NOVEL CONDENSATION REACTIONS OF *N*-CYCLOHEPTATRIENYLIDENE ALKYLAMINE *N*-OXIDES WITH ACETYLENE DERIVATIVES: FACILE FORMATION OF 1-AZAAZULEN-2(1*H*)-ONES

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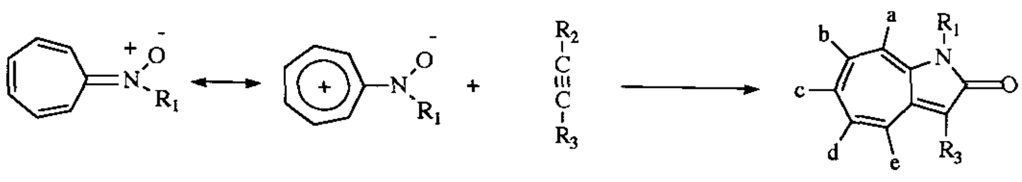
Abstract —Reactions of *N*-cycloheptatrienylidene alkylamine *N*-oxide with acetylene derivatives having electron attracting groups afforded 1-azaazulen-2(1*H*)-one derivatives through a unique condensation process leaving methyl formate or hydrogen.

N-Cycloheptatrienylidene alkylamine *N*-oxides (1), one of fulvenoid dipoles,[1] are considered to draw electrons away from the seven-membered ring moiety toward the *N*-oxide part, resulting in a zwitter ionic form (1'). The lower chemical shifts of C_1 of 1 (1a: 145.6 ppm, 1b: 144.6 ppm)[2] compared with that (135.0 ppm) of *C*-phenyl-*N*-methylnitrone[3] in ^{13}C nmr spectra indicated an existence of a contribution of 1'. It is known that 1 has a bifunctional reactivity, i. e., 1 reacted as nitrones with dipolarophiles such as isocyanates and isothiocyanates[1b] and behaved as cycloheptatrienes in the reaction with *N*-phenyl-1,3,4-triazoline-2,5-dione.[1a]

As a series of the cycloaddition reactions of troponoid compounds,[4] we investigated the reaction of *N*-cycloheptatrienylidene alkylamine *N*-oxides with acetylene derivatives in order to clarify whether the amine *N*-oxides behave as nitrones or as cycloheptatrienes in this reaction. Here the results will be reported.

Reaction of *N*-cycloheptatrienylidene methylamine *N*-oxide (1a) with dimethyl acetylenedicarboxylate (2a) at 80°C for 15 min afforded 1-methyl-3-methoxycarbonyl-1-azaazulen-2(1*H*)-one (3a) in 74% yield.[5] Analogous reaction using *N*-cycloheptatrienylidene ethylamine *N*-oxide (1b) with 2a also gave the corresponding 1-azaazulen-2(1*H*)-one derivative (3b) in 55% yield. The reactions of 1 with ethyl propiolate (2b) under the same reaction conditions gave the corresponding products (3c and 3d) in 38 and 21% yields, respectively.[6] While the reactions using phenylacetylene (2c) and diphenylacetylene (2d) afforded no product except the recovery of acetylene derivatives under several reaction conditions.



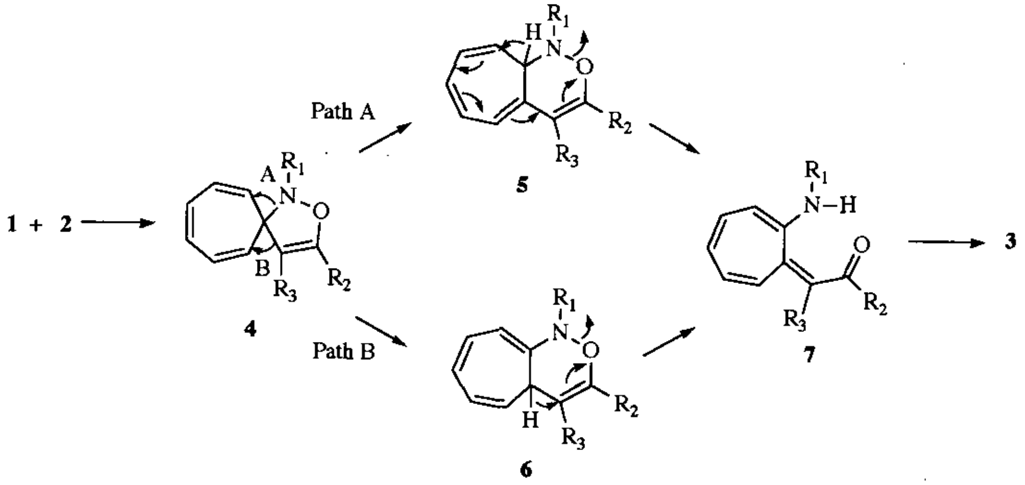
1 1' 2 3

a: R_1 = Me,
b: R_1 = Et

a: R_2 = R_3 = CO_2Me,
b: R_2 = H, R_3 = CO_2Et,
c: R_2 = H, R_3 = Ph,
d: R_2 = R_3 = Ph

a: R_1 = Me, R_3 = CO_2Me,
b: R_1 = Et, R_3 = CO_2Me,
c: R_1= Me, R_3 = CO_2Et,
d: R_1 = Et, R_3 = CO_2Et

The structual elucidation of 3 was accomplished on the basis of the spectral properties. In the ir spectra, the existence of the carbonyl groups was shown by the strong absorption bands at *ca.* 1680 cm^{-1} for amido groups and *ca.* 1700 cm^{-1} for ester groups. Uv spectra showed the characteristic absorption patterns as 1-azaazulen-2(1*H*)-ones with the maxima at 220, 280, and 430 nm.[7] ^{1}H and ^{13}C nmr spectra were compatible to the structures shown in figure.



