Reactions of 2-Hydrazino- and 8-Hydrazinocyclohepta[*b*]pyrroles with Dimethyl Acetylenedicarboxylate

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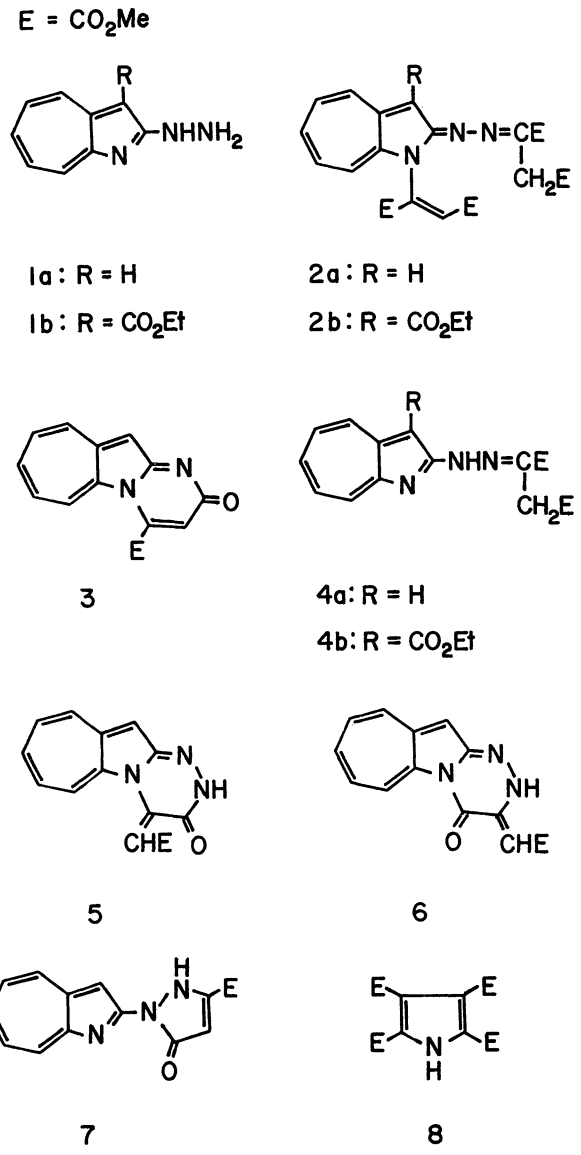
Synopsis. 2-Hydrazinocyclohepta[*b*]pyrrole reacted with dimethyl acetylenedicarboxylate (DMAD) to give the hydrazones (**2a**), the pyrimidinone-fused cyclohepta[*b*]pyrrole (**3**), 1,2,4-triazinone-fused cyclohepta[*b*]pyrroles, and the 1,2-dihydro-3*H*-pyrazol-3-one derivative. Thermolysis of **2a** gave **3** and tetramethyl pyrrole-2,3,4,5-tetracarboxylate. The reaction of ethyl cyclohepta[*b*]pyrrole-3-carboxylate with DMAD at room temperature gave the hydrazone and the spiro-pyrazoline derivative.

It is known that hydrazino-substituted heterocycles react with dimethyl acetylenedicarboxylate (DMAD) to give the hydrazones, and that subsequent cyclization gives either 1,2,4-triazin-5-ones or 5-pyrazolones.[1] Although cyloadditions of azaazulenes are of interest and some studies have been carried out,[2-7] cycloadditions of hydrazinoazaazulenes have not yet been studied. In this paper we report on the reactions of 2-hydrazino- and 8-hydrazinocyclohepta[*b*]pyrroles with DMAD.



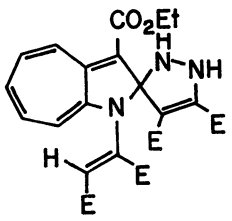
The treatment of 2-hydrazinocyclohepta[*b*]pyrrole (**1a**) with two molar amount of DMAD in benzene at room temperature for 3 h gave dimethyl 2-[1-[(*E*)-1,2-bis(methoxycarbonyl)vinyl]cyclohepta[*b*]pyrrol-2(1*H*)-ylidenehydrazono]succinate (**2a**) (22%), methyl 2-oxo-2*H*-cyclohepta[4,5]pyrrolo[1,2-*a*]pyrimidime-4-carboxylate (**3**)[3] (1%), dimethyl 2-[(cyclohepta[*b*]pyrrol-2-yl)hydrazono]succinate (**4a**) (4%), methyl 3,4-dihydro-4-oxo-2*H*-cyclohepta[4,5]pyrrolo[2,1-*c*][1,2,4]triazin-4-ylideneacetate (**5**) (4.5%), methyl 3,4-dihydro-4-oxo-2*H*-cyclohepta[4,5]pyrrolo[2,1-*c*][1,2,4]triazin-3-ylideneacetate (**6**) (3%), and methyl 1-(cyclohepta[*b*]pyrrol-2-yl)-2,5-dihydro-5-oxo-1*H*-pyrazole-3-carboxylate (**7**) (12%). When **1a** was treated with one molar amount of DMAD in acetonitrile at room temperature, **7** (46%) was obtained as a major product, and **2a** and **3** were not obtained. The treatment of **1a** with three molar amounts of DMAD in acetonitrile at room temperature gave **2a** (43%) as the major product; the yield of **7** was low (2%). For an improvement of the yield of cycloadducts (**5** and **6**), although the reaction was tried under reflux or in the presence of Pd-C, no particular change was observed.

