# PROPELLANES-LVI

# REGIOSPECIFICITY IN DIELS-ALDER REACTIONS OF BROMO-DERIVATIVES OF SOME TETRAENIC PROPELLANE IMIDES<sup>a</sup>

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Abstract—In tetraenic propellane imides substituted at the imide nitrogen atom by relatively large groups both syn and anti-attack occurs when N-phenyltriazolinedione is used as dienophile. However, in formation of the mono-Diels-Alder adducts the unsubstituted cyclohexadiene ring is the one attacked and the bromo-cyclohexadiene ring is attacked only later, during formation of bis-adducts.

During the preparation of several tetraenic propellanes of the type 2 from the corresponding dienes 1 by NBS bromination followed by dehydrobromination using 1,5-diazabicyclo-[4.3.0]non-5-ene (DBN) tetraenic monobromo-derivatives 3 were formed as by-products of 2, in relatively low yields (ca 20%).

The Br atom was always present at C-3. This assignment arises from integration of signals in the appropriate PMR spectra as well as from the calculated spectra (see below).

Since these substrates were available we wanted to study whether or not the bromo-cyclohexadiene ring would be preferentially attacked by 4-phenyl-1,2,4triazoline-3,5-dione 4 as compared to the unsubstituted cyclohexadiene ring in 3 and whether the *synanti* ratio in such attacks will be different from the corresponding unsubstituted substrates of type 2. We have found kinetic data in the literature for the relative rates of reaction of butadiene and 2-chlorobutadiene (as well as the 2,3-dichloro-derivative) as well as those of isoprene and 2-chloro-3-methylbutadiene<sup>1</sup> which indicate that for a conjugated diene substituted in the 2-position the rate is slower by at least one order of magnitude for the halogen derivative as compared to the hydrocarbon.

We therefore expected that the unsubstituted ring would be more reactive towards the PTD than that which contains the bromine atom. This is contrary to our experience with substituted 1,6-methano [10] annulenes 5 where less clearcut results were obtained.<sup>2</sup>

Compounds of type 3 accompanied those of type 2 already described,<sup>a</sup> i.e. 3,  $R=CH_2CH(CH_3)_2$  with  $R'=n-C_6H_{13}$  or *exo*-bornyl as well as  $R=CH_3$ ; R'=exo-bornyl, described herein.

Scheme 1 summarizes the results for the first two bromo-derivatives.

Scheme 2 summarizes the results for the third bromo-derivative and its major accompaniment, the unsubstituted 13.



"Part LV. Peled and Ginsburg, Tetrahedron 37, 151 (1981).



That the Br atom is a substituent in the conjugated dienic system rather than in the side chain attached to the imide nitrogen atom is clear from NMR spectra of the starting materials as well as the mono-adducts in which the ratio of dienic:vinylic:allylic protons is 3:2:2 vs 4:2:2 in the analogs unsubstituted by bromine. In the *bis*-adducts the ratio of vinylic:allylic protons is 3:4 vs 4:4 for the unsubstituted analogs. The same holds for the ratio of cyclobutane protons: bridgehead protons in the cage compounds. Calculation of theoretical NMR spectra of compounds of type 2 and 3 suggest that the Br atom is at C-3 rather than C-2.

Mass spectral fragmentation of the mono-adducts resulting from retro-Diels-Alder reaction leads to an ion m/e = 227 of the constitution  $C_{12}H_9N_3O_2$  but the symmetrical bis-adducts, 8, have in addition ions corresponding to retro-Diels-Alder reaction of the substituted ring, m/e = 305,307 corresponding to  $C_{12}H_8BrN_3O_2$ . Based upon the mass spectral results the two fragmentations occur nearly to the same extent. If PTD had added to both cyclohexadiene rings more or less statistically, we would have expected to obtain more isomers of the mono-adduct than we obtained and were it true that we did not succeed in separating an alleged mixture of such mono-adducts.



the latter should have produced fragment ions of m/e 227,305,307 as in the case of the *bis*-adduct. (For the sake of more rigid comparison we compared only the *syn*-adducts throughout). However in the mono-adducts the ion m/e 227 was observed, unaccompanied by any ion of masses 305 or 307.

