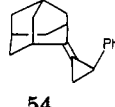
| olefin | products ^a | method ^b (yield, %) ^c | bp, °C (mmHg); n_D or mp, °C (temp, °C) |
|---|--|---|--|
|  23 |  38 | A (65.1) | 92-96 (0.5), 1.5178 (17.0) |
|  24 |  39 | A (56.1) | 95-100 (0.5), 1.5108 (28.0) |
|  25 |  40 | A (73.0) | 71-80 (0.5), 1.5160 (15.0) |
|  26 |  41 | A (47.7) | 75-78 (0.5), 57-60 |
|  9 |  11 | A (70.0) | 72-74 (0.4), 1.5463 (23.0) |
|  27 |  42 | A (92.2) | 105-110 (0.5), 57-59 |
|  28 |  43 | A (70.2) | 92-96 (0.5), 25-27 |
|  29 |  44 | A (77.4) | 115-120 (0.5), 40-41 |
|  30 |  45 ^e | A (31.1) | 108-112 (0.5), 1.5437 (18.0) |
|  31 |  46 ^e | A (61.9) | 108-111 (0.5), 67-70 |
|  32 |  47 ^e | A (19.2) | 112-116 (0.5), 1.5467 (17.0) |
|  33 |  48 | A (76.9) | 86-90 (0.5), 1.5551 (16.5) |

Table II (Continued)

| olefin | products ^a | method ^b (yield, %) ^c | bp, °C (mmHg); n_D or mp, °C (temp, °C) |
|---|---|--|---|
|  34 |  49 | A (37.0) (7.0); B (0) (38.1); C (80.5) (3.4) | 49: 47-49; ^d 50: 100-125 (2.0), 86-88 |
|  35 |  51 | A (trace) (62.4); C (50.7) (0) | 51: 1.5207 ^d (28.0); 52: 70-73 ^d |
|  36 |  53 | A (48.7) | 105-110 (0.5), 1.5566 (18.5) |
|  37 |  54 | D (40.0) | 61-63 ^d |

^a The vinyl ethers 12 (0-32%) and 13 (0-3%) were also produced depending on the reactivity of olefins and the conditions, but they were easily separable from the adducts by chromatography (silica gel, *n*-hexane). ^b A, corresponds to expt 4 in Table I; B, refluxed for 40 h in diglyme instead of toluene of A; C, corresponds to expt 8 in Table I; D, 55 °C for 8 days of A. ^c Isolated yields. ^d Not distilled. ^e Stereochemistry should be considered as tentative.

Table III. Spectral and Analytical Data of Adamantylidene cyclopropane Derivatives

