The Intramolecular Nitrene-Type 1,1-Cycloaddition Reaction of Allyl-Substituted Diazomethanes[1]

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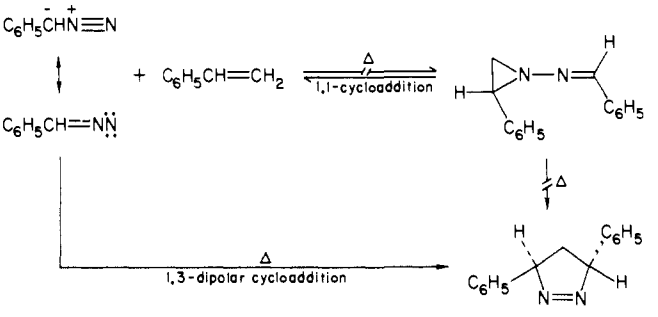
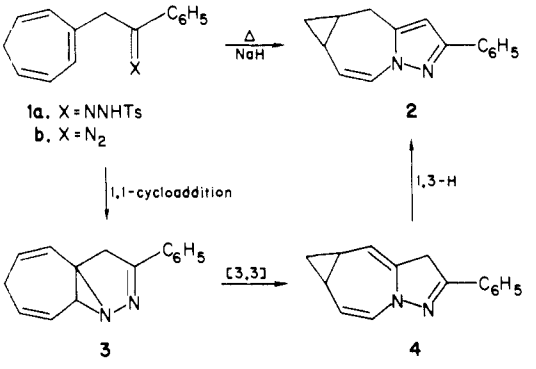
Abstract: Various allyl-substituted diazomethanes generated by pyrolyses of the sodium salts of corresponding tosylhydrazones undergo a reversible intramolecular nitrene-type 1,1-cycloaddition to give 1,2-diazabicyclo[3.1.0]hex-2-enes. Stereochemical results obtained from (*E*)- and (*Z*)-5-phenyl-5-diazopent-2-enes, (*E*)-1,4-diphenyl-4-diazobut-1-ene, and (*Z*)-3-methyl-6-aryl-6-diazohex-3-enes indicated that both the 1,1- and retro-1,1-cycloaddition reactions are stereoselective with complete retention of configuration. Syntheses and reactions of various 2-methyl-5-aryl-5-diazopent-2-enes and rate analyses of the reversible 1,1-cycloaddition revealed that the 1,1-cycloaddition reaction occurs regardless of the nature of the substituent on the aryl group, but the equilibrium constant of the reversible 1,1-cycloaddition largely depends on the nature of a substituent on the aryl group and that electron-withdrawing substituents accelerate both the 1,1- and retro-1,1-cycloadditions. Combining these observations with the fact that the 1,1-cycloaddition reaction is accelerated in polar solvent while the retro-1,1-cycloaddition reaction is decelerated, it can be concluded that the 1,1-cycloaddition reaction occurs concertedly without intervention of a zwitterionic intermediate, being controlled by the electrophilic LUMO energy of diazomethane.

Since the general concept of the 1,3-dipolar cycloaddition was introduced by Huisgen in the early 1960s,[3-7] this reaction has become one of the most general and important methods for the synthesis of five-membered heterocycles.[8] Among various 1,3-dipolar cycloaddition reactions, intermolecular 1,3-dipolar cycloaddition reactions of diazomethanes to olefins have been most thoroughly investigated, and systematic studies by Huisgen and co-workers have provided many fruitful mechanistic conclusions about this reaction.[9,10] Although it had been concluded that the HOMO (diazomethane)–LUMO (olefin) controlled concerted reaction[11,12] occurs without intervention of any intermediate[13] for the reactions of simple diazomethanes with olefins, Huisgen once proposed a mechanistic alternative,[4] i.e., an initial hypothetical nitrene-type 1,1-cycloaddition reaction of phenyldiazomethane to styrene, followed by a vinylcyclopropane–cyclopentene-type 1,3-sigmatropic rearrangement, as shown in Scheme I. This idea was not farfetched, but rather thoughtful, if one may keep in mind that diazomethane can be described by a nitrene-like resonance formula. The elegant control experiments by Huisgen and co-workers, however, soon excluded this hypothesis for the intermolecular 1,3-dipolar cycloaddition reaction of diazomethane.[14] This hypothetical reactivity of the terminal nitrogen of diazomethane had not been uncovered until we[15-17] and then Padwa[18-20] discovered it in intramolecular reactions of allyl-substituted diazomethanes.

Scheme I



Scheme II



During our extensive studies on the intramolecular cyclization of diazomethanes incorporated in the cycloheptatriene ring,[21-23] we found that thermolysis of the sodium salt of α-(1,3,5-cycloheptatrien-3-yl)acetophenone *N*-tosylhydrazone (**1a**) gave 10-phenyl-1,11-diazatricyclo[6.3.0.0^{4,6}]undeca-2,8,10-triene (**2**) via diazomethane **1b** in good yield.[24] (See Scheme II.) This reaction was of interest in the following two points. Among the reported intramolecular cyclization reactions of diazoalkenes,[25] that of

(1) Organic Thermal Reactions, Part 62. Part 61, see ref 2.
(2) Kumagai, T.; Tanaka, S.; Mukai, T. *Tetrahedron Lett.* **1984**, *25*, 5669.
(3) Huisgen, R. *Angew. Chem., Int. Ed. Engl.* **1963**, *2*, 565.
(4) Huisgen, R. *Angew. Chem., Int. Ed. Engl.* **1963**, *2*, 633.
(5) Huisgen, R.; Szeimies, G.; Mobius, L. *Chem. Ber.* **1967**, *100*, 2494.
(6) Huisgen, R.; Stangl, H.; Stern, H. J.; Wagenhofer, H. *Angew. Chem.* **1961**, *73*, 170.
(7) Huisgen, R.; Mobius, L.; Stangl, H.; Szeimies, G.; Vernon, J. M. *Chem. Ber.* **1965**, *98*, 3992.
(8) Recent excellent reviews on the 1,3-dipolar cycloaddition reaction by Huisgen, see ref 9 and 10.
(9) Huisgen, R.; Grashey, R.; Sauer, J. "The Chemistry of Alkenes"; Patai, S., Ed.; Interscience: London, 1964; pp 806–878.
(10) Huisgen, R. "1,3-Dipolar Cycloaddition Chemistry"; Padwa, A., Ed.; John Wiley and Sons: New York, 1983; Vol. 1, p 1–176.
(11) Houk, K. N.; Sims, J.; Watts, C. R.; Luskus, L. J. *J. Am. Chem. Soc.* **1973**, *95*, 7301.
(12) Sustmann, R. *Tetrahedron Lett.* **1971**, 2717.
(13) Huisgen, R. *J. Org. Chem.* **1968**, *33*, 2291; **1976**, *41*, 403.
(14) Huisgen, R.; Sustmann, R.; Bunge, K. *Tetrahedron Lett.* **1966**, 3603; *Chem. Ber.* **1972**, *105*, 1324.
(15) Nishizawa, Y.; Miyashi, T.; Mukai, T. *J. Am. Chem. Soc.* **1980**, *102*, 1176.
(16) Miyashi, T.; Fujii, Y.; Nishizawa, Y.; Mukai, T. *J. Am. Chem. Soc.* **1981**, *103*, 725.
(17) Miyashi, T.; Yamakawa, K.; Kamata, M.; Mukai, T. *J. Am. Chem. Soc.* **1983**, *105*, 6342.
(18) Padwa, A.; Ku, H. *Tetrahedron Lett.* **1980**, *21*, 1009.
(19) Padwa, A.; Rodriguez, A. *Tetrahedron Lett.* **1981**, *22*, 187.
(20) Padwa, A.; Rodriguez, A.; Tohidi, M.; Fukunaga, T. *J. Am. Chem. Soc.* **1983**, *105*, 933.
(21) Tsuruta, H.; Kurabayashi, K.; Mukai, T. *J. Am. Chem. Soc.* **1968**, *90*, 7167.
(22) Tsuruta, H.; Kurabayashi, K.; Mukai, T. *Bull. Chem. Soc. Jpn.* **1972**, *45*, 2822.
(23) Miyashi, T.; Nishizawa, Y.; Mukai, T. *Heterocycles* **1978**, *11*, 293.
(24) Miyashi, T.; Nishizawa, Y.; Sugiyama, T.; Mukai, T. *J. Am. Chem. Soc.* **1977**, *99*, 6109.

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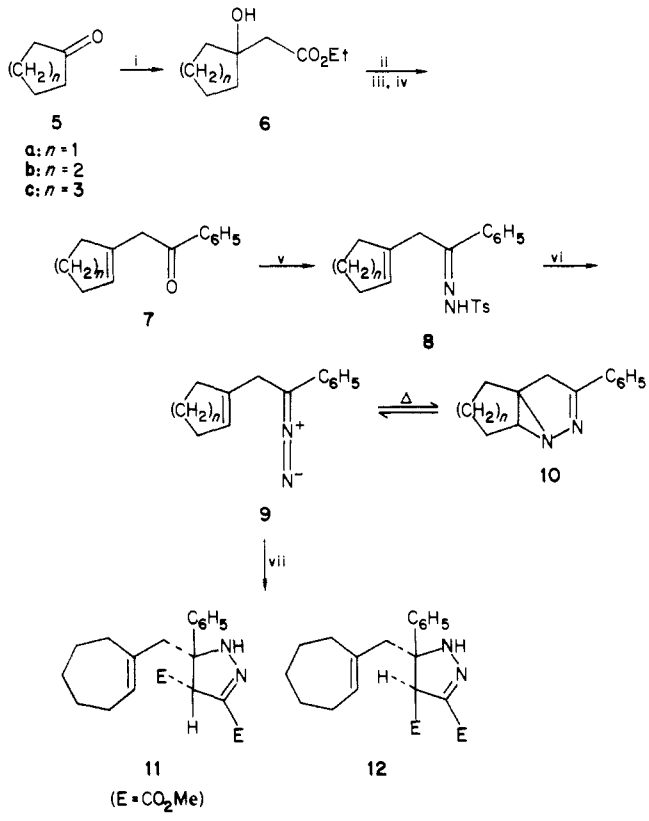
Scheme III[a]



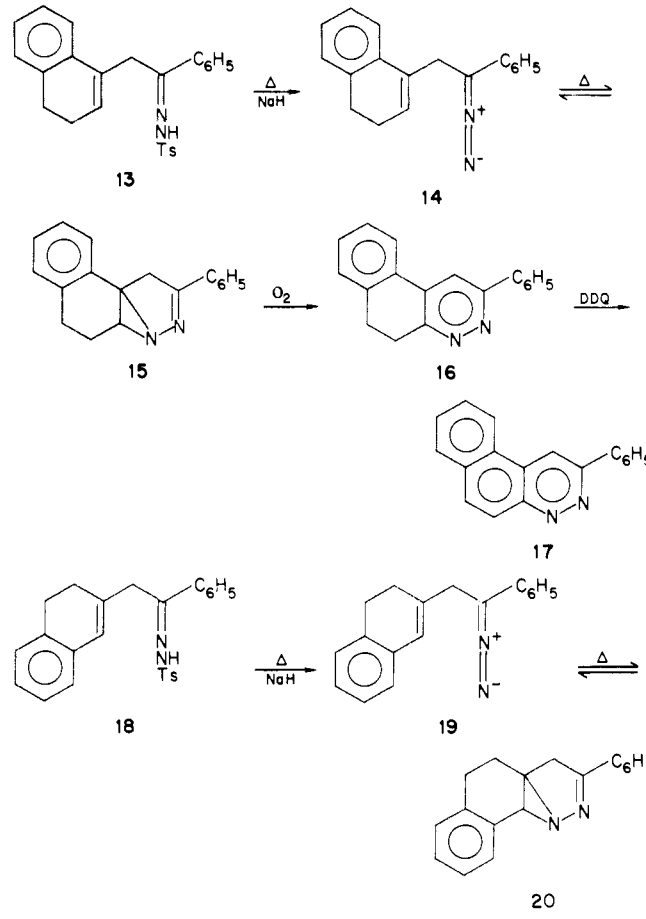
[a] (i) $BrCH_2CO_2Et$; (ii) $SOCl_2$ or P_2O_5; (iii) NaOH; (iv) C_6H_5Li; (v) H_2NHNTs; (vi) Δ/NaH; (vii) dimethyl fumarate.

allyl-substituted diazomethane which contains one methylene carbon between the double bond and the diazo group had been unknown. Secondly, if **2** is afforded by an initial hypothetical 1,1-cycloaddition[4] followed by the Cope rearrangement and the 1,3-hydrogen shift through intermediates **3**[28] and **4**, saturation of two double bonds at the C-1 and C-5 positions might uncover the hitherto unknown nitrene-like reactivity of the terminal nitrogen of diazomethane. This simple idea prompted us to synthesize various allyl-substituted diazomethanes to survey their reactivities. Herein we report the full details of our experimental results on the 1,1-cycloaddition reaction of allyl-substituted diazomethanes.

Results

As our first model compounds, we chose and synthesized α-(cyclopenten-1-yl)-, α-(cyclohexen-1-yl)-, and α-(cyclohepten-1-yl)acetophenone *N*-tosylhydrazones (**8a**, **8b**, and **8c**) whose structures are closely related to **1a** as described in Scheme III, expecting our first observation of the intramolecular 1,1-cycloaddition.[15] Heating the sodium salt of tosylhydrazone **8a** in refluxing carbon tetrachloride[29] immediately developed a red coloration due to **9a** which gradually faded during refluxing. Upon cooling to room temperature, the color faded completely, and **10a** was isolated in 73% yield after separation by silica gel thick-layer chromatography. The structure of **10a** was unequivocally determined by its spectral properties. Similarly, thermal decompositions of the sodium salts of **8b** and **8c** under the same conditions gave rise to the corresponding 1,2-diazabicyclo[3.1.0]-hex-2-enes, **10b** and **10c** in 72 and 86% yields, respectively. Dihydronaphthalene derivative **13** (Scheme IV) also afforded a quantitative yield of **15**. Compound **15** was found to be easily oxidized by air to 3-phenyl-9,10-dihydro-1,2-diazaphenanthrene (**16**), and the structure of **15** was confirmed by further oxidation of **16** to **17** by 2,3-dichloro-5,6-dicyano-1,4-benzoquinone. On the other hand, the isomer **18** afforded in quantitative yield diazomethane **19**, which in turn cyclized slowly to **20** when allowed to stand at −23 °C.

Scheme IV

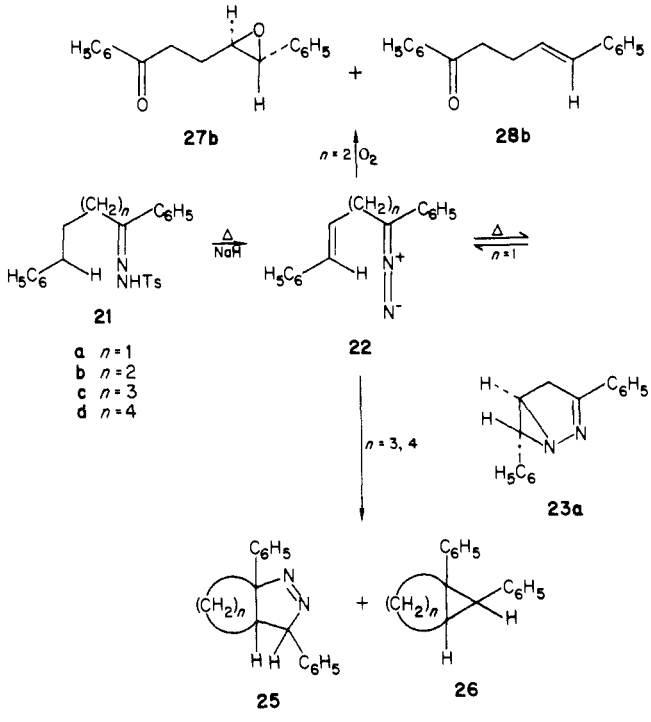


The generation of diazomethanes as intermediates in the formation of those 1,2-diazabicyclo[3.1.0]hex-2-enes was substantiated by the detections of a strong infrared absorption of the diazo group at around 2040 cm^{-1} in each crude reaction mixture and also by the formation of the usual 1,3-dipolar adducts **11** (18%) and **12** (58%) and suppression of the yield of **10c** (20%) when **9c** was decomposed in the presence of dimethyl fumarate.

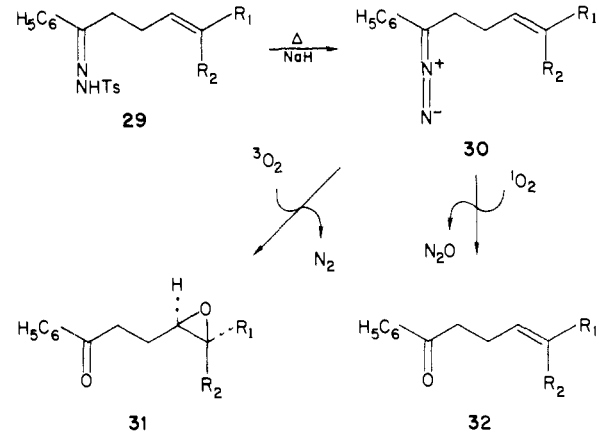
The reversibility of the 1,1-cycloaddition between diazomethanes and 1,2-diazabicyclo[3.1.0]hex-2-enes was directly observed by variable-temperature ^1H NMR analyses. Thus, upon heating a solution of **10a** in toluene-d_8 at 101 °C for 10 min or **10b** at 85 °C in the probe, solutions turned wine-red, and new absorptions appeared due to **9a** and **9b**. Analyses of diazomethane **9a** and **9b** were carried out by integrations of newly appeared signals assigned to side chain methylene hydrogens at δ 2.90 (s), an olefinic hydrogen at 5.65 ppm for **9a**, side chain methylene hydrogens at δ 2.78 (s), and an olefinic hydrogen at 5.47 ppm (m) for **9b**. Analyses indicated the formation of the following mixtures, respectively: **9a** (13%), **10a** (87%), **9b** (24%), and **10b** (76%). The absorptions due to **9a** and **9b** disappeared upon cooling to room temperature, cleanly reproducing the spectra of **10a** and **10b**. Similarly, separate heating of a mixture of **14** (9%) and **15** (91%) at 30 or 90 °C for 10 min in carbon tetrachloride gave mixtures composed respectively of 13% of **14** and 87% of **15** at 30 °C and 50% of **14** and 50% of **15** at 90 °C. The latter mixture, when cooled to 30 °C, gave nearly the same composition (10% of **14**

(25) See excellent reviews on the intramolecular 1,3-dipolar cycloaddition, ref 26 and 27 and references are cited therein.
(26) Padwa, A. *Angew. Chem., Int. Ed. Engl.* **1976**, *15*, 123.
(27) Padwa, A. "1,3-Dipolar Cycloaddition Chemistry"; Padwa, A., Ed.; John Wiley and Sons: New York, 1983, Vol. 2, pp 277-406.
(28) To the best of our knowledge the 1,2-diazabicyclo[3.1.0]hex-2-ene ring system had been known only in one derivative,[60] and the parent compound was recently prepared.[63]
(29) Carbon tetrachloride was a suitable solvent since that dissolved most of the sodium salts of tosylhydrazones and thermolyses could be carried out homogeneously.

Scheme V



Scheme VI[a]



[a] **a**, $R_1 = R_2 = C_6H_5$; **b**, $R_1 = R_2 = H$.

and 90% of **15**) as the starting one. Diazomethane **19**, on the other hand, cyclized rather slowly to **20**; a mixture composed of **19** (74%) and **20** (26%) obtained by heating **20** at 80 °C for 10 min slowly changed its composition to 45% of **19** and 55% of **20** after 30 days at room temperature. During the above ^1H NMR analyses neither a usual 1,3-dipolar cycloadduct nor a side reaction such as nitrogen extrusion was observed. The reversibility of the 1,1-cycloaddition will be discussed later in detail for the more simple models.