Calculation of theoretical NMR spectra of compounds of type 2, 3 and 8 suggest that the bromine atom in 3 is at C-3 rather than at C-2. Figs 1 and 2 indicate the similarities between the measured and calculated spectra for compounds 3a and 8a when for C-3 bromine in 3a and the corresponding derived position in 8a; the spectra are different for the isomeric C-2 bromine position.

#### EXPERIMENTAL

IR spectra were recorded with a Perkin-Elmer 237 spectrometer in CHCl<sub>3</sub> unless otherwise stated. NMR spectra were recorded with a Varian T-60 or a Bruker WP-60 instrument in CDCl<sub>3</sub> unless otherwise stated. r values are given. High resolution mass spectra were obtained with a Varian-MAT-711 spectrometer. M.ps are uncorrected. Chromatographic separations were conducted on 20 × 20 cm plates, each of 70 g silica gel 60PF254 (Merck) with ca. 150 mg material per preparative plate. The eluant was EtOAc: hexane in variable ratios. Diels-Alder reactions were conducted in CH<sub>2</sub>Cl<sub>2</sub> solns. Photocyclizations (300 nm) were carried out overnight in acetone using a Rayonet chamber. n-Hexyl 3'-bromo-11',13'-dioxo-12'-aza[4.4.3]propella-2',4', 7',9'-12(2S)-4-methylpentanoate, 3a.

This was isolated during chromatographic separation of the corresponding unsubstituted compound **2**,<sup>a</sup> in 23 "<sub>o</sub> yield, b.p. 155<sup>c</sup>/0.1 mm. (Found: C. 61.12: H. 6.61: Br. 16.29: N. 2.73. C<sub>24</sub>H<sub>30</sub>BrNO<sub>4</sub> requires: C. 60.50; H. 6.35; Br. 16.77; N. 2.94 "<sub>a</sub>). IR: 2900, 1790, 1730, 1390 cm<sup>-1</sup>. NMR: 3.6-4.2 (m. 7 vinylic H); 5.20 (dd, 1 H, (HN; J = 18 Hz); 5.85 (t, aH, Co<sub>2</sub>CH<sub>2</sub>, J = 8 Hz); 7.2-9.2 (m, 20 aliphatic H). MS: 369 (6); 367 (6); 296 (21); 294 (21); 248 (18); 240 (20); 208 (100); 206 (84).



Fig. 1. Calculated (above) and measured NMR spectra for 3a.



Fig. 2. Calculated (above) and measured NMR spectra for 8a.

Reaction of 3a with 4

(a) At room temp: **3a** (71 mg in 5 ml  $CH_2Cl_2$ ) reacted at once with PTD (15 mg; 0.57 eq in 10 ml). Removal of solvent gave **7a** (37 mg; 43 °<sub>6</sub>) and **6a** (15 mg; 18 °<sub>0</sub>).

Mono-adduct 7a had m.p.  $58-60^{\circ}$  (CH<sub>2</sub>Cl<sub>2</sub>-hexane). IR: 3000, 1790, 1720 (br), 1610, 1510, 1400 cm<sup>-1</sup>. NMR: 2.58 (s, 5 arom H); 3.54 (m, 2 vinylic H); 3.5-4.4 (m, 3 dienic H); 4.6-5.0 (m, 2 allylic H); 5.25 (dd, 1 H, CHN). 5.91 (t, 2 H, CO<sub>2</sub>CH<sub>2</sub>, J = 6 Hz); 7.6-9.2 (m, 20 aliph H). MS: 296 (24); 294 (24); 266 (5); 264 (4); 255 (10); 253 (15); 240 (100); 227 (6); 119 (14).

