syntheses of polyazetidines, polyamines, and polyamino ethers and the mechanisms of these reactions are actively underway.

Registry No. **1a**, 64468-52-6; **1b**, 86863-57-2; **1c**, 86863-58-3; **1d**, 75957-95-8; **1e**, 75958-03-1; **1f**, 86863-61-8; **1g**, 86863-62-9; **1h**, 86863-63-0; **1i**, 86940-70-7; **1j**, 86863-64-1; **1l**, 86863-65-2; **2a**, 86863-66-3; **2c**, 86863-59-4; **2d**, 86863-60-7; **2e**, 86863-67-4; **2f**, 86863-68-5; **2g**, 86863-69-6; **2h**, 86863-70-9; **2i**, 86940-71-8; **2j**, 86863-71-0; **2l**, 86863-72-1; **3a**, 86863-73-2; **3b**, 86863-74-3; **3c**, 86863-75-4; **3d**, 86863-76-5; **4a**, 16311-94-7; **4b**, 16312-06-4; **4c**, 86863-77-6; **4d**, 82166-23-2; **4e**, 86863-78-7; **5a**, 86863-79-8; **5b**, 86863-80-1; **5c**, 86863-81-2; Ac-**5c**, 86863-87-8; **5d**, 86863-82-3; Ac-**5d**, 86863-88-9; **5e**, 86863-83-4; **6g**, 50411-26-2; **6h**, 86863-84-5; Ac-**7c**, 86863-85-6; Ac-**7d**, 86863-86-7; **7e**, 31595-02-5; DiBAL-H, 1191-15-7; AlH_2Cl, 14644-71-4; $AlHCl_2$, 13497-97-7.

Intramolecular 1,1-Cycloaddition Reaction of Allyldiazomethane: Electrophilic Nature of the Terminal Nitrogen of Diazomethane and Geometrical Requirement[1]

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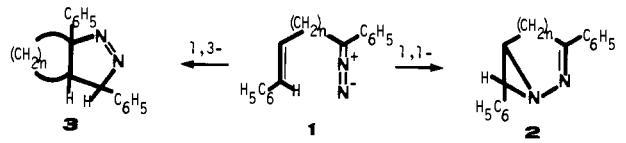
Received April 6, 1983

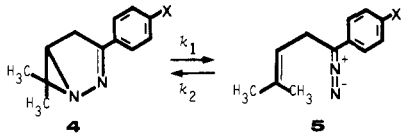
We previously reported that allyldiazomethanes undergo a formal nitrene-type 1,1-cycloaddition reaction to give 1,2-diazabicyclo[3.1.0]hex-2-enes,[2] which occurs reversibly with retention of configuration.[3] It was also of interest to know whether this novel cycloaddition is limited to allyldiazomethanes. We have now compared the reactivities of the homologous diazomethanes **1b** ($n = 2$), **1c** ($n = 3$), and **1d** ($n = 4$) to that of **1a** ($n = 1$), which is known to afford the 1,1-cycloadduct **2a** ($n = 1$) (Scheme I).[3] It was found that **1b**, **1c**, and **1d** do not undergo the 1,1-cycloaddition to give **2b** ($n = 2$), **2c** ($n = 3$), and **2d** ($n = 4$) but undergo 1,3-dipolar cycloadditions giving **3c** ($n = 3$)[4] and **3d** ($n = 4$)[5] from **1c** and **1d**, respectively.[6] This indicates that the 1,1-cycloaddition can compete with the 1,3-dipolar cycloaddition only when the HOMO(dizomethane)-LUMO(olefin) controlled parallel-plane approach required for the 1,3-dipolar cycloaddition becomes geometrically unfavorable, especially in allyldiazomethane. Therefore, the 1,1-cycloaddition reaction of allyldiazomethane is a suitable model to investigate the latent nature of the terminal nitrogen of diazomethane, which is responsible for the 1,1-cycloaddition. Herein we report results obtained from the rate analyses on the reversible 1,1-cycloaddition between 1,2-diazabicyclo[3.1.0]hex-2-enes **4** and allyldiazomethanes **5**, which prove the electrophilic nature of the terminal nitrogen of diazomethane in contrast with the nucleophilic nature[7] of diazomethane as a 1,3-dipole (Scheme II).

