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LETTERS

Establishing cleavage conditions for an anthracene chiral auxiliary using a photochemical retro Diels–Alder reaction

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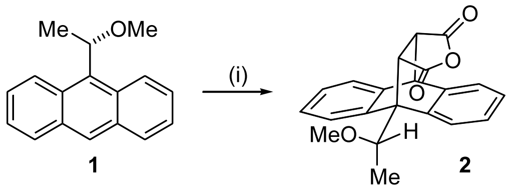
Abstract—Photochemical Diels–Alder additions of chiral 9-anthranyl ethanol derivatives have been conducted giving rise to addition adducts in reasonable yield and excellent diastereoselectivity. Thermal and photochemical retro Diels–Alder additions have also been achieved providing a facile cleavage method for use of this compound as a new chiral auxiliary. © 2002 Elsevier Science Ltd. All rights reserved.

Recent studies from this laboratory and from others have described the potential use of 9-substituted chiral anthracene derivatives as a new class of chiral auxiliary.[1] These differ from those currently used by making use of an alkene to effect the addition process. Studies to-date have involved the synthesis of these compounds and have investigated the diastereoselectivity of the addition process. However, the issue still remains of developing a route that would facilitate the cleavage of the masked alkene from the anthracene addition adduct. One of the most common methods for this process is the use of flash vacuum pyrolysis (FVP),[2] but given the potential value of the auxiliary and the specialist equipment needed to perform this reaction we were interested in developing an easier, cleaner process. Although the diastereoselective addition reaction may be performed using a catalyst or by heating, we were also interested in expanding previous work on the photochemistry of the addition reaction. From the outset of this work, anthracene was attractive as a potential auxiliary as theoretically *both* addition and cleavage steps could be carried out using different wavelengths of UV light. Herein we describe our studies on the photochemical additions of 9-methoxyethylanthracene and attempts to facilitate efficient cleavage of the alkene–anthracene addition adduct.

In previous work, thermal cycloaddition of the auxiliary **1** with maleic anhydride or *N*-methylmaleimide led to exclusive formation of a single diastereoisomer e.g. **2** (Scheme 1). Identical results were obtained when the reaction was carried out using a 2W phosphorescent light source with a peak emission at 254 nm.

In the present work a more powerful 125 W medium pressure mercury lamp was employed in a classical immersion well reactor. This would allow the introduction of filter solutions that would enable us to effectively 'tune' the wavelength of light emitted from the lamp. Reactions were carried out in triplicate by illumination of a 0.1 mM solution of the ether **1** in degassed acetonitrile for 1 h. Either cooling water or a cooled filter solution was passed through the reactor to maintain the temperature of the reaction solution close to 30°C, thus suppressing any unwanted thermal addition reaction. In addition to water, three other filter solutions were used with different absorption spectra (Fig. 1) that would allow illumination at different wavelengths of light. Since the ether **1** and the addition adduct **2** have very different absorption spectra (Fig. 2), it was hoped that selective illumination would only promote the forward (or reverse) reaction. In particular $NiSO_4$-containing solutions should inhibit absorption at the 320–400 nm band of the auxiliary **1**.



Scheme 1. Photochemical addition of maleic anhydride to ether **1**. *Reagents and conditions*: (i) maleic anhydride, solvent, *hν* as text.

Keywords: Diels–Alder; retro Diels–Alder; diastereoselective cycloaddition.

