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Unexpected chlorination of angularly annelated [2.2]paracyclophanes during DDQ oxidation

Lucio Minuti,[a,*] Aldo Taticchi,[a,*] Assunta Marrocchi,[a] Daniela Lanari,[a] Eszter Gacs-Baitz[b] and Agnes Gomory[b]

[a] *Dipartimento di Chimica, Università degli Studi di Perugia, via Elce di Sotto 8, 06123 Perugia, Italy*
[b] *Central Institute for Chemistry, Hungarian Academy of Sciences, PO Box 17, H-1525 Budapest, Hungary*

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Abstract—DDQ treatment of the Diels–Alder products **1** unexpectedly led to chloroderivatives **2**. Chlorination did not occur during DDQ treatment of the fully aromatised compounds **3**. These results point out that DDQ acted as an oxidant and source of chlorine.
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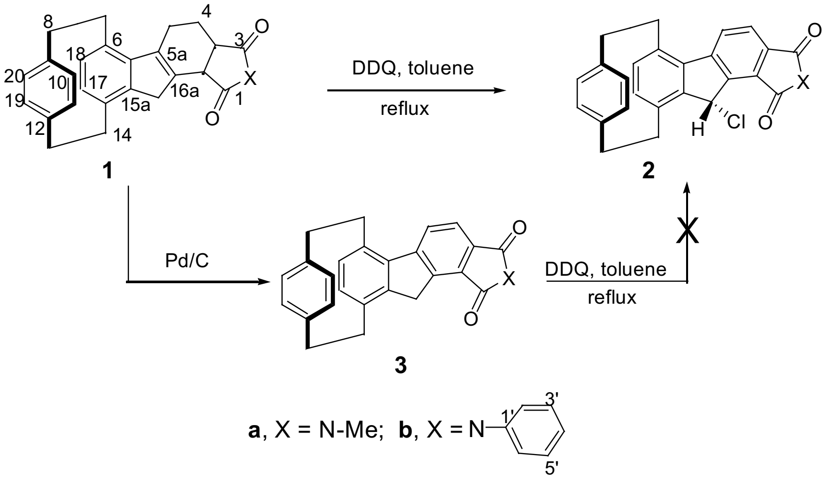
In connection with our studies on angularly annelated [2.2]paracyclophanes we have described the synthesis of a variety of compounds by a simple approach using the Diels–Alder cycloaddition to construct the carbon framework. The subsequent dehydrogenation–oxidation of the cycloadducts was successfully carried out by DDQ treatment.[1] In contrast with previous results, recently we observed that oxidation of Diels–Alder product **1a** by DDQ in toluene at reflux temperature gave, surprisingly, the fully aromatised chloro compound **2a** (Scheme 1) in 30% yield.[2]

The presence of chlorine was established by Beilstein's test[3] as well as by mass spectrum.

The mass spectrum, obtained by a VG ZAB-2SEQ tandem mass spectrometer using electron impact (70 eV) for ionisation, showed a molecular ion [M$^+$] at *m*/*z*



Scheme 1.

Keywords: [2.2]Paracyclophanes; Oxidation; Chlorination.

* Corresponding author. Tel. +39 075 5855537; fax: +39 075 5855560; e-mail: taticchi@unipg.it

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413. In addition two major fragment ions were detected at *m/z* 309 and 104; the fragment $[M-104]^+$ at *m/z* 309 is a result of the rupture of the ethane bridge of [2.2]paracyclophane unit and loss of the $–CH_2–C_6H_4–CH_2$-moiety (*m/z* 104).

The structural assignment has been mainly supported by COSY, $^1H–\{^1H\}$-NOE and long-range hetero-correlation experiments. The chemical shift values of H(16) (singlet at 5.71 ppm) and C(16) (methine at 54.1 ppm) were diagnostic for the chlorine position. The stereochemistry of H(16) followed from the NOE experiments. Selective pre-irradiation of the resonance of H(16) resulted in signal enhancement of the resonances attributed to H(11) and H(14), thus confirming the stereochemistry of the chlorine at C-16.

These results induced us to test the same reaction on another product, the *N*-phenylmaleimide derivative **1b**. When **1b** was treated with DDQ under the same experimental conditions,[2] chloroderivative **2b** was obtained in 51% yield.[4] The structural assignment of **2b** was supported by mass spectrum (molecular ion $[M^+]$ at *m/z* 475 and fragment $[M-104]^+$ at *m/z* 371) and by NMR shift values of H(16) and C(16) ($\delta_H = 5.76$ ppm, $\delta_C = 54.0$ ppm). As for **2a**, the NOEs observed on H(11) and H(14) upon irradiation of H(16), confirmed the stereochemistry of the chlorine at C-16.

In the course of previous studies on the synthesis of IPA[5] and helicenophanes,[1] Diels–Alder cycloadducts were often aromatised by DDQ treatment and chlorination never occurred. When aromatic compounds **3**[6] were treated with DDQ,[7] starting material was recovered thus indicating that the chlorination occurred exclusively on their hydroderivatives. Recently Pragnacharyulu and Abushanab[8] reported the chlorination of 5,6-dihydropyrimidine nucleosides during DDQ oxidation. To our knowledge there is no other precedence for this reaction.