| compd | IR, ^a cm ⁻¹ | ¹ H NMR, ^b δ | formula | anal. calcd/found | |
|-------|--|--|-----------------------------------|-------------------|----------------|
| | | | | C | H |
| 11 | 2920, 2860, 1790 1445, 1095 | 2.66 (br s, 2), 2.20-1.07 (m, 22) | C ₁₇ H ₂₄ | 89.41 89.64 | 10.59 10.36 |
| 38 | 2960, 2920, 2840, 1780, 1465, 1445 | 2.76-2.48 (m, 2), 2.15-1.70 (m, 12), 1.55-0.45 (m, 12) | C ₁₇ H ₂₆ | 88.62 88.40 | 11.38 11.60 |
| 39 | 2975, 2920, 2860, 1790, 1450, 1100 | 2.58 (br s, 2), 2.2-1.6 (m, 12), 1.6-0.6 (m, 7), 1.12 (s, 3) | C ₁₆ H ₂₄ | 88.82 88.75 | 11.18 11.25 |
| 40 | 2960, 2910, 2840, 1775, 1460, 1440 | 2.68-2.38 (m, 2), 2.13-1.69 (m, 12), 1.13 (s, 3), 1.05 (s, 6) | C ₁₆ H ₂₄ | 88.82 88.79 | 11.18 11.21 |
| 41 | 2980, 2910, 2840, 1785, 1465, 1440 | 2.49 (br s, 2), 2.10-1.71 (m, 12), 1.12 (s, 12) | C ₁₇ H ₂₆ | 88.62 88.92 | 11.38 11.43 |
| 42 | 2970, 2920, 2850, 1780, 1460, 1445 | 2.56 (br s, 2), 2.2-0.6 (m, 26) | C ₁₉ H ₂₈ | 88.99 89.00 | 11.01 11.00 |
| 43 | 2920, 2850, 1790, 1770, 1445, 1150 | 3.80 (d, <i>J</i> = 7.5, 1), 3.61-3.15 (m, 2), 2.79 (br s, 1), 2.71 (br s, 1), 2.20-1.62 (m, 12), 1.62-1.19 (m, 4) | C ₁₆ H ₂₂ O | 83.43 83.46 | 9.63 9.52 |
| 44 | 3010, 2910, 2850, 1770, 1630, 1445 | 5.69-5.40 (m, 2), 2.58 (br s, 2), 2.25-1.55 (m, 22) | C ₁₉ H ₂₆ | 89.70 89.70 | 10.30 10.31 |
| 45 | 2980, 2920, 2840, 1780, 1460, 1440 | 2.61 (br s, 1), 2.46 (br s, 1), 2.30-1.55 (m, 17), 1.25 (s, 3), 1.18 (s, 3), 1.07 (s, 3), 1.55-0.72 (m, 2) | C ₂₁ H ₃₀ | 89.29 89.25 | 10.71 10.75 |
| 46 | 2980, 2920, 2840, 1780, 1460, 1440 | 2.61 (br s, 2), 2.42-1.67 (m, 16), 1.67-0.64 (m, 6), 1.20 (s, 3), 1.03 (s, 3) | C ₂₁ H ₃₀ | 89.29 89.37 | 10.71 10.82 |
| 47 | 2920, 2850, 1775, 1470, 1450, 1095 | 2.62 (br s, 2), 2.2-1.7 (m, 14), 1.7-0.6 (m, 8), 0.83 (s, 6) | C ₂₁ H ₃₀ | 89.29 89.19 | 10.71 10.76 |
| 48 | 2920, 2880, 2860, 1790, 1475, 1455 | 2.56 (br s, 2), 2.29 (br s, 2), 2.14-1.05 (m, 18), 0.85 (ABq, <i>J</i> = 9.6, <i>J</i> /Δδ = 0.400, 2) | C ₁₈ H ₂₄ | 89.94 90.09 | 10.06 9.91 |
| 49 | 2960, 2910, 2850, 1765, 1635, 1445, 1310, 1100 | 6.4-6.1 (m, 2), 2.85 (br s, 2), 2.61 (br s, 2), 2.2-1.6 (m, 12), 1.40 (s, 2), 0.98 (ABq, <i>J</i> = 8.0, <i>J</i> /Δδ = 0.444, 2) | C ₁₈ H ₂₂ | 90.70 90.88 | 9.30 9.43 |
| 50 | 3050, 3010, 2910, 2845, 1450, 1438 | 2.75 (br s, 2), 2.20-1.16 (m, 20) | C ₁₈ H ₂₂ | 90.70 90.70 | 9.30 9.31 |
| 51 | 2985, 2930, 2855, 1780, 1450, 1100 | 4.83 (br d, <i>J</i> = 9.0, 1), 2.55 (br s, 2), 2.3-1.4 (m, 13), 1.71 (s, 3), 1.69 (s, 3), 1.21 (s, 3), 1.08 (s, 3) ^c | C ₁₉ H ₂₈ | 88.99 88.90 | 11.01 11.10 |
| 52 | 2985, 2930, 1785, 1445, 1150, 1105 | 4.79 (br d, <i>J</i> = 9.0, 1), 2.3-1.3 (m, 25), 1.3-1.0 (m, 2) ^c | C ₁₉ H ₂₈ | 88.99 89.18 | 11.01 10.82 |
| 53 | 3030, 2910, 2850, 1775, 1625, 1445 | 6.2-5.7 (m, 1), 5.5-5.2 (m, 1), 2.60 (br s, 2), 2.28 (br s, 1), 2.2-0.8 (m, 17) | C ₁₇ H ₂₂ | 90.20 90.28 | 9.80 9.72 |
| 54 | 3020, 2900, 2840, 1775, 1600, 1490, 1440, 743, 685 | 7.4-7.0 (m, 5), 2.9-2.4 (m, 2), 2.56 (q, <i>J</i> = 7.5 and 3.5, 1), 2.2-1.6 (m, 12), 1.75-0.95 (m, 2) | C ₁₉ H ₂₂ | 91.14 91.00 | 8.86 8.95 |

^a Solid compounds were scanned in KBr disks and oils were scanned as neat films. ^b All ¹H NMR spectra were measured in CCl₄ unless otherwise noted. ^c In CDCl₃.