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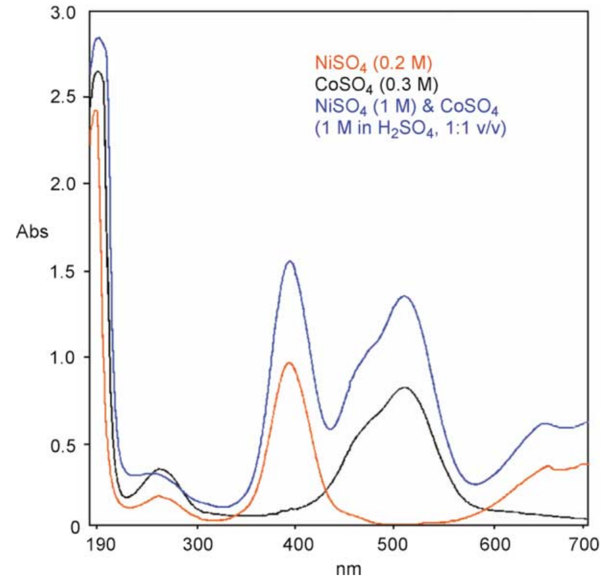


Figure 1. UV spectra of filter solutions used in this study.

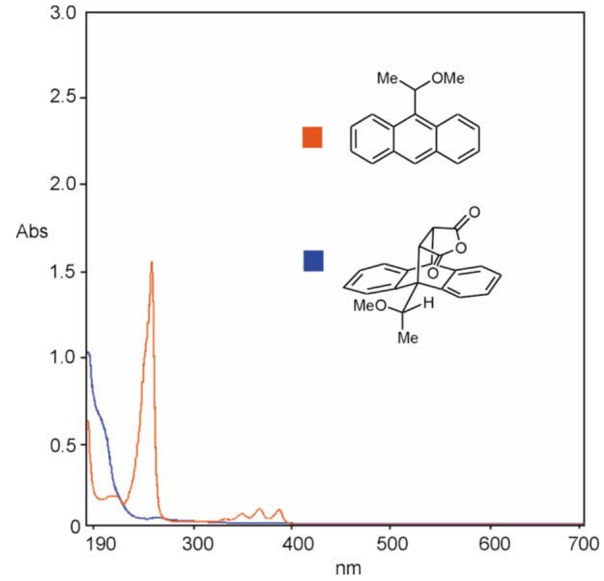
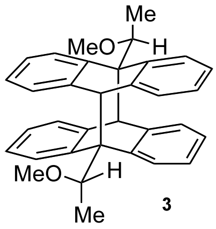


Figure 2. UV spectra of ether **1** and adduct **2**.

The results obtained from the photochemical additions are presented below (Table 1). Although increased quantities of product compared to the thermal reaction were observed with no loss of diastereoselectivity, small quantities (10%) of another component, identified as the dimer **3**, were also observed.[3] The dimer was presumed to be the *trans* isomer, based on steric arguments and literature precedent for this type of dimerization process.[4] Unfortunately, reproducible results could not be obtained from these reactions, which in conjunction with the formation of the unwanted dimer **3**, made the photochemical addition process somewhat limited in the development of our chiral auxiliary at this point.

We next turned our attention to the retro Diels–Alder reaction since this reaction would need to be carried out in an efficient manner to be useful as the ultimate cleavage step for our auxiliary. In the first instance, this was attempted by heating the addition adduct **2** at reflux in mesitylene. After 1 h, only a trace (4%) of auxiliary **1** was recovered indicating that although the reaction appeared to be reversible, thermal cleavage was not viable.



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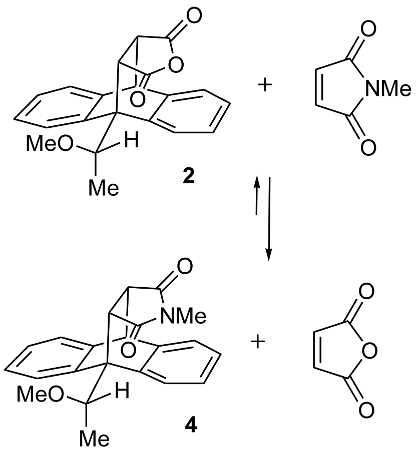
At this temperature the equilibrium for this reaction probably favours formation of product, which correlates with our previous studies of the thermal Diels–Alder additions of anthracene derivatives such as **1**.[1c] However, in these studies we had observed an apparent increase in the rate of the Diels–Alder addition with *N*-methylmaleimide as dienophile. If the Diels–Alder/retro Diels–Alder was indeed proceeding via an equilibrium process, heating the cycloadduct **2** in the presence of *N*-methylmaleimide should lead to preferential formation of the addition product **4** (Scheme 2). In practice, after heating anhydride **2** for 1 h in refluxing mesitylene with 1 equiv. of *N*-methylmaleimide, 23% of the desired imide **4** was formed. This encouraging result led us to consider a similar process under photochemical conditions and photolysis of an acetonitrile solution of the cycloadduct **2** and *N*-methylmaleimide gave the desired product **4** with good conversion (57%) after 1 h. Dimer **3** formation was observed once again. Use of filter solutions offered no real advantage in this reaction (Table 2).

