

CYCLOADDITIONS OF ETHYL 2-AMINO-1-AZAAZULENE-3-CARBOXYLATE  
WITH DIMETHYL ACETYLENEDICARBOXYLATE

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Abstract—Reaction of ethyl 2-amino-1-azaazulene-3-carboxylate with dimethyl acetylenedicarboxylate gave two 1:1-adducts (3 and 4), two 1:2-adducts (5 and 6), and a 1:3-adduct (7). Reaction mechanism is discussed.

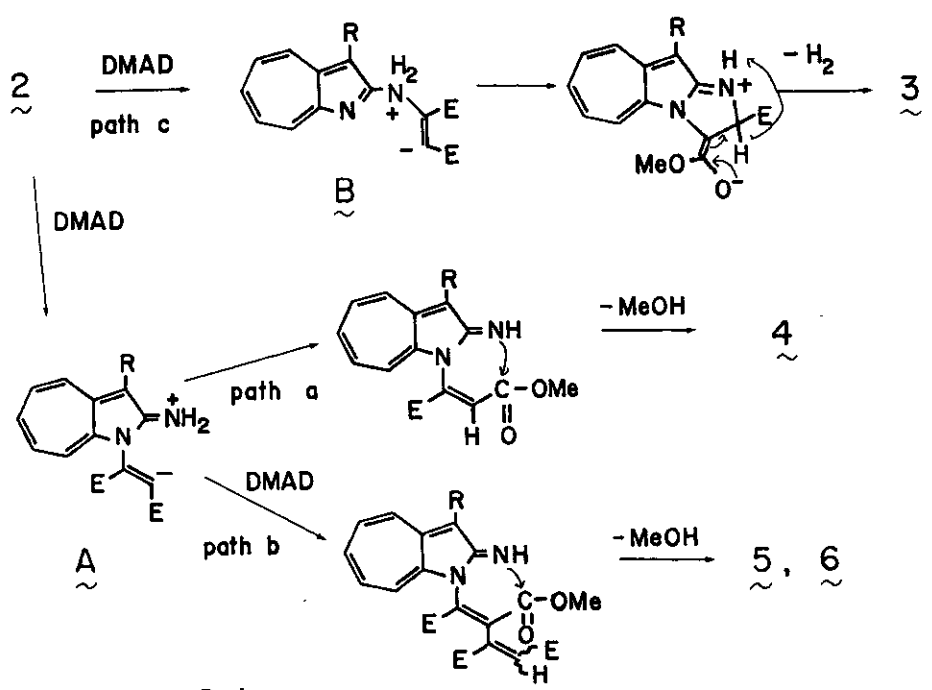
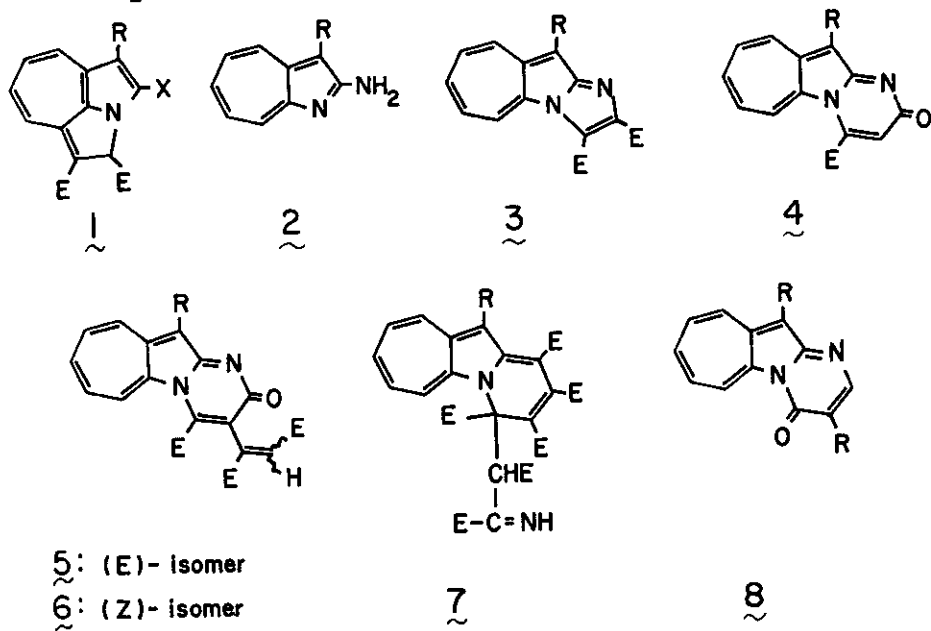
It is known that cycloadditions of nitrogenous heterocycles with dimethyl acetylenedicarboxylate (DMAD) were efficient synthetic methods for N-bridged heterocycles.<sup>1</sup> The author reported that 1-azaazulenes (cyclohepta[b]pyrroles) reacted with DMAD to give 2a-azacyclopent[cd]azulenes (1) via 1,8-dipolar intermediates.<sup>2</sup> 2-Aminobenzazoles are well known to give 2-oxopyrimido[2,1-b]benzazoles upon reactions with DMAD.<sup>3-5</sup> In this paper, the author wish to report on the studies of the reaction of ethyl 2-amino-1-azaazulene-3-carboxylate (2) with DMAD, which afforded different type of cycloaddition products to compare with the reactions of 2-aminobenzazoles or other 2-substituted 1-azaazulenes.

