Tetrahedron Vol. 34, pp. 2167–2169
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0040-4020/78/0715-2167/$02.00/0

PROPELLANES—XLIV

REACTION OF 11-SUBSTITUTED-1,6-METHANO[10]ANNULENES WITH 4-PHENYL-1,2,4-TRIAZOLINE-3,5-DIONE†

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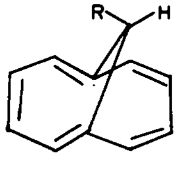
(Received in the UK 22 November 1977; Accepted for publication 22 December 1977)

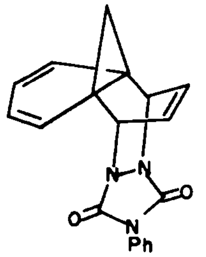
Abstract—Reaction of the bridged annulene derivatives and the dienophile mentioned in the title occurs through attack by the latter from below, *anti*- to the bridge. The mono-adducts obtained contain a substituted cyclopropane ring. Attempted nucleophilic displacement of suitable substituents was unsuccessful.

We have shown that 1,6-methano[10]annulene (**1**, R = H) reacts with one equivalent of 4 - phenyl - 1,2,4 - triazoline - 3,5 - dione (PTD) as well as with its 4-methyl analog, affording in the former case more *bis*-adduct than mono-adduct as well as recovered starting material. In the case of the N-methyl analog one obtains more mono-adduct than *bis*-adduct in the product mixture. However, in either case it is clear that the second equivalent of dienophile adds faster than the first. When the bridged annulene is treated with two equivalents of dienophile it is not surprising that a quantitative yield of *bis*-adduct is obtained.[1] This is one of many cases in which the starting material appreciates its constitution. Since it is aromatic it reacts more slowly with the dienophile than does the mono-adduct whose reactive entity is dienic rather than aromatic.

It was, of course of interest to compare to the above behavior that of 11-substituted derivatives of the same ring system so as to gauge the effect of the particular 11-substituent employed.



1a: R = CN
b: Br
c: $OCOCH_3$
d: OH
e: CO_2H



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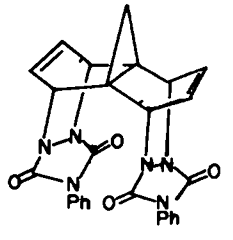

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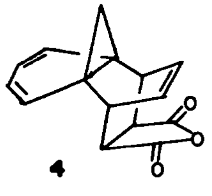
The unexpected result for each of these substrates was the ready obtention of a mono-adduct **2** when treated with PTD. On the contrary, as compared to **1**, R = H, it was not possible readily to obtain a *bis*-adduct **3**. The latter indeed formed but it was always accompanied by a mono-adduct even when the full two equivalents of PTD were supplied (Experimental).

It should also be noted that the 11-substituted compounds all reacted more slowly than their 11-unsubstituted parent. Although accurate kinetics were not carried out the difference in rate is large [1–4 days for the former (see Experimental) vs minutes for the latter[1]]. Thus there is no doubt that the 11-substituent is notably influencing the reaction rate; the question is whether it may in certain cases interact attractively with the dienophile, causing the latter to attack the substrate from above rather than from below. That this does not occur is evident from analysis of the NMR spectra of the products. These are in keeping throughout with the expected attack from below. We know that **1**, R = H, is attacked by maleic anhydride from below and that the resulting mono-adduct **4** affords **5** through attack of **4** again from below. This knowledge is unequivocal since an X-ray structural analysis of **5** has been performed.[2] It should be noted that with respect to the first stage of attack by maleic anhydride, the mono-adduct **4** formed is the *endo*-product. Since much is known about the NMR spectroscopic behavior of derivatives of bridged annulenes,[3] we believe that this criterion is a safe one for concluding that also in **1a–e** attack by PTD occurs exclusively from below. Nevertheless, due to the potential importance of the reverse conclusion, we have submitted a number of the products to the scrutiny of an X-ray beam so as to be in a position to correct the configurational assignment should this become necessary.



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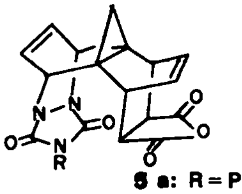

5 a: R = Ph
b: R = Me

Recently a series of fascinating papers has been published with respect to nucleophilic attack upon propellane substrates in which the substituent to be displaced was situated in a cyclopropane ring.[4,5] Since we had in

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†Part XLIII: P. Ashkenazi, J. Kalo, A. Rüttimann and D. Ginsburg, *Tetrahedron* 34, 2161 (1978).

