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ortho-Quinodimethane from anthracene epidioxide: Scope of the Diels–Alder reaction and mild preparation of naphthalene derivatives

ortho-*Quinodiméthane par thermolyse de l'épidioxyde d'anthracène : réaction de Diels–Alder et préparation douce de dérivés naphtaléniques*

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ABSTRACT

The thermal isomerisation of anthracene epidioxide **3** has been known to give phenylenedioxy-*ortho*-quinodimethane **5** as a reactive transient. We presented herein the scope of the Diels–Alder reaction of this transient **5** with some dienophiles. In addition, a mild synthesis of naphthalene derivatives has been developed via base-induced cleavage of the obtained Diels–Alder adducts.

RÉSUMÉ

L'isomérisation thermique de l'épidioxyde de l'anthracène avait été décrite pour donner l'intermédiaire réactif **5** phénylènedioxy-*ortho*-quinodiméthane. Nous présentons les limitations de sa réaction de Diels–Alder avec quelques diénophiles. En complément, nous décrivons une synthèse simple de dérivés naphtaléniques par coupure basique des adduits obtenus.

1. Introduction

Ortho-quinodimethanes are reactive species that are not isolable, but have been suspected as transients in 1959 by Cava et al. [1]. They were originally obtained by the double elimination of α,α'-dibromo-*ortho*-xylenes [1] or by thermal opening of the corresponding benzocyclobutenes [2,3], and several reviews emphasised the importance of these transients as tools for the synthesis of cyclic organic compounds [4–9]. An interesting reaction was the direct formation of the naphthalene derivatives **2** by Diels–Alder reaction with dibromo-*ortho*-xylylene **1** (generated from tetrabromoxylene) with spontaneous loss of HBr [1,10,11] (Scheme 1).

An early study, presented in Scheme 2, showed that the thermal isomerisation of anthracene endoperoxide **3** led to *ortho*-quinodimethane **5** through diepoxide **4** and finally to two successive dimers of **5**, an original [8π+6π] one and the normal [8π+2π] one [12a]. Both isomeric transients **4** and **5** could be trapped with maleic anhydride (**6a**) or

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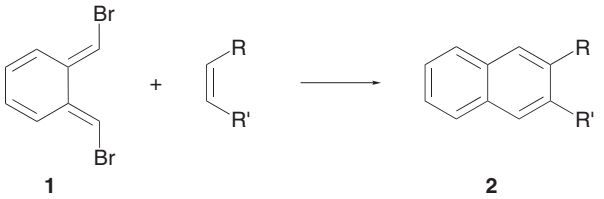


Scheme 1.

N-methylmaleimide (**6b**) to give the isolated *endo* adducts **7b** and **8a,b**, respectively [12b]. From these latter adducts, a base-catalysed or thermal aromatisation into the corresponding naphthalene compounds **9a** and **9b** has been observed, with the release of catechol as a by-product [12b].

This synthesis of naphthalene compounds used only thermal and base-induced transformations and was also suitable to synthetize acid-sensitive compounds. The use of this *ortho*-quinodimethane **5** in organic synthesis has never been studied, although the latter was very easy to obtain from the cheap anthracene. The purpose of this work was to investigate the scope of this Diels–Alder reaction and the further formation of naphthalene derivatives.

2. Results and discussion

2.1. Case of reactive dienophiles

The addition of *N*-methylmaleimide **6a** or maleic anhydride **6b** has already been studied in the initial study of the thermal isomerisation of anthracene epidioxide **3** in refluxing benzene. The corresponding adducts **7b** (10%) and **8a,b** (70–76%) have been isolated along with minute amounts of anthraquinone [12b].

In the present work (Scheme 3), the thermal isomerisation of epidioxide **3** was performed at higher temperature in order to favour the reaction with *ortho*-quinodimethane **5**, i.e. in refluxing chlorobenzene (ca. 132 °C) for 1 h in the presence of a dienophile in slight excess (ca 1.2 equiv.).

Using 1,4-benzoquinone **10a**, 1,4-naphthoquinone **10b** or *trans*-dibenzoylethylene **11** as dienophiles, adducts **14a**, **14b** or **15**, respectively, were isolated in good yields (60–70%).