Although photochemical exchange appeared feasible, photochemical cleavage would be a more desirable process. To our delight, photolysis of an acetonitrile solution of the adduct **2** with water cooling for 1 h led to recovered auxiliary **1** (64%) along with dimer **3** (20%)

Table 1. Photochemical additions of methyl ether **1** and maleic anhydride

Coolant/filter solution	% Diels–Alder adduct **2**	% Dimer **3**
Water	20	5
	62	22
	36	11
$NiSO_4$ (0.2 M)	34	10
	26	10
	42	9
$CoSO_4$ (0.3 M)	49	16
	25	13
	10	6
$NiSO_4$ (1 M) and $CoSO_4$ (1 M in 5% H_2SO_4) (1:1 v/v)	42	11
	35	11
	43	5



Scheme 2. Thermal and photochemical exchange reactions.

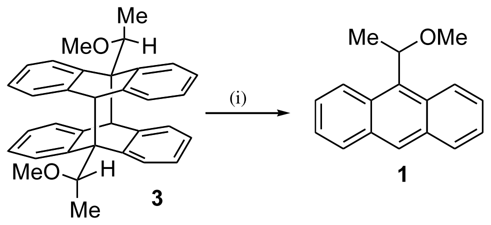
Table 2. Photochemical exchange reactions

Coolant/filter solution	% Diels–Alder adduct **4**	% Dimer **3**
Water	57	9
$NiSO_4$ (0.2 M)	55	13
$CoSO_4$ (0.3 M)	45	10
$NiSO_4$ (1 M) and $CoSO_4$ (1 M in 5% H_2SO_4) (1:1 v/v)	50	6

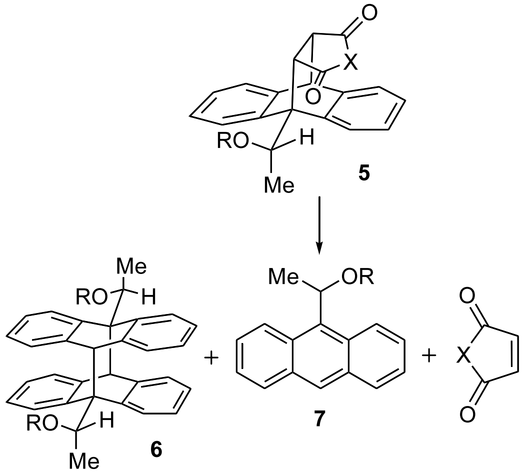
and maleic anhydride which equates to near quantitative cleavage when the dimer is taken into account. At first, dimer formation appeared to be a drawback of this reaction, however, we were able to demonstrate that this can act as a 'masked' auxiliary and itself be recycled. Thus, photolysis of an acetonitrile solution of the isolated dimer **3** for 1 h gave near quantitative conversion to the auxiliary **1**, as did heating in boiling mesitylene for 1 h (Scheme 3).