Our first observation of the reversible intramolecular 1,1-cycloaddition reaction of allyl-substituted diazomethane then developed into an investigation of the generality of this reaction. For this purpose, (*E*)-1,4-diphenyl-3-buten-1-one *N*-tosylhydrazone (**21a**) and its higher homologues, (*E*)-1,5-diphenyl-4-penten-1-one (**21b**), (*E*)-1,6-diphenyl-5-hexen-1-one (**21c**), and (*E*)-1,7-diphenyl-6-hepten-1-one *N*-tosylhydrazone (**21d**), were prepared. It is of interest to note that in diazomethane **22a** the terminal-nitrogen approach to the C=C double bond required for the 1,1-cycloaddition is readily accessible, while the two-plane approach required for the concerted 1,3-dipolar cycloaddition is strictly restricted by geometrical reasons. On the other hand, in the higher homologues **22b**, **22c**, and **22d**, both the terminal-nitrogen and two-plane approaches are geometrically possible. Thus, it was of interest to know whether the 1,1-cycloaddition can compete with the 1,3-dipolar cycloaddition in the higher systems. The results are shown in Scheme V. The 1,1-cycloaddition reaction was only observed for (*E*)-1,4-diphenyl-4-diazobut-1-ene (**22a**). Heating the sodium salt of **21a** in refluxing carbon tetrachloride immediately developed a red coloration due to the generation of diazomethane **22a**, which faded very slowly upon standing at room temperature under argon atmosphere. The crude reaction mixture obtained after 1 h of heating followed by immediate workup was found to include a 1.9:1 mixture of **22a** and *exo*-3,6-diphenyl-1,2-diazabicyclo[3.1.0]hex-2-ene (**23a**). After 10 days the ratio **22a**/**23a** changed to 0.4, and **23a** was isolated in 45% yield when **22a** almost completely disappeared. It was also found that upon thermolysis under air the initially formed **23a** was slowly oxidized to 3,6-diphenylpyridazine.[30] In the crude reaction mixture, neither the 1,3-dipolar cycloadduct 1,4-diphenyl-2,3-diazabicyclo[3.1.0]hex-2-ene nor the isomeric *endo*-3,6-diphenyl-1,2-diazabicyclo[3.1.0]hex-2-ene (**24a**) could be detected at all, indicating the exclusive occurrence of the highly stereoselective 1,1-cycloaddition reaction. Higher diazomethanes **22c** and **22d** expectedly afforded the 1,3-dipolar cycloadducts **25c** and **25d**, respectively. One surprise was the unexpected inertness of diazomethane **22b** toward cyclization. Padwa previously reported that **22b** underwent complex reactions upon refluxing in benzene, but we found that **22b** was stable even under refluxing in carbon tetrachloride and did not change for more than 2 months at ambient temperature when kept under an inert atmosphere. Instead, under aerated conditions, a clean reaction took place and **22b** unexpectedly gave epoxy ketone **27b** as a major product.[31] Upon thermolysis of the sodium salt of **21b** in refluxing carbon tetrachloride under nitrogen atmosphere, there developed a red coloration owing to the generation of **22b** (IR, 2025 cm^{-1} in CCl_4) while sodium toluene-*p*-sulfinate was liberated. When this solution was exposed to air, under stirring at room temperature,[32] the color of the solution rapidly faded owing to the disappearance of **22b**, and upon prolonged stirring the epoxy ketone **27b** and ketone **28b**[33] were isolated in 49% and 27% yields, respectively. Similar results were also obtained when thermolyses of **29a** and **29b** (Scheme VI) were carried out under aerated conditions. Compound **30a** (IR, 2040 cm^{-1} in CCl_4) afforded 71% of **31a**, and 14% of **32a**, **31b**, and **32b**[34] were isolated from **30b** (IR, 2035 cm^{-1} in CCl_4) in 25% and 28% yield, respectively. It is of interest to note that air oxidations under neutral conditions[35] and dye-sensitized photooxidations of **22b**, **30a**, and **30b** by using *meso*-tetraphenylporphine both under basic[32] and neutral conditions exclusively afforded ketones **28b**, **32a**, and **32b**, respectively. The fact that the air oxidation of **22b** in the presence of ketone **32a** under basic conditions did not afford epoxy ketone **31a** excludes a simple intermolecular air epoxidation path from **28b** to **27b** but suggests an internal oxygen atom transfer, possibly via carbonyl oxide as an intermediate. In fact, addition of dimethyl sulfide[36] changed the product ratio, **27b**/**28b** from 62:38 to 15:85. The same air oxidation to give epoxy ketone was also observed for **22c** and **22d** but in rather poor yields. It has been reported that the reaction of diazoalkanes with singlet oxygen generates carbonyl oxide,[37] which in turn intermolecularly transfers an oxygen atom to an olefin to give an epoxide.[38] The efficiencies of intermolecular oxygen-atom transfer in this general method to prepare carbonyl oxides are, however, reported to be low.[39] The results presented

(30) Paal, C.; Schulze, H. *Chem. Dtsch. Ber. Ges.* **1900**, *33*, 3784.

(31) Miyashi, T.; Kamata, M.; Nishizawa, Y.; Mukai, T. *J. Chem. Soc., Chem. Commun.* **1984**, 147.

(32) These reaction conditions are termed "under basic conditions".

(33) Cowan, D. O.; Baum, A. A. *J. Am. Chem. Soc.* **1971**, *93*, 1153.

(34) Conia, M. M.-J. *Bull. Soc. Chim. Fr.* **1950**, 537.

(35) After thermolysis the resulting red carbon tetrachloride solution was washed with water to remove sodium toluene-*p*-sulfinate as well as NaH and then dried over Na_2SO_4.

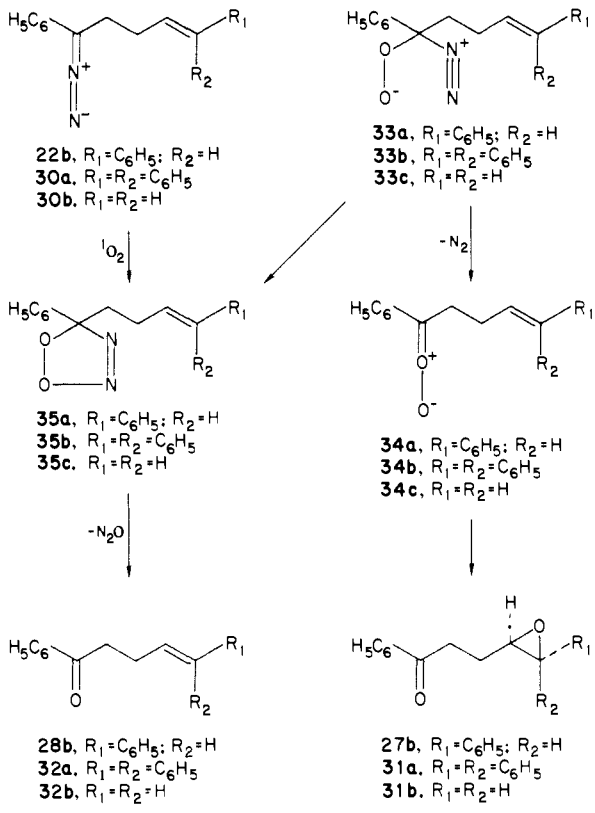
(36) Ando, W.; Miyazaki, H.; Kohmoto, S. *Tetrahedron Lett.* **1979**, 1317.

(37) Higley, D. P.; Murray, R. W. *J. Am. Chem. Soc.* **1974**, *96*, 3330.

(38) Hinricks, T. A.; Ramachadran, V.; Murray, R. W. *J. Am. Chem. Soc.* **1979**, *101*, 1282.

(39) Sawaki, Y.; Kato, H.; Ogata, Y. *J. Am. Chem. Soc.* **1981**, *103*, 3832 and references are cited therein.

Scheme VII



here are, thus, of interest in terms of the first example of oxygen atom transfer via carbonyl oxide observed in the air oxidation of diazoalkene.

Although there still remains some mechanistic ambiguity, a plausible mechanism is shown in Scheme VII. The reactions of **22b**, **30a**, and **30b** with oxygen initially form the zwitterionic species **33** much faster under basic conditions than under neutral conditions, whereas singlet oxygen exclusively forms the 1,3-dipolar cycloadduct **35** as suggested by Bethell and McKeivor[40] under both basic and neutral conditions. Under basic conditions the nitrogen extrusion reaction of **33** giving **34** occurs faster than the cyclization to **35**, while **33** might cyclize to **35** with ease under neutral conditions. Compound **34** then internally transfers an oxygen atom to the double bond to give **27b**, **31a**, and **31b**. In contrast, **35** collapses to ketones **28b**, **32a**, and **32b**, releasing N_2O as the exclusive pathway.

Regardless of the inertnesses of diazomethanes **22b**, **30a**, and **30b** toward cyclization, the above results suggest that the 1,1-cycloaddition reaction generally occurs in allyl-substituted diazomethane.

Next, after studying the generality of the 1,1-cycloaddition reaction, we investigated the stereochemical course of this reaction in order to gain further insights into the mechanism. Similar to the reaction mechanism of the 1,3-dipolar cycloaddition reaction of diazomethanes to olefins, one can envision two different mechanisms. One possible mechanism is a cheletropic concerted cycloaddition,[41] in which (*E*)-**36** and (*Z*)-**36** undergo the stereoselective 1,1-cycloaddition to give *exo*-**37** and *endo*-**37**, respectively. In an alternative stepwise pathway, the electrophilic terminal nitrogen[42] of diazomethanes **36** attack the double bond to form either a six-membered zwitterion **38** or, more preferably, a five-membered zwitterion **39** which, in turn, collapses, randomizing the stereochemistry at the C-6 position to afford a mixture of *exo*-**37** and *endo*-**37** (Scheme VIII). As mentioned previously, (*E*)-1,4-diphenyl-4-diazobut-1-ene (**22a**) stereoselectively gave *exo*-3,6-diphenyl-1,2-diazabicyclo[3.1.0]hex-2-ene (**23a**). This result, however, is not necessarily sufficient to conclude concertedness of this reaction because of the supposed stereochemical inconvenience of the bulky *endo*-phenyl group of the undetected endo-isomer **24a**.[20] Thus, the direct stereochemical courses were determined by the examinations of (*E*)- and (*Z*)-1-phenyl-3-penten-1-one *N*-tosylhydrazone (**44a** and **44b**) (Scheme IX), respectively, and (*Z*)-1-phenyl- and (*Z*)-1-(*p*-bromophenyl)-4-methyl-3-hexen-1-one *N*-tosylhydrazone (**44c** and **44d**), respectively. For the convenience of the stereochemical assignments, 1-phenyl-4-methyl-3-penten-1-one *N*-tosylhydrazone (**44e**) was also examined. Ketones **43a**, **43c**, **43d**, and **43e** were synthesized according to the elegant procedure reported by Steglich.[43] The (*Z*)-isomer **43b** was synthesized by the catalytic reduction of ketone **48** over $Pd/BaSO_4$ in the presence of quinoline. The stereochemical assignment of each ketone was made unequivocally by the ^1H NMR spectrum.

Diazomethane **45a** generated from the sodium salt of **44a** upon heating in refluxing carbon tetrachloride under argon was found to cyclize rather rapidly as compared with the isomer **45b**, and upon standing for 1 day at room temperature **45a** disappeared almost completely. *exo*-3-Phenyl-6-methyl-1,2-diazabicyclo-[3.1.0]hex-2-ene (**46a**) was isolated in 46% yield from a crude pyrolysate, in which neither the ^1H NMR nor liquid chromatographic analysis could detect the endo-isomer **46b**. The structural and stereochemical determinations were made by the comparisons of the ^1H and ^{13}C NMR[44] spectra with those of **46e**.

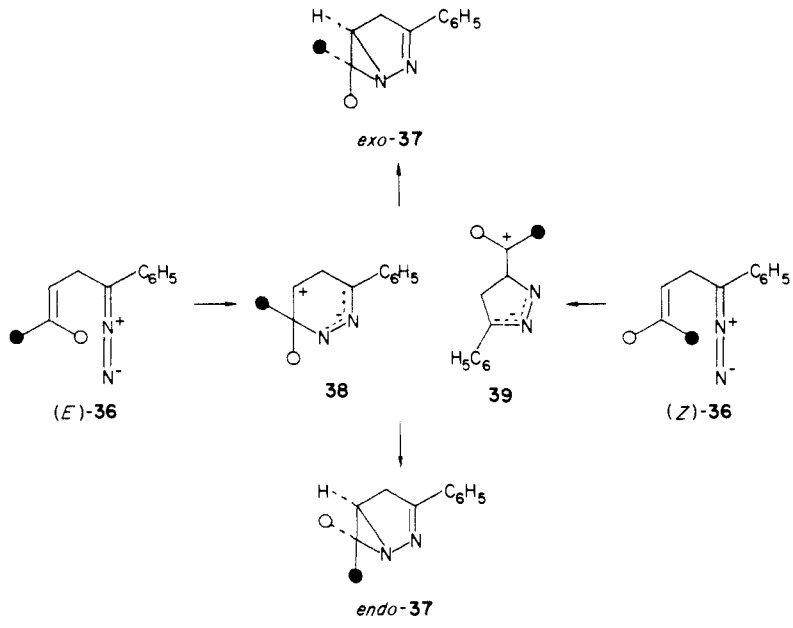
On the other hand, the disappearance of diazomethane **45b** generated from the sodium salt of **44b** under the same conditions was found to be very slow. Thus, the progress of the cyclization of **45b** to **46b** was monitored by the ^1H NMR. Heating the sodium salt of **44b** in carbon tetrachloride for 1 h followed by immediate workup under argon afforded a wine-red colored pyrolysate which was exclusively composed of a mixture of diazomethane **45b** and *endo*-3-phenyl-6-methyl-1,2-diazabicyclo[3.1.0]hex-2-ene (**46b**) in the ratio of 1.5:1. Upon standing at room temperature for 4 days, **45b** slowly converted to **46b**, and the yield of **46b** was found to be 51%. Although ^1H NMR analysis could not detect the exo-isomer **46a**, a small peak of a compound with the same retention time as that of **46a** was detected by liquid chromatographic analysis. Even though this compound is **46a**, the ratio **46a**/**46b** was 1/85, indicating the occurrence of 99% stereoselective 1,1-cycloaddition. Compound **46b** was relatively stable in solution, but evaporation of solvent caused rapid polymerization to ether-insoluble, unidentified compounds. Separation by liquid chromatography followed by careful workup, however, gave rise to a pure compound which was assigned as the endo-isomer **46b** by the NMR spectrum. Similarly, decompositions of the sodium salts of **44c**, **44d**, and **44e** gave **46c**, **46d**, and **46e** in 65%, 70%, and 59% yields, respectively. Since this reaction is essentially reversible as mentioned previously and discussed later, the results shown here indicate that both the 1,1- and retro-1,1-cycloadditions are completely stereoselective. In fact, separate heating of carbon tetrachloride solutions of **46c** and **46d** at 60 °C for 30 min in the NMR probe gave equilibrium mixtures composed respectively of 20% **45c** and 80% **46c** for **46c** and of 23% **45d** and 77% **46d** for **46d**. During heating, their stereoisomers could not be detected at all, and the reformation of **46c** and **46d** was only observed upon cooling those equilibrium mixtures.

The above observations now clearly indicate that the 1,1-cycloaddition of the terminal nitrogen of diazomethane cannot compete energetically with the 1,3-dipolar cycloaddition but occurs reversibly with complete retention of configuration as a general reaction of allyl-substituted diazomethanes.

The systematic experiments[9,10] as well as theoretical considerations[11,12] have already concluded that the HOMO energy of diazomethane controls the 1,3-dipolar cycloaddition of simple

(40) Bethell, D.; McKeivor, R. *J. Chem. Soc., Perkin Trans. 2* **1977**, 327.
(41) Woodward, R. B.; Hoffmann, R. "The Conservation of Orbital Symmetry"; Verlag Chemie: Weinheim/Bergstr., 1970; p 159.
(42) Muller, E.; Rundel, W. *Chem. Ber.* **1956**, *89*, 1065; **1957**, *90*, 1299.
(43) Engel, N.; Kubel, B.; Steglich, W. *Angew. Chem., Int. Ed. Engl.* **1977**, *16*, 394.
(44) For ^{13}C chemical shift, see, for instance: Mison, P.; Chaabouni, R.; Diad, Y.; Martino, R.; Lopez, A.; Lattes, A.; Wehrli, F. M.; Wirthlin, T. *Org. Magn. Reson.* **1976**, *8*, 79.

Scheme VIII



diazomethanes to olefins. In order to compare the reactivity of the terminal nitrogen of diazomethane with that of diazomethane as a 1,3-dipole, we then investigated the substituent effects on the rates of the reversible 1,1-cycloaddition. During the course of this study Padwa and Fukunaga reported that allyl-substituted diazomethane substituted with electron-withdrawing groups cannot be expected to undergo the 1,1-cycloaddition.[20] Thus, it was also of interest to compare the substituent effect with their experimental conclusions which were reported to be supported by the theoretical prognosis.

For this purpose, the additional seven tosylhydrazones **44f–44l** were prepared from the corresponding ketones which were again synthesized according to the procedure reported by Steglich (Scheme X).[43]

Diazomethanes **45f–45l** were generated by heating the corresponding sodium salts of tosylhydrazones **44f–44l** in refluxing carbon tetrachloride for 2 h under a nitrogen or argon atmosphere. It is of interest to note that diazomethanes **45k** and **45l** substituted with strong electron-donating groups, the parent **45e**, and **45i** and **45j** substituted with weak electron-withdrawing groups converted with ease to the corresponding 3-aryl-6,6-dimethyl-1,2-diazabicyclo[3.1.0]hex-2-enes upon standing at room temperature, and the corresponding 1,1-cycloadducts were isolated all as colorless crystals by usual workup in good yields. In contrast, the colors owing to diazomethanes **45f**, **45g**, and **45h** substituted with strong electron-withdrawing groups did not fade at room temperatures, and usual workup at room temperature failed in the isolations of **46f**, **46g**, and **46h** in good yields. However, successful isolations of **46f**, **46g**, and **46h** were performed by cooling the carbon tetrachloride solutions of **45f**, **45g**, and **45h** to −20 °C in order to shift the equilibrium to **46**, followed by freeze–dry evaporations of solvent. It was found that **46f**, **46g**, and **46h** were entirely stable in the crystalline state, but in solution they are in equilibrium with diazomethanes even at room temperature as shown by the NMR spectrum in Figure 1.[45] Our isolation of **46f–46h** with strong electron-withdrawing substituents simply excluded the earlier conclusion[20] reported by Padwa and Fukunaga about the substituent effect on the 1,1-cycloaddition reaction.

The rate analyses were performed according to the equation $-(k_1 + k_2)t = \ln[(KA - B)/(KA_0 - B_0)]$, where A_0 and B_0 are the initial concentrations of 1,2-diazabicyclo[3.1.0]hex-2-enes **45** and diazomethanes **46**, respectively, and $K = k_1/k_2$, by monitoring

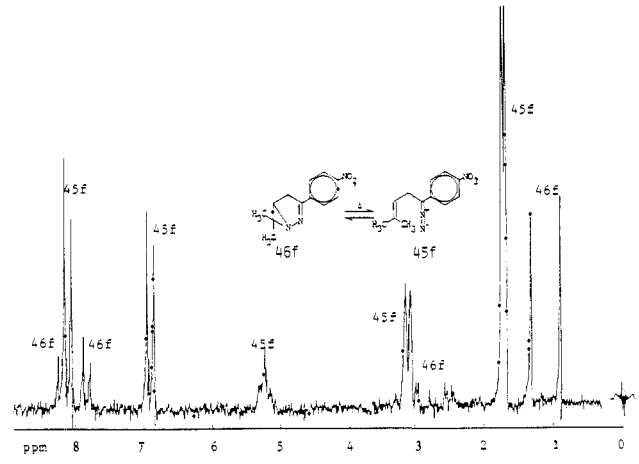


Figure 1. ^{1}H NMR spectrum of **46f** in equilibrium with **45f** (in CCl_4, 30 °C).

Table I. The First-Order Rate Constants, Equilibrium Constants, and Free Energy Change at 50 °C in Carbon Tetrachloride

substitnt (X)	10^3k_1, s^{-1}	10^3k_2, s^{-1}	K^b	ΔG,^{c} kcal/mol
p-NO_2	10.71	2.88	3.71	−0.84
p-CN	4.72	2.16	2.15	−0.49
m-NO_2	2.42	2.88	0.80	0.14
p-Br	0.59	1.89	0.32	0.75
p-Cl	0.49	1.80	0.28	0.84
H	0.40	1.49	0.26	0.86
p-CH_3	0.18	1.23	0.16	1.22
p-OCH_3	0.06[a]	1.16[a]	0.05	1.92

[a] Estimated from $\log k_2^X/k_2^H = 0.36\sigma$ ($r = 0.976$) and $K^{OCH_3} = 0.05$. [b] Obtained by $\log K$ vs. $1/T$ plots. [c] Calculated from equilibrium constants at 50 °C.

the disappearance of **46** and the appearance of **45** while heating a degassed sealed tube containing a carbon tetrachloride solution of 1,2-diazabicyclo[3.1.0]hex-2-enes **46** in the preheated 90-MHz NMR probe. The first-order rate (k_1 and k_2) and equilibrium constants (K) were measured in carbon tetrachloride at various temperatures. In all cases, satisfactory linear $\log K$ vs. $1/T$ plots were obtained. The extrapolated equilibrium constants at 50 °C are listed in Table I. The magnitude of the equilibrium constant increases as the electron-withdrawing nature of the substituent group increases. The difference in the calculated free energy change (ΔG) for the eight derivatives is also listed in Table I. The large dependency of the equilibrium constant on the substituent

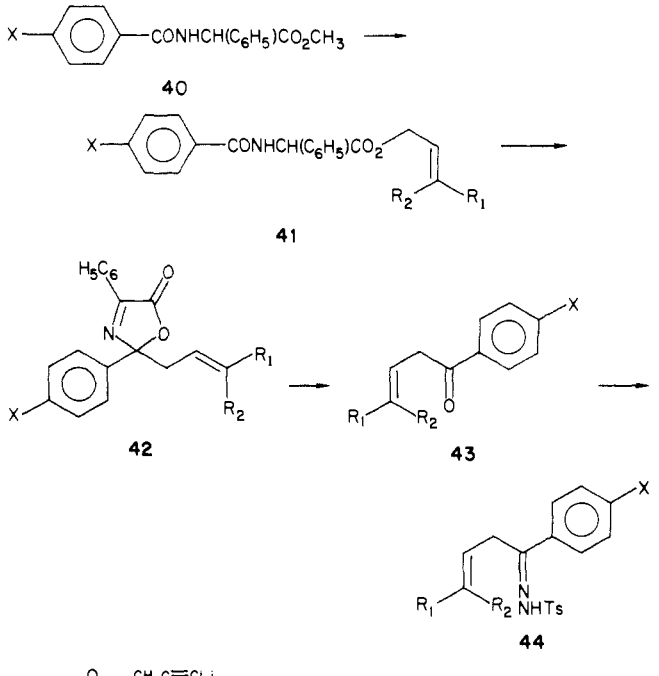
(45) The same results were also observed in the infrared spectra. The infrared spectrum of **46f** in KBr exhibited an absorption at 2030 cm^{-1} due to **45f** as a very weak peak, whereas that appeared as a very strong peak in carbon tetrachloride.