Table IV. Relative Reactivity of 1 and Me₂C=C: with Olefins and Related Differential Orbital Energies^a

| olefin | (π*, eV), ^c (π, eV) ^d | 1 (p = 2.97 eV, σ = -11.74 eV) ^b | | Me ₂ C=C: (p = 2.99 eV, σ = -12.46 eV) ^b | | (p-π, eV), (π*-σ, eV) |
|--------|---|---|-----------|---|---|-----------------------|
| | | rel reactivity 2/ <i>t</i> -BuOK/ 18-crown-6, 100 °C | 8c, 25 °C | rel reactivity triflate/ <i>t</i> -BuOK, -20 °C ⁱ | oxazol- idone/ LiOCH ₂ - CH ₂ OEt, 40 °C ^j | |
| 27 | (2.27), (-8.27) | 0.074 | | 0.027 | 0.02 | (11.24), (14.01) |
| 25 | (2.24), (-8.68) | 0.31 | | 0.30 | | (11.65), (13.98) |
| 9 | (2.07), (-8.94) | 1.00 | 1.00 | 1.00 | 1.00 | (11.91), (13.81) |
| 27 | | 0.68 | | 0.88 | 0.7 | |
| 33 | (-8.97) | 0.58 | 0.61 | 0.54 | | (11.94) |
| 23 | (1.99), ^e (-9.43) ^f | 0.40 | | 0.22 ^k | 0.1 ^k | (12.40), (13.73) |
| 35 | | 0.34 ^h | | | | |
| 37 | (0.25), ^g (-8.43) ^g | 0.40 | 0.48 | 0.49 | 6.2 | (11.40), (11.99) |

^a p-π = LUMO_{carbene}-HOMO_{alkene}, π*-σ = LUMO_{alkene}-HOMO_{carbene}. See ref 26b. ^b INDO calculation. ^c Jordan, K. D.; Burrow, P. D. *Acc. Chem. Res.* 1978, 11, 341. ^d Bieri, G.; Burger, F.; Heilbronner, E.; Maier, J. P. *Helv. Chim. Acta* 1977, 60, 2213. ^e The value of propene. ^f The value of 1-octene: Demeo, D. A.; Elsayed, M. A. *J. Chem. Phys.* 1970, 52, 2622. ^g Burrow, P. D.; Michejda, J. A.; Jordan, K. D. *J. Am. Chem. Soc.* 1976, 98, 6392. Cf. also: Houk, K. N.; Sims, J.; Duke, R. E., Jr.; Strozier, R. W.; George, J. K. *Ibid.* 1973, 95, 7287. ^h Corrected for the statistical factor. ⁱ References 2a and 20. ^j References 2a and 9c. ^k The data reported for 1-octene.

Theoretically, many calculations have predicted a singlet ground state for methylenecarbene with a considerably large singlet-triplet splitting (15.7–51.3 kcal/mol),²⁷ which is suggestive also a singlet ground state of 1.²⁸ Experimentally the similar reactivity (0.34 after correction by the statistical factor) of 2,5-dimethyl-2,4-hexadiene (35) to 2-methyl-2-butene (25) (0.31) (Table IV) supported also the singlet nature of 1 because a diradical resulting from addition of triplet 1 to 35 should be more stable than a radical resulting from 25.²⁰ The electrophilic nature of 1 was also predictable from FMO theory.^{26b,29} The LUMO₁ - HOMO_{alkene} differential energies (p-π) are obviously smaller than HOMO₁ - LUMO_{alkene} (π*-σ) for some selected electron-rich alkenes, predicting the electrophilic nature of 1 (Table IV). This superficial FMO analysis is of course a rough estimation of the real interaction of the carbene with alkenes, but the usefulness of such simple treatment has precedents for prediction of olefinic selectivity of some saturated carbenes (for example, electrophilic CCl₂, ambiphilic MeOCCl, and nucleophilic (MeO)₂C).³⁰ The observed higher reactivity of cyclohexene (9) than that of 1-hexene (23) was consonant with the above prediction. However, the lower reactivities of 2,3-dimethyl-2-butene (26) and 2-methyl-2-butene (25) than that of 9 is apparently due to steric retardation characteristic to alkylidenecarbenes. Without such severe steric hindrance, the relative reactivity of electrophilic carbenes should be proportional to HOMO_{alkene} energies (or p-π). In fact, the plot for dimethylvinylidenecarbene known as not sterically demanding^{26a} gave a linear relationship as shown in Figure 1. However, the plots for 1 and isopropylidenecarbene gave characteristic inverse-U type trends, demonstrating clearly considerable steric retardations for these carbenes.