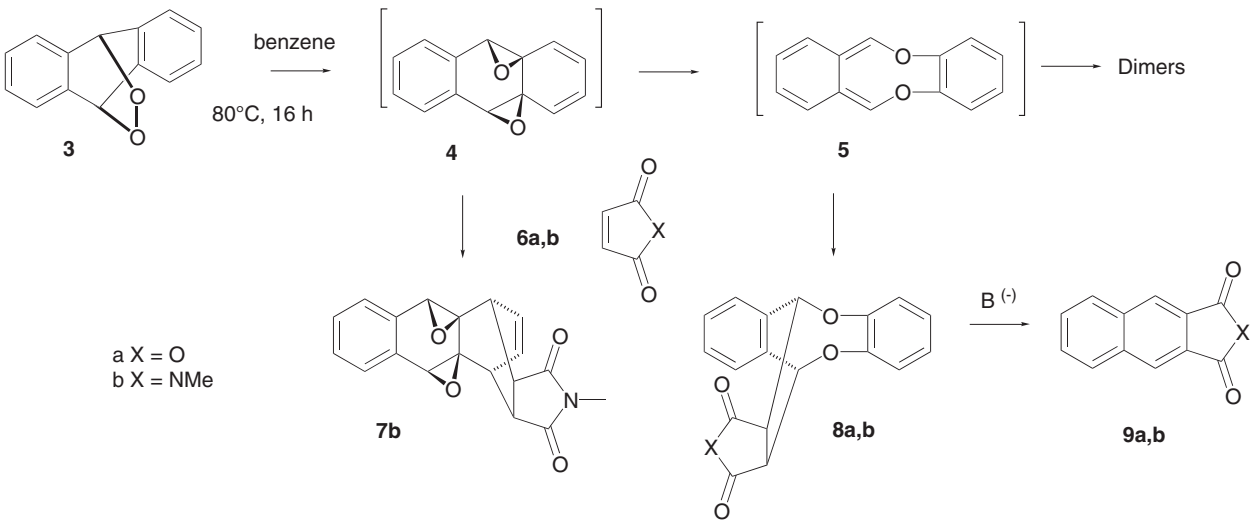
In the particular case of benzoquinone **10a**, a double addition was observed when epidioxide **3** was used in two-fold excess. However, the adduct could not be isolated as a pure compound and was treated directly with a base (see below).

