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Synthesis of Cinnamaldehydes, Esters of Cinnamic Acids and Acylals of Cinnamaldehydes by Oxidation of Arylpropenes with 2,3-Dicyano-5,6-dichlorobenzoquinone (DDQ)

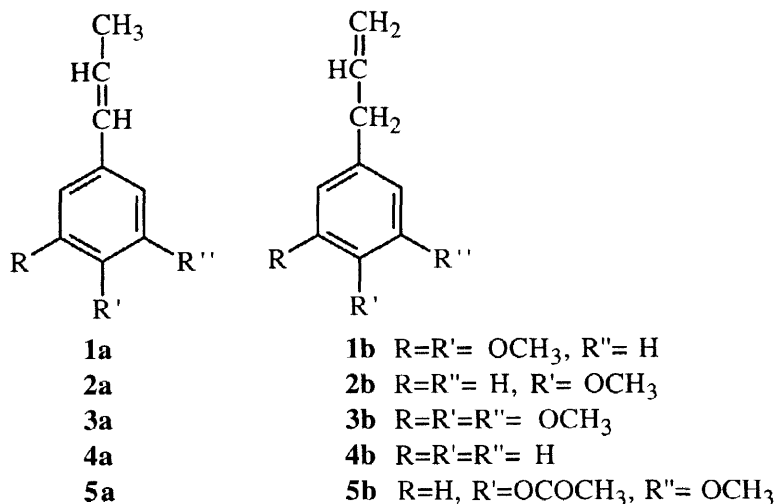
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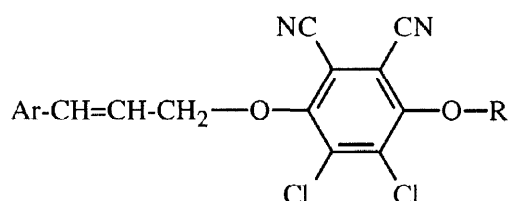
Abstract: 1-Arylpropenes and 3-arylpropenes give cinnamaldehydes (yield ≈ 80%) on oxidation with 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ) in the presence of water. The conversion to aldehydes is promoted by electron-donating groups at the aromatic ring. On DDQ oxidation in the presence of methanol, methyl esters of cinnamic acids are the predominant products. DDQ oxidation of 1- or 3-(3,4-dimethoxyphenyl)-1-propene in the presence of acetic acid gives an acylal [the diacetate of (*E*)-3-(3,4-dimethoxyphenyl)-2-propene-1,1-diol]. © 1998 Elsevier Science Ltd. All rights reserved.

Cinnamaldehydes are formed on oxidation of arylpropenes with 2,3-dichloro-5,6-dicyanoquinone (DDQ)¹⁻⁸ in the presence of water.^{1b,5} To examine the scope of this synthetic method, we have studied the formation of aldehydes on DDQ oxidation of arylpropenes 1-5. It was found that the 1-arylpropenes 1a-3a gave cinnamaldehydes in high yields (77-84 %) on treatment with DDQ (slight excess) at room temperature for 0.5-2 h in the two-phase system dichloromethane-water (4:1). In contrast to what could be expected from



earlier studies,⁵ similar yields of aldehydes (71- 84%) were obtained on oxidation of the 3-arylpropenes **1b** - **3b**. A typical experiment (substrate, **1b**; Fig. 1) is described below. Compounds **4** and **5** were converted into cinnamaldehydes in low to moderate yields on oxidation with a large excess of DDQ in combination with long reaction times (>12 h). The 1-arylpropenes **4a** and **5a** reacted almost immediately with formation of quinol ethers of types **6** and **7** while the 3-arylpropenes **4b** and **5b** were essentially unchanged at an initial stage of the treatment (small amounts of quinol ethers of types **6** and **7** were present in the reaction mixtures). It is evident that electron-donating substituents at the aromatic ring strongly promote the formation of aldehydes. The importance of activating substituents has been underestimated in previous studies.⁵

It has been suggested that quinol ethers of types **6** and **7** are intermediates in the DDQ oxidation of arylpropenes leading to cinnamaldehydes.^{2,5} The aforementioned experiments with **4** and **5** show that quinol ethers formed from these compounds are only slowly oxidised to aldehydes. To obtain further support for the



6 R= H

7 R= Ar-CH=CH-CH₂

8 R= H, Ar= 4-methoxyphenyl

9 R= 4-methoxycinnamyl, Ar= 4-methoxyphenyl

intermediacy of quinol ethers of types **6** and **7**, we examined reaction mixtures obtained on treatment of **1-3** with one half of the amount of DDQ required for the formation of cinnamaldehydes. We found that both types of quinol ethers (**6** and **7**) could be analysed in the crude reaction products by ¹H NMR spectroscopy: signals from the methylene groups appeared at δ≈5 and the signal from **7** was located at somewhat lower field (≈0.05 δ units) than the corresponding signal from **6**. The ¹H NMR spectra of **8** and **9**⁹ exemplify this (quinol ethers **8** and **9** have been isolated by Kiefer and Lutz⁵). The amount of **6** (the main constituent) was considerably larger than the amount of **7** in the reaction mixtures examined. To record the completeness of the oxidation, all the crude oxidation products of **1-5** obtained in this study were analysed for quinol ethers by ¹H NMR spectroscopy.