These structures were deduced on the basis of spectral data, especially ^{1}H NMR spectra, as well as elemental analyses.

Compound **3** was considered to be a thermolyzed product of **2a**. Thus, **2a** was heated in *t*-butylbenzene under reflux for 6 h and gave **3** (19%) and **8**[8] (30%).

The reactions of ethyl 2-hydrazinocyclohepta[*b*]pyrrole-3-carboxylate (**1b**) with DMAD somewhat differed from those of **1a**. Thus, a treatment of **1b** with DMAD in acetonitrile at room temperature gave the ethoxycarbonyl **4b** (65%) and 3-ethyl 4′,5′-dimethyl 1-[(*Z*)-1,2-bis(methoxycarbonyl)vinyl]-1′,2′-dihydrospiro[cyclohepta[*b*]pyrrole-2(1*H*),3′-[3*H*]pyrazole]-3,4′5′-tricarboxylate (**9**) (3%), and a treatment in refluxing xylene gave 1-ethyl 4,5-dimethyl 2-[(*Z*)-1,2-bis(methoxycarbonyl)vinylhydrazono]-2*H*-cyclohepta[*gh*]pyrrolizine-1,4,5-tricarboxylate (**10**) (4%), **4b** (7%), **8** (16%), and 10-ethyl 2,3-dimethyl cyclohepta[4,5]pyrrolo[1,2-*a*]imidazole-2,3,10,-tricarboxylate (**11**)[9] (10%). Compounds **10**, **8**, and **11** would be secondary reaction products. Thus, **4b** was treated with DMAD in refluxing xylene and compounds **10**, **8**, and **11** were obtained.

The formation of the spiro-pyrazoline derivative resembles the reaction of benzophenone phenylhydrazone with DMAD.[10]



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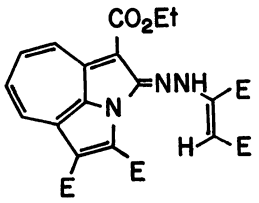

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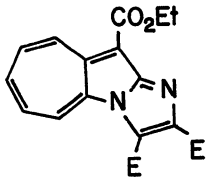

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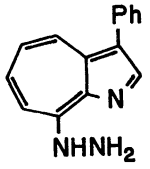

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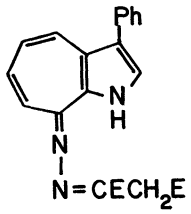

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The reaction of 8-hydrazino-3-phenylcyclohepta[*b*]-pyrrole (**12**) with DMAD gave dimethyl 2-[3-phenylcyclohepta[*b*]pyrrol-8(1*H*)-ylidenehydrazono]succinate (**13**) in 56% yield. From the expectation of cyclization, compound **13** was treated with acetic anhydride or triethylamine, as previously used;[1] no distinct product was obtained.

Experimental

The melting points are uncorrected. ^{1}H NMR spectra (250 MHz) and ^{13}C NMR spectra (62.87 MHz) were taken on a Hitachi R-250H spectrometer using $CDCl_3$ as a solvent (TMS as an internal standard). IR spectra were recorded for Nujol mulls with a Hitachi 270-50 infrared spectrophotometer. High-resolution mass spectra were determined with a JEOL-01SG-2 spectrometer at 70 eV of ionization energy. Column chromatography was performed on Kieselgel 60.

Reaction of 1a with DMAD. a) A mixture of **1a** (0.500 g) and DMAD (0.893 g) in dry benzene (100 ml) was stirred for 3 h at room temperature and evaporated. The residue was chromatographed with chloroform to give **2a** (0.305 g, 22%), **3**[3] (0.005 g, 1%), **4a** (0.040 g, 4%), **5** (0.038 g, 4.5%), **6** (0.028 g, 3%), and **7** (0.102 g, 12%), successively.