The above-described generation of 1 from 2 required relatively higher temperature (>25 °C) in order to com-

plete the reaction compared to the vinyl triflate method developed recently by Stang and co-workers.^{2,6a} Despite of this limitation, the relative ease with which adamantylidenecyclopropane derivatives can be prepared by the method presented here demonstrates the feasibility of extending this method to the synthesis of other methylenecyclopropanes and related compounds.

Experimental Section

General Methods. All boiling points and melting points were measured with a Yanagimoto micro melting point apparatus and are uncorrected. IR spectra were obtained on a JASCO IRA-1 spectrometer. ¹H NMR data were recorded on a JEOL JNM-60HL instrument at 60 MHz. Chemical shifts are reported in δ (ppm) relative to Me₄Si as an internal standard, and coupling constants in Hz. Mass spectra were obtained with a JEOL JMS-D10 mass spectrometer at 75 eV. Microanalyses were performed with a Perkin-Elmer 240B elemental analyzer. GLC analyses were carried out on a JEOL JGC-20K gas chromatograph on a 1- or 2-m silicone SE-30 column at 100–230 °C. Ultrasonic irradiations were performed with a Branson B-220 ultrasonic cleaner. Potassium *tert*-butoxide was purchased from Merck Japan Ltd. (95% purity) and used without further purification. Olefinic substrates were purchased from Tokyo Kasei Co. and/or Aldrich Chemical Co. and used after drying over molecular sieves.

Calculations. The calculations were carried out on a FACOM M-200 computer at the Nagoya University Computation Center. The geometry of adamantylidenecarbene (1) required for the INDO calculation³¹ was estimated from the assumptive molecular model made up by the standard bond lengths and angles.

ω-(Bromomethylene)adamantane (2). A. Bromination-Dehydrobromination Route. To a stirred and cooled (-15 °C) solution of methyleneadamantane (5)³² (2.80 g, 18.9 mmol) in CCl₄ (20 mL) was added dropwise a bromine solution (3 g/5 mL of CCl₄) until the color of bromine persisted. The solvent was removed under reduced pressure at room temperature to afford a solid residue of 6 quantitatively. An analytical sample was obtained after recrystallization from *n*-hexane: mp 63–65 °C; IR (KBr) 2900, 1440, 1250, 890, 730, 675 cm⁻¹; ¹H NMR (CDCl₃) δ 4.18 (s, 2), 2.8–2.1 (m, 4), 2.1–1.5 (m, 10). Anal. Calcd for C₁₁H₁₆Br₂: C, 42.89; H, 5.23. Found: C, 42.90; H, 5.22.

A mixture of the dibromide 6 (1.03 g, 3.34 mmol), *n*-hexane (10 mL), Aliquat 336 (0.1 g), and 51% aqueous KOH (6 mL) was vigorously stirred under an atmosphere of argon for 5 h at room temperature. The mixture was diluted with water, and the organic layer was separated. The water layer was extracted with *n*-hexane

(27) (a) The Hueckel type: Gleiter, R.; Hoffmann, R. *J. Am. Chem. Soc.* 1968, 90, 5457. (b) The MINDO/2: Bodor, N.; Dewar, M. J. S.; Watson, J. S. *Ibid.* 1972, 94, 9095. (c) The ab initio method: Davis, J. H.; Goddard, W. A., III; Harding, L. B. *Ibid.* 1977, 99, 2919. (d) Reference 7 and references cited therein.

(28) Theoretical calculation (INDO method) predicted a singlet ground state for 1 (with a singlet-triplet gap of 49.3 kcal/mol), although the more sophisticated calculations are desirable.

(29) For a recent elaborated ab initio calculation on various saturated singlet carbenes and their cycloadditions, see: Rondan, N. G.; Houk, K. N.; Moss, R. A. *J. Am. Chem. Soc.* 1980, 102, 1770.

(30) For more detailed prediction of carbene philicity, see ref 29.

(31) Pople, J. A.; Beveridge, D. L. "Approximate Molecular Orbital Theory"; McGraw-Hill: New York, 1970; pp 163–193.

(32) Schleyer, P. v. R.; Nicholas, R. D. *J. Am. Chem. Soc.* 1961, 83, 182.