The reaction is considered to proceed *via* a [2+3]-type cycloadduct (4), in which the C-N (Path A) or C-C (Path B) bond of the five membered ring could be cleaved to give a cycloheptatriene derivative (5 or 6). Subsequent migration of the angular proton and cleavage of the O-N bond afforded a heptafulvene derivative (7). The subsequent condensation reaction of 7 led to 1-azaazulen-2(1*H*)-one derivatives (3). The detailed elucidation of the reaction mechanism is now in progress.[8∼10]

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b) S. Kajigaeshi, S. Matsuoka, S. Kanemasa, and M. Noguchi, *Heterocycles*, 1984, 22, 461.

2. The chemical shifts of 1a and 1b in ^{13}C nmr spectra are as follows: 1a: ^{13}C Nmr ($CDCl_3$) δ 46.7, 127.3, 128.7, 129.1, 131.9, 132.2, 145.6. 1b: ^{13}C Nmr ($CDCl_3$) δ 12.1, 53.3, 126.8, 128.8, 129.3, 132.0, 132.2, 133.3, 144.6.

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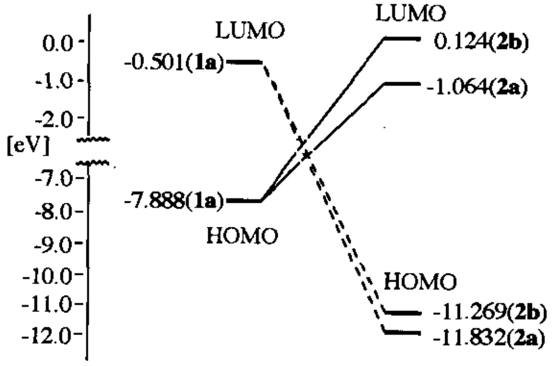
4. K. Ito, Y. Noro, K. Saito, and K. Takahashi, *Bull. Chem. Soc. Jpn.*, 1990, 63, 2573; K. Saito, K. Ito, C. Kabuto, and K. Takahashi, *ibid.*, 1991, 64, 2383; K. Ito, K. Saito, and K. Takahashi, *Heterocycles*, 1991, 32, 1117; K. Ito, K. Saito, S. Takeuchi, and K. Takahashi, *ibid.*, 1992, 34, 1415; K. Ito, K. Saito, and K. Takahashi, *ibid.*, 1992, 34, 2339; *idem*, *ibid.*, 1993, 36, 21.

