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One-step synthesis of 2,9-disubstituted phenanthrenes via Diels–Alder reactions using 1,4-disubstituted naphthalenes as dienophiles

Elisa Paredes, Betina Biolatto, María Kneeteman and Pedro Mancini*

Area de Química Orgánica, Departamento de Química, Facultad de Ingeniería Química, Universidad Nacional del Litoral,
Santiago del Estero 2829, 3000 Santa Fe, Argentina

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Abstract—The normal electron-demand Diels–Alder reaction between 1,4-disubstituted naphthalenes, nitro being one of these two groups, and 1-methoxy-3-trimethylsililoxy-1,3-butadiene gives hydroxyphenanthrene derivatives, the yields being enhanced by placement of more electron-withdrawing groups on the dienophilic system. The nitro group as substituent directs the cycloaddition, and its *cis*-extrusion as nitrous acid along with the loss of methanol from primary adducts leads to the expected aromatized products. © 2002 Elsevier Science Ltd. All rights reserved.

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1. Introduction

The Diels–Alder (D–A) reaction is one of the most useful synthetic reactions and its overwhelming importance is well-known and thoroughly documented in organic chemistry. Its usefulness arises from its versatility and from its remarkable selectivity. By varying the structural nature of diene and dienophile, many different types of compounds can be built.

Table 1. 2,9-Disubstituted phenanthrenes produced via Scheme 1

Entry	Dienophiles	Conditions[a]	Yield (%)[b]
1	**1a**	80°C, 144 h	**4a**, 32
2	**1a**	100°C, 72 h	**4a**, 48
3	**1a**	120°C, 72 h	**4a**, 75
4	**1b**	80°C, 144 h	**4a**, 0
5	**1b**	100°C, 72 h	**4b**, 22
6	**1b**	120°C, 72 h	**4b**, 53
7	**1c**	80°C, 144 h	**4c**, 0
8	**1c**	100°C, 72 h	**4c**, 17
9	**1c**	120°C, 72 h	**4c**, 50

[a] 2 equiv. of diene in benzene.

[b] Based on consumed dienophile.

A great deal of attention has been paid to naphthalenes as dienes in D–A reactions because of their electron-rich constitution.[1] However, their use as dienophiles has been rarely investigated.[2] We have recently confirmed the olefinic nature of naphthalenic double bonds showing that 1-nitronaphthalene, 2-nitronaphthalene and 1,3-dinitronaphthalene exhibit dienophilic behavior of α,β-double bond when they react at relatively mild temperatures with *trans*-1-methoxy-3-(trimethylsilyloxy)-1,3-butadiene (Danishefsky's diene) in a normal D–A reaction. The nitrated compounds obtained as adducts suffer subsequent aromatization toward the phenanthrenic products.[3] In the present work, we explore the effect of the 1,4-disubstitution on the dienophilic behavior of naphthtalene and the efficiency of the cycloaddition when different electron-withdrawing substituents are employed.

2. Results and discussion

The dienophiles used were 1,4-dinitronaphthalene (**1a**),[4a] 1-cyano-4-nitronaphthalene (**1b**)[4b] and 1-acetyl-4-nitronaphthalene (**1c**).[4b] The diene component was the Danishefsky's diene (**2**). Other readily available dienes such as isoprene, *tran*s-1-(*N*-acetyl-*N*-propylamino)-1,3-butadiene, *tran*s-1-methoxy-1,3-butadiene, (1*Z*,3*E*)-1,4-dimetoxy-1,3-butadiene were discarded because these less reactive dienes react under thermal conditions with other nitronaphthalenes affording not the expected phenanthrenes but the corresponding *N*-(naphthyl)-pyrroles.[3]

Keywords: Diels–Alder; dienophiles; phenanthrenes.