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hand additional substrates of this kind, namely our compounds of type **2**, we subjected some of these to potential nucleophilic attack under the same reaction conditions described.[4,5] We observed only recovery of starting materials (see experimental section). We later subjected our substrates to conditions which in other cases[6] afforded relatively high yields of dimers. No such dimers were observed and starting materials were again recovered. We have also treated some of our substrates with "naked" fluoride ion,[7] again to no avail (see experimental section).

EXPERIMENTAL

IR spectra were measured on a Perkin–Elmer model 257 grating spectrometer. NMR spectra were measured on a Varian T-60 spectrometer. Mass spectra were measured on a Varian 711 spectrometer using the heated inlet system. The electron energy was maintained at 100 eV. Only the major fragments are listed. All m.ps are uncorrected. All Diels–Alder reactions were conducted at room temp.

Reaction of 11 - *cyano* - 1,6 - *methano*[10]*annulene*, **1a**, *with PTD*

(a) Reaction between **1a** (46 mg; 1eq) in CH_2Cl_2 (5 ml) with PTD (48 mg; 1eq) in CH_2Cl_2 (5 ml) afforded after 1 hr the mono-adduct **2a** (94 mg; quant), m.p. 231–232° (ethyl acetate). (Found: C, 69.99; H, 4.20; N, 16.25; M.W. 342.1117. $C_{20}H_{14}N_4O_2$ requires: C, 70.16; H, 4.12; N, 16.37%; M.W. 342.1117). IR($CHCl_3$): 1760, 1720, 1400 cm^{-1}. NMR($CDCl_3$): τ 2.55 (m, 5 arom H); 3.30–3.90 (m, 6 vinylic H); 4.70 (m, 2 $C\underline{H}N$); 7.50 (s, 1 cyclopropyl H). MS: M^+, 342 (13); 194 (56); 167 (100); 166 (100); 139 (46); 128 (14); 119 (33).

(b) Reaction of **1a** (32 mg; 1eq) in CH_2Cl_2 (10 ml) with PTD (66 mg; 2eq) in CH_2Cl_2 (10 ml) gave after 2 days a mixture of **2a** (6 parts) and *bis*-adduct **3a** (5 parts). The *bis*-adduct is insoluble in hot EtOAc and had m.p. 222–223°. (Found: C, 65.08; H, 3.99. $C_{28}H_{19}N_7O_4$ requires: C, 64.98; H, 3.70%). IR (KBr): 1760, 1720, 1410 cm^{-1}. NMR ($CDCl_3$): τ 2.50 (m, 10 arom H); 3.30–3.70 (m, 4 vinylic H); 4.20 (m, 4 $C\underline{H}N$); 7.65 (s, 1 cyclopropyl H). MS: 167 (100); 166 (100); 140 (100); 139 (100); 128 (71).

Reaction of 11 - *bromo* - 1,6 - *methano*[10]*annulene*, **1b**, *with PTD*

(a) Reaction of **1b** (36 mg; 1eq) in CH_2Cl_2 (5 ml) with PTD (28 mg; 1eq) in CH_2Cl_2 (5 ml) gave after 1 day the mono-adduct **2b** (62 mg; 97%), m.p. 199–200° (EtOAc–hexane). (Found: C, 57.54; H, 3.88; H, 10.45; Br, 20.34. $C_{19}H_{14}N_3O_2$ Br requires: C, 57.57; H, 3.58; N, 10.60; Br, 20.10%). IR ($CHCl_3$): 1760, 1720, 1400 cm^{-1}. NMR ($CDCl_3$): τ 2.60 (m, 5 arom H); 3.40–4.20 (m, 6 vinylic H); 4.70 (t, 2$C\underline{H}N$); 6.15 (s, 1 cyclopropyl H). MS: M^+-Br, 316 (1.5); 221 (5); 219 (5); 177 (16); 141 (100); 128 (79).

(b) Reaction of **1b** (42 mg; 1eq) in CH_2Cl_2 (5 ml) with PTD (68 mg; 2eq) in CH_2Cl_2 (5 ml) gave after 4 days **2b** (8 parts) and *bis*-adduct **3b** (5 parts) which was insoluble in hot EtOAc and had m.p. 198–199°. (Found: C, 57.04; H, 3.17. $C_{27}H_{19}N_6O_4Br$ requires: C, 56.74; H, 3.35%). IR (KBr): 1760, 1720, 1410 cm^{-1}. NMR ($CDCl_3$): τ 2.60 (m, 10 arom H); 3.55 (m, 4 vinylic H); 4.20 (m, 4$C\underline{H}N$); 6.05 (s, 1 cyclopropyl H). MS: 322 (7); 316 (1); 221 (8); 220 (13); 219 (9); 141 (100).