Table II. The Relative Rates of the 1,1-Cycloaddition, and 1,3-Dipolar Cycloaddition[a]

substituent (X)	*p*-NO_2	*m*-NO_2	*p*-CN	*p*-Br	*p*-Cl	H	*p*-CH_3	*p*-OCH_3
diazoalkene 1,1-cycloadd[b]	1.93	1.93	1.45	1.27	1.21	1	0.83	0.78
aminonitrene 1,1-cycloadd[c]					0.70	1	2.02	3.60
1,3-dipolar cycloadd[d]			0.38		0.96	1	1.41	2.16

[a] The relative rate is based on the rate constant of each reaction for X = H. [b] The reaction of **45** to **46** at 50 °C in CCl_4. [c] The addition of (3,5-diphenyl-1,2,4-triazol-4-yl)nitrene to $XC_6H_4CH{=}CH_2$ at 20 °C in methanol.[49] [d] The addition of $XC_6H_4CHN_2$ to norbornene at 25 °C in dimethylformamide.[48]

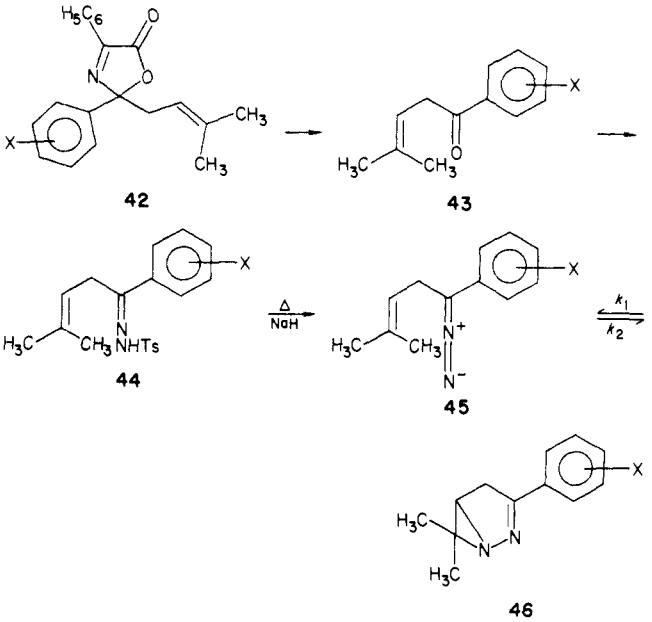
Scheme IX[a]



[a] **a**, $R_1 = CH_3$, $R_2 = H$, X = H; **b**, $R_1 = H$, $R_2 = CH_3$, X = H; **c**, $R_1 = CH_3$, $R_2 = C_2H_5$, X = H; **d**, $R_1 = CH_3$, $R_2 = C_2H_5$, X = Br; **e**, $R_1 = R_2 = CH_3$, X = H.

group directly reflects on the first-order rate constants for both the retro-1,1- (k_1) and 1,1-cycloaddition (k_2) reactions. As shown in Table I,[46] the 1,1-cycloaddition is slightly accelerated by an electron-withdrawing group, obeying the Hammett relation, log $k_2^X/k_2^H = 0.36\sigma$ ($r = 0.976$), whereas the rate acceleration for the retro-1,1-cycloaddition by an electron-withdrawing group was found to be more significant as indicated by the Hammett relation, log $k_1^X/k_1^H = 1.34\sigma^+$ ($r = 0.971$)[47] (Figure 2). It should be noted

Scheme X[a]



[a] **e**, X = H; **f**, X = *p*-NO_2; **g**, X = *m*-NO_2; **h**, X = *p*-CN; **i**, X = *p*-Br; **j**, X = *p*-Cl; **k**, X = *p*-CH_3; **l**, X = *p*-OCH_3.

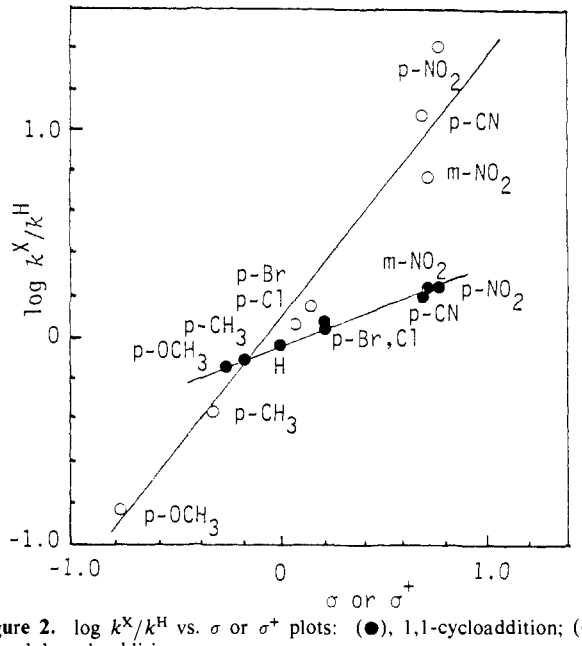


Figure 2. log k^X/k^H vs. σ or σ^+ plots: (●), 1,1-cycloaddition; (○), retro-1,1-cycloaddition.

(46) The activation energies for the 1,1-cycloaddition of **45e** and **45f** were 14.7 (log A = 7.14) and 11.4 (log A = 5.16) kcal/mol, respectively. Those for the retro-1,1-cycloaddition of **46e** and **46f** were 21.2 (log A = 11.0) and 15.5 (log A = 8.51) kcal/mol, respectively.

(47) The correlation of log k_1^X/k_1^H to the Yukawa–Tsuno equation was $1.56[\sigma + 0.48(\sigma^+ - \sigma)]$ ($r = 0.976$) and to the Taft DSP equation was $1.37\sigma_I + 2.88\sigma_R^0$ ($r = 0.989$).

Table III. The Solvent Effects on the First-Order Rate and Equilibrium Constants (at 50 °C)

	solvent			
	CCl_4	C_6D_6	CD_2Cl_2	CD_3CN
E_T, kcal/mol	32.5	34.5	41.1	46.0
		p-NO_2		
K	3.71	2.61	0.96	0.56
10^3k_1, s^{-1}	10.71	7.57	4.59	3.62
10^3k_2, s^{-1}	2.88	2.91	4.77	6.42
		p-CN		
K	2.15	1.34	0.48	0.31
10^3k_1, s^{-1}	4.72	3.86	2.31	2.19
10^3k_2, s^{-1}	2.16	2.88	4.79	7.15
		m-NO_2		
K	0.80	0.47	0.13	0.09
10^3k_1, s^{-1}	2.42	1.87	0.64	0.43
10^3k_2, s^{-1}	2.88	4.01	4.66	4.86
		H		
K	0.26	0.16	0.05	0.04
10^3k_1, s^{-1}	0.40	0.34	0.22	0.15
10^3k_2, s^{-1}	1.49	2.15	3.50	3.72

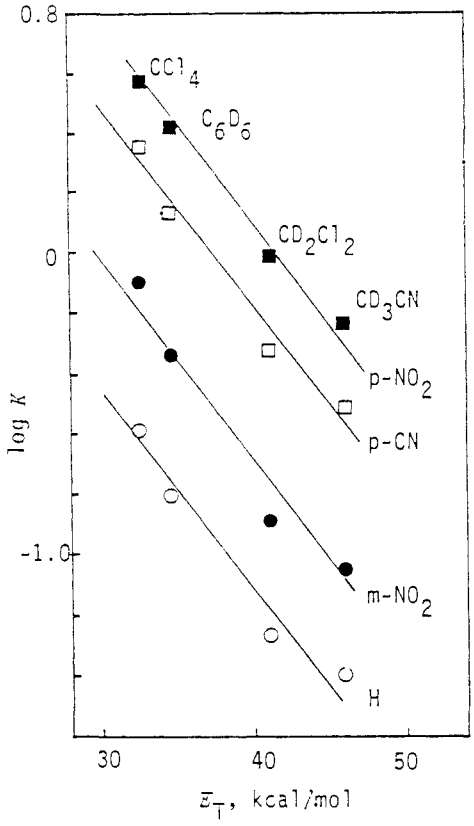


Figure 3. log K vs. E_T plots (50 °C).

that the substituent effect on the rate constant of the 1,1-cycloaddition is opposite to that of intermolecular 1,3-dipolar cycloaddition of the substituted phenyldiazomethanes with norbornene[48] but rather resembles that of the 1,1-cycloaddition[49] of aminonitrene generated from 4-amino-3,5-diphenyl-1,2,4-triazole to para-substituted styrenes as shown in Table II.

In order to gain further insights into the effects on the rates, we investigated the effects of solvent on the first-order rates and equilibrium constants of the reversible 1,1-cycloaddition between **45e–45h** and **46e–46h** in four different solvents. The extrapolated rate and equilibrium constants are listed in Table III. Regardless of the nature of the substituent, the equilibrium constant decreased as the solvent polarity increased, and the linear log K vs. E_T[50] plots were obtained for all derivatives as shown in Figure 3. These

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(49) Schroppel, F.; Sauer, J. *Tetrahedron Lett.* **1974**, 2945.
(50) Reichardt, C. *Angew. Chem., Int. Ed. Engl.* **1965**, *4*, 29.

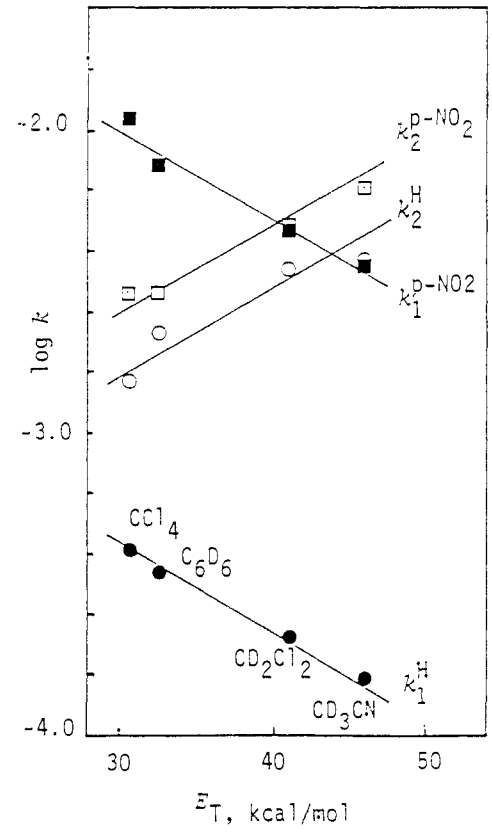


Figure 4. log k vs. E_T plots (50 °C).

results obviously arose from the fact that the 1,1-cycloaddition was accelerated, while the retro-1,1-cycloaddition was decelerated as the solvent polarity increased. The linear correlations between log k and the E_T values are shown in Figure 4 for **46e** and **46f**. The solvent effects on the equilibrium and first-order rate constants, however, are not so large as is expected for the intervention of a zwitterionic intermediate such as **38** or **39**.

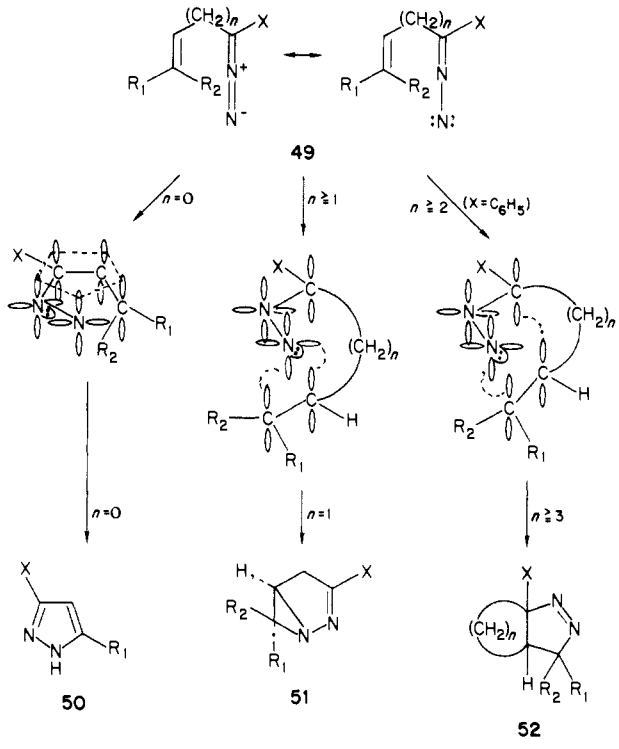
Discussion

Since Huisgen introduced the general principle of the 1,3-dipolar cycloaddition in the early 1960's, a large number of studies dealing with the 1,3-dipolar cycloaddition reaction of diazomethanes to olefins have appeared in literature. In spite of that and Huisgen's pioneering proposal of a hypothetical 1,1-cycloaddition mechanism,[4,14] the nitrene-like nature of the terminal nitrogen of diazomethane had not been uncovered until the late 1970's. This is, however, not a surprise because intramolecular cycloaddition[26,27] reactions of diazoalkenes had not been systematically investigated, in contrast to intermolecular reactions.[9,10] In fact, among many intramolecular cyclizations of diazoalkenes **49** (Scheme XI), that of allyl-substituted diazomethane **49b** (n = 1) had been unknown, and moreover the 1,3-dipolar cycloaddition reaction of **49c** (n = 2) had been reported only in one case from our laboratory.[21,22] All other reactions reported so far were the usual 1,3-dipolar cycloadditions of diazoalkenes containing more than three carbons between the double bond and the diazo group. Our novel observations reported here, thus, elucidate the more general intramolecular cyclization pattern of diazoalkenes.

In general, diazomethane can intermolecularly approach the C=C double bond in three different ways to undergo a cyclization. The first one is an in-plane approach, which is generally available for vinyldiazomethane **49a** (n = 0),[51-54] which is reported to undergo a concerted electrocyclization[55] to form the 1,3-dipolar cycloadduct **50**. In fact, **49a** (n = 0, X = R_1 = C_6H_5; R_2 = H) afforded a quantitative yield of **50** (X = R_1 = C_6H_5). The second

(51) Adamson, D. W.; Kenner, J. *J. Chem. Soc.* **1935**, 286.
(52) Hurd, C. D.; Lui, S. C. *J. Am. Chem. Soc.* **1935**, *57*, 2656.
(53) Ledwith, A.; Parry, D. *J. Chem. Soc. B* **1967**, 41.
(54) Curtin, D. Y.; Gerber, S. M. *J. Am. Chem. Soc.* **1969**, *91*, 711.
(55) Brewbaker, J. L.; Hart, H. *J. Am. Chem. Soc.* **1969**, *91*, 711.

Scheme XI[a]



[a] **a**, $n = 0$; **b**, $n = 1$; **c**, $n = 2$; **d**, $n = 3$; **e**, $n = 4$.

one is a well-known two-plane approach, which is generally accessible in an intermolecular case, but is also possible in diazoalkenes **49** when n is more than 2. The third, terminal-nitrogen approach, in terms of geometry, should be more general because the electrophilic terminal nitrogen can easily approach the C=C double bond in higher homologues than allyl-substituted diazomethane. Nevertheless, the 1,1-cycloaddition occurred only in allyl-substituted diazomethane **49b** in which the usual two-plane approach for the 1,3-dipolar cycloaddition is impossible by geometrical reasons. This indicates, at least, that the 1,1-cycloaddition could not compete energetically with the 1,3-dipolar cycloaddition but was allowed to occur as a "second-best reaction"[10] in consequence of geometrical advantages in **49b**, in preference to 1,3-dipolar cycloaddition as the "best-reaction".[10] When the terminal nitrogen of diazomethane intramolecularly approaches the neighboring double bond, one can envision two mechanistic alternatives, a one-step and a two-step process, to account for the 1,1-cycloaddition. In the latter mechanism, the electrophilic terminal nitrogen attack would involve 1,6- and/or 1,5-ring closure to form **38** and/or **39** (Scheme VIII), respectively. Regardless of an initial ring closure mode,[56] one may think that the product analysis can simply exclude the possibility of a two-step mechanism because both **38** and **39** are capable of giving formal 1,3-dipolar cycloadducts, 2,3-diazabicyclo[3.1.0]hex-2-enes, together with the 1,1-cycloadducts, 1,2-diazabicyclo[3.1.0]hex-2-enes, in contrast to the observed experimental results. This, however, is not correct since the formation of 1,2-diazabicyclo[3.1.0]hex-2-enes would be more favored than that of 2,3-diazabicyclo[3.1.0]hex-2-enes, as seen by comparison of the difference in the energy gained from forming the new bonds: 122 (N=C) +73 (C-N) kcal/mol for 1,2-diazabicyclo[3.1.0]hex-2-enes and 93 (N=N) +83 (C—C) kcal/mol for 2,3-diazabicyclo[3.1.0]hex-2-enes. In addition, the ring-strain of the aziridine ring (27.7 kcal/mol) is almost the same as that of the cyclopropane ring (27.6 kcal/mol).[59] In fact, the

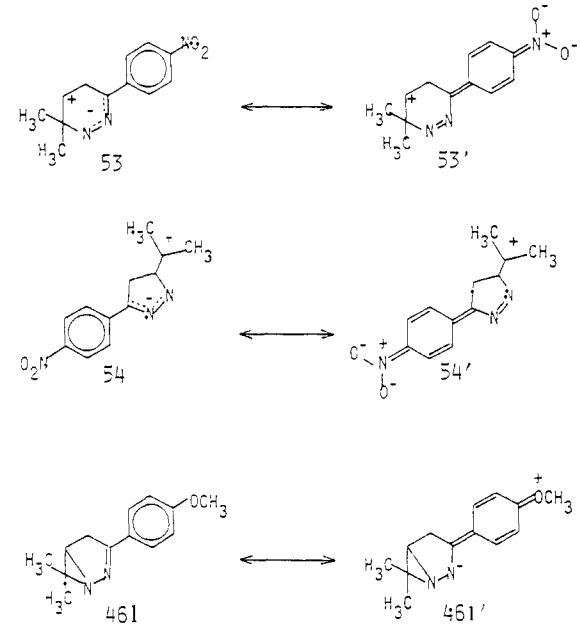


Figure 5.

recent studies on photosensitized rearrangements of cyclic 1,2-diazenes to 1,2-diazabicyclo[3.1.0]hex-2-enes[60-63] likely support this assertion. Thus, the product analyses support neither a one-step nor a two-step mechanism, and then we investigated stereochemistry and substituent and solvent effects on the reversible 1,1-cycloaddition.

First of all the observed complete stereoselectivity for both the 1,1- and retro-1,1-cycloadditions can exclude the intermediacy of **39**,[63] but **38** might still be viable if the ring closure in **38** is much faster than ring-flipping.[20] In this context, substituent and solvent effects on the rates are more informative. If such intermediates intervened, it is obvious that the direct resonance interactions with *p*-NO_2 and *p*-CN would induce strong stabilization of zwitterionic intermediates **53** and **54**, which then would result in significant rate accelerations of the 1,1-cycloaddition; log k_2 should correlate with σ^- substituent constants. The observed small rate acceleration for the 1,1-cycloaddition shown in Table I, thus, likely excludes the possibility of a two-step mechanism involving a zwitterionic intermediate. The small change in the rate induced by changing the solvent polarity similarly contradicts a two-step mechanism. For the retro-1,1-cycloaddition, the same argument is also available. In a two-step mechanism through either **38** or **39**, the retro-1,1-cycloaddition should be accelerated by electron-withdrawing groups since zwitterion **38** or **39** can be stabilized by the resonance stabilization such as **53**–**53′** or **54**–**54′**. This, however, contradicts the fact that the retro-1,1-cycloaddition was decelerated in the more polar solvents. On the contrary, a one-step mechanism is consistent with the observed results. Compound **46** substituted with electron-donating groups should be stabilized by the direct resonance such as **46l**–**46l′** shown in Figure 5, but such stabilization cannot be expected for **46** substituted with electron-withdrawing groups. Destabilization of **46** thus resulted in the acceleration of the retro-1,1-cycloaddition with an increase in the electron-withdrawing nature of the substituent. On the other hand, regardless of the substituent, the more polar solvents would stabilize **46** relative to the transition state and diazomethanes **45** if **46** is more polar than the transition state and **45**. The deceleration of the retro-1,1-cycloaddition with an increase in the solvent polarity, thus, can be ascribed to the stabilization of **46** in the more polar

(56) An experiental "rules for ring closure"[57] favors both **38** and **39** in ionic processes, but a radical intermediate type **39** is favored in a radical process.[58]

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(62) Adam, W.; DeLucchi, O. *Angew. Chem., Int. Ed. Engl.* **1980**, *20*, 400.

(63) Chang, M. H.; Dougherty, D. A. *J. Am. Chem. Soc.* **1982**, *104*, 2333.