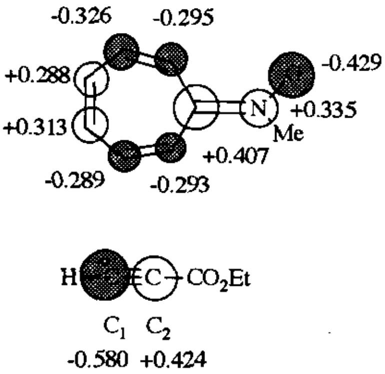
5. Physical data of 3 are as follows: 3a: yellow crystals. mp 170–171°C (from dichloromethane–ethyl acetate). Hrms: m/z 217.0737. Calcd for $C_{12}H_{11}NO_3$: m/z 217.0738. Ms m/z (rel intensity): 217 (M^+, 47), 186 (M^+–OMe, 100), 159 (M^+–CO_2Me, 30). Uv (MeOH): 429 nm (log ε, 3.65), 281 (4.00), 224 (3.72). Ir (KBr): 1698, 1678 cm^{-1}. ^1H Nmr ($CDCl_3$) δ 3.60 (s, 3H, Me), 3.98 (s, 3H, Me), 8.31 (dd, H_c), 8.33 (d, H_a), 8.54 (dd, H_b), 8.59 (dd, H_d), 9.08 (d, H_e). Coupling constants in Hz; J_{ab}= 8.8, J_{bc}= 10.0, J_{cd}= 9.4, J_{de}= 11.3. ^{13}C Nmr ($CDCl_3$) δ 26.5, 51.4, 115.9, 130.1, 131.5, 134.3, 136.3, 146.2, 148.3, 165.1, 165.6. 3b: Yellow crystals. mp 136–137°C (from dichloromethane–ethyl acetate). Hrms: m/z 231.0899. Calcd for $C_{13}H_{13}NO_3$: m/z 231.0894. Ms m/z (rel intensity): 231 (M^+, 100), 200 (M^+–OMe, 100), 172 (M^+–CO_2Me, 41). Uv (MeOH): 429 nm (log ε, 3.62), 280 (4.00), 221 (3.88). Ir (oil): 1703, 1680 cm^{-1}. ^1H Nmr ($CDCl_3$) δ 1.32 (t, 3H, Me, J=7.2 Hz), 3.95(s, 3H, Me), 4.17 (q, 2H, CH_2, J=7.2 Hz), 7.23 (dd, H_c), 7.36 (d, H_a), 7.54 (dd, H_b), 7.58 (dd, H_d), 9.10 (d, H_e). Coupling constants in Hz; J_{ab}= 9.3, J_{bc}= 10.5, J_{cd}= 9.0, J_{de}= 11.2. ^{13}C Nmr ($CDCl_3$) δ 13.7, 34.9, 51.4, 115.6, 130.1, 131.4, 134.3, 136.2, 145.3, 148.5, 165.2, 165.3. 3c: yellow oil. Hrms: m/z 231.0920. Calcd for $C_{13}H_{13}NO_3$: m/z 231.0894. Ms m/z (rel intensity): 231 (M^+, 28), 186 (M^+–OEt, 73), 159 (M^+–CO_2Et, 100). Uv (MeOH): 428 nm (log ε, 3.88), 280 (4.24), 233 (3.88). Ir (oil): 1698, 1678 cm^{-1}. ^1H Nmr ($CDCl_3$) δ 1.42 (t, 3H, Me, J= 7.2 Hz), 3.58 (s, 3H, Me), 4.40 (q, 2H, CH_2, J= 7.2 Hz), 7.20–7.30 (m, 2H, H_a and H_c), 7.40–7.60 (m, 2H, H_b and H_d), 9.03 (d, H_e, J_{de}= 11.1 Hz). ^{13}C Nmr ($CDCl_3$) δ 14.5, 26.5, 60.1, 115.8, 130.1, 131.3, 134.2, 136.1, 146.1, 148.1, 164.6, 165.6. 3d: yellow oil. Hrms: m/z 245.1066. Calcd for $C_{14}H_{15}NO_3$: m/z 245.1051. Ms m/z (rel intensity): 245 (M^+, 64), 200 (M^+–OEt, 56), 173 (M^+–CO_2Et, 100). Uv (MeOH): 428 nm (log ε, 4.08), 281 (4.42), 233 (4.06). Ir (oil): 1707, 1672 cm^{-1}. ^1H Nmr ($CDCl_3$)

δ 1.33 (t, 3H, Me, J= 7.2 Hz), 1.44 (t, 3H, Me, J= 7.2 Hz), 4.17 (q, 2H, CH_2, J= 7.2 Hz), 4.43 (q, 2H, CH_2, J= 7.2 Hz), 7.28 (dd, H_c), 7.33 (d, H_a), 7.52 (dd, H_b), 7.56 (dd, H_d), 9.07 (d, H_e). Coupling constants in Hz; J_{ab}= 8.8, J_{bc}= 10.7, J_{cd}= 9.3, J_{de}= 11.0. ^{13}C Nmr ($CDCl_3$) δ 13.7, 14.5, 34.8, 60.2, 115.5, 130.1, 131.3, 134.2, 136.0, 145.8, 148.3, 164.8, 165.3.

6. The degree of difficulty in the elimination of the leaving moieties is considered to be responsible to the difference of the product yield.
7. K. Ito, K. Saito, and K. Takahashi, *Bull. Chem. Soc. Jpn.*, 1992, 65, 812.
8. The attempted isolation of the intermediates (4, 5, 6, or 7) had no success, even in the reaction at 0°C. The low reaction temperature only caused the low yield of 3.
9. D. P. Curran, "Advances in Cycloaddition", Vol. 1, JAI Press Inc., (London), 1988, 79.
10. The peri- and regioselectivities on the addition reaction process were explained by FMO theory. The energy gaps between the HOMO of 1 and the LUMO of 2 were smaller than the other combinations, suggesting that the reactions were governed by the interaction between the HOMO of 1 and the LUMO of 2. In the HOMO of 1, the coefficients on the carbon and the oxygen atoms of the nitrone moiety were larger than those of any other carbon atoms of the cycloheptatriene moiety to explain that the periselectivity of 1 as nitrone was higher than that as cycloheptatriene. The regioselectivity in the reaction of 2b was explained as that the oxygen atom of 1, with the largest HOMO coefficient, should attack preferencially the C_1 carbon atom of 2b, with the largest LUMO coefficient.[11]



HOMO-LUMO interaction of cycloheptatrienylidene methylamine *N*-oxide(**1a**) with acetylene derivatives (**2a** and **2b**)



Values of the coefficients of the HOMO of **1a** and the LUMO of **2b**

11. The PM3 MO calculations on 1 and 2 were carried out using an NEC PC-9801 RA 32-bit personal computer with "PASOCON MOPAC/386" program, which is based on the MOPAC (Ver. 5.0 QCPE No. 455) by Toray System Center.

Received, 21st January, 1993