Mono-adduct **6a** had m.p. 144-145 (CH<sub>2</sub>Cl<sub>2</sub> hexane). (Found: N, 8.44. C<sub>32</sub>H<sub>35</sub>BrN<sub>4</sub>O<sub>6</sub> requires: N, 8.61°, ). IR (KBr): 2900, 1780, 1730 (br), 1600, 1500, 1400, 1250 cm<sup>-1</sup>. NMR: 2.62 (s, 5 arom H); 3.34 (m, 2 vinylic H); 3.6-4.3 (m, 3 dienic H); 4.73 (m, 2 allylic H); 5.20 (dd, 1 H, CHN, J = 15 Hz); 5.87 (t, 2 H, CO<sub>2</sub>CH<sub>2</sub>, J = 5 Hz); 7.6-9.2 (m, 20 aliph H). MS: 239 (3); 237 (3); 227 (100), 119 (98).

Bis-adduct **9a** was obtained during 30 min reaction from **7a** (13 mg in 3 ml) and PTD (4 mg in 2 ml), affording after

removal of solvent **9a** (15 mg; 91 °<sub>0</sub>), m.p. 125 (dec, CH<sub>2</sub>Cl<sub>2</sub>-hexane). (Found: C, 57.37; H, 4.96; Br, 9.98. C<sub>40</sub>H<sub>40</sub>BrN<sub>7</sub>O<sub>8</sub> requires: C, 58.11; H, 4.88; Br, 9.67 °<sub>0</sub>). IR (KBr): 2900, 1780, 1730 (br), 1600, 1500, 1400, 1250 cm<sup>-1</sup>. NMR: 2.57 (s, 10 arom H); 3.0–3.5 (m, 3 vinylic H); 4.2–4.8 (m, 4 allylic H); 5.30 (dd, 1 H, CHN, J = 16 Hz); 5.89 (t, 2 H, CO<sub>2</sub>CH<sub>2</sub>, J = 8 Hz); 7.6–9.2 (m, 20 aliph H). MS: 231 (24); 221 (18); 112 (100).

Bis-adduct 8a was obtained during 20 min reaction from 6a (21 mg in 5 ml) with PTD (6 mg in 2 ml), affording 8a (25 mg; 93 °<sub>0</sub>), m.p. 195-198' (CH<sub>2</sub>Cl<sub>2</sub>-hexane). (Found: Br. 10.01: N. 11.95; M.W. 825.2088, 827.2061.  $C_{40}H_{40}BrN_7O_8$  requires: Br. 9.67; N. 11.86 °<sub>0</sub>; M.W. 825.2121, 827.2071). IR (KBr): 2900, 1780, 1730, 1600, 1500, 1400 cm<sup>-1</sup>. NMR: 2.59 (s, 10 arom H); 3.0-4.0 (m, 3 vinylic H); 4.4 4.7 (m, 4 allylic H); 5.15 (dd, 1 H, CHN, J = 16 Hz); 5.95 (t, 2 H, CO<sub>2</sub>CH<sub>2</sub>, J = 8 Hz); 7.3-9.2 (m, 20 aliph H). MS: M<sup>+</sup> (5): 307 (45); 305 (49); 240 (6); 227 (70); 119 (100).

(b) At room temp with 2 eq PTD: 3a (292 mg in 5 ml) reacted during 30 min with PTD (200 mg in 5 ml) affording 9a (322 mg;  $63^{\circ}$ ,) and 8a (146 mg;  $29^{\circ}$ ,).

(c)  $At - 78^{\circ}$ ; **3a** (115 mg in 10 ml) reacted with PTD (75 mg in 10 ml) during 1 hr, giving **9a** (95 mg; 48 "<sub>o</sub>) and **8a** (64 mg; 32 "<sub>o</sub>).

Photochemical cyclization of **8a** gave **10a** in 98", yield, m.p. 132-134° CH<sub>2</sub>Cl<sub>2</sub>-hexane). (Found: Peak matching 825.2097, 827.2125), IR (KBr): 3000, 1730 (br), 1500, 1400 cm<sup>-1</sup>. NMR: 2.53 (s, 10 arom H); 4.6-5.2 (m, 4 bridgehead H + 1 H. CHN): 5.96 (t, 2 H, CO<sub>2</sub>CH<sub>2</sub>, J = 6 Hz); 6.40 (m, 3 cyclobutane H); 7.2-9.2 (m, 20 aliph H). MS: 163 (20); 162 (27); 137 (11); 131 (9); 119 (10).