2a: Red prisms; mp 186—187 °C (from hexane); ^{1}H NMR δ=3.65 (3H, s), 3.75 (3H, s), 3.82 (2H, s), 3.87 (3H, s), 3.88 (3H, s), 6.40 (1H, s), 6.65—6.95 (6H, m), and 7.26 (1H, d, J=11.0 Hz); ^{13}C NMR δ=32.55 (t), 51.74 (q), 52.31 (q), 52.50 (q), 52.85 (q), 102.23 (d), 112.62 (d), 128.74 (d), 129.44 (d), 129.66 (d), 131.98 (d), 133.00 (d), 133.97 (s), 145.25 (s), 147.09 (s), 147.24 (s), 147.28 (s), 162.18 (s), 164.05 (s), 165.44 (s), 165.70 (s), and 169.64 (s); IR 1752, 1740, 1726, 1706 (C=O), and 1660 cm^{-1} (C=N). Found: C, 57.19; H, 4.79; N, 9.15%. Calcd for $C_{21}H_{21}N_3O_8$: C, 56.88; H, 4.78; N, 9.48%.

4a: Orange prisms; mp 165—167 °C (from hexane); ^{1}H NMR δ=3.73 (3H, s), 4.01 (3H, s), 4.77 (2H, s), 6.17 (1H, s), 7.06 (1H, s), 7.45—7.70 (3H, m), 8.21 (1H, d, J=10.4 Hz) and 8.23—8.29 (1H, m); IR 3348 (NH), 1738, 1704 (C=O), and 1640 cm^{-1} (C=N). Found: C, 59.68; H, 4.95; N, 13.98%. Calcd for $C_{15}H_{15}N_3O_4$; C, 59.80; H, 5.02; N, 13.95%.

5: Brown needles; mp 242—244 °C (from hexane–dichloromethane); ^{1}H NMR δ=3.74 (3H, s), 5.98 (1H, brd, J=7.9 Hz), 6.14 (1H, s), 6.40—6.60 (3H, m), 6.69 (1H, s), 6.93 (1H, d, J=11.6 Hz), and 9.05 (1H, brs); IR 3160 (NH), 1696, 1652 (C=O), and 1622 cm-1 (C=C). Found: C, 62.59; H, 4.24; N, 15.65%. Calcd for $C_{14}H_{11}N_3O_3$: C, 62.45; H, 4.12; N, 15.61%.

6: Red brown needles; mp 201—202 °C (from hexane–dichloromethane); ^{1}H NMR δ=3.86 (3H, s), 6.08 (1H, s), 6.34 (1H, s), 6.35—6.55 (3H, m), 6.86 (1H, d, J=10.4 Hz), 6.90 (1H, brd, J=6.7 Hz), and 8.79 (1H, brs); IR 3160 (NH), 1710, 1660 (C=O), and 1610 cm^{-1} (C=C). Found: C, 62.43; H, 4.55; N, 15.25%. Calcd for $C_{14}H_{11}N_3O_3$: C, 62.45; H, 4.12; N, 15.61%.

7: Yellow brown needles; mp 190—191 °C (from hexane–dichloromethane); ^{1}H NMR δ=3.98 (3H, s), 6.14 (1H, s), 7.65 (1H, s), 7.70—7.95 (3H, m), 8.53 (1H, d, J=9.2 Hz), and 8.55 (1H, d, J=9.8 Hz); IR 3100 (NH), 1720, 1715, 1652 (C=O), and 1622 cm-1 (C=C). Found: C, 62.68; H, 4.29; N, 15.20%. Calcd for $C_{14}H_{11}N_3O_3$: C, 62.45; H, 4.12; N, 15.61%.

b) A mixture of **1a** (0.318 g) and DMAD (0.290 g) in dry acetonitrile (100 ml) was stirred for 3 h at room temperature and evaporated. The residue was chromatographed with chloroform to give **4a** (0.006 g, 1%), **5** (0.015 g, 2.5%), **6** (0.014 g, 2%), and **7** (0.274 g, 46%), successively.

Thermolysis of 2a. A solution of **2a** (0.180 g) in *t*-butylbenzene (15 ml) was refluxed for 6 h and evaporated. The residue was chromatographed with benzene–chloroform (1:1) to give **3** (0.020 g, 19%) and **8**[8] (0.037 g, 30%).

Reaction of 1b with DMAD. a) A mixture of **1b** (1.000 g) and DMAD (1.230 g) in dry acetonitrile (100 ml) was stirred for 3 h at room temperature and evaporated. The residue was chromatographed with chloroform to give **4b** (1.050 g, 65%) and **9** (0.074 g, 3%), successively.