2.2. Case of less reactive dienophiles

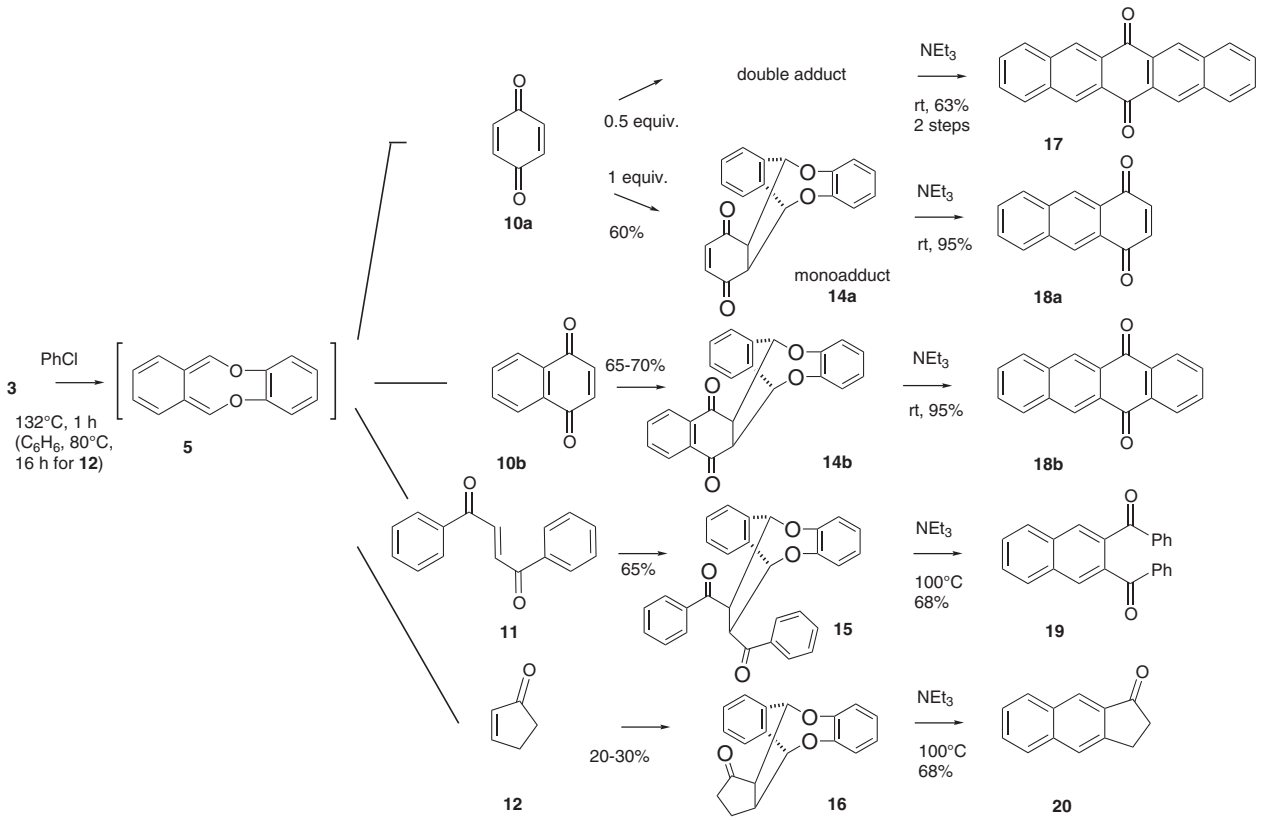
Cyclohex-2-en-1-one, cyclohexene, and coumarin were unreactive and dimers of **5** were only observed. In the case of the cyclopentenone **12**, the adduct **16** was isolated in poor yield (20–30%) and required to heat under refluxing benzene for 16 h with an 8-fold excess of the dienophile (Scheme 3). An inactivated double bond or a double bond activated by only one carbonyl function was also too less reactive for this Diels–Alder reaction to compete with dimerization. The more reactive 5-membered ring **12** gave only poorly the desired adduct.

2.3. Structure of the adducts

In all cases, we obtained a single adduct. Adduct **15** possessed the benzoyl groups in *trans* relation, as indicated by the important coupling between the protons in α-position to the carbonyl functions (J = 8 Hz). We assumed that adducts **14a,b** and **16** possessed an *endo*-configuration (see Scheme 3) as it has already been demonstrated for **8b** [12b]. This was confirmed in ^{1}H NMR spectra of **14a** and **14b** by the clear deshielding of the protons H-α in α-position to the carbonyl groups (δ 4.40 and 4.05 ppm, respectively) in comparison to the corresponding protons

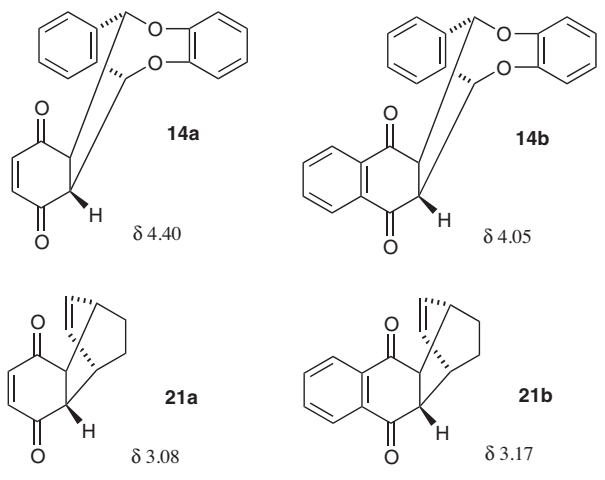


Scheme 2.



Scheme 3.

of the similar adducts **21a** [13] and **21b** [14] of the quinones **10a** and **10b** with cyclohexadiene (δ 3.22 and 3.17, respectively), as depicted in Scheme 4. This deshielding was due to the influence of the nearby intracyclic oxygen atoms of the veratrole moiety. In the case of the non-symmetrical adduct **15**, this important effect shifted one of the H-α protons at 5.90 ppm, with also a deshielding of 1.4 ppm with respect to the other H-α (at 4.50 ppm).