# exo-Bornyl 3'-bromo-11'.13'-dioxo-12'-aza[4.4.3]propella-2',4',7',9-tetraene-12'-(2S)-4-methylpentanoate, **3b**

This compound was isolated in 17 ", yield as a by-product of the unsubstituted product." It is unstable and decomposes on standing at room temp. (Found: M.W. 487.1222, 485.1219.  $C_{25}H_{28}BrNO_4$  requires: N.W. 487.1180, 485.1201), NMR: 3.8-4.6 (m, 7 vinylic H); 5.0-5.5 (m, 1 H, CHN + 1 H,  $CO_2CH$ ); 8.0 9.5 (m, 25 aliph H). MS: 348 (11); 346 (9); 208 (46); 206 (40).

#### Reaction of 3b with PTD

(a) At room temp: 3b (324 mg in 10 ml) underwent immediate reaction with PTD (75 mg; 0.75 eq in 5 ml), giving recovered 3b (55 mg), mono-adduct 7b (163 mg;  $45^{\circ}_{o}$ ) and mono-adduct 6b (91 mg;  $25^{\circ}_{o}$ ).

Mono-adduct **7b** had m.p.  $133 \cdot 135^{\circ}$  (CH<sub>2</sub>Cl<sub>2</sub>-hexane). (Found: Br, 11.29. C<sub>36</sub>H<sub>39</sub>BrN<sub>4</sub>O<sub>6</sub> requires: Br, 11.35<sup>°°</sup><sub>v</sub>). IR (KBr): 2900, 1800, 1740, 1400 cm<sup>-1</sup>. NMR: 2.6 (s. 5 arom H); 3.3-3.5 (m, 2 vinylic H); 3.6-4.2 (m, 3 dienic H); 4.7-4.9 (m, 2 allylic H); 5.0-5.5 (m, 1 H, C<u>H</u>N + 1 H, CO<sub>2</sub>C<u>H</u>); 8.0-9.5 (m, 25 aliph H). MS: 297 (3); 296 (9); 295 (6); 294 (11); 240 (9); 238 (9); 227 (39).

Mono-adduct **6b** had m.p. 223- 224<sup>-</sup> (CH<sub>2</sub>Cl<sub>2</sub>- hexane). (Found: Br, 11.49<sup>*w*</sup><sub>0</sub>). IR (KBr): 2900, 1800, 1740, 1400 cm<sup>-1</sup>. NMR: 2.6 (s, 5 arom H); 3.3 3.6 (m, 2 vinylic H); 3.9 4.3 (m, 3 dienic H); 4.7-4.9 (m, 2 allylic H), 5.0-5.5 (m, 1 H, CHN + 1 H, CO<sub>2</sub>CH); 8.0-9.5 (m, 25 aliph H). MS: 296 (9); 294 (6); 227 (100).

Bis-adduct 9b was prepared in a 2 min reaction between 7b (38 mg in 3 ml) with PTD (10 mg in 2 ml) giving 9b (45 mg; 94 " $_{0}$ , m.p. 284' (dec, CH<sub>2</sub>Cl<sub>2</sub>-hexane). (Found: Br, 8.38. C<sub>44</sub>H<sub>44</sub>BrN-O<sub>8</sub> requires: Br, 9.09 " $_{0}$ ). IR (KBr): 2900, 1790, 1730, 1400 cm<sup>-1</sup>. NMR: 2.4 (s. 10 arom H); 3 2- 3.4 (m, 3 vinylic H); 4.4-4.7 (m, 4 allylic H); 5.0- 5.5 (m, 1 H, CHN + 1 H, CO<sub>2</sub>CH); 8.0 9.5 (m, 25 aliph H). MS: 296 (15); 294 (18); 284 (5); 282 (6); 253 (9); 251 (9); 239 (19); 237 (19); 227 (45); 177 (19); 119 (100).