* Corresponding author. Tel.: +54-342-4571164; fax: +54-342-4571162; e-mail: pmancini@fiqus.unl.edu.ar

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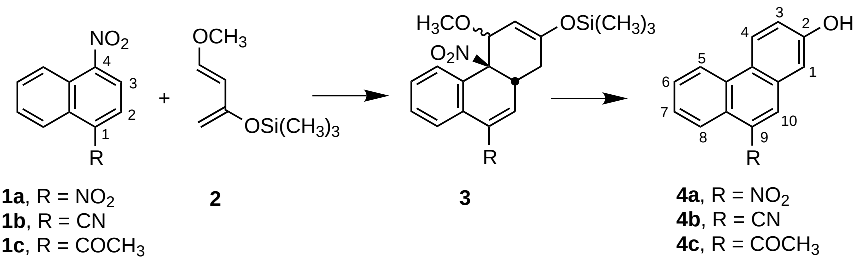

Scheme 1. Diels–Alder reactions of nitronaphthalene derivatives and Danishefsky's diene.

The D–A reactions were carried out in a sealed tube at different temperatures and times, using 2:1 diene:dienophile molar ratios.[5] The reaction conditions and yields for each dienophile are given in Table 1. The catalysis of reactions with boron trifluoride etherate was also performed, but no further improvement in the yields were observed.

When 1,4-dinitronaphthalene, 1-cyano-4-nitronaphthalene and 1-acetyl-4-nitronaphthalene were reacted with Danishefsky's diene, the observed products were 2-hydroxy-9-cyanophenanthrene (**4a**) (Table 1, entries 1–3), 2-hydroxy-9-cyanophenathrene (**4b**) (Table 1, entries 4–6) and 2-hydroxy-9-acetylphenanthrene (**4c**) (Table 1, entries 7–9), respectively.[6] These products resulted from the expected aromatization of the 1:1 nitro-adducts **3** promoted by the loss of the nitro and methoxyl groups as nitrous acid and methanol, respectively (Scheme 1), according to observed results with previously studied nitronaphthalenes.[3] Attempts to isolate the primary adducts were not successful because of their instability.

Table 1 shows that the combination high temperature/short time is more effective than low temperature/long time. It should also be noted that 1-acetyl-4-nitronaphthtalene and 1-cyano-4-nitronaphthalene did not produce significantly better yields than 1-nitronaphthalene (51%, 120°C 72 h),[3] despite the placement of a second electron-withdrawing group in the naphthalene ring.

The reactions proceeded for dienophiles **1b** and **1c** by addition of the diene selectively to the nitro-substituted double bond of the naphthalene, indicating the strong directing effect of the nitro group.

The resulting regioespecificity of reaction was under frontier orbital control, interpreted as the preferred interaction between atoms of each reactant moiety with the higher atom orbital coefficient in the frontier molecular orbital, HOMO of diene and LUMO of dienophile, as is the case for normal electron-demand Diels–Alder cycloadditions.[7] The experimental findings were in good agreement with a first theoretical approach of atomic orbital coefficients of diene's HOMO and dienophile's LUMOs obtained from extended Hückel calculations of MM+ optimized geometries.[8]

The addition of a second diene molecule to the C9–C10 double bond of phenanthrenes was not observed. Indeed, the calculated LUMOs of the species **4** are higher than the LUMOs of corresponding starting dienophiles, proving that the addition of a second molecule of diene is less favored after the addition of the first one.[8]

The observed reactivity for the studied dienophiles was in order with the electron-withdrawing character of the substituents (**1a**>**1b**>**1c**). Extended Hückel calculations of LUMOs correctly assign the first place in the reactivity sequence to **1a** but they predict that 1-acetyl-4-nitronaphthalene would be more reactive than 1-cyano-4-nitronaphthalene.[8]

3. Conclusions

It was demonstrated that naphthalene, when 1,4-disubstituted, nitro being one of these groups, can undergo D–A reaction regiospecifically with Danishefsky's diene. It was also demonstrated that the reactivity of nitronaphthalene nucleus increases substantially when the second group is another nitro substituent. In the reactions of 1-acetyl-4-nitronaphthalene and 1-cyano-4-nitronaphthalene, the nitro group orients the cycloaddition selectively towards the double bond to which it is directly attached. On the other hand, it was shown from computational results that Hückel semiempirical calculations present a high level of coincidence with the experimental results.