Reaction of 11 - *acetoxy* - 1,6 - *methano*[10]*annulene*, **1c**, *with PTD*

(a) Reaction between **1c** (39 mg; 1eq) in CH_2Cl_2 (5 ml) with PTD (34 mg; 1eq) in CH_2Cl_2 (5 ml) gave after 1 day mono-adduct **2c** (73 mg; quant), m.p. 187–188° (benzene–hexane). (Found: C, 66.73; H, 4.92; N, 11.56. $C_{21}H_{17}N_3O_4$ requires: C, 67.19; H, 4.57; N, 11.20%). IR ($CHCl_3$): 1760, 1720, 1400 cm^{-1}. NMR ($CDCl_3$): τ 2.50 (m, 5 arom H); 3.40–4.20 (m, 6 vinylic H); 4.70 (t, 2$C\underline{H}N$); 5.50 (s, 1 cyclopropyl H). MS: M^+-$OCOCH_3$, 315 (5); 200 (8); 194 (25); 177 (25); 158 (47); 128 (95); 119 (100).

(b) Reaction between **1c** (24 mg; 1eq) in CH_2Cl_2 (5 ml) with PTD (43 mg; 2eq) in CH_2Cl_2 (5 ml) gave after 4 days mono-adduct **2c** (7 parts) and *bis*-adduct **3c** (6 parts) which was insoluble in benzene, m.p. 202–203°. (Found: C, 62.49; H, 4.22; N, 14.78. $C_{29}H_{22}N_6O_6$ requires: C, 63.27; H, 4.03; N, 15.27%). IR ($CHCl_3$): 1760, 1720, 1400, 1050 cm^{-1}. NMR ($CDCl_3$): τ 2.50 (m, 10 arom H); 3.60 (m, 4 vinylic H); 4.20 (m, 4$C\underline{H}N$); 5.50 (s, 1 cyclopropyl H); 7.95 (s, 3$C\underline{H}_3CO$). MS: 177 (70); 158 (100); 141 (43); 140 (68); 129 (100); 128 (100).

Reaction of 11 - *hydroxy* - 1,6 - *methano*[10]*annulene*, **1d**, *with PTD*

(a) A soln of **1d** (20 mg; 1eq) in CH_2Cl_2 (5 ml) treated with one of PTD (22 mg; 1eq) in CH_2Cl_2 (5 ml) gave after 1 day the oily mono-adduct **2d** (42 mg; quant). It eventually crystallized after long standing, m.p. 111–112°. (Found: N, 13.28. $C_{18}H_{15}N_3O_3$ requires: N, 13.08%). IR ($CHCl_3$): 3560, 1760, 1720, 1400 cm^{-1}. NMR ($CDCl_3$): τ 2.55 (m, 5 arom H); 3.10–4.10 (m, 6 vinylic H); 4.55 (m, 2 $C\underline{H}N$); 7.00 (m, 1 cyclopropyl H). MS: 177 (7); 168 (4); 146 (10); 128 (100); 119 (17).

(b) Reaction between **1d** (23 mg; 1eq) in CH_2Cl_2 (10 ml) and PTD (47 mg; 2eq) in CH_2Cl_2 (5 ml) gave after 10 days mainly mono-adduct **2d** and *bis*-adduct **3d** (10 mg) which was insoluble in EtOAc, m.p. 207–208°. IR (KBr): 1800, 1720, 1440 cm^{-1}. MS: 177 (39); 156 (100); 155 (100); 128 (100).

Reaction of 11 - *carboxy* - 1,6 - *methano*[10]*annulene*, **1e**, *with PTD*

A soln of **1e** (11.5 mg; 1eq) in CH_2Cl_2 (5 ml) when treated with one of PTD (12 mg; 1eq) in CH_2Cl_2 (5 ml) gave after 1 day mono-adduct **2e** (23 mg; quant), m.p. 190–192° (EtOAc–hexane). (Found: C, 65.40; H, 4.28; N, 12.15. $C_{19}H_{15}N_3O_4$ requires: C, 65.32; H, 4.33; N, 12.03%). IR ($CHCl_3$): 1760, 1720, 1450 cm^{-1}. NMR ($CDCl_3$): τ 2.50 (m, 5 arom H); 3.40–4.00 (m, 6 vinylic H); 4.70 (m, 2$C\underline{H}N$); 7.40 (s, 1 cyclopropyl H).