Bis-adduct **8b** was prepared in a 2 min reaction between **6b** (50 mg in 5 ml) with PTD (12 mg in 2 ml), giving **8b** (60 mg; 97", m.p. 291° (dec,  $CH_2CI_2$  hexane). (Found: Br, 8.52", IR (KBr): 2900, 1790, 1740, 1400 cm<sup>-1</sup>. NMR: 2.4 (s, 10 arom H): 3.3-36 (m, 3 vinylic H); 4.4 4.7 (m, 4 allylic H); 5.0 5.5 (m, 1 H, CHN + 1 H,  $CO_2CH$ ); 8.0-9.5 (m, 25 aliph H). MS: 307 (27): 305 (25); 227 (54); 181 (7): 160 (12); 137 (11); 119 (100).

Photochemical cyclization of **8b** gave **10b** in 88 ", yield, m.p. 292-293" (CH<sub>2</sub>Cl<sub>2</sub>-hexane). (Found: Br, 9.12", IR (KBr): 2900, 1790, 1740, 1400 cm<sup>-1</sup>. NMR: 2.4 (s, 10 arom H); 4.5-5.5 (m, 4 bridgehead H + 1 H, CHN + 1 H, CO<sub>2</sub>CH); 6.3-6.6 (m, 3 cyclobutane H); 8.0-9.5 (m, 25 aliph H). MS: 366 (26); 363 (12); 355 (55); 149 (100); 146 (27); 112 (100).

# exo-Bornyl 11',13'-dioxo-12'-aza[4.4.3]propella-3',8'-diene-12'-(2S)-propionate, **12**

This was prepared in 50°, yield from the free acid as previously described," b.p. 142 (0.01 mm. (Found: C, 72.90; H, 8.12; N, 3.32; M.W. 411.2341.  $C_{25}H_{33}NO_4$  requires: C, 72.96; H, 8.08; N, 3.40°, M.W. 411.2409). IR: 3000 -2850,

1780, 1730, 1700, 1400 cm<sup>-1</sup>. NMR: 4.0-4.3 (m, 4 vinylic H); 5.0  $\cdot$ 5.5 (m, 1 H, CHN + 1 H, CHO); 7.1-9.2 (m, 27 aliph H). MS: M<sup>-</sup>, 411 (1); 258 (10); 230 (45); 174 (8); 137 (70); 136 (40).

## exo-Bornyl 11',13'-dioxo-12'-aza[4.4.3]propella-2',4',7',9'tetraene-12'-(2S)-propionate, 13

The tetraene was prepared using benzene<sup>a</sup> in 74  $_{0.0}^{a}$  yield but the product was composed of 13 (84  $_{0.0}^{a}$ ) and its 3'-bromoderivative, 3c (16  $_{0.0}^{a}$ ). This composition was based upon the NMR spectrum of the mixture of 13 and 3c. It had b.p. 125' (0.01 mm. (Found for 13: M.W. 407.2135. C<sub>25</sub>H<sub>29</sub>NO<sub>4</sub> requires: M.W. 407.2096). IR (mixture): 2900, 1780, 1740, 1710, 1380 cm<sup>-1</sup>. NMR (mixture): 3.8–4.5 (A<sub>2</sub>B<sub>2</sub>, 8 vinylic H): 4.9–5.4 (m, 1 H, CHN + 1 H, CHO); 8.0–9.3 (m, 19 aliph H). MS: M' of 13, 407 (5): 226 (3); 205 (6); 137 (17): 128 (100).

# Reaction of mixture with PTD

(a) At room temp. The mixture (345 mg in 20 ml) was heated with PTD until stable red color persisted, giving 14 (122 mg;  $19^{\circ}_{\circ}$ ), 15 (390 mg;  $61^{\circ}_{\circ}$ ) and 8c (100 mg;  $17^{\circ}_{\circ}$ ).