This method appears general for anhydride type addition products and alcohol **5** (R = H; X = O) was cleaved to give dimer **6** (R = H) and monomer **7** (R = H)[5] in 40 and 12% conversion, respectively, after 1 h (Scheme 4). The somewhat reduced conversion again supports the hypothesis that the addition adduct **5** (R = H; X = O) is more thermodynamically stable than ether **2**. With maleimide products (R = H, Me; X = NMe) extensive decomposition was observed. These compounds should have a slow retro-Diels–Alder reaction compared to the anhydrides due to their increased stability and in this case illumination gives rise to another reaction pathway, ultimately leading to adduct decomposition.

In conclusion we have investigated the photochemical Diels–Alder and thermal and photochemical retro Diels–Alder reactions of chiral 9-anthracylethanol derivatives. The latter provides a clean and efficient method for the cleavage of anhydride substrates from the addition adduct. Having now established both addition and cleavage conditions for our anthracene auxiliary, further work will focus on the asymmetric reactions that may be possible with these compounds.



Scheme 3. Recycling of dimer **3**. *Reagents and conditions*: (i) either *hν*, CH_3CN, 1 h (93%) or mesitylene, 1 h, Δ (99%).



Scheme 4.

Acknowledgements

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2. (a) Kaupp, G. *Liebigs Ann. Chem.* **1977**, 254–275; (b) Lasne, M.-C.; Ripoll, J.-L. *Synthesis* **1985**, 121–143.
3. Selected data for compound **3** (accurate MS or CHN analysis could not be obtained due to decomposition to the monomeric compound upon heating or ionisation); mp 219–221°C; δ_H (300 MHz; $CDCl_3$) 7.56 (2H, m, ArC*H*), 7.00 (2H, m, ArC*H*), 6.86–6.62 (12H, m, ArC*H*), 4.53 (2H, s, C*H*CHC-O), 4.43 (2H, m, C*H*C-O), 3.75 (6H, s, OCH_3) and 1.44 (6H, d, *J* 6.2, CH_3); δ_C (125 MHz; $CDCl_3$) 144.7 (Ar*C*), 144.5 (Ar*C*), 144.2 (Ar*C*), 144.1 (Ar*C*), 143.4 (Ar*C*), 142.3 (Ar*C*), 141.7 (Ar*C*), 128.9 (Ar*C*H), 128.5 (Ar*C*H), 128.5 (Ar*C*H), 128.2 (Ar*C*H), 127.9 (Ar*C*H), 127.6 (Ar*C*H), 125.4 (Ar*C*H), 125.1 (Ar*C*H), 125.0 (Ar*C*H), 124.9 (Ar*C*H), 124.9 (Ar*C*H), 124.6 (Ar*C*H), 124.5 (Ar*C*H), 124.2 (Ar*C*H), 82.2 (*C*CH), 60.9 (CH*C*), 58.8 (CH_3*C*H), 58.2 (O*C*H_3) and 15.9 (*C*H_3). *m*/*z* (CI^+) 236 (15%, $C_{17}H_{16}O^+$), 221 (10), 205 (100, $C_{16}H_{13}^+$). All other compounds in this study have been described previously.

4. Bouas-Laurent, H.; Castellan, A.; Desvergne, J.-P.; Lapouyade, R. *Chem. Soc. Rev.* **2000**, *29*, 43–55.

5. Selected data for compound **6** (R = H; accurate MS or CHN analysis could not be obtained due to decomposition to the monomeric compound upon heating or ionisation; ^{13}C was not possible due to limited solubility in DMSO); mp 232–234°C; δ_H (300 MHz; DMSO) 7.73 (2H, m, ArC*H*), 7.03 (2H, m, ArC*H*), 6.87–6.65 (12H, m, ArC*H*), 5.92 (2H, t, *J* 4.5, O-*H*), 5.01 (2H, m, C*H*C-O), 4.83 (2H, s, C*H*CHC-O) and 1.39 (6H, d, *J* 6.2, C*H*$_3$); *m*/*z* (CI$^+$) 233 (15%), 222 (100, $C_{16}H_{14}O^+$), 205 (96, $C_{16}H_{13}{}^+$), 179 (83).