Scheme I



a: n=1; b: n=2; c: n=3; d: n=4

Scheme II



a: $X=NO_2$; b: X=Br; c: X=Cl
d: X=H; e: $X=CH_3$; f: $X=OCH_3$

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

substituent	10^3k_1, s^{-1}	10^3k_2, s^{-1}	K^b	ΔG,[c] kcal/mol
NO_2	10.71	2.88	3.71	−0.84
Br	0.59	1.89	0.32	0.75
Cl	0.49	1.80	0.28	0.84
H	0.40	1.49	0.26	0.86
CH_3	0.18	1.23	0.16	1.22
OCH_3	0.06[a]	1.16[a]	0.05	1.92

[a] Estimated from $\log k_2^X/k_2^H = 0.38\sigma_p$ ($r = 0.996$) and $K^{OCH_3} = 0.05$. [b] Obtained by $\log K$ vs. $1/T$ plots. [c] Calculated from equilibrium constants at 50 °C.

The 1,2-diazabicyclo[3.1.0]hex-2-ene derivatives **4a-f**[8] were synthesized in good yields by the same procedure[3] we reported previously. In particular, the *p*-nitro derivative **4a** was quantitatively isolated by freeze-dry evaporation of carbon tetrachloride at −30 °C after decomposition followed by cooling at −20 °C for 3 days. The rate analyses were performed by monitoring the disappearance of **4b-e** and the appearance of **5b-e** while heating a degassed sealed tube containing a carbon tetrachloride solution of **4** in the preheated 90-MHz NMR probe and vice versa for the *p*-nitro derivatives **4a** and **5a**.[10] The equlibrium constants (K) were measured at temperature ranges between 20 and 75 °C for **4a**, 42 and 76 °C for **4b**, 45 and 65 °C for **4c**, 45 and 75 °C for **4d**, 50 and 80 °C for **4e**, and 60 and 85 °C for **4f**. In all cases

(1) Organic Thermal Reaction. 56. Part 55, see: Satake, K.; Kumagai, T.; Mukai, T., *Chem. Lett.* **1983**, 743.

(2) Nishizawa, Y.; Miyashi, T.; Mukai, T. *J. Am. Chem. Soc.* **1980**, *102*, 1176.

(3) Miyashi, T.; Fujii, Y.; Nishizawa, Y.; Mukai, T. *J. Am. Chem. Soc.* ***103***, 725. see also: Padawa, A.; Ku, H. *Tetrahedron Lett.* **1980**, 1009. Padawa, A.; Rodriguez, A. *Ibid.* **1981**, 187.

(4) **3c**: mp 54.5 °C (dec 105 °C); *m/e* 262 (M^+, 3%), 234 (100%); UV λ_{max} (cyclohexane) 254 (ε 440), 260 (ε 480), 265.5 (ε 300), 333 (ε 230) nm; ^1H NMR ($CDCl_3$), δ 0.85–1.53 (1 H, m), 1.60–2.25 (4 H, m), 2.50–2.85 (2 H, m), 5.35 (1 H, d, $J = 4.0$ Hz), 6.85–7.09 (2 H, 7), 7.10–7.53 (8 H, m).

(5) **3d**: mp 119 °C; *m/e* 276 (M^+, 4.5%), 248 (100%); UV λ_{max} (cyclohexane) 254 (ε 740), 259 (ε 630), 265 (ε 390), 340 (ε 230) nm; ^1H NMR ($CDCl_3$) δ 1.10–2.24 (8 H, m), 2.35–2.56 (1 H, m), 5.16 (1 H, d, $J = 11.5$ Hz), 7.08–7.60 (8 H, m), 7.62–7.90 (2 H, m).

(6) Padwa and Fukunaga reported that **1b** undergoes complex reactions upon heating in benzene.[11] We found that **1b** is very stable even under refluxing in CCl_4 and did not change for more than 2 months at ambient temperatures when kept under N_2 atmosphere. Chemical behavior of **1b** will be separately reported soon.

(7) Huisgen, R.; Geittner, J. *Heterocycles* **1978**, *11*, 105.