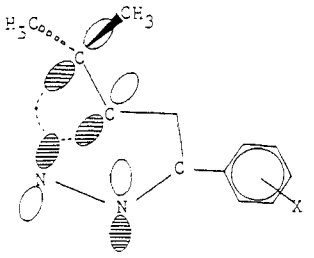

Figure 6.

solvents. Judging from the substituent and solvent effects on the rates, the stereochemical integrity can be concluded to arise from the concertedness of the reversible 1,1-cycloaddition.

The observation that the substituent effect on the rate constant of the 1,1-cycloaddition is similar to that on the aminonitrene 1,1-cycloaddition[49] but opposite to that on the 1,3-dipolar cycloaddition of diazomethane[48] indicates the electrophilic nitrene character of the terminal nitrogen of diazomethane in contrast with the nucleophilic nature of diazomethane as a 1,3-dipole and then provides an intriguing mechanistic rationale.

When the terminal nitrogen approaches the C=C double bond in a manner that resembles the nonlinear nitrene 1,1-cycloaddition as shown in Figure 6, the highest stabilization should be gained by interaction between the LUMO (diazomethane) and the HOMO (olefin). This interaction is strongly reinforced by the cyclic geometry which prevents the HOMO (diazomethane)–LUMO (olefin) controlled two-plane approach. Thus, the substituent effect on the rate of the 1,1-cycloaddition reaction of allyl-substituted diazomethane is a result of the change of the electrophilic LUMO energy level of diazomethane.

In conclusion, our experimental observations indicate that the nitrene-type 1,1-cycloaddition controlled by the LUMO energy of diazomethane occurs reversibly with complete retention of configuration in allyl-substituted diazomethane and demonstrates the novel as well as the divergent reactivity of diazomethane. Another intriguing aspect is a mechanistic application of this reaction to elucidate complex reaction pathways of diazoalkenes, which cannot be simply accounted for by the 1,3-dipolar reactivity. The recently reported rearrangement of diazoallene to 1,4-dihydropyridazine may be one example.[64] The (diazomethyl)-cyclopropene–pyridazine rearrangement[65,66] may also be a typical example for which the concerted 1,1-cycloaddition mechanism can be applicable.

Experimental Section

General Methods. All melting points and boiling points are uncorrected. Elemental analyses were performed by the Instrumental Analyses Center for Chemistry, Faculty of Science, Tohoku University. IR spectra were recorded on a Shimadzu IR-27G or a Shimadzu IR-435 spectrophotometer. UV spectra were recorded on a Hitachi 340 or Cary 219 spectrophotometer. MS data were collected on a Hitachi M-52 mass spectrometer. ^{1}H NMR spectra were obtained at 60 MHz on a Varian EM-360, at 90 MHz on a Varian EM-390, at 100 MHz on a JEOL PS100, or at 200 MHz on a Varian XL-200 spectrometer. ^{13}C NMR spectra were obtained at 50 MHz on a Varian XL-200 spectrometer. Gas chromatographic and liquid chromatographic analyses were performed on a Hitachi 633 and a Waters liquid chromatographic system equipped with Waters 730 data module, respectively. Preparative thick-layer chromatography was performed on 0.5 mm × 20 cm × 20 cm silica gel (E. Merck 60PF$_{254}$) plates. Wako Q-22 silica gel was used for column chromatography. Ethereal solvents were dried and distilled from lithium aluminum hydride. Methylene chloride, carbon tetrachloride, and amines were dried and distilled from calcium hydride. NMR multiplicities were reported by using the following abbreviations: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad; J = coupling constant (hertz).

Preparation of α-(Cyclopenten-1-yl)acetophenone *N*-Tosylhydrazone (8a). Zinc (25.8 g, 394 mmol) and trace amounts of iodine under nitrogen at 70 °C were treated with a solution of cyclopentanone (26.4 g, 314 mmol) and ethyl bromoacetate (65.5 g, 392 mmol) in 300 mL of dry tetrahydrofuran (THF) over 2 h. After an additional 2 h of refluxing, the solution was cooled with ice–water and treated with dilute hydrochloric acid. After the separation of the organic layer, the aqueous layer was extracted with ether. The combined organic layer was washed with water and dried over Na_2SO_4. Removal of solvents followed by distillation in vacuo gave 28.0 g (53% yield) of **6a** as a colorless oil: bp 85–87 °C (3 mmHg); ^{1}H NMR (60 MHz, CCl_4), δ 1.3 (t, 3 H, J = 7.2 Hz), 1.2–2.0 (m, 8 H), 2.5 (s, 2 H), 3.4 (br s, 1 H), 4.1 (q, 2 H, J = 7.2 Hz). To an ice–water-cooled solution of **6a** (28 g, 163 mmol) in dry pyridine (300 mL) was added thionyl chloride (35.1 g, 295 mmol) dropwise under stirring over a 10-min period. After 46 h of stirring, the reaction mixture was poured into ice–water and extracted with ether. The ether layer was washed with water and dried over Na_2SO_4. Removal of solvent followed by distillation gave 15.9 g (63% yield) of a colorless oil (bp 72–74 °C, 3 mmHg) which was found to be composed of 20% 1-(carbethoxymethyl)cyclopentene and the α,β-unsaturated isomer (80%) by gas chromatographic analysis. Distillation using a spinning band column (a Nester/Faust 10 mm × 650 mm column) concentrated 1-(carbethoxy)-cyclopentene in a lower boiling distillate. The residue composed of two isomers was treated with sodium ethoxide in dry ethanol to isomerize the α,β-isomer to 1-(carbethoxymethyl)cyclopentene. The resulting mixture was then subjected to spinning band column distillation to concentrate 1-(carbethoxymethyl)cyclopentene in a lower boiling distillate. Repeating these procedures finally afforded 8.80 g of 1-(carbethoxymethyl)cyclopentene (purity 97%): IR (neat) 2950, 2850, 1738, 1650, 1288, 1148, 1117, 1035 cm^{-1}; ^{1}H NMR (CCl_4, 60 MHz) δ 1.22 (t, 3 H, J = 7.2 Hz), 1.7–2.5 (m, 6 H), 3.00 (m, 2 H), 4.05 (q, 2 H, J = 7.2 Hz), 5.45 (m, 1 H). A solution of 1-(carbethoxymethyl)cyclopentene (8.80 g, 57 mmol) in ethanol (30 mL) was treated with aqueous NaOH (1 N, 80 mL) under stirring for 20 h at room temperature to give 6.42 g (89% yield) of (cyclopenten-1-yl)acetic acid: mp 48–51 °C; IR (KBr), 3000, 2950, 1690 cm^{-1}; ^{1}H NMR ($CDCl_3$, 60 MHz) δ 1.6–2.6 (m, 6 H), 3.13 (br s, 2 H), 5.55 (m, 1 H), 11.52 (br s, 1 H). To a solution of PhLi prepared from Li (3.74 g, 539 mmol) and bromobenzene (32.7 g, 215 mmol) in dry ether (200 mL) was added a solution of (cyclopenten-1-yl)acetic acid (6.31 g, 50.1 mmol) in ether (50 mL) dropwise at room temperature. After 1 h of stirring, the reaction mixture was decomposed with aqueous NH_4Cl and extracted with ether. The ether layer was washed with water and dried over Na_2SO_4. The residue (6.5 g) obtained after removal of solvent was chromatographed on a silica gel column. Elutions with n-hexane–ether (10:1) gave **7a** (3.74 g) which, without further purification, was treated with p-toluenesulfonyl hydrazide (3.40 g, 18.3 mmol) in ethanol (50 mL). The resulting white precipitates were filtered and recrystallized from ethanol to afford **8a** as colorless prisms (1.90 g): mp 123–124 °C; mass spectrum, 25 eV, m/e (relative intensity) 354 (M^+, 14), 355 (7), 200 (15), 199 (100), 171 (29), 141 (7), 91 (7); ^{1}H NMR ($CDCl_3$, 60 MHz) δ 1.4–2.7 (m, 6 H), 2.39 (s, 3 H), 3.33 (br s, 1 H), 5.01–5.79 (m, 1 H), 7.1–8.0 (m, 10 H).

Anal. Calcd for $C_{20}H_{22}N_2O_2S$: C, 67.78; H, 6.26; N, 7.91. Found: C, 67.61; H, 6.32; N, 7.84.

Preparations of α-(Cyclohexen-1-yl)acetophenone *N*-Tosylhydrazone (8b) and α-(Cyclohepten-1-yl)acetophenone *N*-Tosylhydrazone (8c). Compounds **8b** and **8c** were prepared by the same procedures as those for **8a** except for dehydrations of **6b** and **6c** which were dehydrated by P_2O_5 in refluxing benzene. Compound **6b** (28.7 g, 154 mmol) was treated with P_2O_5 (31 g, 219 mmol) in refluxing benzene (200 mL) for 2.5 h. After the mixture was cooled to room temperature, the benzene layer was washed with water and dried over Na_2SO_4. Removal of benzene followed by distillation in vacuo gave 20.6 g (80% yield) of 1-(carbethoxymethyl)cyclohexene (bp 88 °C, 10 mmHg) as a colorless oil. The similar treatment of 37.2 g (186 mmol) of **6c** with 25 g (176 mmol) of P_2O_5 afforded 28.4 g of a colorless oil which is composed of 1-(carbethoxymethyl)cycloheptene and its α,β-unsaturated isomer (2:5). The same procedures as those for **6a** gave 29.7 g of 1-(carbethoxymethyl)cyclopentene from 41.8 g of the crude reaction mixture.

8b: mp 125–127 °C; mass spectrum, 25 eV, m/e (relative intensity), 368 (M^+, 15), 214 (8), 213 (100), 157 (7), 141 (7), 91 (16); ^{1}H NMR ($CDCl_3$, 60 MHz), δ 7.1–8.0 (m, 10 H), 5.08–5.48 (m, 1 H), 3.23 (br s, 2 H), 2.38 (s, 3 H), 1.2–2.0 (m, 8 H).

Anal. Calcd for $C_{21}H_{24}N_2O_2S$: C, 68.46; H, 6.57; N, 7.60. Found: C, 68.23; H, 6.66; N, 7.63.

8c: mp 120 °C; mass spectrum, 25 eV, m/e (relative intensity), 382 (M^+, 13), 228 (17), 227 (100); ^{1}H NMR ($CDCl_3$, 60 MHz) δ 7.2–8.3 (m, 10 H), 5.2 (m, 1 H), 3.3 (s, 2 H), 2.4 (s, 3 H), 1.0–2.2 (m, 10 H).

Anal. Calcd for $C_{22}H_{26}N_2O_2S$: C, 69.09; H, 6.85; N, 7.33. Found: C, 69.19; H, 6.60; H, 7.22.

Pyrolysis of the Sodium Salt of α-(Cyclopenten-1-yl)acetophenone *N*-Tosylhydrazone (8a). To 25 mg of sodium hydride (55% oil disper-

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sion) was added a solution of **8a** (300 mg, 0.847 mmol) in 30 mL of dry carbon tetrachloride under a nitrogen atmosphere. After being stirred for 15 min at room temperature, the mixture was heated under reflux for 2 h and then cooled to room temperature. Filtration of the resulting sodium toluene-*p*-sulfinate followed by removal of solvent gave a viscous oil. Addition of ether–*n*-hexane to this oil afforded 130 mg of colorless crystals. Thick-layer chromatography of the residue (6:5, *n*-hexane–ether) afforded an additional 25 mg of colorless crystals. Recrystallization from *n*-hexane–ether gave 122 mg (73% yield) of **10a** as colorless needles: mp 91 °C; IR (KBr) 1560 cm^{-1}; UV (ethanol) 253.5 nm (log ϵ 4.09); mass spectrum, 25 eV, *m/e* (relative intensity) 198 (M^+, 62), 170 (45), 169 (35), 155 (52), 141 (100); ^1H NMR (toluene-d_8, 100 MHz) δ 1.2–2.2 (m, 7 H), 2.72 (d, 1 H, J = 17.3 Hz), 2.91 (d, 1 H, J = 17.3 Hz), 7.0–7.2 (m, 3 H), 7.6–7.8 (m, 2 H).

Anal. Calcd for $C_{13}H_{14}N_2$: C, 78.75; H, 7.12; N, 14.13. Found: C, 78.88; H, 7.27; N, 14.32.

Pyrolysis of the Sodium Salt of α-(Cyclohexen-1-yl)acetophenone *N*-Tosylhydrazone (8b). Similarly, the sodium salt of **8b** prepared from 470 mg (1.28 mmol) of **8b** and 34.7 mg of sodium hydride (55% oil dispersion) was heated in refluxing carbon tetrachloride (30 min) under a nitrogen atmosphere. The resulting viscous oil obtained by the above procedures afforded 196 mg (72% yield) of colorless crystals upon thick-layer chromatography (8:7 *n*-hexane–ether). Recrystallization from *n*-hexane–ether gave **10b** as colorless prisms: mp 71.5 °C; IR (KBr) 3050, 2950, 2850, 1590, 1560, 1495, 1450, 940, 750, 690, 550 cm^{-1}; UV (ethanol) 254.5 nm (log ϵ 4.10); mass spectrum, 25 eV, *m/e* (relative intensity) 212 (M^+, 8.5), 184 (30), 169 (28), 155 (45), 142 (47), 141 (100), 128 (46), 115 (38), 91 (42), 77 (37); ^1H NMR (toluene-d_8, 90 MHz) δ 7.5–7.8 (m, 2 H), 6.9–7.2 (m, 3 H), 2.91 (d, 1 H, J = 17.5 Hz), 2.57 (dd, 1 H, J = 17.5 and 1.8 Hz), 1.0–2.2 (m, 9 H).

Anal. Calcd for $C_{14}H_{16}N_2$: C, 79.21; H, 7.60; N, 13.20. Found: C, 78.99; H, 7.64; N, 13.14.

Pyrolysis of the Sodium Salt of α-(Cyclohepten-1-yl)acetophenone *N*-Tosylhydrazone (8c). The sodium salt of **8c** prepared from 300 mg (0.785 mmol) of **8c** and 23 mg of sodium hydride (55% oil dispersion) was heated under reflux for 30 min in 30 mL of dry carbon tetrachloride. Thick-layer chromatography (1:1 *n*-hexane–ether) afforded 153 mg (86%) of colorless crystals which upon recrystallization from *n*-hexane–ether afforded **10c** as colorless needles: mp 65–67 °C; IR (KBr) 2920, 1560, 1494, 1455, 1432, 1328, 1008, 938, 820, 750, 685, 650, 550 cm^{-1}; UV (ethanol) 254 nm (log ϵ 4.13); mass spectrum, 25 eV, *m/e* (relative intensity) 226 (M^+, 8), 198 (23), 183 (28), 169 (23), 156 (28), 155 (61), 142 (47), 141 (100), 129 (71), 128 (37), 115 (30), 91 (34); ^1H NMR (benzene-d_6, 100 MHz), δ 7.6–7.8 (m, 2 H), 7.0–7.2 (m, 3 H), 2.99 (d, 1 H, J = 17.5 Hz), 2.53 (d, 1 H, J = 17.5 Hz), 1.0–2.1 (m, 11 H).

Anal. Calcd for $C_{15}H_{18}N_2$: C, 79.60; H, 8.02; N, 12.38. Found: C, 79.90; H, 7.81; N, 12.37.

Pyrolysis of the Sodium Salt of 8c in the Presence of Dimethyl Fumarate. The sodium salt of **8c** prepared from 327 mg (0.856 mmol) of **8c**, 29 mg of sodium hydride (55% oil dispersion), and 247 mg (1.72 mmol) of dimethyl fumarate were heated in refluxing carbon tetrachloride for 30 min and then cooled to room temperature. Filtration of the resulting precipitates followed by removal of solvent afforded a viscous oil from which thick-layer chromatography (1:1 *n*-hexane–ether) afforded 56 mg (18% yield) of **11**, 185 mg (58% yield) of **12**, and 38 mg of **10c** (20% yield).

11: mp 124–126 °C; IR (KBr) 3370, 1740, 1677, 1547, 1210 cm^{-1}; mass spectrum, 25 eV, *m/e* (relative intensity) 370 (M^+, 1), 261 (88), 229 (18), 217 (100), 171 (20); ^1H NMR (CCl_4, 60 MHz) 7.2–7.6 (m, 5 H), 6.9 (s, 1 H), 5.6 (t, 1 H, J = 6 Hz), 4.0 (s, 1 H), 3.8 (s, 3 H), 3.7 (s, 3 H), 2.6 (br s, 2 H), 0.7–2.2 (m, 10 H).

Anal. Calcd for $C_{21}H_{26}N_2O_4$: C, 68.09; H, 7.07; N, 7.56. Found: C, 67.45; H, 7.11; N, 7.29.

12: IR (CCl_4) 3350, 1740, 1565, 1440, 1210 cm^{-1}; mass spectrum, 25 eV, *m/e* (relative intensity) 370 (M^+, 2), 261 (85), 229 (9), 217 (100), 171 (34); ^1H NMR (CCl_4, 60 MHz) δ 7.2–7.8 (m, 6 H), 5.7 (t, 1 H, J = 6.5 Hz), 4.1 (s, 1 H), 3.8 (s, 3 H), 3.2 (s, 3 H), 2.7 (br s, 2 H), 0.8–2.3 (m, 10 H).

Anal. Calcd for $C_{21}H_{26}N_2O_4$: C, 68.09; H, 7.07; N, 7.56. Found: C, 67.95; H, 7.01; N, 7.43.

Preparation of α-(1,2-Benzo-1,3-cyclohexadien-3-yl)acetophenone *N*-Tosylhydrazone (13). To zinc (10.2 g, 156 mmol) and trace amounts of iodine was added dropwise a solution of α-tetralone (20.8 g, 142 mmol) and ethyl bromoacetate (26.1 g, 156 mmol) in 90 mL of dry THF over a 1.5-h period under refluxing. After an additional 2 h of refluxing, the mixture was cooled with ice–water and treated with dilute aqueous hydrochloric acid. The organic layer was separated, and the aqueous layer was extracted with ether. The combined organic layer was washed with water and dried over Na_2SO_4. Removal of solvents followed by distillation in vacuo gave 1-(carbethoxymethyl)-1-hydroxy-1,2,3,4-tetrahydronaphthalene (26.7 g, 80% yield): bp 130 °C (0.6 mmHg); IR (CCl_4) 3520, 2950, 1720, 1320, 1180, 1165, 1020 cm^{-1}; ^1H NMR (CCl_4, 60 MHz) δ 7.52 (m, 1 H), 6.9–7.2 (m, 3 H), 4.11 (q, 2 H, J = 7.2 Hz), 2.74 (m, 2 H), 2.69 (s, 2 H), 1.90 (m, 2 H), 1.21 (t, 3 H, J = 7.2 Hz). A solution of this alcohol (26.7 g, 114 mmol) in benzene (130 mL) was treated with P_2O_5 (40 g) under reflux for 2 h. The reaction mixture was cooled to room temperature and then poured into ice–water. The organic layer was separated, and the aqueous layer was neutralized with dilute aqueous sodium hydroxide and extracted with ether. The combined organic layer was washed with water and dried over Na_2SO_4. Removal of solvents followed by distillation gave 23.2 g of a 7:1 mixture of 4-(carbethoxymethyl)-1,2-dihydronaphthalene and the isomeric α,β-unsaturated ester (bp 110 °C, 0.4 mmHg). A solution of this mixture (23.2 g) in 30 mL of dry ethanol was treated with sodium ethoxide prepared from sodium (5.75 g, 0.25 mol) and 170 mL of dry ethanol under stirring at room temperature for 45 h. To this was added 500 mL of water, and stirring was continued for 2 days. The mixture was acidified with dilute hydrochloric acid and extracted with ether. The ether extract was washed with water and dried over Na_2SO_4. Removal of solvent afforded 15.4 g of (1,2-benzo-1,3-cyclohexadien-3-yl)acetic acid, which was recrystallized from *n*-hexane as colorless prisms: mp 106.5–108 °C; IR (KBr) 3120, 2930, 1690, 1410, 1240, 1215, 1180, 765 cm^{-1}; ^1H NMR ($CDCl_3$, 60 MHz) δ 10.99 (br s, 1 H), 7.19 (m, 4 H), 6.02 (td, 1 H, J = 4.5, 1.1 Hz), 3.46 (d, 2 H, J = 1.1 Hz), 2.78 (m, 2 H), 2.30 (m, 2 H).

To a solution of PhLi prepared from lithium (1.56 g, 0.223 mol) and bromobenzene (14.7 g, 94.2 mmol) in 100 mL of dry ether was added dropwise a solution of (1,2-benzo-1,3-cyclohexadien-3-yl)acetic acid (4.29 g, 22.8 mmol) in dry ether (45 mL) over a 15-min period at room temperature. After an additional 35 min of stirring, the mixture was poured into ice–water, and the organic layer was separated. The aqueous layer was acidified with dilute hydrochloric acid and then extracted with water. The combined organic layer was washed with water and dried over Na_2SO_4. Removal of solvent gave 6.5 g of an oil which was chromatographed on silica gel. Elutions with *n*-hexane–ether (30:1) afforded 3.38 g (60% yield) of α-(1,2-benzo-1,3-cyclohexadien-3-yl)acetophenone: ^1H NMR (CCl_4, 60 MHz) δ 7.8–8.0 (m, 2 H), 7.2–7.5 (m, 3 H), 7.02 (s, 4 H), 5.79 (td, 1 H, J = 4.5, 1.0 Hz), 3.99 (q, 2 H, J = 1.0 Hz), 2.70 (m, 2 H), 2.20 (m, 2 H).