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References and notes

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2. Experimental procedure. A toluene solution (10 mL) of compound **1a**[6] (0.2 g, 0.52 mmol) was treated with DDQ (0.8 g, 3.5 mmol) at reflux temperature for 8 h. The solvent was removed in vacuo and the crude product was chromatographed on silica gel with hexane–ethyl acetate (7:3) to afford 0.064 g (30%) of the chloroderivative **2a** as pink crystals; mp 218–219 °C (EtOAc); IR ($CHCl_3$): 1706 (s, C=O) cm^{-1}; ^1H NMR, δ 2.85–3.07 (m, 5H, H-7, H-8, Hs-13, H-14), 3.26 (s, 3H, Me), 3.30 (m, 1H, H-8), 3.55 (m, 1H, H-14), 3.87 (m, 1H, H-7), 5.71 (s, 1H, H-16), 5.79 (dd, 1H, J = 8.0, 1.6 Hz, H-10), 6.24 (dd, 1H, J = 8.0, 1.7 Hz, H-11), 6.56 (dd, 1H, J = 7.9, 1.6 Hz, H-20), 6.61 (dd, 1H, J = 7.9, 1.7 Hz, H-19), 6.65 (d, 1H, J = 7.8 Hz, H-17), 6.68 (d, 1H, J = 7.8 Hz, H-18), 7.98 (d, 1H, J = 7.8 Hz, H-4), 8.04 (d, 1H, J = 7.8 Hz, H-5); ^{13}C NMR, δ 24.1 (Me), 31.8 (C-8), 33.2, 33.9 (C-13, C-14), 34.2 (C-7), 54.1 (C-16), 125.1 (C-4), 126.9 (C-11), 127.2 (C-5), 128.4 (C-16b), 128.5 (C-10), 128.9 (C-3a), 133.5 (C-19), 133.8 (C-20), 135.4 (C-18), 137.0, 137.6, 138.8 (C-6, C-15, C-5b), 137.7 (C-17), 139.2, 139.3 (C-9, C-12), 140.5 (C-16a), 145.6 (C-15a), 148.3 (C-5a), 167.2 (C-1), 168.2 (C-8); MS, *m/z* (rel. int.) 413 (M^+, 62), 365 (10), 359 (5.8), 309 (50), 217 (10), 190 (18), 189 (44), 104 (100). Anal. Calcd for $C_{26}H_{20}ClNO_2$: C, 75.45; H, 4.87. Found: C, 75.40; H, 4.89.
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4. Chloroderivative **2b**: Reaction yield (51%); chromatographed on silica gel with dichloromethane; orange crystals; mp 256-257 °C (EtOAc); IR ($CHCl_3$): 1718 (s, C=O) cm^{-1}; ^1H NMR, δ 2.88–3.55 (m, 7H, H-7, Hs-8, Hs-13, Hs-14), 3.88 (m, 1H, H-7), 5.76 (s, 1H, H-16), 5.84 (dd, 1H, J = 8.0, 1.6 Hz, H-10), 6.28 (dd, 1H, J = 8.0, 1.7 Hz, H-11), 6.58 (dd, 1H, J = 7.9, 1.6 Hz, H-20), 6.61 (dd, 1H, J = 7.9, 1.7 Hz; H-19), 6.66 (d, 1H, J = 7.8 Hz, H-17), 6.69 (d, 1H, J = 7.8 Hz, H-18), 7.45 (m, 1H, H-4′), 7.54 (m, 4H, H-2′, H-3′, H-5′, H-6′), 8.07 (d, 1H, J = 7.8 Hz, H-4), 8.10 (d, 1H, J = 7.8 Hz, H-5); ^{13}C NMR, δ 31.8 (C-8), 33.2 (C-13), 33.9 (C-14), 34.1 (C-7), 54.0 (C-16), 125.6 (C-4), 126.6(C-2′, C-6′), 126.9 (C-11), 127.7 (C-5), 127.8 (C-16b), 128.1 (C-4′), 128.5 (C-10), 129.1 (C-3′, C-5′), 129.8 (C-3a), 131.8 (C-1′), 133.5, 133.8 (C-19, C-20), 135.5 (C-18), 137.1, 137.6, 138.7 (C-15, C-16, C-5b), 137.7 (C-17),, 139.1, 139.2 (C- 9, C-12), 140.9 (C-16a), 145.7 (C-15a), 148.8 (C-5a), 165.8 (C-1), 167.0 (C-3); MS, *m/z* (rel. int.) 475 (M^+, 12), 441 (60), 439 (6.7), 371 (10), 337 (100), 218 (8.4), 189 (19), 104 (62). Anal. Calcd for $C_{26}H_{20}ClNO_2$: C, 75.45; H, 4.87. Found: C, 75.40; H, 4.89.
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7. DDQ treatment of compounds **3**. A toluene solution (25 mL) of the aromatic compounds **3a** or **3b**[6] (0.052 mmol) and DDQ (0.09 mmol) was heated at reflux temperature and the course of the reaction was checked by analysing a small aliquot of the reaction mixture at different times. After 24 h the reaction mixture was worked up as usual. All the TLC analyses showed that only the reactants were present in the reaction mixture.
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