(10 mL \times 2). The combined organic layer and the extracts were washed with water and dried (Na_2SO_4). Removal of the solvent under reduced pressure gave an oily residue that was purified by a short silica gel (or alumina) column with *n*-hexane as eluant to give the vinyl bromide 2 as a colorless oil (0.700 g, 91.4%): n_D^{27} 1.5612 (solidified material on cooling had mp 26–28 °C); IR (neat) 3060, 2910, 2840, 1630, 1445, 1270, 770, 680 cm^{-1} ; $^1\text{H NMR}$ (CDCl_3) δ 5.78 (s, 1), 3.10 (br s, 1), 2.57 (br s, 1), 2.2–1.7 (m, 12); mass spectrum, m/e (relative intensity) 228 ($\text{M}^+ + 2$, 7.8), 226 (M^+ , 8.8), 147 (17), 135 (13), 105 (24), 97 (46), 91 (37), 83 (43), 81 (42), 71 (43), 69 (73), 67 (43), 57 (91), 55 (100), 44 (95), 43 (99), 41 (99). Anal. Calcd for $\text{C}_{11}\text{H}_{15}\text{Br}$: C, 58.17; H, 6.66. Found: C, 58.32; H, 6.51.

B. Bromination of 5 with NBS. A mixture of 5 (1.14 g, 7.70 mmol), NBS (2.74 g, 15.4 mmol), and dibenzoyl peroxide (20 mg) in anhydrous CCl_4 (50 mL) was heated under reflux for 30 h.¹² The resulting precipitates were removed by filtration, and the filtrate was evaporated under reduced pressure to give an oily residue that was purified on a silica gel column with *n*-hexane as eluant to afford the bromide 2 (751 mg, 43.0%).

C. The Wittig Reaction of Adamantanone (4). To a mixture of (bromomethyl)triphenylphosphonium bromide¹¹ (1.05 g, 2.40 mmol) in anhydrous ether (4 mL) were added piperidine (0.30 mL, 3.0 mmol) and an ether solution of phenyllithium (3.5 mL, 3.1 mmol) at room temperature with stirring under argon atmosphere. After 5 min, 4 (150 mg, 1.00 mmol) was added to the mixture and the stirring was continued for 3 h. The precipitates were filtered and washed with ether. The combined filtrate and washings were washed with 2 N H_2SO_4 , H_2O , and 5% NaHCO_3 , successively, and dried (Na_2SO_4). Removal of the solvent gave an oil that was purified on a silica gel column (*n*-hexane) to afford the bromide 2 (44 mg, 51% for the reacted 4).

2-[(*N*-Acetylamino)methyl]-2-adamantanol (7c). A mixture of 2-(aminomethyl)-2-adamantanol (7b) hydrochloride^{14a} (390 mg, 1.79 mmol) and acetic anhydride (184 mg, 1.80 mmol) in anhydrous pyridine (15 mL) was stirred overnight at room temperature. The diluted mixture was extracted with CHCl_3 (5 mL \times 3), and the combined extracts were concentrated under reduced pressure to precipitate crystals that were filtered and washed with water to give 7c (280 mg, 70.0%): mp 295–298 °C; IR (KBr) 3325, 1630, 1570 cm^{-1} ; $^1\text{H NMR}$ (CDCl_3) δ 5.9 (br s, 1, D_2O exchangeable), 3.52 (d, $J = 6.0$, 2), 2.35 (br s, 1, D_2O exchangeable), 2.02 (s, 3), 2.4–1.3 (m, 14). Anal. Calcd for $\text{C}_{13}\text{H}_{21}\text{NO}_2$: C, 69.92; H, 9.48; N, 6.27. Found: C, 69.87; H, 9.28; N, 6.29.

2-[(*N*-Acetyl-*N*-nitrosoamino)methyl]-2-adamantanol (3). To an ice-cooled and stirred mixture of 7c (135 mg, 0.600 mmol), CH_3COOK (238 mg, 2.76 mmol), and P_2O_5 (25 mg, 0.18 mmol) in glacial acetic acid (3 mL) was added an acetic acid solution of NOCl (5.5 mL, 2.24 mmol). After the stirring was continued for 1 h under ice-cooling and 10 min at room temperature, the mixture was diluted with ice-water and extracted with CH_2Cl_2 (5 mL \times 2). The combined extracts were washed with water and dried (Na_2SO_4). Removal of the solvent under reduced pressure gave a faintly yellowish crystalline residue of 3 (82 mg, 53.8%): mp 205–207 °C dec; IR (KBr) 3315, 1625, 1575, 1450 cm^{-1} . The nitroso compound 3 was very unstable and used directly without further purification.