Scheme 4.

2.4. Base-induced cleavage of the adducts

Instead of an aqueous sodium carbonate solution under refluxing THF as originally described [12b], we have preferred to use the triethylamine as a more suitable and efficient base (Scheme 3). For mono-adducts **14a** and **14b**, the addition of an excess of triethylamine at room temperature was sufficient to cleave these adducts into 1,4-anthraquinone **18a** or naphthacene-5,12-quinone **18b**, which were isolated in good yields by simple crystallisation and washing in order to discard the formed catechol. It is worth noting that this transformation could be carried out in a one-pot process. For instance, endoperoxide **3** was refluxed with a slight excess of benzoquinone **10a** for 1 h. The solvent was then partially evaporated, and after addition of an excess of triethylamine, quinone **18a** was isolated. However, using half the amount of **10a** led to a double addition of *ortho*-quinodimethane **5** onto this benzoquinone, followed by a double cleavage after the addition of triethylamine to give pentacenequinone **17**. In both the cases, the overall yield of quinones **18a** or **17** was similar (ca 65%). Concerning adducts **15** and **16**, their cleavage with triethylamine was more difficult and was achieved under refluxing 1-propanol for one day to give the known 2,3-dibenzoylnaphthalene **19** [15] and benzo[*f*]indanone **20** [11] in 68% yield, respectively. In these cases, the catechol by-product was discarded by oxidation of the crude product on silica gel plates (see Experimental part).

Actually, the dibromo-*ortho*-quinodimethane transient **1** was more reactive than the *ortho*-quinodimethane **5** intermediate. This was exemplified with benzoindenone **20** [11], which was obtained in better yield with dibromo **1**. However, the formation of reactive hydrobromic acid limited its use, even if the addition of calcium carbonate improved the conditions [16].

3. Conclusion

We have studied the scope of the Diels–Alder reaction of the transient phenylenedioxy-*ortho*-quinodimethane **5,** issued from the thermal isomerisation of anthracene epidioxide **3**. We have then developed a very mild preparation of naphthalene derivatives by triethylamine-catalysed cleavage of the corresponding adducts. This method allows the synthesis of acid-sensitive compounds and offers certain advantages over the classical method using dibromo-*ortho*-quinodimethane **1**, but seems limited to reactive dienophiles as quinones **10a,b** or dibenzoylethylene **11**.

4. Experimental part

4.1. General

Flash chromatography (FC): silica gel (Merck 60, 230–400 mesh). TLC: Al-roll silica gel (Merck 60, F_{254}). Mp: Kofler hot bench. IR spectra (ν in cm^{-1}): PerkinElmer 297. UV spectra: Spectrometer Cary 15. ^1H and ^{13}C NMR spectra (80 MHz and 20 MHz resp.): Varian FT 80A, tetramethylsilane (TMS) as an internal standard. Microanalyses were carried out by the Laboratoire de microanalyses, Université Paris-6, France.

4.2. Reagents and solvents

Usual solvents and PhCl were freshly distilled, dry Et_2O and benzene were distilled and stored over Na, $CHCl_3$ was distilled over P_2O_5 and kept over Na_2CO_3.

4.2.1. Preparation of the 9,10-epidioxy-9,10-dihydroxyanthracene (3) [12b]

To a solution of anthracene (4.0 g, 22 mmol) in $CHCl_3$ (600 mL) was added a solution of hematoporphyrin hydrochloride (50 mg) in EtOH (100 mL) and this solution was irradiated with a halogen lamp whose light was filtered through an aqueous solution of Na_2CrO_4 (20 g/L). The anthracene disappearing was monitored by UV-spectroscopy or TLC. The dye was discarded by the addition of solid Na_2CO_3 and filtration. The solution was then evaporated, the residue crystallised and washed in EtOH and Et_2O to give cream crystals of **3** (4.2 g, 84%).

4.3. Preparation of the adducts

4.3.1. General procedure

A solution of **3** (0.2 g, 0.95 mmol) and the dienophile (ca 1.2 equiv.) in chlorobenzene (20 mL) was heated under reflux for 1 h. The solvent was then evaporated and the adduct isolated by crystallisation and washing in the given solvent.

