

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

Noritaka ABE* and Kumiko YATABE

Department of Chemistry, Faculty of Science, Yamaguchi University, Yamaguchi 753

(Received January 16, 1991)

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 cycloadditions 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*]pyrimidine-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.

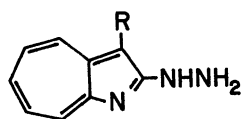
These structures were deduced on the basis of spectral data, especially ¹H NMR spectra, as well as elemental analyses.

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 8⁸⁾ (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.

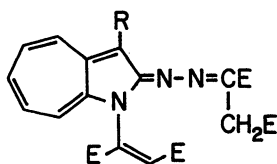
The formation of the spiro-pyrazoline derivative resembles the reaction of benzophenone phenylhydrazone with DMAD.¹⁰⁾

E = CO₂Me



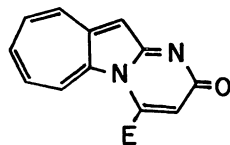
1a: R = H

1b: R = CO₂Et

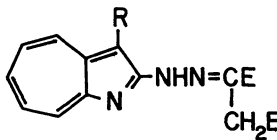


2a: R = H

2b: R = CO₂Et

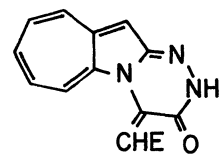


3

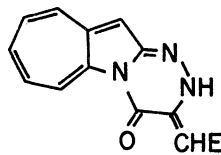


4a: R = H

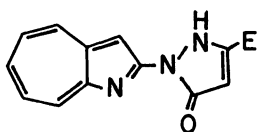
4b: R = CO₂Et



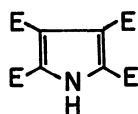
5



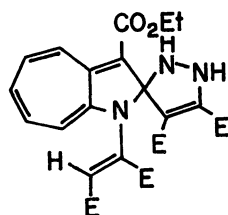
6



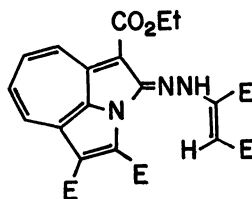
7



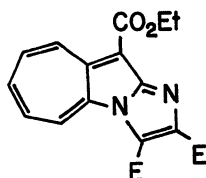
8



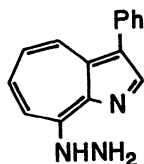
9



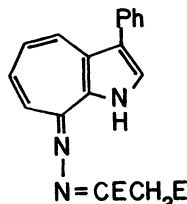
10



11



12



13

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. ¹H NMR spectra (250 MHz) and ¹³C NMR spectra (62.87 MHz) were taken on a Hitachi R-250H spectrometer using CDCl₃ 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%), **3³⁾** (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); ¹H 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); ¹³C 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 C₂₁H₂₁N₃O₈: C, 56.88; H, 4.78; N, 9.48%.

4a: Orange prisms; mp 165–167 °C (from hexane); ¹H 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 C₁₅H₁₅N₃O₄: C, 59.80; H, 5.02; N, 13.95%.

5: Brown needles; mp 242–244 °C (from hexane–dichloromethane); ¹H 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 C₁₄H₁₁N₃O₃: C, 62.45; H, 4.12; N, 15.61%.

6: Red brown needles; mp 201–202 °C (from hexane–dichloromethane); ¹H 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 C₁₄H₁₁N₃O₃: C, 62.45; H, 4.12; N, 15.61%.

7: Yellow brown needles; mp 190–191 °C (from hexane–dichloromethane); ¹H 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 C₁₄H₁₁N₃O₃: 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 **8⁸⁾** (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); ¹H 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 C₁₈H₁₉N₃O₆: C, 57.91; H, 5.13; N, 11.25%.

9: Red brown prisms, mp 197–198 °C (from hexane–dichloromethane); ¹H 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 C₂₄H₂₅N₃O₁₀: 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 **11⁹⁾** (0.079 g, 10%), successively.

10: Red prisms, mp 210–212 °C (from hexane–dichloromethane); ¹H 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 $\text{C}_{24}\text{H}_{23}\text{N}_3\text{O}_{10}$: M, 513.1382.

11: Dark violet needles, mp $162\text{--}163^\circ\text{C}$ (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 $120\text{--}121^\circ\text{C}$; ^1H NMR $\delta=3.61$ (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 $\delta=35.01$ (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 $\times 2$), 129.27 (d $\times 2$), 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 $\text{C}_{21}\text{H}_{19}\text{N}_3\text{O}_4$: C, 66.83; H, 5.07; N, 11.03%.

We thank Dr. Akira Mori, Kyushu University, for the measurements of the mass spectra and elemental analyses.

References

- 1) D. J. LeCount and A. T. Greer, *J. Chem. Soc., Perkin Trans. I*, **1974**, 297.
- 2) T. Nishiwaki and N. Abe, *Heterocycles*, **15**, 547 (1981).
- 3) N. Abe and T. Takehiro, *Bull. Chem. Soc. Jpn.*, **61**, 1225 (1988), and references cited therein.
- 4) N. Abe and T. Ueno, *Bull. Chem. Soc. Jpn.*, **63**, 2121 (1990), and references cited therein.
- 5) O. Meth-Cohn, C. Moore, and P. H. van Rooyen, *J. Chem. Soc., Perkin Trans. I*, **1985**, 1793.
- 6) K. Hafner, *Lect. Heterocycl. Chem.*, **3**, 33 (1976), and references cited therein.
- 7) G. R. Tian, A. Mori, and H. Takeshita, *Bull. Chem. Soc. Jpn.*, **62**, 3727 (1989).
- 8) T. Zaima, Y. Matsunaga, and K. Mitsunashi, *J. Heterocycl. Chem.*, **20**, 1 (1983).
- 9) N. Abe, *Heterocycles*, **26**, 51 (1987).
- 10) M. K. Saxena, M. N. Gudi, and M. V. George, *Tetrahedron*, **29**, 101 (1973).
- 11) K. Yamane, K. Fujimori, J.-K. Sin, and T. Nozoe, *Bull. Chem. Soc. Jpn.*, **50**, 1184 (1977).