4b: Yellow prisms; mp 150—151 °C (from hexane–dichloromethane); ^{1}H NMR δ=1.53 (3H, t, J=7.3 Hz), 3.71 (3H, s), 3.81 (2H, s), 3.92 (3H, s), 4.58 (2H, q, J=7.3 Hz), 7.50—7.90 (3H, m), 8.54 (1H, d, J=9.8 Hz), 9.17 (1H, d, J=9.8 Hz), and 14.01 (1H, s); IR 3248 (NH), 1734, 1710, and 1668 cm^{-1} (C=O). Found: C, 58.15; H, 5.18; N, 11.14%. Calcd for $C_{18}H_{19}N_3O_6$: C, 57.91; H, 5.13; N, 11.25%.

9: Red brown prisms, mp 197—198 °C (from hexane–dichloromethane); ^{1}H NMR δ=1.43 (3H, t, J=7.3 Hz), 3.50 (1H, brs), 3.68 (3H, s), 3.76 (3H, s), 3.80 (3H, s), 3.95 (3H, s), 4.35 (2H, dq, J=11.6 and 7.3 Hz), 5.08 (1H, brs), 5.56 (1H, s), 6.31 (1H, d, J=9.2 Hz), 6.69 (1H, dd, J=11.0 and 9.2 Hz), 6.94 (1H, dd, J=11.0 and 9.2 Hz), 6.97 (1H, d, J=11.6 and 9.2 Hz), and 8.41 (1H, d, J=11.6 Hz); IR 1760, 1744, 1694, and 1678 cm^{-1} (C=O). Found: m/z 515.1538. Calcd for $C_{24}H_{25}N_3O_{10}$: M, 515.1538.

b) A mixture of **1b** (0.500 g) and DMAD (0.920 g) in dry xylene (50 ml) was refluxed for 5 h and evaporated. The residue was chromatographed with benzene–chloroform (1:1) to give **10** (0.040 g, 4%), **4b** (0.054 g, 7%), **8** (0.101 g, 16%), and **11**[9] (0.079 g, 10%), successively.

10: Red prisms, mp 210—212 °C (from hexane–dichloromethane); ^{1}H NMR δ=1.42 (3H, t, J=7.3 Hz), 3.43

(3H, s), 3.61 (3H, s), 3.83 (3H, s), 3.97 (3H, s), 4.41 (2H, q, J=7.3 Hz), 6.08 (1H, s), 6.56 (1H, dd, J=11.6 and 9.2 Hz), 6.89 (1H, dd, J=11.6 and 9.2 Hz), 7.69 (2H, d, J=11.6 Hz), and 10.62 (1H, brs, exch.); IR 3356 (NH), 1746, 1734, 1712, and 1690 cm^{-1} (C=O). Found: m/z 513.1376. Calcd for $C_{24}H_{23}N_3O_{10}$: M, 513.1382.

11: Dark violet needles, mp 162—163 °C (from hexane–dichloromethane) (lit,[9] mp 161 °C).

Reaction of 4b with DMAD. A mixture of **4b** (0.250 g) and DMAD (0.190 g) in dry xylene (50 ml) was refluxed for 3 h and evaporated. The residue was chromatographed with benzene–chloroform (1:1) to give **10** (0.015 g, 4%), **4b** (0.164 g, 47.5%), **8** (0.072 g, 30%), and **11** (0.010 g, 4%), successively.

Reaction of 12 with DMAD. a) A mixture of **12**[11] (0.235 g) and DMAD (0.285 g) in dry acetonitrile (100 ml) was stirred for 1 h and evaporated. The residue was chromatographed with chloroform to give **13** (0.210 g, 56%), which was recrystallized from cyclohexane to give yellow needles, mp 120—121 °C; ^{1}H NMR δ=3.61 (3H, s), 3.85 (2H, s), 3.96 (2H, s), 6.72 (1H, dd, J=10.4 and 8.9 Hz), 7.17 (1H, dd, J=12.2 and 8.9 Hz), 7.41 (1H, s), 7.38—7.55 (5H, m), 7.61 (1H, d, J=10.4 Hz), 8.11 (1H, d, J=12.2 Hz), and 10.30 (1H, brs); ^{13}C NMR δ=35.01 (t), 51.93 (q), 52.57 (q), 122.81 (d), 123.52 (d), 123.90 (d), 126.78 (s), 127.00 (d), 127.60 (s), 128.52 (d×2), 129.27 (d×2), 131.37 (d), 133.33 (s), 134.20 (s), 135.15 (d), 147.01 (s), 156.34 (s), 165.35 (s), and 171.92 (s); IR 3288 (NH), 1706 (C=O), 1622 (C=N), and 696 cm^{-1} (phenyl). Found: C, 67.03; H, 5.05; N, 10.96%. Calcd for $C_{21}H_{19}N_3O_4$: C, 66.83; H, 5.07; N, 11.03%.

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