4.3.2. Benzoquinone adduct 14a: general procedure with 3 (0.3 g, 1.43 mmol) and 10a (0.19 g, 1.76 mmol, 1.23 equiv.)

Cream crystals from acetone, 60% yield, mp (dec) > 290 °C (C_6H_5Cl).

IR (KBr): 1670 (C=O), 1485, 1240, 810, 760 cm^{-1}. UV (THF), λ_{max}(log ε): 385 (1.78); 283 (3.19); 270 (3.26); 262 (3.25) nm. ^1H NMR ($CDCl_3$): δ 4.40 (m, 2 H, 2 H-α); 5.80 (m, 2 H, H-6, H-11); 6.80 (s, 4 H, H-1 to H-4); 7.20 (s, 6 H, 2 H-β, H-7 to H-10). ^{13}C NMR ($CDCl_3$): δ 52.1 (2 C-α); 81.1 (C-6, C-11); 123.2, 124.6 (C-1 to C-4); 129.6, 130.4 (C-7 to C-11); 133.5 (C-6a, C-10a); 141.1 (2 C-β); 149.0 (C-4a, C-12a); 195.7 (2 C=O) ppm. Anal. calcd for $C_{20}H_{14}O_4$ (318.0): C, 75.46; H, 4.43; O, 20.10. Found: C, 75.7; H, 4.6; O, 20.2.

4.3.3. Naphthalenequinone adduct 14b: general procedure with 3 (0.2 g, 0.95 mmol) and 10b (0.20 g, 1.28 mmol, 1.35 equiv.)

Cream crystals, 65–70% yield, mp 271 °C (benzene).

IR (KBr): 1670 (C=O), 1240, 980, 950, 800, 745 cm^{-1}. UV (THF), λ_{max}(log ε): 385 (2.26); 295 (3.39); 278 (3.51) nm. ^1H NMR ($CDCl_3$): δ 4.05 (m, 2 H, 2 H-α); 6.00 (m, 2 H, H-6, H-11); 6.80 (s, 4 H, H-1 to H-4); 7.20 (s, 4 H, H-7 to H-10); 7.50–8.00 (m, 4 H, 2 H-γ, 2 H-δ). ^{13}C NMR ($CDCl_3$): δ 52.8 (2 C-α); 81.2 (C-6, C-11); 123.3, 124.5 (C-1 to C-4); 127.0 (2 C-β); 129.7, 130.2 (C-7 to C-11); 133.9 (C-6a, C-10a); 134.6, 134.8 (2 C-γ, 2 C-δ); 149.0 (C-4a, C-12a); 195.2 (2 C=O) ppm. Anal. calcd for $C_{24}H_{16}O_4$ (368.4): C, 78.25; H, 4.38; O, 17.37. Found: C, 78.3; H, 4.4; O, 17.2.

4.3.4. trans-2,3-Dibenzoylethylene adduct 15: general procedure with 3 (0.5 g, 2.4 mmol) and 11 (0.65 g, 2.75 mmol, 1.16 equiv.)

Cream crystals from boiling cyclohexane, 65% yield, mp 210–211 °C. IR (KBr): 1670 (C=O), 1490, 1440 cm^{-1}. UV (THF), λ_{max}(log ε): 316 (2.38); 277.5 (3.55); 272.5 (3.55); 244 (4.50) nm. ^1H NMR ($CDCl_3$): δ 4.50 (dd, J = 1.7, 8.2 Hz, 1H, H-α); 5.75 (d, J = 0.9 Hz, 1 H, H-11); 5.79 (d, J = 1.7 Hz, 1 H, H-6); 5.90 (dd, J = 0.9, 8.2 Hz, 1 H, H-α′); 6.73 (s, 4 H, H-1 to H-4); 7.21 (s, 4 H, H-7 to H-10); 7.30–7.70 (m, 6 Har); 7.90-8.10 (m, 4 Har). ^{13}C NMR ($CDCl_3$, partial data without aromatic C between 125–139 ppm): δ 49.0, 53.3 (C-α, C-α′); 80.2, 82.2 (C-6, C-11); 148.9, 150.7 (C-4a, C-12a); 195.6, 196.2 (2 C=O) ppm. Anal. Calcd for $C_{30}H_{22}O_4$ (446.5): C, 80.70; H, 4.97; O, 14.33. Found: C, 80.5; H, 5.0; O, 14.3.