A solution of α-(1,2-benzo-1,3-cyclohexadien-3-yl)acetophenone (3.30 g, 13.3 mmol) and *p*-toluenesulfonyl hydrazide (2.56 g, 13.8 mmol) in ethanol (30 mL) was stirred for 22 h. Recrystallization of the resulting precipitates from ethanol afforded 2.36 g (42% yield) of α-(1,2-benzo-1,3-cyclohexadien-3-yl)acetophenone *N*-tosylhydrazone (**13**) as colorless prisms: mp 136–138 °C; IR (KBr) 3220, 1595, 1345, 1165, 1075, 1005, 900, 805, 760 cm^{-1}; mass spectrum, 25 eV, *m/e* (relative intensity) 416 (M^+, 2), 278 (10), 261 (25), 260 (100), 259 (25), 245 (16), 139 (22), 91 (28); ^1H NMR ($CDCl_3$, 60 MHz) δ 7.1–7.9 (m, 14 H), 6.30 (m, 1 H), 3.67 (m, 2 H), 2.5–2.9 (m, 2 H), 2.40 (s, 3 H), 1.8–2.2 (m, 2 H).

Anal. Calcd for $C_{23}H_{24}N_2O_2S$: C, 72.10; H, 5.81; N, 6.73. Found: C, 72.30; H, 6.09; N, 6.64.

Preparation of α-(1,2-Benzo-1,3-cyclohexadien-4-yl)acetophenone *N*-Tosylhydrazone (18). To a suspension of 6.37 g (146 mmol) of sodium hydride (55% oil dispersion) in 70 mL of dry benzene a solution of diethyl carbonate (80 mL) in 70 mL of dry benzene was added. To this mixture was added a solution of α-tetralone (8.86 g, 60.9 mmol) in 50 mL of dry benzene dropwise over a 30 min period, and the mixture was heated under reflux for 14 h and cooled to room temperature. The organic layer was separated after addition of 150 mL of water, and the aqueous layer was extracted with ether. The combined organic layer was washed with water and dried over Na_2SO_4. Removal of solvents followed by distillation in vacuo gave 12.2 g of β-(ethoxycarbonyl)tetralone (92% yield) as a colorless oil. A solution of β-(ethoxycarbonyl)tetralone (1.49 g, 6.83 mmol) in 15 mL of ethanol was treated with sodium borohydride (132 mg, 3.49 mmol) at room temperature for 6 h. After addition of saturated aqueous ammonium chloride followed by extraction, the organic layer was washed with water and dried over Na_2SO_4. Removal of solvent gave 1.26 g of 1-hydroxy-2-(ethoxycarbonyl)-1,2,3,4-tetrahydronaphthalene [^1H NMR ($CDCl_3$, 60 MHz) δ 7.0–7.6 (m, 4 H), 5.0 (d, 1 H, J = 3.0 Hz), 4.2 (q, 2 H, J = 7.5 Hz), 3.7 (m, 1 H), 2.3–3.2 (m, 4 H), 1.3 (t, 3 H, J = 7.5 Hz)], which, without further purification, was treated with 1 g of P_2O_5 in 50 mL of dry benzene under reflux for 6 h. After being cooled to room temperature, the mixture was poured into ice–water and the organic layer was separated. The aqueous layer was extracted with ether. The combined organic layer was washed with water and dried over Na_2SO_4. Removal of solvents followed by distillation gave 923 mg (67% yield from β-(ethoxycarbonyl)tetralone) of 3-(ethoxycarbonyl)-1,2-dihydronaphthalene: bp 110 °C (0.2 mmHg); IR (CCl_4) 1710, 1630, 1450, 1370, 1270, 1190, 1065, 1020 cm^{-1}; ^1H NMR (CCl_4, 60 MHz) δ 7.41 (t, 1 H, J = 1.5 Hz), 7.10 (s, 4 H), 4.20 (q, 2 H, J = 6.6 Hz), 2.4–3.1 (m, 4 H), 1.33 (t, 3 H, J = 6.6 Hz). To a suspension of 3.15 g (82.9

mmol) of lithium aluminum hydride in 50 mL of dry benzene was added a solution of 3-(ethoxycarbonyl)-1,2-dihydronaphthalene (13.6 g, 67.3 mmol) in 50 mL of dry benzene dropwise at 50–60 °C over a 2 h period, and heating was continued for 15 h under stirring. After being cooled to room temperature, the mixture was decomposed with saturated aqueous NH_4Cl, the resulting precipitates were filtered, and the aqueous layer was extracted with ether. The combined organic layer was washed with water and dried over Na_2SO_4. Removal of solvent followed by distillation in vacuo gave 7.17 g (67% yield) of 3-(hydroxylmethyl)-1,2-dihydronaphthalene: bp 114–120 °C (0.3 mmHg); ^1H NMR (CCl_4, 60 MHz) δ 6.98 (m, 4 H), 6.30 (t, 1 H, J = 1.4 Hz), 4.08 (br s, 2 H), 3.35 (br s, 1 H), 2.71 (m, 2 H), 2.15 (m, 2 H). To a solution of 7.17 g (44.8 mmol) of 3-(hydroxylmethyl)-1,2-dihydronaphthalene and 2 mL of pyridine in 160 mL of dry ether was added a solution of phosphorus tribromide (6.56 g, 24.2 mmol) in 10 mL of dry ether at 0 °C. After 40 h of stirring, the mixture was poured into ice–water, and the organic layer was separated. The aqueous layer was extracted with ether, and the combined organic layer was washed with water and dried over Na_2SO_4. Removal of solvent followed by distillation gave 3-(bromomethyl)-1,2-dihydronaphthalene (5.48 g, 55% yield) as a colorless oil: bp 106–109 °C (0.3 mmHg); IR (neat) 3020, 2940, 2840, 1485, 1453 cm^{-1}; ^1H NMR (CCl_4, 60 MHz) δ 7.03 (m, 4 H), 6.50 (m, 1 H), 4.08 (s, 2 H), 2.85 (m, 2 H), 2.40 (m, 2 H). To a solution of benzoin (1.06 g, 5.0 mmol) in 12 mL of dimethyl sulfoxide were added 2.6 mL of 10% aqueous sodium hydroxide and a solution of 3-(bromomethyl)-1,2-dihydronaphthalene (1.15 g, 5.14 mmol) in 5 mL of dimethyl sulfoxide dropwise under a nitrogen atmosphere over a 5-min period. Additional stirring for 7 h at room temperature followed by addition of water resulted in precipitation of crystals. Filtration followed by recrystallization from *n*-hexane–benzene afforded 3-(1,2-benzo-1,3-cyclohexadien-4-yl)-2-hydroxy-1,2-diphenylpropan-1-one as colorless needles (1.12 g, 63% yield): mp 153–155 °C; IR (KBr) 3490, 2930, 1669, 1597, 1578, 1486 cm^{-1}; mass spectrum, 25 eV, *m/e* (relative intensity) 354 (M^+, 0.9), 146 (17), 143 (20), 128 (16), 105 (100), 77 (63). Then, 3-(1,2-benzo-1,3-cyclohexadien-4-yl)-2-hydroxy-1,2-diphenylpropan-1-one was treated with sodium borohydride in ethanol to give 3-(1,2-benzo-1,3-cyclohexadien-4-yl)-1,2-dihydroxy-1,2-diphenylpropane (mp 216–218 °C). To a solution of this diol (3.60 g, 10.1 mmol) in ethanol (230 mL) was added a solution of sodium periodate (2.49 g, 11.6 mmol) in 25 mL of water at room temperature, and the resulting mixture was stirred for 26 h. The resulting crystals were filtered, and concentration of the filtrate afforded additional crystals. Combined crystals were washed with 1:1 water–ethanol and dried. Recrystallization from *n*-hexane–benzene afforded α-(1,2-benzo-1,3-cyclohexadien-4-yl)acetophenone (702 mg, 28% yield) as colorless prisms: mp 115–117 °C; IR (KBr) 2880, 1678, 1447, 1198 cm^{-1}; ^1H NMR ($CDCl_3$, 60 MHz) 7.8–8.1 (m, 2 H), 7.3–7.6 (m, 3 H), 7.05 (m, 4 H), 6.34 (m, 1 H), 3.82 (d, 2 H, J = 0.8 Hz), 2.83 (m, 2 H), 2.32 (m, 2 H). A solution of α-(1,2-benzo-1,3-cyclohexadien-4-yl)-acetophenone (675 mg, 2.72 mmol) and *p*-toluenesulfonohydrazide (560 mg, 3.01 mmol) in 10 mL of ethanol was heated under reflux for 10 min and stirred at room temperature for 26 h. Filtration of the resulting crystals followed by recrystallization from ethanol gave α-(1,2-benzo-1,3-cyclohexadien-4-yl)acetophenone *N*-tosylhydrazone (**18**) (817 mg, 71% yield) as colorless plates: mp 158–159 °C; IR (KBr) 3225, 1600, 1390, 1345 cm^{-1}; mass spectrum, 25 eV, *m/e* (relative intensity) 416 (M^+, 0.6), 262 (29), 261 (100), 259 (45), 232 (38), 230 (24), 229 (23), 141 (26), 128 (23); ^1H NMR ($CDCl_3$, 60 MHz) δ 6.9–7.9 (m, 14 H), 5.77 (m, 1 H), 3.47 (br s, 2 H), 3.77 (m, 2 H), 2.38 (s, 3 H), 2.20 (m, 2 H).

Anal. Calcd for $C_{25}H_{24}O_2S$: C, 72.10; H, 5.81; N, 6.73. Found: C, 71.44; H, 6.24; N, 6.21.

Pyrolysis of the Sodium Salt of α-(1,2-Benzo-1,3-cyclohexadien-3-yl)acetophenone *N*-Tosylhydrazone (13). The sodium salt of **13** was prepared from **13** (384 mg, 0.92 mmol) and sodium hydride (26.4 mg, 1.10 mmol) in dry THF (5 mL). After removal of THF, the sodium salt of **13** was heated under reflux in 30 mL of dry carbon tetrachloride for 1 h under nitrogen. The mixture was cooled with ice–water until the red color due to **14** (IR, 2045 cm^{-1} in CCl_4) faded, and the resulting precipitates were filtered. Removal of solvent gave 244 mg of a viscous oil which is composed of 87% 9-phenyl-5,6-benzo-1,10-diazatricyclo-[5.3.0.$0^{2,7}$]deca-5,9-diene (**15**) and 13% diazomethane **14**. This viscous oil was subjected to pyrolysis in a NMR probe. Compound **15** was found to be easily oxidized to 3-phenyl-9,10-dihydro-1,2-diazaphenanthrene (**16**) by air during attempted crystallization or purification by thick-layer chromatography. Thus, further purification of **15** was abandoned. When pyrolysis of the sodium salt of **14** was carried out under aerated conditions, **16** was exclusively afforded. Thus, pyrolysis of the sodium salt of **14** prepared from 838 mg (2.01 mmol) and 59 mg of sodium hydride (2.46 mmol) followed by the same workup afforded 618 mg of a viscous oil, which upon thick-layer chromatography (3:2 *n*-hexane–ether) afforded 440 mg (84%) of **16** as colorless prisms.

15: ^1H NMR (CCl_4, 100 MHz) δ 7.5–7.7 (m, 2 H), 7.1–7.4 (m, 3 H), 6.7–7.1 (m, 4 H), 3.81 (d, 1 H, J = 17.5 Hz), 3.30 (d, 1 H, J = 17.5 Hz), 2.96 (m, 1 H), 2.1–2.7 (m, 3 H), 1.48 (m, 1 H).

16: mp 111–113 °C (from ether–*n*-hexane); IR (KBr) 3050, 2950, 1590, 1410, 1400, 787, 748 cm^{-1}; UV (ethanol) 262 nm (log ϵ 4.36); mass spectrum, 70 eV, *m/e* (relative intensity) 258 (M^+, 100), 259 (23), 229 (37), 228 (19), 115 (15); ^1H NMR ($CDCl_3$, 60 MHz) δ 7.0–8.1 (m, 10 H, including a singlet at d 7.85), 2.7–3.4 (m, 4 H).

Anal. Calcd for $C_{18}H_{14}N_2$: C, 83.69; H, 5.46; N, 10.85. Found: C, 83.54; H, 5.62; N, 10.64.

Dehydrogenation of 3-Phenyl-9,10-dihydro-1,2-diazaphenanthrene (16). A solution of **16** (249 mg, 0.965 mmol) and 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (300 mg, 1.32 mmol) in 50 mL of benzene was heated under reflux for 2 h. The resulting mixture was passed through an alumina short column after having been cooled to room temperature, and removal of solvent gave 159 mg of crystals, which upon recrystallization from benzene gave 159 mg (64% yield) of 3-phenyl-1,2-diazaphenanthrene (**17**) as colorless plates: mp 133–134 °C; UV (ethanol) 214 (log ϵ 4.47), 233 (log ϵ 4.32), 271 (log ϵ 4.72), 273.5 (log ϵ 4.72), 355 (log ϵ 3.42), 371 (log ϵ 3.37) nm; mass spectrum, 25 eV, *m/e* (relative intensity) 256 (M^+, 83), 257 (15), 229 (20), 228 (100), 227 (36), 226 (84), 202 (15), 200 (13), 126 (8).

Anal. Calcd for $C_{18}H_{12}N_2$: C, 84.35; H, 4.72; N, 10.93. Found: C, 84.62; H, 4.79; N, 10.76.

Pyrolysis of the Sodium Salt of α-(1,2-Benzo-1,3-cyclohexadien-4-yl)acetophenone *N*-Tosylhydrazone (18). The sodium salt of **18** prepared from 208 mg (0.5 mmol) of **18** and 15 mg (0.63 mmol) of sodium hydride was similarly heated under reflux in 40 mL of dry carbon tetrachloride for 85 min. After having been cooled to room temperature, the resulting precipitates were filtered, and the red solution was concentrated in vacuo to 1 mL. ^1H NMR spectrum revealed that this red solution included diazomethane **19** exclusively. This red solution was allowed to stand in a refrigerator at −25 °C for 3 weeks. The resulting crystals were filtered to afford 66 mg (50% yield) of 9-phenyl-3,4-benzo-1,10-diazatricyclo-[5.3.0.$0^{2,7}$]deca-2,8-diene (**20**) as colorless prisms.

19: IR (CCl_4) 2040 cm^{-1}; ^1H NMR (CCl_4, 60 MHz) δ 6.8–7.4 (m, 9 H), 6.29 (t, 1 H, J = 1.5 Hz), 3.24 (d, 2 H, J = 0.7 Hz), 2.77 (m, 2 H), 2.22 (m, 2 H).

20: mp 93.5–95 °C; IR (KBr) 3040, 2930, 1554, 1490, 1442, 1428, 1336, 935, 790, 744, 723, 682 cm^{-1}; mass spectrum, 25 eV, *m/e* (relative intensity) 260 (M^+, 1), 232 (8), 143 (27), 142 (26), 141 (28), 128 (82), 115 (15), 105 (100), 78 (27), 77 (77); ^1H NMR ($CDCl_3$, 100 MHz) δ 2.1–2.4 (m, 2 H), 2.60 (ddd, 1 H, J = 16.0, 5.0, 2.0 Hz), 3.10 (ddd, 1 H, J = 8.5, 7.4, 3.6 Hz), 3.40 (d, 1 H, J = 17.2 Hz), 3.69 (d, 1 H, J = 17.2 Hz), 6.9–7.5 (m, 7 H), 7.7–7.9 (m, 2 H).

Anal. Calcd for $C_{18}H_{16}N_2$: C, 83.04; H, 6.20; N, 10.76. Found: C, 83.22; H, 6.07; N, 10.33.

Preparation of (*E*)-1,4-Diphenyl-3-buten-1-one *N*-Tosylhydrazone (21a). (*E*)-1,4-Diphenyl-3-buten-1-one was prepared according to the reported procedures.[67-70] A solution of (*E*)-1,4-diphenyl-3-buten-1-one (4.08 g, 18.4 mmol) and *p*-toluenesulfonyl hydrazide (3.61 g, 19.4 mmol) in 40 mL of ethanol was stirred at room temperature. Filtration of the resulting crystals followed by recrystallization from ethanol gave **21a** (3.92 g, 55%) as colorless prisms: mp 140–141.5 °C; mass spectrum, 70 eV, *m/e* (relative intensity) 390 (M^+, 1.5), 155 (23), 128 (31), 115 (32), 91 (100), 78 (26), 77 (46); ^1H NMR ($CDCl_3$, 60 MHz) δ 6.9–8.2 (m, 15 H), 5.9–6.3 (m, 2 H), 3.5 (m, 2 H), 2.36 (br s, 3 H).

Anal. Calcd for $C_{23}H_{22}N_2O_2S$: C, 70.75; H, 5.68; N, 7.18. Found: C, 70.51; H, 5.97; N, 7.22.

Preparation of (*E*)-1,5-Diphenyl-4-penten-1-one *N*-Tosylhydrazone (21b). A solution of (*E*)-1,5-diphenyl-4-penten-1-one (**28b**) (7 g, 0.03 mol) and *p*-toluenesulfonohydrazide (6.07 g, 0.03 mol) in methanol was stirred at room temperature for 2 days. Filtration of the resulting crystals followed by recrystallization from methanol gave **21b** (10.9 g, 91%) as colorless needles: mp 120–122 °C; mass spectrum, 25 eV, *m/e* (relative intensity) 404 (M^+, 26.1), 205 (100); ^1H NMR ($CDCl_3$, 90 MHz) δ 2.20–2.55 (m, 5 H), 2.55–2.90 (m, 2 H), 6.05 (dt, 1 H, J = 16.0, 6.0 Hz), 6.35 (d, 1 H, J = 16.0 Hz), 7.00–8.40 (m, 15 H).

Anal. Calcd for $C_{24}H_{24}N_2O_2S$: C, 71.26; H, 5.98; N, 6.92; S, 7.93. Found: C, 71.13; H, 5.91; N, 6.97; S, 8.01.

Preparation of (*E*)-1,6-Diphenyl-5-hexen-1-one *N*-Tosylhydrazone (21c). Compound **21c** was prepared from (*E*)-1,6-diphenyl-5-hexen-1-one and *p*-toluenesulfonohydrazide in 65% yield as colorless needles: mp

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116–118 °C (from methanol); mass spectrum, 13.5 eV, *m/e* (relative intensity) 418 (M^+, 12.5), 143 (100); ^1H NMR ($CDCl_3$, 90 MHz) δ 1.40–1.90 (m, 2 H), 2.10–2.37 (m, 2 H), 2.37 (s, 3 H), 2.50–2.75 (m, 2 H), 6.05 (dt, 1 H, *J* = 16, 6.0 Hz), 6.30 (d, 1 H, *J* = 16.0 Hz), 7.10–7.45 (m, 10 H), 7.45–7.75 (m, 2 H), 7.80–8.05 (m, 2 H), 8.25 (br s, 1 H).

Anal. Calcd for $C_{25}H_{26}N_2O_2S$: C, 71.74; H, 6.26; N, 6.69; S, 7.66. Found: C, 71.79; H, 6.31; N, 6.58; S, 7.61.

Preparation of (*E*)-1,7-Diphenyl-6-hepten-1-one *N*-Tosylhydrazone (21d). Compound **21d** was prepared from (*E*)-1,7-diphenyl-6-hepten-1-one[71] and *p*-toluenesulfonohydrazide in 80% yield as colorless prisms (from methanol): mp 128–130 °C; mass spectrum, 13.5 eV, *m/e* (relative intensity) 432 (M^+, 2.3), 144 (100); ^1H NMR ($CDCl_3$, 90 MHz) δ 1.20–1.65 (m, 4 H), 1.90–2.25 (m, 2 H), 2.33 (s, 3 H), 2.40–2.80 (m, 2 H), 6.05 (dt, 1 H, *J* = 16.0, 6.0 Hz), 6.30 (d, 1 H, *J* = 16.0 Hz), 6.95–8.30 (m, 15 H).

Anal. Calcd for $C_{26}H_{28}N_2O_2S$: C, 72.19; H, 6.52; N, 6.48; S, 7.41. Found: C, 72.05; H, 6.55; N, 6.46; S, 7.12.

Preparation of 1,5,5-Triphenyl-4-penten-1-one *N*-Tosylhydrazone (29a). Compound **29a** was prepared from 1,5,5-triphenyl-4-penten-1-one and *p*-toluenesulfonohydrazide in methanol as colorless needles (96% yield): mp 135–136.5 °C (from methanol); mass spectrum, 13.5 eV, *m/e* (relative intensity) 480 (M^+, 3.6), 205 (39), 296 (100); ^1H NMR ($CDCl_3$, 90 MHz) δ 2.05–2.50 (m, 5 H), 2.50–2.90 (m, 2 H), 6.08 (t, 1 H, *J* = 7.5 Hz), 6.90–7.90 (m, 20 H).

Anal. Calcd for $C_{30}H_{28}N_2O_2S$: C, 74.98; H, 5.87; N, 5.83; S, 6.66. Found: C, 74.88; H, 5.90; N, 5.90; S, 6.77.