[(*Tosylazo*)methylene]adamantane (8c). A mixture of 2-adamantanecarboxaldehyde tosylhydrazone^{3b} (8a) (100 mg, 0.301 mmol) and phenyltrimethylammonium perbromide (113 mg, 0.301 mmol) in anhydrous THF (10 mL) was stirred at –15 to –10 °C for 2 h under argon atmosphere. The mixture was diluted with ether (30 mL), washed with cold saturated Na_2CO_3 (5 mL), water, and saturated NaCl , successively, and dried (Na_2SO_4). Removal of the solvent under reduced pressure gave a yellowish solid of 8c (72 mg, 72%), which was very unstable, decomposing rapidly at room temperature, and used directly without further purification.

General Procedure of Adamantylidenecyclopropanation with 2. Method A. A mixture of an appropriate olefin (20 mmol), the bromide 2 (1.0 mmol), 18-crown-6-ether (0.11 mmol), and *t*-BuOK (2.0 mmol, commercially available 95% reagent of Merck Co. was used in general) in anhydrous toluene (2 mL) was heated with stirring under an atmosphere of argon at 100 °C for 40 h in a sealed tube. The cooled mixture was diluted with *n*-hexane (20 mL), washed with water, and dried (Na_2SO_4). Removal of

the solvent and remaining olefin gave a crude adduct that was purified on a silica gel column (*n*-hexane) and/or by Kugelrohr distillation (see Tables I, II, and III). For the somewhat modified conditions, see Tables I and II.

Method B. Instead of toluene as in method A, a high-boiling solvent such as diglyme was used for the higher temperature reactions.

Method C. For the lower temperature reactions, the reaction mixture was irradiated with an ultrasonic cleaner (see experiment 8 of Table I).

Dehydrobromination of 2 with *t*-BuOK in the Absence of Olefin. Adamantylidenemethyl *tert*-Butyl Ether (12) and Bis(adamantylidenemethyl) Ether (13). A mixture of 2 (115 mg, 0.507 mmol), 18-crown-6 ether (20 mg, 0.076 mmol), and *t*-BuOK (200 mg of 90% purity reagent, 1.69 mmol) in toluene (2 mL) was heated under an argon atmosphere at 150 °C for 8 h. The cooled mixture was diluted with *n*-hexane (10 mL), washed with water, and dried (Na_2SO_4). Removal of the solvent under reduced pressure gave a crude product that was purified on an alumina TLC plate, eluting with *n*-hexane, to afford ether 13 as the upper fraction (8.0 mg, 10.2%): mp 246–249 °C (recrystallized from *n*-hexane); IR (KBr) 2910, 2850, 1660, 1445, 1375, 1155, 809 cm^{-1} ; $^1\text{H NMR}$ (CCl_4) δ 5.85 (s, 2), 3.00 (br s, 2), 2.20 (br s, 2), 2.1–1.5 (m, 24); mass spectrum, m/e (relative intensity) 311 ($\text{M}^+ + 1$, 11), 310 (M^+ , 49), 147 (12), 135 (11), 119 (20), 105 (40), 93 (29), 91 (100), 81 (29), 79 (65), 77 (40), 67 (54), 55 (37), 41 (74). Anal. Calcd for $\text{C}_{22}\text{H}_{30}\text{O}$: C, 85.11; H, 9.74. Found: C, 85.02; H, 9.83.

The lower fraction gave the *tert*-butyl ether 12 as a very volatile oil (96 mg, 86.0%): n_D^{17} 1.5119; IR (neat) 2960, 2890, 2835, 1665, 1440, 1355, 1180, 1120 cm^{-1} ; $^1\text{H NMR}$ (CDCl_3) δ 5.93 (s, 1), 3.00 (br s, 1), 2.27 (br s, 1), 2.11–1.50 (m, 12), 1.23 (s, 9); mass spectrum, m/e (relative intensity) 220 (M^+ , 2.8), 164 (52), 107 (26), 91 (29), 79 (67), 77 (29), 67 (24), 57 (95), 55 (24), 41 (100), 39 (48). Anal. Calcd for $\text{C}_{15}\text{H}_{22}\text{O}$: C, 81.76; H, 10.98. Found: C, 81.77; H, 10.70.