(8) **4a**: mp 98 °C dec; ^1H NMR (CCl_4) 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); *m/e* 231 (M^+, 1.7%), 203 (100%), 156 (23%). **4b**: mp 76 °C; ^1H NMR (CCl_4) 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); *m/e* 266 ($M^+ + 2$, 2.2%), 264 (M^+, 2.0%), 238 (32.3%), 236 (42.2%), 221 (16.2%), 142 (100%). **4c**: mp 67 °C; ^1H NMR (CCl_4) δ 0.93 (s, 3 H), 1.3[illegible] (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); *m/e* 222 ($M^+ + 2$, 1.8%), 194 (15%), 177 (100%). **4d**: see ref 3. **4e**: mp 63.5 °C; ^1H NMR (CCl_4) 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); *m/e* 200 (M^+, 3.0 %), 172 (28%), 157 (100%). **4f**: mp 102 °C; ^1H NMR (CCl_4) 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); *m/e* 216 (M^+, 3.2%) 188 (12%), 173 (100%). The precursors tosylhydrazones were prepared from the corresponding ketones, which were synthesized according to the procedures reported by Steglich.[9]

(9) Engel, S.; Borries, K.; Steglich, W. *Angew. Chem., Int. Ed. Engl.* **1977**, *16*, 394.

(10) Rate constants $k_1^{NO_2}$ and $k_2^{NO_2}$ were measured by monitoring the disappearance of **5a** and the appearance of **4a** using a mixture containing ca. 80% of **5a** and 20% of **4a**, which was prepared by heating a carbon tetrachloride solution of **4a** at 72 °C for 10 min in a degassed sealed NMR tube. The rate constants $k_1^{OCH_3}$ and $k_2^{OCH_3}$ could not be accurately measured because of a low conversion of **4f** to **5f** and were estimated from $\log k_2^X/k_2^H = 0.38\sigma_p$ ($r = 0.996$, X = NO_2, Br, Cl, H, and CH_3) and $K = 0.05$.

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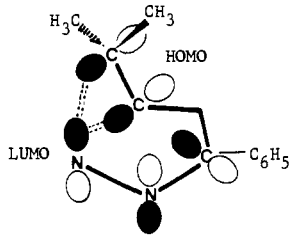

Figure 1.

satisfactory linear log K vs. $1/T$ plots were obtained. The calculated equlibrium constants at 50 °C were listed in Table I, from which the Hammett relation, log $K^X/K^H = 1.12\sigma_p^+$ ($r = 0.975$), was derived. The magnitude of the equlibrium constant increases as the electron-withdrawing nature of the substituent increases. This coincides with the difference in the calculated free energy change (ΔG) for the six derivatives and implies that the more electron-withdrawing substituent destabilizes **4** but stabilizes **5**. Thus, when **4a** was dissolved in carbon tetrachloride, yellow orange color due to **5a** spontaneously developed and a mixture containing 31% of **4a** and 69% of **5a** was obtained even at 25 °C. In contrast, **4f** was stable at 25 °C. Destablization of **4** and stabilization of **5** by the more electron-withdrawing group reflects on the rate acceleration of the retro-1,1-cycloaddition by the more electron-withdrawing substituent as shown in the table. The same substituent effect on the first-order rate constants was also observed in the 1,1-cycloaddition, but the rate acceleration by a strong electron-withdrawing group such as the nitro group is not significant as compared with that of the retro-1,1-cycloaddition as the Hammett relation, log $k_2^X/k_2^H = 0.38\ \sigma_p$ ($r = 0.996$), shows. The observed rate acceleration of the 1,1-cycloaddition by the more electron-withdrawing substituent contradicts the conclusion reached by Padwa and Fukunaga that allyldiazomethane substituted with an electron-withdrawing group cannot be expected to undergo 1,1-cycloaddition.[11] Their conclusion unfortunately was based on a single experimental result that prolonged heating of *trans*-1-phenyl-4-(*p*-nitrophenyl)-4-diazobut-1-ene did not afford any clear product but not on a rate analysis based on the reverisibility of this reaction.

It should be noted that the substituent effect on the rate of the 1,1-cycloaddition is opposite to that of the intermolecular 1,3-dipolar cycloaddition of the substituted phenyldiazomethanes with dipolarophile[7] but resembles that of the amino-nitrene 1,1-cycloaddition to the C=C double bonds.[12] This observation indicates the electrophilic nature of the terminal nitrogen of diazomethane and provides an intriguing mechanistic rationale for the 1,1-cycloaddition reaction of allyldiazomethane. 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 1, the highest stabilization should be gained by interaction between the LUMO(diazomethane)[13] and the HOMO(olefin). This interaction is strongly reinforced by the cyclic geometry which prevents the HOMO(diazomethane)-LUMO(olefin) controlled parallel-plane approach.[14] Thus, the substituent effect on the rate of the 1,1-cycloaddition reaction of allyldiazomethane is a result of the change of the electrophilic LUMO energy level of diazomethane.[15] Further mechanistic investigations of the intramolecular 1,1-cycloaddition reaction of diazoalkenes are in progress and will be soon reported elsewhere.