Treatment of 2 with DMAD in hot acetonitrile for 5 h gave a complex mixture. From the mixture, six products, 3 (3.2%, dark violet needles, mp 161 °C), 4 (18.5%, red needles, mp 184 °C), 5 (21.1%, red needles, mp 171 °C), 6 (4.4%, red needles, mp 192 °C), recovered 2 (23.5%), and 7 (2.4%, purple prisms, mp 164 °C), were isolated by means of silica gel column chromatography. When the reaction was carried out in dry benzene, compounds, 3 (13.8%), 4 (10.8%), 5 (6.5%), 6 (0.7%), 2 (23.5%), and 7 (1.6%), were isolated.

Compound 3<sup>6</sup> was a 1:1-cycloadduct [MS m/z 356 (M<sup>+</sup>)] and characterized as 2,3-dimethyl 10-ethyl cyclohepta[4,5]pyrrolo[1,2-a]imidazole-2,3,10-tricarboxylate<sup>7</sup> on the basis of the spectral data. In the <sup>1</sup>H NMR spectrum of 3, two protons of seven membered ring resonated at rather low field [ $\delta$  9.52 (d, J=11.8 Hz, H-9) and 9.85 (d, J=10.0 Hz, H-5)], which would be deshielded by the ester groups at C-10 and C-3, respectively.

R = CO<sub>2</sub>Et.

E = CO<sub>2</sub>Me



Scheme

Compound 4<sup>8</sup> was a 1:1-cycloadduct [MS m/z 326 (M<sup>+</sup>)] and characterized as 11-ethyl 4-methyl 2H-2-oxo-cyclohepta [4,5] pyrrolo [1,2-a] pyrimidine-4,11-dicarboxylate, which corresponds to methyl 2-oxopyrimido [2,1-b] benzazole-4-carboxylates on the reactions of 2-aminobenzazoles with DMAD.<sup>3-5</sup> Treatments of 4 under the similar conditions of deesterification (heating with 48% HBr or 48% HBr-PPA) or hydrolysis (heating with ethanolic alkali) of 4-oxo-cyclohepta [4,5] pyrrolo [1,2-a] pyrimidinecarboxylates<sup>8</sup> (8) gave no definitive products.

Compounds 5<sup>10</sup> [MS m/z 468 (M<sup>+</sup>)] and 6<sup>11</sup> [MS m/z 468 (M<sup>+</sup>)] were 1:2-adducts and would be isomers for the similarity of their spectral data. In the <sup>1</sup>H NMR spectra of 5 and 6, vinylic protons were seen at  $\delta$  7.22 and 6.44, respectively. Higher resonated vinylic proton should be assigned as one of maleate and lower as one of fumarate, therefore compounds 5 and 6 were characterized as fumarate and maleate derivatives of 4, respectively. Since 4 did not react with DMAD under the conditions as for 2, 5 and 6 would be directly produced from 2 with two eq. molar amount of DMAD.

Compound 7<sup>12</sup> was a 1:3-adduct and tentatively assigned as cyclohepta [4,5]-pyrrolo [1,2-a] pyridine derivatives on the basis of its spectral data, at present.

A plausible mechanism for the reaction is shown in Scheme. When DMAD attacks at ring-nitrogen of 2, dipolar species A should be produced as earlier studies.<sup>2</sup> When condensation occurred between imine-nitrogen and ester group (path a and b), compounds 4, 5, and 6 are produced. When DMAD attacks at amino group, dipolar species B should be produced (path c), which drive another type of cyclization to give 3.

#### REFERENCES

1. M. V. George, S. K. Khetan, and R. K. Gupta, Adv. Heterocyclic Chem., 1976, 19, 279; R. M. Acheson and N. F. Elmore, ibid., 1978, 23, 263; R. M. Acheson, Lect. Heterocyclic Chem., 1982, 6, 59.
2. N. Abe, Y. Tanaka, and T. Nishiwaki, J. Chem. Soc., Perkin Trans. 1, 1978, 185; N. Abe and T. Nishiwaki, Bull. Chem. Soc. Jpn., 1981, 54, 1277.
3. H. Ogura, M. Kawano, and T. Itoh, Chem. Pharm. Bull., 1973, 21, 2019.
4. C-K. Chan, J. C. N. Ma, and T. C. W. Mak, J. Chem. Soc., Perkin Trans. 2, 1977, 1070.
5. J. J. Wada, R. F. Hegel, and C. B. Toso, J. Org. Chem., 1979, 44, 1811.