Preparation of 1-Phenyl-4-penten-1-one *N*-Tosylhydrazone (29b). Compound **29b** was prepared quantitatively from 1-phenyl-4-penten-1-one[34] and *p*-toluenesulfonohydrazide in methanol: mp 118–120 °C (colorless prisms from methanol); mass spectrum, 25 eV, *m/e* (relative intensity) 328 (M^+, 6.1), 144 (100); ^1H NMR ($CDCl_3$, 90 MHz) δ 2.05–2.40 (m, 2 H), 2.40 (s, 3 H), 2.50–2.81 (m, 2 H), 4.80–5.10 (m, 2 H), 5.46–5.93 (m, 1 H), 7.15–7.43 (m, 5 H), 7.45–7.65 (m, 2 H), 7.77–7.95 (m, 2 H), 8.05 (br s, 1 H).

Anal. Calcd for $C_{18}H_{20}N_2O_2S$: C, 65.83; H, 6.14; N, 8.53; S, 9.76. Found: C, 65.90; H, 6.01; N, 8.55; S, 9.81.

Pyrolysis of the Sodium Salt of (*E*)-1,4-Diphenyl-3-buten-1-one (21a). To a suspension of 120 mg (2.4 mmol) of sodium hydride (55% oil dispersion) in 2 mL of dry THF was added a solution of **21a** (495 mg, 1.3 mmol) in 10 mL of dry THF, and the mixture was stirred for 15 min. Solvent was removed by using a rotary pump, and the system was replaced several times with dry argon by using a Firestone valve. Dry carbon tetrachloride (50 mL) was then introduced, and the mixture was heated under reflux for 1 h. The resulting red-colored solution with white precipitates was cooled to room temperature, 50 mL of distilled water was added through a syringe under stirring to decompose excess sodium hydride and dissolve sodium toluene-*p*-sulfinate, and then the aqueous layer was removed through a syringe. Washing with distilled water was repeated 3 times. A 200-mL round-bottomed flask equipped with a 100 mL pressure equalized dropping funnel with a one-way stopcock in a pressure equalization arm was connected to a Firestone valve. After appropriate amounts of Na_2SO_4 were placed in a dropping funnel and the system was evacuated by using a rotary pump and replaced with dry argon several times, the system was kept under a negative pressure. The above red-colored carbon tetrachloride solution was introduced to a dropping funnel through a syringe to dry a solution over Na_2SO_4, keeping stopcocks of a dropping funnel and a pressure equalization arm off. After 30 min of drying, a stopcock of a dropping funnel was opened to move the dried solution to a 200-mL flask while a one-way stopcock was closed, and then the system was filled with dry argon through a Firestone valve. This solution was allowed to stand at room temperature or under ice–water cooling until the red color faded almost completely. Removal of solvent in vacuo at temperatures less than 40 °C gave 409 mg of an oily product, to which addition of ether gave 185 mg of crystals. Recrystallization from methylene chloride–ether gave 122 mg (45% yield) of *exo*-3,6-diphenyl-1,2-diazabicyclo[3.1.0]hex-2-ene (**23a**) as colorless plates.

When pyrolysis was carried out under an incomplete inert atmosphere, 3,6-diphenylpyridazine[30] was often formed.

This general experimental procedure was employed for all pyrolyses of the sodium salt of tosylhydrazones described hereinafter to prevent an unexpected air-oxidation of diazomethanes or 1,2-diazabicyclo[3.1.0]-hex-2-enes.

Anal. Calcd for $C_{16}H_{14}N_2$: C, 82.02; H, 6.02; N, 11.96. Found: C, 81.75; H, 6.00; N, 11.67.

Pyrolysis of the Sodium Salt of (*E*)-1,5-Diphenyl-4-penten-1-one *N*-Tosylhydrazone (21b). A solution of the sodium salt of **21b** prepared from 500 mg (1.24 mmol) and 72 mg (1.49 mmol) of sodium hydride in 75 mL of dry carbon tetrachloride was heated under reflux for 1 h. The resulting red-colored solution was washed with water and dried over Na_2SO_4 as described before and was allowed to stand at room temperature or under cooling at −25 °C in a refrigerator. The progress of the reaction was followed by IR spectra. The absorption due to diazomethane **22b** at 2025 cm^{-1} did not weaken, and **22b** remained unchanged for more than 3 months when kept under argon.

Air-Oxidation of 22b under Basic Conditions.[32] The crude pyrolysate obtained from pyrolysis of the sodium salt of **21b** prepared from 500 mg of **21b** and 72 mg of sodium hydride which included diazomethane **22b**, exclusively, together with a slight excess of sodium hydride and liberated sodium toluene-*p*-sulfinate was exposed to air under stirring. The red color began to fade quickly, and **22b** completely disappeared within 2 h. Stirring was continued additionally for 12 h. Washing with water and drying over Na_2SO_4 followed by removal of solvent gave 325 mg of an oil, which upon thick-layer chromatography (1:3 ether–*n*-hexane) afforded epoxy ketone **27b** (147 mg, 47%) and ketone **28b** (79 mg, 27%). Compound **27b** was independently synthesized by epoxidation of **28b** by using *m*-chloroperbenzoic acid.

27b: mp 38–39 °C; IR (KBr) 1675, 1278, 1200 cm^{-1}; UV (ethanol) 241 (log ε 4.29), 219 (log ε 4.30) nm; mass spectrum, 13.5 eV, *m/e* (relative intensity) 252 (M^+, 11.4), 105 (100); ^1H NMR (CCl_4, 90 MHz), δ 1.90 (m, 1 H), 2.25 (m, 1 H), 2.90 (m, 1 H), 3.10 (t, 2 H, *J* = 7.5 Hz), 3.54 (d, 1 H, *J* = 2.2 Hz), 6.90–7.50 (m, 8 H), 7.80–8.00 (m, 2 H).

Anal. Calcd for $C_{17}H_{16}O_2$: C, 80.93; H, 6.39. Found: C, 80.23; H, 6.53.

Dye-Sensitized Photooxidation and Air-Oxidation of 22b under Basic Conditions. The crude pyrolysate obtained from pyrolysis of the sodium salt of **21b** prepared from **21b** (700 mg, 1.74 mmol) and sodium hydride (100 mg, 2.09 mmol) in 100 mL of carbon tetrachloride was divided into two parts without washing with water. One part was stirred under air. Compound **22b** disappeared within 30 min. After an additional 76 h of stirring, the solution was washed and dried over Na_2SO_4. Liquid chromatographic analysis (column, reverse phase Waters C_{18} Radial Pak; solvent, 3:1 methanol–water; flow rate, 1.3 mL/min) showed the formation of **27b** (retention time, 8.90 min) and **28b** (16.3 min) in the ratio of 81:19. The other was subjected to dye-sensitized photooxidation in the presence of 2 mg of *meso*-tetraphenylporphine. Upon irradiation with Na lamps under vigorous oxygen bubbling **22b** disappeared within 10 min. Liquid chromatographic analysis showed the formation of **27b** and **28b** in the ratio of 22:78.

Dye-Sensitized Photooxidation and Air-Oxidation of 22b under Neutral Conditions. The crude pyrolysate obtained from pyrolysis of the sodium salt of **21b** prepared from **21b** (1.0 g, 2.48 mmol) and sodium hydride (238 mg, 4.96 mmol) in 150 mL of carbon tetrachloride was washed with water and dried over Na_2SO_4 as described before. The resulting carbon tetrachloride solution was divided into two parts. One part was stirred under air for 23 h until **22b** completely disappeared. The other was similarly irradiated with Na lamps under oxygen bubbling in the presence of 2 mg of *meso*-tetraphenylporphine for 10 min. Liquid chromatographic analyses of both solutions revealed the exclusive formation of **28b**, but **27b** could not be detected. In dye-sensitized photooxidation, oxygen gas from the exit of the system was collected in a spiral trap at −196 °C. Oxygen was removed in vacuo at −196 °C, and the remaining white solids were gasified. Mass spectral analysis showed the formation of dinitrogen oxide (*m/e*, 44) after the subtraction of the background carbon dioxide.

Air-Oxidation of 22b in the Presence of Dimethyl Sulfide under Basic Conditions. Similar to the experiment described for air-oxidation of **22b** under basic condition, the crude pyrolysate (from 1.00 g of **21b** and 200 mg of sodium hydride) was divided into two parts. One part was exposed to air under stirring. The other was stirred in the presence of dimethyl sulfide (666 mg, 10.4 mmol) under air. Liquid chromatographic analyses showed that the formation ratios of **27b** and **28b** without and with dimethyl sulfide were 62:38 and 15:85, respectively.

Pyrolysis of the Sodium Salt of 1,5,5-Triphenyl-4-penten-1-one *N*-Tosylhydrazone (29a) and Air-Oxidation and Dye-Sensitized Photooxidation of 30a. (a) Air-Oxidation under Basic Conditions. The sodium salt of **29a** from 700 mg (1.46 mmol) of **29a** and 140 mg (2.92 mmol) of sodium hydride was decomposed in refluxing carbon tetrachloride (70 mL) for 1 h. The resulting red-colored solution was allowed to stand at room temperature or −25 °C. Diazomethane **30a** (IR, 2040 cm^{-1} in CCl_4) did not change for more than 1 month when kept under nitrogen. When exposed to air under stirring, the red color faded within 2 h. After washing with water and drying over Na_2SO_4, removal of solvent followed by the separation with thick-layer chromatography (1:4 ether–*n*-hexane) gave 310 mg (71% yield) of **31a** and 44 mg (14% yield) of **32a**.

31a: mp 50–51 °C (colorless prisms from *n*-hexane); IR (KBr) 1688, 1600, 1278, 1198 cm^{-1}; UV (ethanol) 242 (log ε 4.10) nm; mass spec-

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trum, 25 eV, *m/e* (relative intensity) 328 (M^+, 1), 146 (100); ^1H NMR (CCl_4, 90 MHz) δ 1.50 (m, 1 H), 1.96 (m, 1 H), 3.02 (t, 2 H, J = 7.5 Hz), 3.40 (dd, 1 H, J = 7.5, 4.5 Hz), 7.05–7.55 (m, 13 H), 7.70–7.93 (m, 2 H).

Anal. Calcd for $C_{23}H_{20}O_2$: C, 84.12; H, 6.14. Found: C, 84.12; H, 6.26.

(b) Air-Oxidation and Dye-Sensitized Photooxidation under Neutral Conditions. The crude pyrolysate from 1.0 g (2.48 mmol) of **29a** and 238 mg (4.96 mmol) of sodium hydride in 150 mL of dry carbon tetrachloride was washed with water and dried over Na_2SO_4 and then divided into 2 parts. One part was stirred under air. The other part was irradiated with Na lamps under oxygen bubbling in the presence of 2 mg of *meso*-tetraphenylporphine. Liquid chromatographic analyses (column: Waters C_{18} Radial Pak; solvent, 4:1 methanol–water; flow rate, 1.3 mL/min) showed the exclusive formation of **32a** for both reactions.

Pyrolysis of the Sodium Salt of 1-Phenyl-4-penten-1-one *N*-Tosylhydrazone (29b) and Air-Oxidation of 30b under Basic Conditions. The sodium salt of **29b** from 500 mg (1.52 mmol) of **29b** and 110 mg (2.29 mmol) of sodium hydride was decomposed in refluxing carbon tetrachloride (70 mL) for 1 h. Diazomethane **30b** (IR, 2035 cm^{-1} in CCl_4) in the resulting red solution remained unchanged for more than 2 months when kept under nitrogen at room temperature or −25 °C. When exposed to air under stirring, **30b** disappeared within 2 h. Removal of solvent after washing with water and drying over Na_2SO_4 followed by thick-layer chromatography (3:5 ether–*n*-hexane) gave 66 mg (25% yield) of **31b** and 66 mg (27%) of **32b**.

31b: mp 29–31 °C; IR (neat) 1690, 1595, 1446, 1205 cm^{-1}; UV (ethanol) 241.5 (log ϵ 4.08), 279 (log ϵ 3.0) nm; mass spectrum, 25 eV, *m/e* (relative intensity) 176 (M^+, 12.6), 105 (100); ^1H NMR (CCl_4, 90 MHz) δ 1.70 (m, 1 H), 2.10 (m, 1 H), 2.38 (dd, 1 H, J = 5.2, 5.1 Hz), 2.61 (dd, 1 H, J = 5.2, 4.0 Hz), 2.90 (m, 1 H), 3.05 (t, 2 H, J = 7.0 Hz), 7.20–7.60 (m, 3 H), 7.80–8.05 (m, 2 H).

Anal. Calcd for $C_{11}H_{12}O_2$: C, 74.97; H, 6.86. Found: C, 74.69; H, 6.87.

Air-Oxidation of 30b under Neutral Conditions. The sodium salt of **29b** from 500 mg (1.52 mmol) of **29b** and 110 mg (2.28 mmol) of sodium hydride was decomposed in carbon tetrachloride (75 mL). After washing the mixture with water and drying over Na_2SO_4, the resulting solution was stirred under air for 62 h. Removal of solvent followed by thick-layer chromatography (3:5 ether–*n*-hexane) afforded **32b** (137 mg, 56.3 % yield).

Air-Oxidation of 22b in the Presence of Ketone 32a under Basic Conditions. The sodium salt of **21b** from 500 mg (1.24 mmol) of **21b** and 72 mg (1.49 mmol) of sodium hydride was decomposed in refluxing carbon tetrachloride (50 mL) for 1 h. After having been cooled to room temperature, ketone **32a** (387 mg, 1.24 mmol) was added, and the resulting solution was stirred under air for 3 h. Liquid chromatographic analysis showed the formations of **27b** and **28b** but not that of **31a** at all.

Pyrolysis of (*E*)-1,6-Diphenyl-5-hexen-1-one *N*-Tosylhydrazone (21c). The sodium salt of **21c** from 500 mg (1.20 mmol) of **21c** and 86 mg (1.79 mmol) of sodium hydride was heated under reflux in 50 mL of carbon tetrachloride for 1 h. The same workup as that for **21a** followed by thick-layer chromatography (1:2 ether–*n*-hexane) afforded **25c** (196 mg, 69% yield): mp 53.5–54.5 °C (colorless prisms); IR (KBr) 3050, 2950, 2860, 1600, 1550, 1490 cm^{-1}; UV (*n*-hexane) 254 (log ϵ 2.64), 260 (log ϵ 2.68), 265.5 (log ϵ 2.48), 333 (log ϵ 2.36) nm; mass spectrum, 13.5 eV, *m/e* (relative intensity) 262 (M^+, 3), 234 (100); ^1H NMR ($CDCl_3$, 90 MHz) δ 0.85–1.53 (m, 1 H), 1.60–2.25 (m, 4 H), 2.50–2.85 (m, 2 H), 5.35 (d, 1 H, J = 4.0 Hz), 6.85–7.09 (m, 2 H), 7.10–7.53 (m, 8 H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 24.22 (t), 35.38 (t), 40.72 (t), 49.81 (d), 102.55 (d), 107.90 (s), 125.53, 127.03, 126.61, 128.596, 128.73.

Anal. Calcd for $C_{18}H_{18}N_2$: C, 82.40; H, 6.92; N, 10.68. Found: C, 82.70; H, 6.98; N, 10.71.

Pyrolysis of the Sodium Salt of (*E*)-1,7-Diphenyl-6-hepten-1-one *N*-Tosylhydrazone (21d). The sodium salt of **21d** from 500 mg of **21d** and 83 mg (1.74 mmol) of sodium hydride was heated in refluxing carbon tetrachloride (50 mL) for 1 h. Stirring was continued for 68 h at room temperature until **22d** completely disappeared. The same workup as that described before followed by thick-layer chromatography (1:2 ether–*n*-hexane) gave 47 mg (16% yield) of **26d**, 35 mg (12% yield) of (*E*)-1,7-diphenyl-6-hepten-1-one, and 160 mg (50% yield) of **25d** together with trace amounts of epoxide of (*E*)-1,7-diphenyl-6-hepten-1-one. When pyrolysis was carried out under air, epoxide was isolated in 8% yield together with three other compounds.

25d: mp 118–119 °C (colorless prisms); IR (KBr) 3050, 1600, 1492, 1450, 1065 cm^{-1}; UV (*n*-hexane) 252 (log ϵ 2.87), 259 (log ϵ 2.80), 265 (log ϵ 2.59), 340 (log ϵ 2.36) nm; mass spectrum, 13.5 eV, *m/e* (relative intensity) 276 (M^+, 4.5), 248 (100); ^1H NMR ($CDCl_3$, 200 MHz) δ 1.10–2.24 (m, 8 H), 2.35–2.56 (m, 1 H), 5.16 (d, 1 H, J = 11.5 Hz), 7.08–7.60 (m, 8 H), 7.62–7.90 (m, 2 H).

Anal. Calcd for $C_{19}H_{20}N_2$: C, 82.57; H, 7.29; N, 10.14. Found: C, 82.46; H, 7.41; N, 10.05.

26d: mp 83–84 °C (colorless needles); IR (KBr) 3050, 1600, 1490 cm^{-1}; UV (*n*-hexane) 260 (log ϵ 2.79), 266.5 (log ϵ 2.75), 277 (log ϵ 2.53) nm; mass spectrum, 13.5 eV, *m/e* (relative intensity) 248 (M^+, 100); ^1H NMR ($CDCl_3$, 200 MHz) δ 1.30–1.64 (m, 4 H), 1.76–2.04 (m, 3 H), 2.12 (d, 1 H, J = 6.0 Hz), 2.06–2.36 (m, 2 H), 6.62–6.80 (m, 2 H), 6.94–7.24 (m, 8 H).

Anal. Calcd for $C_{19}H_{20}$: C, 91.88; H, 8.12. Found: C, 92.17; H, 8.19.

Preparations of (*Z*)-1-Phenyl-3-penten-1-one (43b) and Its *N*-Tosylhydrazone 44b. Compound **47** was prepared from styrene oxide and propyne in 55% yield according to the reported procedure.[72] To a stirred solution of 31.5 g (196 mmol) of **47** in 200 mL of acetone was added the Jones reagent in acetone dropwise under ice–water cooling until the solution turned to pale red. Stirring was continued for 6 h, and the resulting solution was extracted with ether after addition of water. Ether extracts were washed with water and dried over Na_2SO_4. Removal of solvent gave 33.6 g of an oil, which crystallized upon standing. Recrystallization from *n*-hexane–ether gave **48** (22.1 g, 72% yield) as colorless needles (mp 53.5 °C).

Anal. Calcd for $C_{11}H_{10}O$: C, 83.51; H, 6.37. Found: C, 83.34; H, 6.43.

In a hydrogenation apparatus, 2.1 g (12.9 mmol) of **48** was hydrogenated in 15 mL of methanol with 3 drops of quinoline over 5% palladium on barium sulfate at atmospheric pressure. Filtration of the catalyst and removal of solvent followed by column chromatography (4:1 *n*-hexane–ether) gave 1.9 g of a yellow oil. Distillation using a Kugelrohr apparatus gave 1.8 g (86% yield) of **43b** as a colorless oil: bp 150 °C (oven temperature) (0.08 mmHg); ^1H NMR (CCl_4, 60 MHz) δ 1.70 (dd, 3 H, J = 6.0, 1.5 Hz), 3.65 (m, 2 H), 5.4–5.90 (m, 2 H), 7.4–8.1 (m, 5 H).

Anal. Calcd for $C_{11}H_{12}O$: C, 82.46; H, 7.55. Found: C, 82.34; H, 7.69.

A solution of 92 mg (5.8 mmol) of **43b** and *p*-toluenesulfonohydrazide (1.32 g, 7.1 mmol) in 20 mL of ethanol was stirred for 2 days at room temperature. Filtration followed by recrystallization from ethanol gave 1.4 g of **44b** as colorless prisms: mp 129.5–130 °C; mass spectrum, 25 eV, *m/e* (relative intensity) 328 (M^+, 11.3), 174 (24), 173 (100), 130 (26), 129 (65), 119 (21), 115 (24), 105 (19), 91 (47), 77 (23), 65 (26); ^1H NMR ($CDCl_3$, 90 MHz), δ 1.73 (dd, J = 6.0, 1.5 Hz), 2.40 (s, 3 H), 3.36 (m, 2 H), 5.20 (m, 1 H), 5.60 (m, 1 H), 7.2–8.0 (m, 5 H), J = 10.5 Hz by simultaneous irradiations of methylene and methyl hydrogens.

Anal. Calcd for $C_{18}H_{20}N_2O_2S$: C, 65.55; H, 6.16; N, 8.55. Found: C, 65.84; H, 6.14; N, 8.53.

Preparations of (*E*)-1-Phenyl-3-penten-1-one (43a), (*Z*)-1-Aryl-4-methyl-3-hexen-1-ones 43c and 43d, 1-Aryl-4-methyl-3-penten-1-ones 43e–43l, and Their *N*-Tosylhydrazones 44a and 44c–44l. Ketones **43a** and **43c–43l** were prepared starting from **40** through **41** and **42** according to the procedures reported by Steglich,[43] which were converted with ease to the corresponding tosylhydrazones **44a** and **44c–44l**. NMR spectra of **43** and **44** were described.

(*E*)-1-Phenyl-3-penten-1-one (43a):[73] colorless oil; ^1H NMR (CCl_4, 90 MHz) δ 1.70 (m, 3 H), 3.60 (m, 2 H), 5.60 (m, 2 H), 7.3–8.3 (m, 5 H), J = 15.0 Hz by simultaneous irradiations of methylene and methyl hydrogens.

Anal. Calcd for $C_{11}H_{12}O$: C, 82.46; H, 7.55. Found: C, 82.41; H, 7.60.

