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

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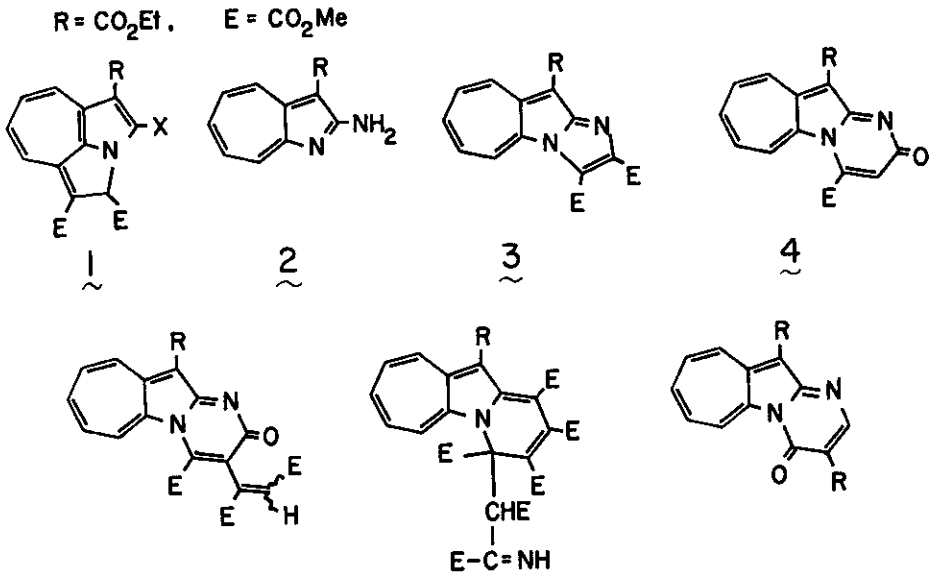
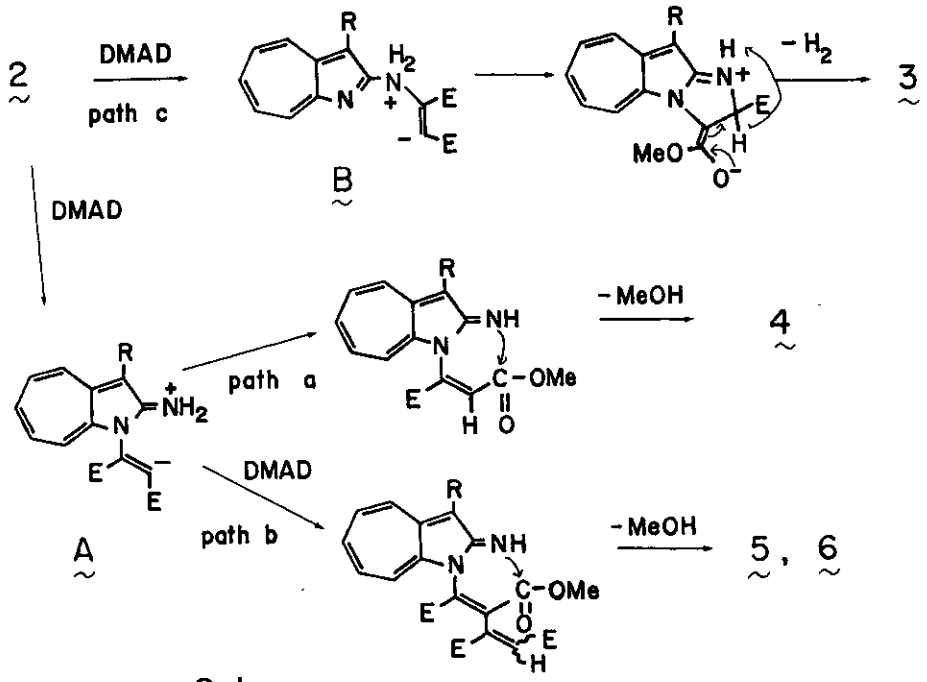
Abstract—Reaction of ethyl 2-amino-1-azaazulene-3-carboxylate with dimethyl acetylenedicarboxylate gave two 1:1-adducts (3 and 4), two 1:2-adducts (5 and 6), and a 1:3-adduct (7). Reaction mechanism is discussed.

It is known that cycloadditions of nitrogeneous heterocycles with dimethyl acetylenedicarboxylate (DMAD) were efficient synthetic methods for N-bridged heterocycles.[1] The author reported that 1-azaazulenes (cyclohepta[b]pyrroles) reacted with DMAD to give 2a-azacyclopent[cd]azulenes (1) via 1,8-dipolar intermediates.[2] 2-Aminobenzazoles are well known to give 2-oxopyrimido[2,1-b]benzazoles upon reactions with DMAD.[3-5] 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 ℃), 4 (18.5%, red needles, mp 184 ℃), 5 (21.1%, red needles, mp 171 ℃), 6 (4.4%, red needles, mp 192 ℃), recovered 2 (23.5%), and 7 (2.4%, purple prisms, mp 164 ℃), 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[6] was a 1:1-cycloadduct [MS m/z 356 (M^+)] and characterized as 2,3-dimethyl 10-ethyl cyclohepta[4,5]pyrrolo[1,2-a]imidazole-2,3,10-tricarboxylate[7] on the basis of the spectral data. In the ^1H NMR spectrum of 3, two protons of seven membered ring resonated at rather low field [δ 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 = CO2Et, E = CO2Me
1
2
3
4
5: (E)- isomer
6: (Z)- isomer
7
8


2
DMAD
path c
B
3
DMAD
path a
path b
A
-MeOH
4
-MeOH
5, 6

Scheme

Compound 4[8] was a 1:1-cycloadduct [MS m/z 326 (M^+)] 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.[3-5] 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[9] (8) gave no definitive products.

Compounds 5[10] [MS m/z 468 (M^+)] and 6[11] [MS m/z 468 (M^+)] were 1:2-adducts and would be isomers for the similarity of their spectral data. In the ^{1}H NMR spectra of 5 and 6, vinylic protons were seen at δ 7.22 and 6.44, respectively. Higher resonated vinylic proton should be assigned as one of maleate and lower as one of fumalate, 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[12] 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.[2] 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.

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6. ^{1}H NMR δ =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, 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}H NMR δ =1.56 (3H, t, J=7 Hz, Me), 4.03 (3H, s, OMe), 4.57 (2H, q, J=7 Hz, 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}C NMR δ =14.23 (q, Me), 53.08 (q, OMe), 61.19 (t, 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}H NMR δ =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, OCH_2), 7.22 (1H, s, H-vinylic), 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}H NMR δ =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, OCH_2), 6.44 (1H, s, H-vinylic), 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}H NMR δ =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, 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}C NMR δ =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, 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×2, ester C=O), 166.42 (s×2, ester C=O), 170.42 (s, ester C=O). IR 3150 cm^{-1} (NH).

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