Formation of an ester occurs on DDQ oxidation of the 1-arylpropene dehydrodiisoeugenol in the presence of methanol or ethanol (a methyl or ethyl cinnamate derivative is obtained).⁴ We have examined the oxidation of the 3-arylpropene **1b** with DDQ in the presence of methanol (Fig. 1). The yield of ester **11** was 55 %. Minor amounts of aldehyde **10** (≈ 6%) were present in the crude reaction mixtures. To examine the possibility that aldehyde **10** is an intermediate in the formation of **11**, we treated **10** with DDQ in the presence of methanol. Contrary to what could be expected from previous work,⁴ this led to the formation of **11** but rather large amounts of **10** remained unchanged. Ester **11** may be reaction product of **10** but the formation of **11** may alternatively proceed via initially formed acetal intermediates. Oxidation of such intermediates probably produces ortho esters and hydrolysis of such esters is expected to give **11**. It is notable that attempts to detect cinnamic acids in the DDQ/H₂O and DDQ/CH₃OH oxidation mixtures failed.

Oxidation of **1a** and **1b** with DDQ in the presence of acetic acid gave the acylal **12** in high yield. This acylal has previously been obtained by treating aldehyde **10** with acetic anhydride.¹⁰ The formation of an acylal rather than products of higher degree of oxidation could be speculated to be due to an electron-withdrawing effect of the acetate group that renders the intermediates and final products less susceptible to oxidation.

DDQ oxidation of arylpropenes represents a new method for the synthesis of acylals of cinnamaldehydes. Acylals of this type have hitherto been prepared using cinnamaldehydes as starting material.^{11,12}

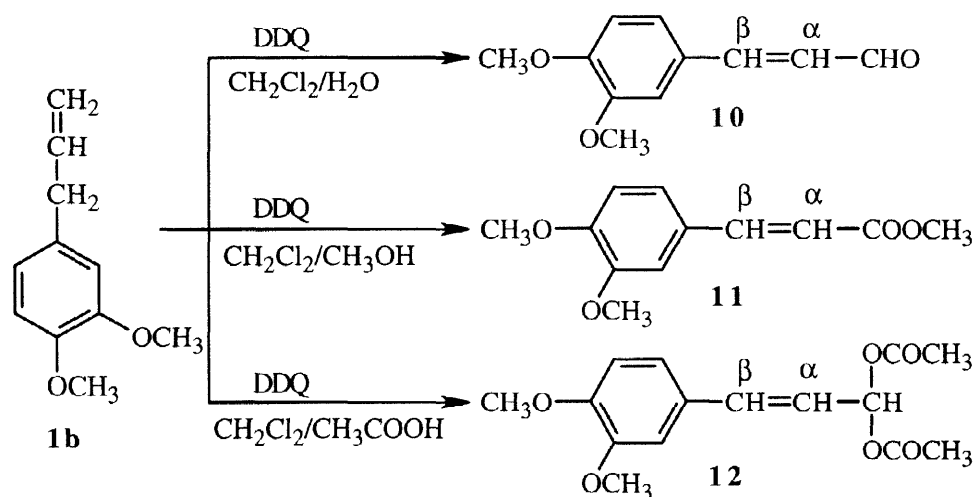


Fig. 1. Preparation of **10-12** by oxidation of **1b** with DDQ.