Reaction of 12 with 1. A mixture of 12 (35 mg, 0.16 mmol), 2 (36 mg, 0.16 mmol), 18-crown-6 ether (10 mg, 0.038 mmol), and *t*-BuOK (37 mg of 97% purity reagent, 0.34 mmol) in toluene (1 mL) was heated at 100 °C for 40 h in a sealed tube. The cooled mixture was diluted with *n*-hexane, washed with water, and dried (Na_2SO_4). Removal of the solvent gave an oily residue, which was purified on an alumina plate to afford 13 (10 mg, 20.3%) and 12 (40 mg, 34.6% after correction for the recovery).

Generation of 1 from 3 in Cyclohexene. To a vigorously stirred and cooled (–10 °C) mixture of freshly prepared 3 (30 mg, 0.12 mmol), cyclohexene (1.0 mL, 9.8 mmol), and BTAC (2.0 mg, 0.0087 mmol) in CH_2Cl_2 was added 51% aqueous KOH (0.30 mL). The stirring was continued for 0.5 h at the same temperature and 1 h at 25 °C. The mixture was diluted with water and extracted with CH_2Cl_2 (5 mL \times 3). The combined extracts were washed, dried (MgSO_4), and evaporated to afford a crude adduct that was filtered through a short silica gel column (*n*-hexane). GLC analysis indicated the formation of adduct 11 (44.2%).

Generation of 1 from 8c in Cyclohexene. Freshly prepared 8c from 8a (10 mg, 0.030 mmol) in cyclohexene (202 mg, 2.46 mmol) was allowed to stand at 20–25 °C for 12 h. The mixture was passed through a short silica gel column using *n*-hexane as eluant and analyzed on GLC to indicate the formation of 11 (10.1%).

General Procedure for the Relative Reactivity Studies. A mixture of cyclohexene (2.0 mmol) and an appropriate olefin (2.0 mmol), the bromide 2 (0.20 mmol), 18-crown-6 ether (0.02 mmol) and *t*-BuOK (0.40 mmol of 95% reagent) in dry toluene (10 mL) was stirred magnetically under an atmosphere of argon at 100 \pm 2 °C for 40 h in a sealed tube. The cooled mixture was purified on a short silica gel column, eluting with *n*-hexane, to give the two product adducts, which were analyzed on a flame ionization GLC. Each reaction mixture was analyzed three times and averaged. For the analysis, appropriate calibration mixture of the adducts were used and the relative reactivity was calculated by the Doering–Skell equation.²³ The decomposition of 8c was carried out similarly in the presence of appropriate olefin mixtures (Table IV).

Registry No. 1, 85203-15-2; 2, 68251-94-5; 3, 85203-16-3; 8c, 85203-17-4; 9, 110-83-8; 11, 68251-95-6; 12, 68251-99-0; 13,

68252-00-6; 23, 592-41-6; 24, 563-46-2; 25, 513-35-9; 26, 563-79-1; 27, 931-88-4; 28, 110-87-2; 29, 111-78-4; 30, 80-56-8; 31, 127-91-3; 32, 79-92-5; 33, 498-66-8; 34, 121-46-0; 35, 764-13-6; 36, 592-57-4; 37, 100-42-5; 38, 85203-18-5; 39, 85203-19-6; 40, 85203-20-9; 41,

85203-21-0; 42, 85203-22-1; 43, 85220-71-9; 44, 85203-23-2; 45, 85203-24-3; 46, 85220-72-0; 47, 85203-25-4; 48, 68251-96-7; 49, 85203-26-5; 50, 68251-97-8; 51, 85203-27-6; 52, 68251-98-9; 53, 85203-28-7; 54, 85203-29-8.

Immature Hydronium Ion Implicated in Water-Catalyzed Immonium Ion Hydrolysis¹

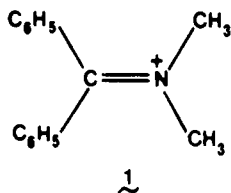
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The water-catalyzed hydrolysis of the dimethylimmonium ion of benzophenone exhibits a solvent deuterium isotope effect of $k_{\text{H}_2\text{O}}/k_{\text{D}_2\text{O}} = 2.19$. Proton inventory studies in protium oxide-deuterium oxide mixtures of atom fraction deuterium n indicate identical contributions of three protons to the observed effect. Each proton exhibits an isotope effect of about 1.30. The downwardly curved proton inventory can be fit to the equation $k_n/k_0 = (1 - n + n\phi^*)^3$ where $\phi^* = 0.768$. The data support a transition-state structure involving an immature hydronium ion.