(b) Reaction with 2eq PTD gave only mono-adduct even after 10 days standing.

Reaction of 4 with PTD

The mono-adduct **4** (38 mg) in CH_2Cl_2 (5 ml) reacted at once with PTD (29 mg) in CH_2Cl_2 (5 ml), affording the di-adduct **5a** (56 mg; 84%), m.p. 217–218°. (Found: C, 67.12; H, 4.48; N, 9.57; M.W. 415.1180. $C_{23}H_{17}N_3O_5$ requires: C, 66.50; H, 4.13; N, 10.12%; M.W. 415.1168). IR ($CHCl_3$): 1850, 1770, 1710, 1400 cm^{-1}. NMR ($CDCl_3$): τ 2.55 (s, 5 arom H); 3.70 (m, 4 vinylic H); 4.60 (t, 2$C\underline{H}N$); 5.50 (t, 2 $C\underline{H}CO$); 6.20 (m, 2 = CH–C$\underline{H}$); 9.00, 9.30 (AB, J = 8 Hz, 2 cyclopropyl H). MS: M^+, 415 (0.4); 317 (1); 265 (1.1); 240 (21); 177 (2); 167 (16); 142 (100); 119 (38).

Reaction of 4 with MTD

Immediate reaction occurred between **4** (58 mg) in CH_2Cl_2 (5 ml) and 4 - methyl - 1,2,4 - triazoline - 3,5 - dione (27 mg) in CH_2Cl_2 (5 ml) giving the di-adduct **5b** (66 mg; 78%), m.p. 248–250° (ethyl acetate). (Found: C, 60.89; H, 4.31; N, 11.89, M.W. 353.1038. ($C_{18}H_{15}N_3O_5$ requires: C, 61.19; H, 4.28; N, 11.89%; M.W. 353.1011). IR (KBr): 1850, 1770, 1700, 1440 cm^{-1}. NMR ($CDCl_3$). τ 3.80 (t, 4 vinylic H); 4.70 (t, 2$C\underline{H}N$); 5.60 (t, 2 $C\underline{H}CO$); 6.25 (m, 2 = CH–C$\underline{H}$); 7.00 (s, 3 $NC\underline{H}_3$); 9.00, 9.30 AB, J = 7 Hz, 2 cyclopropyl H). MS: M^+, 353 (2.7); 255 (5); 2.40 (10); 167 (11); 142 (79); 141 (100).

Attempted displacement of bromine in **2b**

(a) A mixture of **2b** (28 mg), tetraethylammonium acetate (dried in vacuum over P_2O_5; 96 mg) and dry acetone (10 ml) was stirred for 4 days at room temp.[4] The solvent was evaporated and distilled water was added to the residue and extracted with CH_2Cl_2 (3 × 25 ml). Removal of solvent showed quant recovery of **2b** identical spectroscopically with the starting material. The aqueous phase contained no bromide ion (Volhard titration) and there was no sign of acetate absorption, spectroscopically.

(b) Repetition at reflux for 3 hr,[5] followed by the same workup afforded the same result as in (a).

(c) A mixture of **2b** (95 mg) in DMF (3 ml, dried and distilled) was stirred under dry N_2 for 16 hr at 0°.[6] Water was added and the whole was extracted thrice with CH_2Cl_2. The aqueous phase contained no bromide ion (Volhard) and only **2b** (91 mg) recovered from the extract. No dimer was obtained.[6]

(d) Increasing the KOAc tenfold gave the same results as in (c).

(e) A mixture of **2b** (31 mg), dry KOAc (32 mg), 18-crown-6 (285 mg) and acetonitrile (10 ml) was heated under reflux for 8 hr.[7] The solvent was removed and the residue extracted with benzene. After drying and removal of solvent the hexane-insoluble portion (to remove crown ether; 42 mg) was crystallized. It had m.p. 199–200° (benzene–hexane) identical with authentic **2b**. There was neither sign of acetate absorption nor of bromide ion in the aqueous phase.

A mixture of **2b** (30 mg), dry KF (423 mg), 18-crown-6 (77 mg) and acetonitrile (10 ml) was heated under reflux for 8 hr.[8] The solvent was removed and the residue extracted with EtOAc which removed 116 mg of the residue. Inorganic matter (378 mg) was not extracted. Recrystallization afforded the bromide **2b** (30 mg), m.p. 197–199°. Again there was no sign of displacement by fluoride ion.

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