Therefore, normal electron-demand Diels–Alder reactions with the unusual dienophiles presented in this work can be translated into a one-step method for the preparation of 2,9-disubstituted phenanthrenes.

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4. (a) Hodgson, H.; Mahadevan, A.; Ward, E. *J. Chem. Soc.* **1947**, 1392; (b) The same method, mentioned at 4(a), for preparation of 1,4-dinitronaphthalene, was used to obtain 1-acetyl-4-nitronaphthalene and 1-cyano-4-nitronaphthalene in good yields from 1-acetyl-4-aminonaphthalene and 1-amino-4-cyanonaphthalene, respectively.
5. General procedure. The temperature, the length of reaction and the diene/dienophile ratio are given in Table 1. An ampule containing 1.0 mmol of the dienophile and the required amount of diene in 0.5 ml of dry benzene was cooled in liquid nitrogen, sealed and then heated in an oil bath. After the reaction time was completed, it was cooled once more in liquid nitrogen and opened. The solution was evaporated and the residue purified by column chromatography in silica gel using hexane/ethyl acetate mixtures as eluent. Biolatto, B.; Kneeteman, M.; Paredes, E.; Mancini P. *J. Org. Chem.* **2001**, *66*, 3906.
6. Spectral data: **4a** ^{1}H NMR (200 MHz) $CDCl_3$, δ 6.70 (s, 1H), 7.34 (d, 1H, $J=1.8$ Hz), 7.39 (dd, 1H, $J=10.0$, 1.8 Hz), 7.53 (td, 1H, $J=7.3$, 1.8 Hz), 7.66 (td, 1H, $J=7.3$, 1.8 Hz), 8.29 (s, 1H), 8.42 (dd, 1H, $J=7.3$, 1.8 Hz), 8.54 (d, 1H, $J=10.0$ Hz), 8.61 (dd, 1H, $J=7.3$, 1.8 Hz); MS (EI) m/z M^+ 239; IR 3280, 1521, 1343 cm^{-1}. **4b** ^{1}H NMR (200 MHz) $CDCl_3$, δ 6.00 (s, 1H), 7.31 (d, 1H, $J=2.7$ Hz), 7.38 (dd, 1H, $J=9.0$, 2.7 Hz), 7. 63 (td, 1H, $J=7.2$, 1.6 Hz), 7.71 (td, 1H, $J=7.2$, 1.6 Hz), 8.11 (s, 1H), 8.16 (dd, 1H, $J=7.7$, 1.6 Hz), 8.52 (d, 1H, $J=9.0$ Hz), 8.55 (dd, 1H, $J=7.2$, 1.6 Hz); MS (EI) m/z M^+ 219; IR 3320, 2224 cm^{-1}. **4c** ^{1}H NMR (200 MHz) $CDCl_3$, δ 2.73 (s, 3H), 5.50 (s, 1H), 7.30 (d, 1H, $J=2.2$ Hz), 7.32 (dd, 1H, $J=7.30$, 2.2 Hz), 7.53 (td, 1H, $J=7.9$, 1.3 Hz), 7.60 (td, 1H, $J=7.1$, 1.7 Hz), 7.95 (s, 1H), 8.46 (dd, 1H, $J=7.0$, 1.5 Hz), 8.51 (d, 1H, $J=9.5$ Hz), 8.55 (dd, 1H, $J=7.8$, 1.7 Hz); MS (EI) m/z M^+ 236; IR 3059, 1682 cm^{-1}.
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8. LUMO: **1a** $=-10.9865$ eV, **1b** $=-10.7629$ eV, **1c** $=-10.8840$ eV, **4a** $=-10.5802$ eV, **4b** $=-9.7708$ eV, **4c** $=-10.0899$ eV. HOMO: **2** $=-11.9298$ eV. Atomic orbital coefficients in LUMO: **1a** C1 $=+0.22301$, C2 $=-0.22319$; **1b** C4 $=+0.15737$, C3 $=-0.32048$; **1c** C4 $=+0.21295$, C3 $=-0.28422$. Atomic orbital coefficients in HOMO: **2** C1 $=-0.4405$, C4 $=+0.6300$.