6.  $^1\text{H NMR } \delta = 1.48$  (3H, t,  $J=7$  Hz, Me), 3.98 (3H, s, OMe), 3.99 (3H, s, OMe), 4.55 (2H, q,  $J=7$  Hz,  $\text{OCH}_2$ ), 7.53-7.77 (3H, m, H-6, 7, and 8), 9.52 (1H, d,  $J=11.8$  Hz), 9.85 (1H, d,  $J=10.0$  Hz).
7. Cyclohepta [4,5]pyrrolo [1,2-a]imidazole system was synthesized. N. Abe, T. Nishiwaki, H. Yamamoto, and N. Kunishige, Bull. Chem. Soc. Jpn., 1983, 56, 3703.
8.  $^1\text{H NMR } \delta = 1.56$  (3H, t,  $J=7$  Hz, Me), 4.03 (3H, s, OMe), 4.57 (2H, q,  $J=7$  Hz,  $\text{OCH}_2$ ), 7.24 (1H, s, H-3), 7.70-7.84 (3H, m, H-7, 8, and 9), 9.38-9.51 (1H, m, H-10), 10.38-10.48 (1H, m, H-6).  $^{13}\text{C NMR } \delta = 14.23$  (q, Me), 53.08 (q, OMe), 61.19 (t,  $\text{OCH}_2$ ), 106.12 (s, C-11), 107.63 (d, C-3), 129.03 (d, C-9), 134.50 (d, C-7), 135.16 (d, C-8), 136.23 (d, C-6), 139.02 (d, C-10), 141.46 (s, C-10a), 146.22 (s, C-5a), 150.76 (s, C-4), 154.54 (s, C-11a), 161.79 (s, C-2), 162.91 (s, ester C=O), 164.86 (s, ester C=O).
9. Compound 8 was easily deesterified and gave non-substituted compound. Behavior of 4 was different from 8. N. Abe, Bull. Chem. Soc. Jpn., submitted for publication.
10.  $^1\text{H NMR } \delta = 1.56$  (3H, t,  $J=7$  Hz, Me), 3.61, 3.75, 3.95 (each 3H, s, OMe), 4.57 (2H, q,  $J=7$  Hz,  $\text{OCH}_2$ ), 7.22 (1H, s, H-vinyl), 7.66-7.80 (3H, m, H-7, 8, and 9), 9.37-9.49 (1H, m, H-10), 10.26-10.36 (1H, m, H-6).
11.  $^1\text{H NMR } \delta = 1.51$  (3H, t,  $J=7$  Hz, Me), 3.80, 3.85, 3.96 (each 3H, s, OMe), 4.54 (2H, q,  $J=7$  Hz,  $\text{OCH}_2$ ), 6.44 (1H, s, H-vinyl), 7.75-7.88 (3H, m, H-7, 8, and 9), 9.42-9.55 (1H, m, H-10), 10.34-10.45 (1H, m, H-6).
12.  $^1\text{H NMR } \delta = 1.54$  (t,  $J=7$  Hz, Me), 3.57 (1H, s, H-methine), 3.44, 3.62, 3.75, 3.76, 3.88, 3.95 (each 3H, s, OMe), 4.65 (2H, q,  $\text{OCH}_2$ ), 7.50-7.85 (3H, m, H-7, 8, and 9), 8.42 (1H, dd,  $J=8.5$  and  $2.5$  Hz, H-6), 9.08 (1H, dd,  $J=11.5$  and  $2.0$  Hz, H-10), 12.60 (1H, bs, exchangeable, NH).  $^{13}\text{C NMR } \delta = 14.47$  (q, Me), 40.89 (s, C-4), 48.83 (d, C-methine), 50.83, 51.06, 52.30, 53.24, 53.47, 54.95 (each q, OMe), 62.42 (t,  $\text{OCH}_2$ ), 100.89 (s, C-3), 101.36 (s, C-1), 105.71 (s, C-2), 112.48 (s, C-11), 124.48 (s, C-10a), 125.71 (d, C-9), 134.0 (d, C-7), 137.13 (d, C-8), 138.18 (d, C-10), 140.07 (d, C-6), 147.01 (s, C-5a), 150.60 (s, C-11a), 155.48 (s, C-imine), 162.66 (s, ester C=O), 165.83 (s, ester C=O), 165.95 (s $\times$ 2, ester C=O), 166.42 (s $\times$ 2, ester C=O), 170.42 (s, ester C=O). IR  $3150\text{ cm}^{-1}$  (NH).

Received, 11th September, 1986