4.3.5. Cyclopentenone adduct 16

A solution of **3** (0.5 g, 2.4 mmol) and distilled **12** (1.6 mL, 19.2 mmol, 8.1 equiv.) in benzene (250 mL) was refluxed for 16 h. The solvent was evaporated to give a mixture of adduct **16** and 9,10-anthraquinone. After purification by column chromatography (SiO_2, eluent CH_2Cl_2), **16** was isolated (0.15–0.2 g, 20–30% yield).

Cream crystals, mp 228–229 °C (benzene). IR (KBr): 1740, 1485, 1240, 770 cm^{-1}. ^1H NMR ($CDCl_3$): δ 1.80–2.80 (m, 4 H); 3.52, 3.60 (2 m, each 1 H, H-α, H-α′); 5.32, 5.62 (2 m, each 1 H, H-6, H-11); 6.76 (s, 4 H, H-1 to H-4); 7.21 (s, 4 H, H-7 to H-10). Anal. calcd for $C_{19}H_{16}O_3$ (292.2): C, 78.06; H, 5.52. Found: C, 77.9; H, 5.7.

4.4. Cleavage of the adducts

4.4.1. Pentacene-6,13-quinone (17)

4.4.1.1. From anthracene epidioxide 3. A solution of **3** (0.1 g, 0.47 mmol), **10a** (24 mg, 0.22 mmol, 0.47 equiv.) was refluxed in PhCl (25 mL) for 1 h. The solvent was evaporated until 5–10 mL, and NEt_3 (0.5 mL) was added at room temperature. The precipitated yellow crystals of **17** (40 mg, 63%) were isolated after 1 h of stirring. Mp 394 °C (lit. [1] 395–398 °C). Same IR and ^1H NMR data as in the literature [17].

4.4.2. 1,4-Anthraquinone (18a)

4.4.2.1. From adduct 14a. To a solution of adduct **14a** (0.22 g, 0.68 mmol) in $CHCl_3$ (5 mL) was added NEt_3 (0.5 mL) at room temperature and the solution was stirred for 1 h. The solution was evaporated and the yellow plates of **18a** (135 mg, 95%) were washed with Et_2O.

4.4.2.2. From anthracene epidioxide 3. Same procedure as for **17** with **3** (0.2 g, 0.95 mmol), **10a** (0.15 g, 1.39 mmol, 1.46 equiv.) in PhCl (20 mL), to give **18a** (130 mg, 65%) as yellow plates. Mp 225 °C (lit. [1] 219–223 °C). Same IR, ^1H NMR and ^{13}C NMR data as in the literature [17].

4.4.3. Naphthacene-5,12-quinone (18b)

Same procedure as for **18a**, from adduct **14b** (0.25 g, 0.68 mmol) in $CHCl_3$ (5 mL) and NEt_3 (0.5 mL) to give **18b** (165 mg, 95%) as yellowish crystals. Mp > 280 °C (lit. [1] 290–292 °C). Same IR data as in the literature [17].

4.4.4. 2,3-Dibenzoylnaphthalene (19)

A solution of **15** (0.13 g, 0.29 mmol) in propan-1-ol (35 mL) was refluxed with NEt_3 (5 mL) for 24 h. The solvents were evaporated, the residue dissolved in $CHCl_3$ (20 mL) and silica gel (Kieselgel 60, 4 g) was added. This mixture was left to dry for 16 h in order to oxidize the formed pyrocatechol, then extracted with CH_2Cl_2 and the solvent evaporated to give **19** (66 mg, 68%) as colourless crystals after recrystallisation in AcOH. Mp 145 °C (AcOH) (lit. [15] 145 °C). Same IR data as in the literature [18].

4.4.5. Benzo[f]indanone (20)

Same procedure as for **19** to give **20** as colourless crystals (68% yield). Same ^1H NMR as in lit. [11]. IR (KBr): 2940, 1705, 1630, 870 cm^{-1}.

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