Registry No. (*E*)-**1b**, 87013-62-5; (*E*)-**1c**, 87013-63-6; (*E*)-**1d**, 87013-64-7; **3c**, 87013-65-8; **3d**, 87039-24-5; **4a**, 87013-66-9; **4b**, 87013-67-0; **4c**, 87013-68-1; **4d**, 76620-31-0; **4e**, 87013-69-2; **4f**, 87013-70-5; **5a**, 87013-71-6; **5b**, 87013-72-7; **5c**, 87013-73-8; **5d**, 76620-33-2; **5e**, 87013-74-9; **5f**, 87013-75-0.

(11) Padwa, A.; Rodriguez, A.; Tohidi, M.; Fukunaga, T. *J. Am. Chem. Soc.* **1983**, *105*, 933.
(12) Schroppel, F., Sauer, J. *Tetrahedron Lett.* **1974**, 2945.
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Stereospecificity in the Biosynthesis of Phytosterol Side Chains: ^{13}C NMR Signal Assignments of C-26 and C-27

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Received April 15, 1983

The biosynthetic mechanism of phytosterol side-chain formation has been postulated to include transalkylation at C-24 from the methyl group of methionine (Scheme I).[1,2] The hydrogen migration from C-24 to C-25 was demonstrated to be stereospecific by examining isofucosterol (**3**-I). Thus, the *pro-R* methyl group (C-26) in **3**-I originates from the *E* methyl group in lanosterol (**1**).[3] Double-bond migration (**3** → **4** or **5**) followed by reduction was suggested to produce sitosterol.[2,4] From the stereochemical viewpoint, each migration and hydrogenation reaction occurs in two ways, leading to opposite configurations at C-25 (**6** or **7**). Recently, we demonstrated that the sitosterol side chain (**6**) is formed stereospecifically from [1,2-^{13}C]acetate, although ^{13}C NMR signals of C-26 and C-27 (*pro-R* and *pro-S* methyl group at C-25, respectively) could not be unambiguously assigned.[5]

Here we report the assignments of these signals and the biosynthetic stereospecificity of phytosterol side chains. We established cell cultures of *Physalis peruviana* from which isofucosterol as well as 24-methylenecholesterol, sitosterol, and stigmasterol, but not withanolide,[6] were isolated. [1,2-^{13}C]Acetate was incorporated into the sterols, which were isolated as their acetates.

Of the ^{13}C-labeling patterns of the phytosterols obtained from [1,2-^{13}C]acetate, the singlet at δ 20.93 and the doublet at δ 21.01 of [^{13}C]isofucosteryl acetate (**3**-II) can be assigned to C-26 and C-27, respectively, according to Nicotra et al.[3]

On catalytic deuteration, **3**-II was converted into an acetate mixture of [^{13}C,24,28-^{2}H]sitosterol (**10**-I) and [^{13}C,24,28-^{2}H]-clionasterol (**11**-I) (M^+ of **10**-II and **11**-II, m/z 456:457:458 = 6:7:5). As no signals arisen from 25-^{2}H could be observed, the labeling patterns of C-26 and C-27 should be almost the same as those of **3**-II.

To analyze the labeling patterns of the methyl groups at C-25 in the mixture, we applied the "INADEQUATE" pulse sequence, which was originally proposed for observing naturally abundant ^{13}C-^{13}C couplings.[8] ^{13}C-^{13}C coupled signals due to doubly enriched carbons from [1,2-^{13}C]acetate were observed selectively. Carbon-13 NMR spectral analysis of the **10**-II and **11**-II mixture was done at 50.309 MHz with a Varian XL-200 NMR spectrometer. The sample was dissolved in [^{2}H]chloroform (40.7 mg in 0.5 mL) in a 10-mm spherical cell. The "INADEQUATE" pulse sequence was optimized for $^{1}J_{CC} = 37$ Hz {$\tau = 1/(4J)$}: 32K data points were acquired with a frequency range of 3200 Hz giving a digital resolution of 0.2 Hz/point. To suppress the single ^{13}C signals, an optimal 90° pulse was set for the sample and steady-state condition was employed before data accumulation (number of transients, 29K). Results are shown in Figure 1,[9] and

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(9) See text and ref 10 for ^{13}C NMR measurement conditions. Exponential resolution enhancement and Gaussian apodization were applied.

0002-7863/83/1505-6343$01.50/0