Typical experiments (Fig. 1): (E)-3-(3,4-Dimethoxyphenyl)propenal (**10**). Water (60 ml) and DDQ (13.2 mmol) were added to a solution of **1b** (6 mmol) in water-saturated dichloromethane (240 ml). The mixture was stirred for 30 min at room temperature. A solution of ascorbic acid (13.2 mmol) in 60 ml water was added to the reaction mixture and stirring was continued for 10 min. Solids were filtered off and the liquid layers were separated. The organic layer was washed with brine and dried (Na_2SO_4). The residue obtained on evaporation of the solvents was chromatographed on a column (40 g SiO_2 with 15 g neutral Al_2O_3 at the top of the column) with toluene-ethyl acetate (10:1) as the eluent. The fractions containing **10** were pooled on the basis of examination by thin layer chromatography. Evaporation of the solvents gave a product (1.03 g) consisting of essentially pure **10** (^1H NMR). Recrystallization from benzene/hexane gave crystals of m.p. 80-82 °C (lit.¹³ 81-82 °C). Yield: 80 %. ^1H NMR (CDCl_3 , 400 MHz): δ 3.93 (3H, s; OCH_3), 3.94 (3H, s; OCH_3), 6.62 (1H, dd, $J=7.8$ and 16 Hz; $\text{H}\alpha$), 6.85-7.2 (3H, m; H-Ar), 7.43 (1H, d, $J=16$ Hz; $\text{H}\beta$), 9.67 (1H, d, $J=7.8$ Hz; CHO). Methyl (E)-3-(3,4-dimethoxyphenyl)propenoate (**11**). Compound **1b** (4 mmol) was dissolved in dichloromethane (160 ml) and methanol (8 ml). DDQ (14.4 mmol) was added and the resulting mixture was stirred for 1 h. Work-up and purification was accomplished as in the experiment describing the preparation of **10**. A product (0.49 g) of m.p. 67 °C was obtained. Recrystallization from methanol raised the m.p. to 68 °C (lit.¹⁴ 68-69 °C). ^1H NMR (CDCl_3 , 400 MHz): δ 3.80 (3H, s; COOCH_3), 3.92 (6H, s; OCH_3), 6.32 (1H, d, $J=15.8$ Hz; $\text{H}\alpha$), 6.87 (1H, d, $J=8.3$ Hz; H-Ar), 7.05 (1H, d, $J=1.9$ Hz; H-Ar), 7.11 (1H, dd,

$J=1.9$ and 8.3 Hz; H-Ar), 7.64 (1H, d, $J=15.8$ Hz; H β). The diacetate of (*E*)-3-(3,4-dimethoxyphenyl)-2-propene-1,1-diol (**12**). Compound **1b** (4 mmol) was dissolved in dichloromethane (160 ml) and acetic acid (8 ml). After addition of DDQ (9.6 mmol) the reaction mixture was stirred for 1h. Solids were filtered off. The liquid phase was washed with saturated NaHCO₃ solution and precipitates formed were filtered off. The layers were separated and the organic phase was washed with brine (50 ml) and dried (Na₂SO₄). The material in the organic layer was chromatographed on neutral Al₂O₃ (30 g) using dichloromethane as the eluent. A fraction (0.92 g) consisting of acylal **12** contaminated with aldehyde **10** was obtained (¹H NMR). To remove the aldehyde the product was dissolved in ether and the solution extracted with 10 % NaHSO₃ solution. Drying (Na₂SO₄) of the ether layer and evaporation of the solvent gave pure acylal **12** (0.88 g) (¹H NMR). Yield: 75 %. ¹H NMR (CDCl₃, 400 MHz): 2.13 (6H, s; COCH₃), 3.89 (3H, s; OCH₃), 3.91 (3H, s; OCH₃), 6.08 (1H, dd, $J=6.8$ and 16 Hz; H α), 6.8-7.0 (3H, m; H-Ar), 6.81 (1H, d (broad), $J=16$ Hz; H β), 7.30 (1H, dd, $J=0.8$ and 6.8 Hz; O-CH-O). ¹³C NMR: δ 21.2 (2C, CH₃-C), 56.0 (OCH₃), 56.1 (OCH₃), 90.2 (O-CH-O), 109.2, 111.1, 119.7 (C α), 120.9, 128.2, 135.7 (C β), 149.2, 149.9, 168.9 (2C, CO). The assignments are based on HETCOR experiments.

References and Notes

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- ¹H NMR (400 MHz, CDCl₃). **8**: δ 3.82 (3H, s; OCH₃), 4.86 (2H, dd, $J=1.0$ and 7.0 Hz; CH₂), 6.32 (1H, dt, $J=16$ and 7.0 Hz; vinyl H), 6.61 (1H, d, $J=16$ Hz; vinyl H), 6.87 (2H, m; H-Ar), 7.35 (2H, m; H-Ar). **9**: δ 3.82 (6H, s; OCH₃), 4.90 (4H, dd, $J=1.0$ and 7.0 Hz; CH₂), 6.315 (2H, dt, $J=16$ and 7.0 Hz; vinyl H), 6.62 (2H, d, $J=16$ Hz; vinyl H), 6.87 (4H, m; H-Ar), 7.35 (4H, m; H-Ar).
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