(*E*)-1-Phenyl-3-penten-1-one *N*-Tosylhydrazone (44a): mp 121 °C (colorless prisms from ethanol); ^1H NMR ($CDCl_3$, 90 MHz) δ 1.53 (dd, 3 H, J = 6.0, 3.0 Hz), 2.40 (s, 3 H), 3.23 (m, 2 H), 5.33 (m, 2 H), 7.2–7.9 (m, 5 H), J = 15.0 Hz by simultaneous irradiations of methylene and methyl hydrogens.

Anal. Calcd for $C_{18}H_{20}N_2O_2S$: C, 65.94; H, 6.21; N, 8.54. Found: C, 65.84; H, 6.14; N, 8.53.

(*Z*)-1-Phenyl-4-methyl-3-hexen-1-one (43c): oil (bp 80 °C (0.05 mm Hg)); ^1H NMR (CCl_4, 90 MHz) δ 1.00 (t, 3 H, J = 7.8 Hz), 1.74 (br s, 3 H), 2.11 (q, 2 H, J = 7.8 Hz), 2.57 (d, 2 H, J = 7.2 Hz), 5.36 (m, 1 H), 7.2–7.8 (m, 5 H).

Anal. Calcd for $C_{13}H_{16}O$: C, 82.94; H, 8.57. Found: C, 82.73; H, 8.55.

(*Z*)-1-Phenyl-4-methyl-3-hexen-1-one *N*-Tosylhydrazone (44c): mp 115.5 °C (colorless prisms from ethanol); ^1H NMR ($CDCl_3$, 90 MHz) δ 1.01 (t, 3 H, J = 8.1 Hz), 1.70 (br s, 3 H), 2.19 (q, 2 H, J = 8.1 Hz), 2.40 (s, 3 H), 3.33 (br d, 2 H, J = 6.5 Hz), 4.80 (br t, 1 H, J = 6.5 Hz), 7.0–8.0 (m, 10 H).

(72) Shulte, K. E.; Reiss, K. P. *Chem. Ber.* **1957**, *87*, 964.
(73) Weerdt, J. A.; Cerfontain, H. J. *J. Chem. Soc., Perkin Trans. 2* **1980**, 592.

Anal. Calcd for $C_{20}H_{24}O_2N_2S$: C, 67.39; H, 6.79; N, 7.86; S, 8.99. Found: C, 67.33; H, 6.81; N, 7.73; S, 9.01.

(*Z*)-(*p*-Bromophenyl)-4-methyl-3-hexen-1-one (43d): bp 110 °C (0.1 mmHg); ^{1}H NMR (CCl_4, 90 MHz) δ 1.00 (t, 3 H, J = 8.7 Hz), 1.72 (br s, 3 H), 2.08 (q, 2 H, J = 8.7 Hz), 3.54 (d, 2 H, J = 6.6 Hz), 5.31 (t, 1 H, J = 6.5 Hz), 7.55 (d, 2 H, J = 9.0 Hz), 7.78 (d, 2 H, J = 9.0 Hz).

Anal. Calcd for $C_{13}H_{15}OBr$: C, 58.44; H, 5.66; Br, 29.91. Found: C, 58.31; H, 5.76; Br, 29.68.

(*Z*)-1-(*p*-Bromophenyl)-4-methyl-3-hexen-1-one *N*-Tosylhydrazone (44d): mp 108–112 °C (colorless needles from ethanol); ^{1}H NMR (CD_2Cl_2, 90 MHz) δ 0.99 (t, 3 H, J = 7.5 Hz), 1.67 (br s, 3 H), 2.17 (q, 2 H, J = 7.5 Hz), 2.39 (s, 3 H), 3.30 (br d, J = 6.5 Hz), 4.77 (br t, 1 H, J = 6.5 Hz), 7.38 (d, 2 H, J = 9.0 Hz), 7.5 (br s, 5 H), 7.85 (d, 2 H, J = 9.0 Hz).

Anal. Calcd for $C_{20}H_{23}O_2N_2BrS$: C, 55.17; H, 5.33; N, 6.44; Br, 18.35; S, 7.36. Found: C, 55.06; H, 5.38; N, 6.27; Br, 18.59; S, 7.47.

1-Phenyl-4-methyl-3-penten-1-one (43e): colorless oil (bp 110 °C (Kugelrohr oven temperature) (0.03 mmHg)); ^{1}H NMR (CCl_4, 90 MHz) δ 1.70 (s, 3 H), 1.77 (s, 3 H), 3.57 (d, 2 H, J = 7.0 Hz), 5.40 (br t, 1 H, J = 7.0 Hz), 7.49 (m, 3 H), 7.94 (m, 2 H).

1-Phenyl-4-methyl-3-penten-1-one *N*-Tosylhydrazone (44e): 120 °C (colorless needles from ethanol); ^{1}H NMR ($CDCl_3$, 90 MHz) δ 1.76 (m, 6 H), 2.41 (br s, 3 H), 3.31 (br d, 2 H, J = 7.2 Hz), 4.87 (br t, J = 7.2 Hz), 7.36 (m, 3 H), 7.80 (m, 2 H).

Anal. Calcd for $C_{19}H_{22}N_2O_2S$: C, 66.64; H, 6.48; N, 8.18; S, 9.36. Found: C, 66.45; H, 6.52; N, 8.13; S, 9.34.

1-(*p*-Nitrophenyl)-4-methyl-3-penten-1-one (43f): mp 53–54 °C (yellow needles from *n*-hexane); ^{1}H NMR (CCl_4, 90 MHz) δ 1.73 (s, 3 H), 1.79 (s, 3 H), 3.77 (d, 2 H, J = 6.6 Hz), 5.37 (m, 1 H), 8.21 (m, 4 H).

Anal. Calcd for $C_{12}H_{13}O_3N$: C, 65.74; H, 5.98; N, 6.39. Found: C, 65.12; H, 6.01; N, 6.32.

1-(*p*-Nitrophenyl)-4-methyl-3-penten-1-one *N*-Tosylhydrazone (44f): mp 122–124 °C (yellow needles from ethanol); ^{1}H NMR (CD_2Cl_2, 90 MHz) δ 1.75 (br s, 6 H), 2.45 (s, 3 H), 3.36 (br d, 2 H, J = 6.0 Hz), 4.85 (br t, 1 H, J = 6.0 Hz), 7.3–8.25 (m, 9 H).

Anal. Calcd for $C_{19}H_{21}O_4N_3S$: C, 58.90; H, 5.46; N, 10.85; S, 8.27. Found: C, 58.87; H, 5.32; N, 10.90; S, 8.41.

1-(*m*-Nitrophenyl)-4-methyl-3-penten-1-one (43g): mp 39–41 °C (yellow prisms from *n*-hexane); ^{1}H NMR (CCl_4, 90 MHz) δ 1.73 (s, 3 H), 1.75 (s, 3 H), 3.70 (d, 2 H, J = 7.2 Hz), 5.37 (m, 1 H), 7.69 (t, 1 H, J = 7.8 Hz), 8.31 (m, 2 H), 8.67 (m, 1 H).

Anal. Calcd for $C_{12}H_{13}O_3N$: C, 65.74; H, 5.98; N, 6.39. Found: C, 65.23; H, 5.90; N, 6.31.

1-(*m*-Nitrophenyl)-4-methyl-3-penten-1-one *N*-Tosylhydrazone (44g): mp 134–136 °C (colorless needles from ethanol); ^{1}H NMR (CD_2Cl_2, 90 MHz) δ 1.75 (br s, 6 H), 2.45 (s, 3 H), 3.35 (br d, 2 H, J = 6.5 Hz), 4.85 (br t, 1 H, J = 6.5 Hz), 7.25–8.40 (m, 9 H).

Anal. Calcd for $C_{19}H_{21}O_4N_3S$: C, 58.90; H, 5.46; N, 10.85; S, 8.27. Found: C, 58.98; H, 5.47; N, 10.91; S, 8.29.

1-(*p*-Cyanophenyl)-4-methyl-3-penten-1-one (43h): mp 74.5–75.5 °C (colorless plates from *n*-hexane); ^{1}H NMR (CCl_4, 90 MHz) δ 1.73 (s, 3 H), 1.76 (s, 3 H), 3.62 (d, 2 H, J = 7.2 Hz), 5.35 (m, 1 H), 7.11 (d, 2 H, J = 8.0 Hz), 8.03 (d, 2 H, J = 8.0 Hz).

Anal. Calcd for $C_{13}H_{13}ON$: C, 78.36; H, 6.58; N, 7.03. Found: C, 78.25; H, 6.67; N, 7.00.

1-(*p*-Cyanophenyl)-4-methyl-3-penten-1-one *N*-Tosylhydrazone (44h): mp 139–140 °C (colorless plates from ethanol); ^{1}H NMR (CD_2Cl_2, 90 MHz) δ 1.72 (br s, 6 H), 2.41 (s, 3 H), 3.33 (br d, 2 H, J = 6.0 Hz), 4.85 (br t, 1 H, J = 6.0 Hz), 7.25–8.20 (m, 9 H).

Anal. Calcd for $C_{20}H_{21}O_2N_3S$: C, 65.37; H, 5.76; N, 11.44; S, 8.72. Found: C, 65.47; H, 5.76; N, 11.45; S, 8.70.

1-(*p*-Bromophenyl)-4-methyl-3-penten-1-one (43i): mp 43–44 °C (colorless needles from *n*-hexane); ^{1}H NMR (CCl_4, 90 MHz) δ 1.66 (s, 3 H), 1.73 (s, 3 H), 2.52 (d, 2 H, J = 7.0 Hz), 5.33 (br t, 1 H, J = 7.0 Hz), 7.50 (d, 2 H, J = 8.7 Hz), 7.75 (d, 2 H, J = 8.7 Hz).

Anal. Calcd for $C_{12}H_{13}OBr$: C, 56.94; H, 5.18; Br, 31.57. Found: C, 56.85; H, 5.09; Br, 31.46.

1-(*p*-Bromophenyl)-4-methyl-3-penten-1-one *N*-Tosylhydrazone (44i): mp 134–135 °C (colorless needles from ethanol); ^{1}H NMR (CD_2Cl_2, 90 MHz) δ 1.74 (br s, 6 H), 2.40 (s, 3 H), 3.30 (br d, 2 H, J = 6.5 Hz), 4.80 (br t, 1 H, J = 6.5 Hz), 7.30 (d, 2 H, J = 9.0 Hz), 7.50 (m, 5 H), 7.80 (d, 2 H, J = 9.0 Hz).

Anal. Calcd for $C_{19}H_{21}O_2N_2SBr$: C, 54.16; H, 5.02; N, 6.65; S, 7.61; Br, 18.96. Found: C, 54.33; H, 5.09; N, 6.56; S, 7.44; Br, 18.72.

1-(*p*-Chlorophenyl)-4-methyl-3-penten-1-one (43j): mp 38–40 °C (colorless prisms from *n*-hexane); ^{1}H NMR (CCl_4, 90 M Hz) δ 1.66 (s, 3 H), 1.73 (s, 3 H), 3.55 (d, 2 H, J = 7.5 Hz), 5.34 (br t, 1 H, J = 7.5 Hz), 7.34 (d, 2 H, J = 9.0 Hz), 7.84 (d, 2 H, J = 9.0 Hz).

Anal. Calcd for $C_{12}H_{13}OCl$: C, 69.06; H, 6.24; Cl, 17.03. Found: C, 69.14; H, 6.21; Cl, 16.83.

1-(*p*-Chlorophenyl)-4-methyl-3-penten-1-one *N*-Tosylhydrazone (44j): mp 130–132 °C (colorless needles from ethanol); ^{1}H NMR ($CDCl_3$, 90 MHz) δ 1.74 (br s, 6 H), 2.41 (s, 3 H), 3.28 (d, 2 H, J = 6.6 Hz), 4.84 (br t, 1 H, J = 6.6 Hz), 7.30 (d, 2 H, J = 8.7 Hz), 7.31 (d, 2 H, J = 7.5 Hz), 7.36 (s, 1 H), 7.57 (d, 2 H, J = 8.7 Hz), 7.84 (d, 2 H, J = 7.5 Hz).

Anal. Calcd for $C_{19}H_{21}N_2O_2SCl$: C, 60.55; H, 5.62; N, 7.43; S, 8.51; Cl, 9.41. Found: C, 60.39; H, 5.68; N, 7.39; S, 8.56; Cl, 9.52.

1-(*p*-Tolyl)-4-methyl-3-penten-1-one (43k): bp 115 °C (0.007 mmHg) (colorless oil); ^{1}H NMR (CCl_4, 90 MHz) δ 1.67 (s, 3 H)8, 1.73 (s, 3 H), 2.38 (s, 3 H), 3.51 (d, 2 H, J = 6.6 Hz), 5.37 (br t, 1 H, J = 6.6 Hz), 7.16 (d, 2 H, J = 7.8 Hz), 7.78 (d, 2 H, J = 7.8 Hz).

Anal. Calcd for $C_{13}H_{16}O$: C, 82.93; H, 8.57. Found: C, 82.76; H, 8.43.

1-(*p*-Tolyl)-4-methyl-3-penten-1-one *N*-Tosylhydrazone (44k): mp 116–117.5 °C (colorless needles from ethanol); ^{1}H NMR ($CDCl_3$, 90 MHz) δ 1.75 (br s, 6 H), 2.35 (s, 3 H), 2.40 (s, 3 H), 3.30 (d, 2 H, J = 6.6 Hz), 4.85 (br t, 1 H, J = 6.6 Hz), 7.14 (d, 2 H, J = 8.4 Hz), 7.29 (d, 2 H, J = 8.1 Hz), 7.54 (d, 2 H, J = 8.1 Hz), 7.85 (d, 2 H, J = 8.4 Hz).

Anal. Calcd for $C_{20}H_{24}N_2O_2S$: C, 67.38; H, 6.79; N, 7.86; S, 8.99. Found: C, 67.18; H, 6.85; N, 7.83; S, 8.71.

1-(*p*-Anisyl)-4-methyl-3-penten-1-one (43l): bp 160 °C (Kugelrohr oven temperature) (0.004 mmHg); ^{1}H NMR (CCl_4, 90 MHz) δ 1.68 (s, 3 H), 1.75 (s, 3 H), 3.50 (d, 2 H, J = 7.5 Hz), 3.83 (s, 3 H), 5.37 (br t, 1 H, J = 7.5 Hz), 6.83 (d, 2 H, J = 9.0 Hz), 7.76 (s, 1 H), 7.84 (d, 2 H, J = 9.0 Hz).

Anal. Calcd for $C_{13}H_{16}O_2$: C, 76.44; H, 7.90. Found: C, 76.62; H, 7.78.

1-(*p*-Anisyl)-4-methyl-3-penten-1-one *N*-Tosylhydrazone (44l): mp 107–109 °C (colorless needles from ethanol); ^{1}H NMR ($CDCl_3$, 90 MHz) δ 1.76 (br s, 6 H), 2.41 (s, 3 H), 3.29 (d, 2 H, J = 7.2 Hz), 3.80 (s, 3 H), 4.85 (br t, 1 H, J = 7.2 Hz), 6.86 (d, 2 H, J = 9.0 Hz), 7.07 (m, 1 H), 7.32 (d, 2 H, J = 8.4 Hz), 7.62 (d, 2 H, J = 9.0 Hz), 7.88 (d, 2 H, J = 8.4 Hz).

Anal. Calcd for $C_{20}H_{24}N_2O_3S$: C, 64.49; H, 6.49; N, 7.52; S, 8.61. Found: C, 64.31; H, 6.47; N, 7.48; S, 8.61.

Pyrolysis of the Sodium Salt of (*E*)-1-Phenyl-3-penten-1-one *N*-Tosylhydrazone (44a). The sodium salt of **44a** prepared from **44a** (310 mg, 0.95 mmol) and 40 mg (1.67 mmol) of sodium hydride was heated under reflux for 1 h in 25 mL of dry carbon tetrachloride, and the resulting solution was allowed to stand at room temperature for 1 day and then washed and dried over Na_2SO_4 as described for pyrolysis of the sodium salt of **21a**. Removal of solvent gave 369 mg of a reddish oil, which upon thick-layer chromatography (1:1 *n*-hexane–ether) gave 75 mg (46% yield) of **46a**. The liquid chromatographic analysis (column, Waters Radial Pak A; solvent, ether; flow rate, 2 mL/min, 1,2-dimethoxybenzene as an internal standard) showed that the yield of **46a** was 72%. **46a**: mp 52 °C (colorless prisms from *n*-pentane); IR (KBr) 3050, 1590, 1450, 1340, 750, 685 cm^{-1}; mass spectrum, 25 eV, *m/e* (relative intensity) 173 (M^+ + 1, 1.4), 172 (M^+, 2.6), 144 (30.2), 129 (100); ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.34 (d, 3 H, J = 6 Hz), 1.54 (dd, 1 H, J = 4.2, 6 Hz), 2.70 (ddd, 1 H, J = 3, 4.2, 6 Hz), 3.40 (d, 2 H, J = 20 Hz); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 16.89 (CH_3), 37.90 (C4), 46.71 (C5), 48.82 (C6), 168.27 (C3).

Anal. Calcd for $C_{11}H_{12}N_2$: C, 76.71; H, 7.02; N, 16.27. Found: C, 76.67; H, 7.13; N, 16.40.

Pyrolysis of the Sodium Salt of (*Z*)-1-Phenyl-3-penten-1-one *N*-Tosylhydrazone (44b). The sodium salt of **44b** prepared from 264 mg (0.8 mmol) of **44b** and 20 mg (0.8 mmol) of sodium hydride was similarly decomposed in 69 mL of refluxing carbon tetrachloride. The resulting red solution was washed with water, dried over Na_2SO_4, and then allowed to stand for 4 days at room temperature. Removal of solvent gave 72 mg of a red oil, which included a 1.5:1 mixture of **45b** and **46b**. However, the isolation of **46b** either by using thick-layer chromatography or by crystallization was unsuccessful, because **46b** decomposed on silica gel. The yield of **46b** (51%) was determined by the liquid chromatographic analysis (column, Waters Radial Pak A; solvent, 4:1 ether–tetrahydrofuran; flow rate, 2 mL/min; diphenyldimethylsilane as an internal standard; retention time, diphenyldimethylsilane 1.73 min, **46b**, 8.70 min). In this chromatogram, a very small peak (retention time 3.93 min) which could be assigned to **46a** was detected. The pure sample of **46b** for ^{1}H and ^{13}C NMR spectra was separated by a Waters Semi Prep Porasil column (7.8 mm × 30 cm). Elutions with ether were removed by a rotary pump. The residual colorless oil was covered with nitrogen and quickly diluted with $CDCl_3$, and the spectra were recorded.

46b: ^{1}H NMR (CCl_4, 90 MHz) δ 0.94 (d, 3 H, J = 6.4 Hz), 2.66 (dd, 1 H, J = 6.4, 6.4 Hz), 2.86 (1 H, ddd, J = 2.6, 6.4, 8.4 Hz), 3.08 (dd,

1 H, J = 2.6, 18.4 Hz), 3.32 (dd, 1 H, J = 8.4, 18.4 Hz); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 5.74 (CH_3), 34.28 (C4), 41.68 (C5), 42.24 (C6), 171.13 (C3).

Pyrolyses of the Sodium Salts of 44c–44e and 44i–44l. Pyrolyses of these sodium salts were carried out by the same procedures as those described for **21a**. The spectral properties of the isolated 1,2-diazabicyclo[3.1.0]hex-2-enes were described.

3-Phenyl-6-*endo*-ethyl-6-*exo*-methyl-1,2-diazabicyclo[3.1.0]hex-2-ene (46c): mp 58.5 °C (colorless needles from *n*-hexane–ether, 65% yield); mass spectrum, 25 eV, *m/e* (relative intensity) 200 (M^+, 6.1) 172 (73.8), 157 (87), 143 (100); ^{1}H NMR (CCl_4, 90 MHz) 0.80–1.25 (m, 5 H), 1.28 (s, 3 H), 2.62 (dd, 1 H, J = 3, 9.2 Hz), 3.03 (dd, 1 H, J = 3, 18 Hz), 3.30 (dd, 1 H, J = 9.2, 18 Hz); ^{13}C ($CDCl_3$, 50 MHz) δ 10.48 (CH_3), 18.49 (CH_2), 22.71 (CH_3), 35.09 (C4), 50.59 (C5), 51.07 (C6), 170.49 (C3).

Anal. Calcd for $C_{13}H_{16}N_2$: C, 77.96; H, 8.05; N, 13.99. Found: C, 77.89; H, 8.02; N, 13.87.

3-(*p*-Bromophenyl)-6-*endo*-ethyl-6-*exo*-methyl-1,2-diazabicyclo[3.1.0]hex-2-ene (46d): mp 75–76 °C (colorless needles from *n*-hexane–ether, 70% yield); mass spectrum, 25 eV, *m/e* (relative intensity) 280 (M^+ + 2, 3.1), 278 (M^+, 4.4), 252 (44.2), 250 (44.5), 171 (26.1), 156 (100), 142 (83.3); ^{1}H NMR (CCl_4, 90 MHz) δ 0.8–1.25 (m, 5 H), 1.26 (s, 3 H), 2.47 (dd, 1 H, J = 3.0, 8.7 Hz), 2.85 (dd, 1 H, J = 3.0, 18.0 Hz), 3.24 (dd, 1 H, J = 8.7, 18.0 Hz), 7.3–7.7 (m, 4 H).

