

IPSO NITRATION: NITRATION OF 2-ALKYLPHENOLS IN ACETIC ANHYDRIDE.  
FORMATION OF 6-ALKYL-6-NITROCYCLOHEXA-2,4-DIENONES

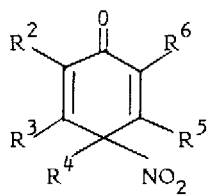
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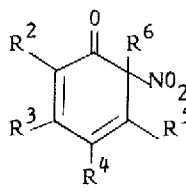
Summary: Low temperature nitration of 2-alkylphenols in acetic anhydride gives 6-alkyl-6-nitrocyclohexa-2,4-dienones. The dienones undergo a regiospecific rearrangement to give *o*-nitrophenols.

Formation of 4-alkyl-4-nitrocyclohexa-2,5-dienones (e.g. **1a**) in the nitration of phenols which are fully substituted in the reactive 2, 4 and 6 positions (e.g. mesitol) has long been known.<sup>1,2</sup> More recently 4-alkyl-4-nitrocyclohexa-2,5-dienones (e.g. **1b**) have been obtained from simple 4-alkylphenols (e.g. *p*-cresol) and their derivatives.<sup>3-6</sup> The analogous formation of the 6-alkyl-6-nitrocyclohexa-2,4-dienones, from 2-alkylphenols, has not been established. Coombes and co-workers suggested the possible intermediacy of 6-methyl-6-nitrocyclohexa-2,4-dienone (**2c**) in the nitration of 2-methylanisole, in order to account for the formation of 6-nitro-*o*-cresol.<sup>7</sup> However, they did not detect the formation of a dienone intermediate in the similar nitration of *o*-cresol although under the same conditions they were able to detect (uv) the formation of an intermediate, assumed to be the 2,5-dienone **1b**, in the nitration of *p*-cresol.

We wish to report the ready formation of 6-alkyl-6-nitrocyclohexa-2,4-dienones (**2**) in the low temperature nitration of 2-alkylphenols in acetic anhydride and their specific 1,3 rearrangement to give 2-alkyl-6-nitrophenols. Nitration of *o*-cresol using nitric acid in acetic anhydride (mole ratio of substrate : nitric acid : acetic anhydride = 1 : 1.5 : 20) at -60 °C for 3 h gave **2c** (60%), 4-nitro-*o*-cresol (17%) and 6-nitro-*o*-cresol (23%). When the mixture was warmed to -20 °C, the dienone rearranged with a half-life of 8 min to give 6-nitro-*o*-cresol. Nitration of *p*-xylenol at -40 °C for 30 min gave dienone **2d** (95%), 2,5-dimethyl-6-nitrophenol (4%) and 2,5-dimethyl-4-nitrophenol (1%). When the reaction mixture was worked up by the ammonia method<sup>8</sup> the dienone **2d** rearranged to give 2,5-dimethyl-6-nitrophenol as the only isolatable product.



1



2

a  $R^2=R^4=R^6=Me; R^3=R^5=H$   
c  $R^6=Me; R^2=R^3=R^4=R^5=H$   
e  $R^6=Me; R^2=R^4=D; R^3=R^5=H$   
g  $R^3=R^5=R^6=Me; R^2=R^4=H$   
i  $R^3=Me; R^6=i-Pr; R^2=R^4=R^5=H$

b  $R^4=Me; R^2=R^3=R^5=R^6=H$   
d  $R^3=R^6=Me; R^2=R^4=R^5=H$   
f  $R^5=R^6=Me; R^2=R^3=R^4=H$   
h  $R^4=R^6=Me; R^2=R^3=R^5=H$

In a separate experiment, monitored by nmr, the temperature of the reaction mixture was raised to 0°C and the dienone was observed to rearrange to the same nitrophenol.

The dienone **2c** was identified from its <sup>1</sup>H nmr spectrum at -60 °C in acetic anhydride: δ 6.17 (d, 1, 2-H), 6.58 (4-H), 6.60 (5-H) and 7.31 ppm (8 lines, 1, 3-H),  $J_{2,3} = 9.9$ ,  $J_{3,4} = 6.7$ ,  $J_{3,5} = 0.8$ ,  $J_{4,5} = 9.8$  Hz. Chemical shifts and coupling constants were obtained by computer refinement of the simulated spectrum. Assignment of the peaks in the spectrum was facilitated by the spectrum of the dideuteriodienone **2e** (δ 6.60 (br s, 1, 5-H) and 7.31 ppm (br s, 1, 3-H)) obtained by the nitration of the 4,6-dideuterio-*o*-cresol as well as by the spectrum of the dienone **2d** (δ 6.03 (br s, 1, 2-H), 6.47 (d, 1,  $J_{4,5} = 10$  Hz, 4-H), and 6.57 ppm (d, 1,  $J = 10$  Hz, 5-H)). Further evidence for the formation of dienone(s) comes from nitrations carried out in [<sup>2</sup>H<sub>6</sub>] acetic anhydride in which it was possible to observe the upfield shift of the *o*-methyl group due to the change in the hybridization of the ring carbon to which it is attached. Thus in the case of *o*-cresol, the methyl group shifted from δ 2.17 to 1.74 ppm. Similarly in *p*-xylenol it shifted from δ 2.11 to 1.71 ppm.

The rearrangement of the 2,5-dienones **1** to give *o*-nitrophenols is well established.<sup>3,5,9</sup> However, the rearrangement of the 2,4-dienones **2** to give *o*-nitrophenols, observed here, takes place even when the equally reactive *para* position is vacant. This implies that there is some bonding interaction between the oxygen and the migrating nitro group.<sup>7</sup> The formation of 2,4 dienones **2** and their rearrangement to *o*-nitrophenols suggests that the high *ortho-para* ratios observed<sup>7</sup> in the nitration of 2-alkylphenols may, at least in part, be attributed to the formation and rearrangement of these intermediates.

Dienones **2f** and **2g** were obtained on nitration of the corresponding phenols. 2,4-Dimethylphenol gave both **1h** and **2h**. Thymol gave **2i**. The formation of 6-alkyl-6-nitrocyclohexa-2,4-dienones thus appears to be a general reaction of 2-alkylphenols.

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