Several detailed studies of the base-catalyzed and water-catalyzed hydrolysis of Schiff bases have been reported.³⁻⁹ Much of the impetus for these studies derives from the occurrence of such compounds in the catalytic mechanism of several enzymes, including acetoacetate decarboxylase¹⁰ and aldolase¹¹ among others. Since proton transfer and solvent participation are of major importance in the hydrolysis of such compounds, we felt that proton inventory studies would be useful in elucidating the details of the transition-state structure for such a reaction. The compound chosen for study models the protonation state of Schiff bases at low-pH values and has been the object of much investigation.^{3,4,9} The dimethylimmonium ion of benzophenone (1) exhibits a pH-independent region for



hydrolysis between pH 2 and 6.5 due to the cationic nature of the compound (i.e., further protonation of nitrogen is prevented). Previous studies have shown that this pH region corresponds to water-catalyzed hydrolysis of 1.^{3,4,9}

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(3) Cordes, E. H.; Jencks, W. P. *J. Am. Chem. Soc.* **1963**, *85*, 2843.

(4) Koehler, K.; Sandstrom, W.; Cordes, E. H. *J. Am. Chem. Soc.* **1964**, *86*, 2413.

(5) do Amaral, L.; Sandstrom, W. A.; Cordes, E. H. *J. Am. Chem. Soc.* **1966**, *88*, 2225.

(6) Hand, E. S.; Jencks, W. P. *J. Am. Chem. Soc.* **1975**, *97*, 6221.

(7) Pollack, R. M.; Brault, M. *J. Am. Chem. Soc.* **1976**, *98*, 247.

(8) Hogg, J. L.; Jencks, W. P. *J. Am. Chem. Soc.* **1976**, *98*, 5643.

(9) Fischer, H.; DeCandis, F. X.; Ogden, S. D.; Jencks, W. P. *J. Am. Chem. Soc.* **1980**, *102*, 1340.

(10) Warren, S. G.; Zerner, B.; Westheimer, F. H. *Biochemistry* **1966**, *5*, 817.

(11) Rose, I. A.; O'Connell, E. L. *J. Biol. Chem.* **1969**, *244*, 126.

Table I. First-Order Rate Constants for the Water-Catalyzed Hydrolysis of 1 at 50.00 ± 0.05 °C in $\text{H}_2\text{O}-\text{D}_2\text{O}$ Mixtures of Atom Fraction of Deuterium n^a

| deuterium atom fraction (n) | no. of runs | $10^6 k_n, \text{s}^{-1}$ | |
|---------------------------------|-------------|---------------------------|--------------------|
| | | obsd | calcd ^b |
| 0.000 | 5 | 1409 ± 6^c | 1409 |
| 0.248 | 5 | 1179 ± 8 | 1180 |
| 0.495 | 4 | 978 ± 3 | 978 |
| 0.743 | 5 | 801 ± 4 | 800 |
| 0.990 ^d | 4 | 644 ± 3 | 645 |

^a The pH(D) was maintained at 3.0 by using 10^{-3} M HCl (DCl). Ionic strength was kept at 0.5 M with KCl.

^b Calculated on the basis of eq 8 for transition state 6 with $\phi_a^* = 0.768$. ^c Error limits are standard deviations.

^d Atom fraction of deuterium in "pure" 10^{-3} M DCl solution as determined by Josef Nemeth.³¹

Table II. First-Order Rate Constants for the Water-Catalyzed Hydrolysis of 1 as a Function of Volume Fraction of Acetonitrile in the Solvent at 25.00 ± 0.05 °C^a

| volume fraction of CH_3CN^b | $10^6 k, \text{s}^{-1}$ |
|---|-------------------------|
| 0.0 | 220 ± 3^c |
| 0.1 | 270 ± 5 |
| 0.2 | 336 ± 4 |
| 0.3 | 414 ± 4 |
| 0.4 | 493 ± 4 |
| 0.5 | 536 ± 5 |
| 0.6 | 568 ± 2 |

^a The pH was maintained at 3.0 by using 10^{-3} M HCl, and the ionic strength was kept at 0.5 M with KCl. ^b Before mixing. ^c Average of at least two determinations. Error limits are standard deviations.

Results

Table I summarizes the data obtained for the hydrolysis of 1 at 50 °C in protium oxide, deuterium oxide, and mixtures of atom fraction of deuterium n of the two at pH 3.0 or the equivalent pD. This table also contains the calculated rate constants predicted on the basis of a chemical model to be discussed. The proton inventory plot (Figure 1) for the data of Table I is clearly downwardly