Anal. Calcd for $C_{13}H_{15}N_2Br$: C, 55.93; H, 5.38; N, 10.04; Br, 28.65. Found: C, 55.79; H, 5.21; N, 9.97; Br, 28.38.

1-Phenyl-6,6-dimethyl-1,2-diazabicyclo[3.1.0]hex-2-ene (46e): mp 52.5 °C (colorless prisms from *n*-pentane, 59% yield); UV (ethanol) 254 nm (log ϵ 4.14); mass spectrum, 25 eV, *m/e* (relative intensity) 186 (M^+, 4), 158 (23), 143 (100), 128 (62), 115 (33); ^{1}H NMR (CCl_4, 90 MHz) δ 0.92 (3 H), 1.33 (3 H), 2.45 (dd, 1 H, J = 4, 8 Hz), 2.90 (dd, 1 H, J = 4, 18 Hz), 3.10 (dd, 1 H, J = 8, 18 Hz); ^{13}C NMR ($CDCl_3$, 50 MHz) 11.88 (CH_3), 25.87 (CH_3), 35.30 (C4), 47.10 (C6), 50.07 (C5), 171.03 (C3).

Anal. Calcd for $C_{12}H_{14}N_2$: C, 77.38; H, 7.58; N, 15.04. Found: C, 77.29; H, 7.43; N, 14.98.

3-(*p*-Bromophenyl)-6,6-dimethyl-1,2-diazabicyclo[3.1.0]hex-2-ene (46i): mp 76 °C (colorless needles from *n*-hexane–ether, 65% yield); mass spectrum, 25 eV, *m/e* (relative intensity) 266 (M^+ + 2, 2.2), 264 (M, 2.0), 238 (32.3), 236 (42.2), 221 (16.2), 142 (100); ^{1}H NMR (CCl_4, 90 MHz) δ 0.90 (s, 3 H), 1.32 (s, 3 H), 2.47 (dd, 1 H, J = 3.0, 8.2 Hz), 2.85 (dd, 1 H, J = 3.0, 18.0 Hz), 3.25 (dd, 1 H, J = 8.2, 18.0 Hz), 7.46 (m, 4 H).

Anal. Calcd for $C_{12}H_{13}N_2Br$: C, 54.36; H, 4.91; N, 10.57. Found: C, 54.21; H, 4.79; N, 10.34.

3-(*p*-Chlorophenyl)-6,6-dimethyl-1,2-diazabicyclo[3.1.0]hex-2-ene (46j): mp 67 °C (colorless needles from *n*-hexane–ether, 68% yield); mass spectrum, 25 eV, *m/e* (relative intensity) 222 (M^+ + 2, 2.2), 194 (15), 177 (100); ^{1}H NMR (CCl_4, 90 MHz) δ 0.93 (s, 3 H), 1.33 (s, 3 H), 2.47 (dd, 1 H, J = 3.0, 8.1 Hz), 2.85 (dd, 1 H, J = 3.0, 18.0 Hz), 3.21 (dd, 1 H, J = 8.1, 18.0 Hz), 7.31 (d, 2 H, J = 8.7 Hz), 7.64 (d, 2 H, J = 8.7 Hz).

Anal. Calcd for $C_{12}H_{13}N_2Cl$: C, 65.31; H, 5.90; N, 12.70. Found: C, 65.22; H, 5.77; N, 12.56.

3-(*p*-Tolyl)-6,6-dimethyl-1,2-diazabicyclo[3.1.0]hex-2-ene (46k): 63.5 °C (pale yellow prisms from *n*-hexane–ether, 60% yield); mass spectrum, 25 eV, *m/e* (relative intensity) 200 (M^+, 3.0), 172 (28), 157 (100); ^{1}H NMR (CCl_4, 90 MHz) δ 0.90 (s, 3 H), 1.29 (s, 3 H), 2.35 (s, 3 H), 2.47 (dd, 1 H, J = 3.0, 8.2 Hz), 2.85 (dd, 1 H, J = 3.0, 18.0 Hz), 3.19 (dd, 1 H, J = 8.2, 18.0 Hz), 7.08 (d, 2 H, J = 8.1 Hz), 7.54 (d, 2 H, J = 8.1 Hz).

Anal. Calcd for $C_{13}H_{16}N_2$: C, 77.96; H, 8.05; N, 13.99. Found: C, 78.06; H, 8.11; N, 13.78.

3-(*p*-Anisyl)-6,6-dimethyl-1,2-diazabicyclo[3.1.0]hex-2-ene (46l): mp 102 °C (pale yellow needles from *n*-pentane–ether, 62% yield); mass spectrum, 25 eV, *m/e* (relative intensity) 216 (M^+, 3.2), 188 (12), 173 (100); ^{1}H NMR (CCl_4, 90 MHz) δ 0.91 (s, 3 H), 1.30 (s, 3 H), 2.41 (dd, 1 H, J = 3.0, 8.2 Hz), 2.82 (dd, 1 H, J = 3.0, 18.0 Hz), 3.19 (dd, 1 H, J = 8.2, 18.0 Hz), 3.79 (s, 3 H), 6.79 (d, 2 H, J = 8.7 Hz), 7.59 (d, 2 H, J = 8.7 Hz).

Anal. Calcd for $C_{13}H_{16}N_2O$: C, 72.19; H, 7.46; N, 12.95. Found: C, 72.30; H, 7.33; N, 12.88.

Pyrolysis of the Sodium Salt of 1-(*p*-Nitrophenyl)-4-methyl-3-penten-1-one (44f). The sodium salt of **44f** prepared from 480 mg (1.24 mmol) of **44f** and 35.8 mg (1.49 mmol) of sodium hydride was heated under reflux for 2 h in 90 mL of carbon tetrachloride. The mixture was washed with water, and the resulting orange-colored solution was dried over Na_2SO_4 and then allowed to stand at −25 °C. When the solution turned to yellow, it was frozen with dry ice. Carbon tetrachloride was removed at −40 to 50 °C (0.01 mmHg), with use of a liquid nitrogen trap. When about 70% of the carbon tetrachloride was removed, carbon tetrachloride was thawed at −30 °C, and the resulting yellow crystals were filtered. The filtrate was refrozen and concentrated. This procedure was repeated 3 times to afford 261 mg (91% yield) of yellow crystals. Recrystallization from methylene chloride–*n*-pentane at −30 °C gave 3-(*p*-nitrophenyl)-6,6-dimethyl-1,2-diazabicyclo[3.1.0]hex-2-ene (**46f**) as orange-yellow needles: mp 98 °C; IR (KBr) 3100, 2960, 2040 (very weak), 1608, 1596, 1571, 1510, 1348, 1318, 1222, 1104, 924, 858, 848 cm^{-1}; IR (CCl_4) 3100, 2040 (very strong), 1600, 1510, 1340, 1260 cm^{-1}; mass spectrum, 12 eV, *m/e* (relative intensity) 231 (M^+, 1.7), 203 (100), 156 (23); ^{1}H NMR (CCl_4, 90 MHz) δ 0.92 (s, 3 H), 1.37 (s, 3 H), 2.58 (dd, 1 H, J = 3.0, 9.0 Hz), 2.96 (dd, 1 H, J = 3.0, 18.0 Hz), 3.30 (dd, 1 H, J = 9.0, 18.0 Hz), 7.84 (d, 2 H, J = 9.0 Hz), 8.20 (d, 2 H, J = 9.0 Hz).

Anal. Calcd for $C_{12}H_{13}O_2N_3$: C, 62.32; H, 5.67; N, 18.17. Found: C, 62.19; H, 5.48; N, 18.22.

Pyrolyses of the Sodium Salts of 1-(*m*-Nitrophenyl)-4-methyl-3-penten-1-one and 1-(*p*-Cyanophenyl)-4-methyl-3-penten-1-one *N*-Tosylhydrazones 44g and 44h. Pyrolyses of these tosylhydrazones were carried out essentially by the same procedures as described for that of **44f**.

3-(*m*-Nitrophenyl)-6,6-dimethyl-1,2-diazabicyclo[3.1.0]hex-2-ene (46g): mp 90 °C (yellow needles from methylene chloride–*n*-pentane, 61% yield); mass spectrum, 25 eV, *m/e* (relative intensity) 231 (M^+, 5.6), 203 (100), 156 (64.6); ^{1}H NMR (CCl_4, 90 MHz) δ 0.64 (s, 3 H), 1.04 (s, 3 H), 2.23 (dd, 1 H, J = 3.6, 8.7 Hz), 2.65 (dd, 1 H, J = 3.6, 18.6 Hz), 3.02 (dd, 1 H, J = 8.7, 18.6 Hz), 7.11 (m, 1 H), 7.86 (m, 3 H).

Anal. Calcd for $C_{12}H_{13}O_2N_3$: C, 62.32; H, 5.67; N, 18.17. Found: C, 62.48; H, 5.76; N, 18.22.

3-(*p*-Cyanophenyl)-6,6-dimethyl-1,2-diazabicyclo[3.1.0]hex-2-ene (46h): mp 78.5 °C (yellow needles from ether–*n*-pentane, 61% yield); mass spectrum, 25 eV, *m/e* (relative intensity), 211 (M^+, 2.4), 183 (57.3), 168 (100); ^{1}H NMR (CCl_4, 90 MHz) δ 0.93 (s, 3 H), 1.37 (s, 3 H), 2.57 (dd, 1 H, J = 3.0, 8.4 Hz), 2.92 (dd, 1 H, J = 3.0, 18.0 Hz), 3.26 (dd, 1 H, J = 8.4, 18.0 Hz), 7.63 (d, 2 H, J = 9.0 Hz), 7.85 (d, 2 H, J = 9.0 Hz).

Anal. Calcd for $C_{13}H_{13}N_3$: C, 73.90; H, 6.20; N, 19.89. Found: C, 73.79; H, 6.11; N, 19.92.

Rate Analyses of the Reversible 1,1-Cycloaddition Reactions between 3-Aryl-6,6-dimethyl-1,2-diazabicyclo[3.1.0]hex-2-enes 46 and 1-Diazo-1-aryl-4-methyl-3-pentenes 45. A NMR tube containing a solution of 15

Table IV. The Observed Rate and Equilibrium Constants for the Reversible 1,1-Cycloaddition of **45e–46e** and **45f–46f** in Four Solvents

solvent	substitnt	temp, °C	$10^3(k_1 + k_2)$, s^{-1}	K
CCl_4	*p*-NO_2	20.0	1.40	1.91
		22.5	1.57	2.08
		29.0	3.03	2.30
		34.0	4.02	2.70
		73.0		6.44
	H	46.5	1.54	0.24
		49.5	1.71	0.25
		52.0	2.22	0.29
		55.0	2.90	0.32
		62.5		0.38
C_6D_6	*p*-NO_2	39.5	4.44	1.94
		40.8	4.85	2.02
		46.0	7.58	2.35
		52.0	12.0	2.75
	H	37.0	0.61	0.12
		46.6	1.79	0.14
		51.9	2.72	0.17
		57.3	5.29	0.19
CD_2Cl_2	*p*-NO_2	36.2	3.14	0.63
		42.3	5.25	0.75
		48.6	8.75	0.92
		50.2	9.22	0.99
	H	46.6	3.18	0.05
		51.8	4.15	0.06
		56.5	4.95	0.07
		60.2	5.14	0.07
CD_3CN	*p*-NO_2	32.0	3.01	0.35
		39.0	5.15	0.43
		40.0	5.32	0.44
		45.6		0.50
	H	46.6	3.14	0.03
		52.5	4.45	0.04
		57.3	5.78	0.05
		60.5	7.63	0.06

mg of **46** in 0.5 mL of solvent (carbon tetrachloride, benzene-d_6, methylene-d_2 chloride, or acetonitrile-d_3) was connected to a vacuum line, degassed by repeating 3 freeze(−196 °C)–pump(10^{-4}–10^{-5} torr)–thaw(0 °C) cycles, and then sealed at 10^{-4}–10^{-5} torr. The NMR tube was placed into a preheated Varian EM-390 90-MHz NMR probe whose temperature was controlled by an EM-3940 Variable Temperature Controller. The concentrations of **45** and **46** were obtained by integrations of methyl signals of **46** and methyl signals of **45** appearing at around 1.9 ppm, and an equilibrium constant was obtained when the ratio of **45** and **46** became constant. The temperature of a probe was calibrated twice before and the ends of the measurements by the standard ethylene glycol or methanol sample. During heating under the conditions employed for rate analyses, any significant side reaction did not take place. The first-order rate constants, k_1 (the retro-1,1-cycloaddition) and k_2 (the 1,1-cycloaddition), were obtained by least-squares treatments of $1/T$ vs. ln $[(KA - B)/(KA_0 - B_0)]$ (A_0 and B_0 are initial concentrations of **45** and **46**, respectively) plots and the equilibrium constant ($K = k_1/k_2$). The first-order rate and equilibrium constants were measured over temperature ranges as follow; for instance in carbon tetrachloride, 20–73 °C for *p*-NO_2, 20.5–48 °C for *p*-CN, 32.8–62.5 °C for *m*-NO_2, 50–76 °C for *p*-Br, 42–62 °C for *p*-Cl, 41.5–62.5 °C for H, 48–67 °C for *p*-CH_3, and 60–71 °C for *p*-OCH_3. The first-order rate and equilibrium constants at 50 °C shown in Tables I and III were the extrapolated values from the linear log k and log K vs. $1/T$ plots. As typical examples, the observed rate and equilibrium constants for the reversible 1,1-cycloaddition of **45e–46e** and **45f–46f** were shown in Table IV.

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Registry No. 5a, 120-92-3; **6a**, 3197-76-0; **6b**, 5326-50-1; **6c**, 95019-29-7; **7a**, 100188-61-2; **7b**, 1017-23-8; **7c**, 6465-15-2; **8a**, 100188-60-1; **8a**·Na, 73594-32-8; **8b**, 73594-33-9; **8b**·Na, 100188-62-3; **8c**, 73594-34-0; **8c**·Na, 100188-63-4; **10a**, 73594-35-1; **10b**, 73594-36-2; **10c**, 73594-37-3; **11**, 100188-64-5; **12**, 100188-65-6; **13**, 73594-41-9; **13**·Na, 100188-72-5; **14**, 100188-73-6; **15**, 73594-38-4; **16**, 100188-74-7; **17**, 100188-75-8; **18**, 73594-39-5; **18**·Na, 100188-76-9; **19**, 73599-36-7; **20**, 73594-40-8; **21a**, 74457-33-3; **21a**·Na, 74457-34-4; **21b**, 100188-77-0; **21b**·Na, 100189-15-9; **21c**, 100188-78-1; **21c**·Na, 100188-83-8; **21d**, 100188-79-2; **21d**·Na, 100188-84-9; **22b**, 87013-62-5; **23a**, 74457-37-7; **25c**, 87013-65-8; **25d**, 87039-24-5; **26d**, 100188-85-0; **27b**, 100188-80-5; **27d**, 100188-86-1; **28a**, 3420-52-8; **28b**, 28069-36-5; **28c**, 28069-37-6; **28d**, 28069-38-7; **29a**, 90466-88-9; **29a**·Na, 100188-81-6; **29b**, 90466-89-0; **29b**·Na, 100188-82-7; **30a**, 90466-91-4; **30b**, 90466-92-5; **31a**, 90466-94-7; **31b**, 90466-95-8; **32a**, 90466-96-9; **32b**, 3240-29-7; **43a**, 74157-93-0; **43b**, 61752-45-2; **43c**, 100188-87-2; **43d**, 100188-89-4; **43e**, 36597-09-8; **43f**, 100188-91-8; **43g**, 100188-93-0; **43h**, 100188-95-2; **43i**, 100188-97-4; **43j**, 62045-83-4; **43k**, 88299-58-5; **43l**, 73172-57-3; **44a**, 77764-70-6; **44a**·Na, 76620-26-3; **44b**, 77764-70-6; **44b**·Na, 76620-26-3; **44c**, 100188-88-3; **44c**·Na, 100189-02-4; **44d**, 100188-90-7; **44d**·Na, 100189-03-5; **44e**, 76620-32-1; **44e**·Na, 84066-53-5; **44f**, 100188-92-9; **44f**·Na, 100189-10-4; **44g**, 100188-94-1; **44g**·Na, 100189-11-5; **44h**, 100188-96-3; **44h**·Na, 100189-12-6; **44i**, 100188-98-5; **44i**·Na, 100189-04-6; **44j**, 100188-99-6; **44j**·Na, 100189-05-7; **44k**, 100189-00-2; **44k**·Na, 100189-06-8; **44l**, 100189-01-3; **44l**·Na, 100189-07-9; **45b**, 76620-29-6; **46a**, 76633-73-3; **46b**, 76620-30-9; **46c**, 100189-08-0; **46d**, 100189-09-1; **46e**, 76620-31-0; **46f**, 87013-66-9; **46g**, 100189-13-7; **46h**, 100189-14-8; **46i**, 87013-67-0; **46j**, 87013-68-1; **46k**, 87013-69-2; **46l**, 87013-70-5; **47**, 4885-09-0; **48**, 76620-28-5; $BrCH_2CO_2CH_2CH_3$, 105-36-2; $H_3CO_2CCH{=}CHCO_2CH_3$, 624-49-7; $C_6H_5CH(OH)COC_6H_5$, 579-44-2; 1-(carbethoxymethyl)-cyclopentene, 57647-92-4; (carbethoxymethylene)cyclopentane, 1903-22-6; (cyclopenten-1-yl)acetic acid, 21622-08-2; 1-(carbethoxymethyl)-cyclohexene, 4709-59-5; 1-(carbethoxymethyl)cycloheptene, 92599-53-6; (carbethoxymethylene)cycloheptane, 1903-23-7; (cyclohepten-1-yl)acetic acid, 18294-87-6; (cyclohexen-1-yl)acetic acid, 73961-73-6; α-tetralone, 529-34-0; 1-(carbethoxymethyl)-1-hydroxy-1,2,3,4-tetrahydronaphthalene, 91111-41-0; 4-(carbethoxymethyl)-1,2-dihydronaphthalene, 54125-45-0; 4-(carbethoxymethylene)-1,2,3,4-tetrahydronaphthalene, 62677-71-8; (1,2-benzo-1,3-cyclohexadien-3-yl)acetic acid, 4709-55-1; α-(1,2-benzo-1,3-cyclohexadien-3-yl)acetophenone, 100188-66-7; β-(ethoxycarbonyl)tetralone, 6742-26-3; 1-hydroxy-2-(ethoxycarbonyl)-1,2,3,4-tetrahydronaphthalene, 100188-67-8; 3-(ethoxycarbonyl)-1,2-dihydronaphthalene, 100046-58-0; 3-(hydroxymethyl)-1,2-dihydronaphthalene, 100046-59-1; 3-(bromomethyl)-1,2-dihydronaphthalene, 100188-68-9; 3-(1,2-benzo-1,3-cyclohexadien-4-yl)-2-hydroxy-1,2-diphenylpropan-1-one, 100188-69-0; 3-(1,2-benzo-1,3-cyclohexadien-4-yl)-1,2-dihydroxy-1,2-diphenylpropane, 100188-70-3; α-(1,2-benzo-1,3-cyclohexadien-4-yl)acetophenone, 100188-71-4.

Metal Ion Catalysis of Amide Hydrolysis

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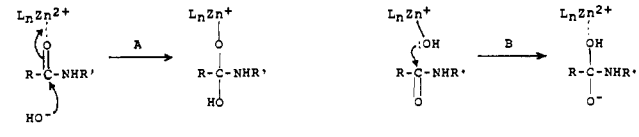
Abstract: Hydrolysis of amides at neutral pH is known to proceed with rate-limiting breakdown of the tetrahedral intermediate (TI). A hypothesis is presented which rationalizes the catalytic effect of metal ions in terms of an acceleration of this step. Coordination of a metal ion to an alkoxide oxygen of the TI greatly diminishes the basicity of the alkoxide oxygen without substantially decreasing its nucleophilicity, resulting in an overall facilitation of expulsion of the leaving nitrogen. General acid catalysis of C–N cleavage by metal-bound water may also be important in certain cases. If TI breakdown is facilitated to such an extent that TI formation becomes partly or wholly rate-limiting, then an additional catalytic benefit of the metal ion in terms of carbonyl activation or metal-hydroxide participation may be realized.

Although the detailed three-dimensional structure of carboxypeptidase A (CPA) has been known for 18 years, the mechanism of peptide bond hydrolysis and the role of the active site zinc remain to this day an open question.[1] Much current research has aimed at distinguishing between two kinetically equivalent pathways leading to the tetrahedral intermediate (TI): (1) the electrophilic activation of the carbonyl moiety by zinc (Scheme IA) and (2) provision of a better nucleophile (Zn–OH mechanism,

Scheme I



Scheme II

Scheme IB). However, this distinction may be academic in view of the substantial evidence which has been accrued indicating that

(1) Rees, D. C.; Lewis, M.; Lipscomb, W. N. *J. Mol. Biol.* **1983**, *168*, 367. Lipscomb, W. N. *Proc. Natl. Acad. Sci. U.S.A.* **1980**, *77*, 3875. Lipscomb, W. N.; Hartsuck, J. A.; Reeke, G. N., Jr.; Quiocho, F. A.; Bethge, P. H.; Ludwig, M. L.; Steitz, T. A.; Muirhead, H.; Coppola, J. C. *Brookhaven Symp. Biol.* **1968**, *21*, 24.

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