Bis-adduct 14 had m.p. 190–191° ( $CH_2CI_2$ -hexane). (Found: N, 12.11; M.W. 757.2871.  $C_{41}H_{39}N_7O_8$  requires: N, 12.94°,; M.W. 757.2860). IR (KBr): 2950, 1780, 1730 (br), 1400 cm<sup>-1</sup>. NMR: 2.5 (s, 10 arom H); 3.2–3.7 (m, 4 vinylic H); 4.2–4.8 (m, 4 allylic H); 5.0–5.5 (m, 1 H, CHN + 1 H, CHO); 8.0–9.3 (m, 19 aliph H). MS: M<sup>+</sup>, 757 (1); 227 (11); 193 (5); 174 (7); 136 (14); 121 (32); 119 (50).

Bis-adduct 15 had m.p. 293 294° ( $CH_2Cl_2$ -hexane). (Found: N, 12.14; M.W. 757.2865 (peak matching)). IR (KBr): 2950, 1800, 1730 (br), 1500, 1400, 1220 cm<sup>-1</sup>. NMR: 2.5 (s, 10 arom H); 3.5-3.8 (m, 4 vinylic H); 4.5-4.7 (m, 4 allylic H); 5.0-5.5 (m, 1 H, CHN + 1 H, CHO); 8.0-9.3 (m, 19 allph H). MS: 227 (55); 163 (13); 119 (5).

Bis-adduct & had m.p.  $204-205^{\circ}$  (CH<sub>2</sub>Cl<sub>2</sub> hexane). (Found: N, 11.50; Br, 9.27. C<sub>4.1</sub>H<sub>38</sub>BrN<sub>7</sub>O<sub>8</sub> requires: N, 11.72; Br, 9.55°<sub>a</sub>). IR (KBr): 2950, 1780, 1730, 1400 cm<sup>-1</sup>. NMR: 2.6 (s, 10 arom H); 2.9–3.9 (m, 3 vinylic H); 4.3–4.8 (m, 4 allylic H); 5.0–5.5 (m, 1 H, CHN + 1 H, CHO); 8.0–9.3 (m, 19 aliph H). MS: 340 (13); 307 (5), 305 (5); 254 (12); 252 (13); 227 (10); 136 (14); 121 (11); 119 (100).

(b) At = -78. Mixture (106 mg in 10 ml) reacted during 15 min with PTD (95 mg in 5 ml), giving 14 (25 mg; 13 "<sub>o</sub>), 15 (126 mg; 68 "<sub>o</sub>) and 8c (25 mg; 16 "<sub>o</sub>).

Photochemical cyclization of 15 gave 16 in 93 ", yield, m.p. 188 (CH<sub>2</sub>Cl<sub>2</sub>-hexane). (Found: N,  $12.52^{\circ}$ , M.W. 757.2860). IR (KBr): 2950, 1780, 1740 (br); 1400 cm<sup>-1</sup>. NMR: 4.7 5.6 (m, 4 bridgehead H + 1 H, CHN + 1 H, CHO); 6.5-7.0 (m, 4 cyclobutane H); 8.0 -9.3 (m, 19 aliph H). MS: M<sup>+</sup>, 757 (0.5); 576 (4); 227 (33); 183 (10); 136 (41); 121 (77); 119 (7).

Photochemical cyclization of **8c** gave **17** in 93  $^{\circ}$ , yield, m.p. 183-184 (CH<sub>2</sub>Cl<sub>2</sub>-hexane). (Found: M.W. 837.1955, 835.1980. C<sub>41</sub>H<sub>38</sub>BrN<sub>7</sub>O<sub>8</sub> requires: M.W. 837.1873, 835.1965). IR (KBr): 2950, 1780, 1730 (br), 1400 cm<sup>-1</sup>. NMR: 2.5 (s, 10 arom H): 4.3-5.6 (m, 4 bridgehead H + 1 H, CHN + 1 H, CHO); 6.0-6.6 (m. 3 cyclobutane H); 8.5 9.2 (m, 19 aliph H). MS: M<sup>+</sup>, 837 (1), 835 (1); 318 (16); 231 (47); 136 (58); 121 (100).

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