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Oxidative Cyclisation of Chalcones with Thallium(III)-Nitrate: Synthesis of (*Z*)-2-Phenylmethylene-7-nitro-3(2*H*)-benzofuranones

Short Communication

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Oxidation of 2′-hydroxy-3′-nitrochalcones with thallium(III) nitrate gives (*Z*)-2-phenylmethylene-7-nitrobenzofuran-3(2*H*)-one derivatives, rather than the more usual 1,2-diaryl-3,3-dimethoxypropan-1-ones or the corresponding isoflavones.

(Keywords: Oxidative cyclisation of chalcones; (Z)-2-Phenylmethylene-7-nitro-3(2H)-benzofuranones; Thallium(III)nitrate]

Oxydative Cyclisierung von Chalconen mit Thallium(III)nitrat: Synthese von (Z)-2-Phenylmethylen-7-nitro-3(2H)-benzofuranonen (Kurze Mitteilung)

Die Oxidation von 2′-Hydroxy-3′-nitrochalconen mit Thallium(III)nitrat ergab (*Z*)-2-Phenylmethylen-7-nitro-3(2*H*)-benzofuranon-Derivate und nicht die üblichen 1,2-Diaryl-3,3-dimethoxypropan-1-one bzw. die entsprechenden Isoflavone.

Thallium(III) nitrate (*TTN*) has found widespread use as an oxidising agent in organic synthesis[1]. In the case of chalcones oxidation with *TTN* is normally accompanied by rearrangement providing easy access to a variety of compounds[2] including isoflavones. In the preparation of isoflavone from 2′-hydroxychalcone using thallium(III) nitrate, a nitro derivative **1** was also isolated as the product of a minor side reaction[3]. Since thallium(III) nitrate is a trihydrate, presumably nitration of the chalcone would have taken place due to a build up of nitric acid concentration in the system thus changing the course of reaction. Alternatively, the nitro group might have been introduced only after the abnormal reaction had occurred. In order to study the effect of a 3′-nitrosubstituent, we have now examined the reaction of 2′-hydroxy-3′-nitrochalcones (**2 a–c**) with thallium(III) nitrate.

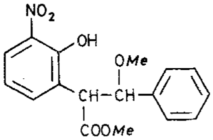
Results and Discussion

The reaction of 2′-hydroxy-3′-nitrochalcones (**2 a–c**) in methanol with thallium(III) nitrate afforded intermediates which upon heating in refluxing methanolic hydrochloric acid or in contact with alkali in the cold gave (*Z*)-7-nitro aurone derivatives. The infrared spectra of these products revealed carbonyl absorption around 1 705 cm^{-1}, typical for a cyclopentanone ring system with a conjugated exocyclic double bond and the structural assignments were confirmed by UV and ^{1}H-NMR spectral data (see experimental). The (*Z*)-configuration could be established on the basis of chemical shifts of the β- and 2′- and 6′-protons[4–6] and the IR spectra[6] of the compounds. The stereochemistry of (*Z*)- and (*E*)-aurones has already been established by X-ray[7] and dipole moment[6] measurements and a correlation with their characteristic IR spectra exists to make appropriate assignments of the geometrical isomers. That the reactions proceed through 2-(α-methoxybenzyl) benzofuranone derivatives could be demonstrated, in one case, (**2 c**), by isolating the intermediate **4** which clearly has a ketonic carbonyl group in a five-membered ring (IR: 1 737 cm^{-1}). Furthermore, treatment of this compound with refluxing acid or, more importantly, with potassium hydroxide at room temperature generated the aurone (**3 c**) in high yield.

This oxidative cyclisation appears to be the only example in the otherwise extensively studied oxidation reactions of chalcones[2] with thallium(III) nitrate where no rearrangement has taken place, the behaviour being reminiscent of chalcone oxidation reactions with oxidants like lead tetraacetate[5], manganic acetate[5] and alkaline hydrogen peroxide[8]. The striking difference is that unlike other oxidants no side products could be observed in this reaction with *TTN*. Furthermore, we have found that this oxidative cyclisation takes place only when the nitro substituent is at the 3′-position; 5′-nitro and 4-nitro chalcones did not give aurones under similar conditions. The best yields of cyclised products were observed when the chalcones were reasonably soluble in methanol. With highly insoluble chalcones yields were drastically reduced.

The apparent structural factor which determines the course of the *TTN* oxidation would appear to be the presence or absence of the nitro group *ortho* to the phenolic hydroxyl group in the A-ring. It is therefore tempting to suggest that the controlling factor in the formation of **4** is the increased dissociation of the phenolic hydroxyl group[9]. It may be that participation occurs in the expected intermediate **5**.

It is also apparent that in the original work[3] involving the formation of **1** by oxidation of 2′-hydroxychalcone nitration was not the first step in the reaction.



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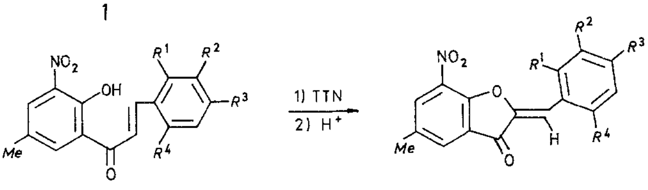
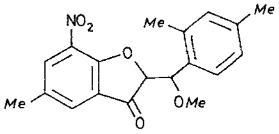


2 3

a $R^1 = R^2 = R^3 = R^4 = H$

b $R^1 = H;\ R^2 = R^3 = -OCH_3;\ R^4 = -NO_2$

c $R^1 = R^3 = -CH_3;\ R^2 = R^4 = H$



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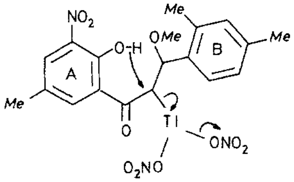

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Experimental

Melting point were determined with a Reichert hot stage apparatus and are uncorrected. Unless otherwise mentioned ^{1}H-NMR spectra were recorded on Perkin-Elmer R 34 spectrometer operating at 220 MHz for solutions in $CDCl_3$

with *TMS* as internal standard. IR spectra were recorded for KBr discs on a Perkin-Elmer 125 spectrometer, UV spectra for solutions in methanol with a Pye Unicam SP 8-100 spectrophotometer, and mass spectra on an AE 1 MS 12 spectrometer by direct inlet technique.

(Z)-2-phenylmethylene-5-methyl-7-nitro-3(2H)-benzofuranone (**3a**)

To a solution of 1-(2-hydroxy-3-nitro-5-methylphenyl)-3-phenyl propen-1-one (**2a**) (0.14 g) in methanol (60 ml) was added thallium(III) nitrate (0.45 g, 2.0 mol equiv.) and the mixture was stirred at 20 °C for 3 days. The precipitated thallium(I) nitrate was filtered and the methanol was removed *in vacuo* on water bath (50 °C). The residue was taken in methylene chloride (50 ml) and the solution was passed through a small column of basic alumina to remove traces of unreacted chalcone. The reaction product was taken in methanol (50 ml) and was refluxed with 10% hydrochloric acid 75 °C for 4 h when yellow needles of (**3a**) (54%) separated, mp 235-236 °C (*Me*OH).

IR: 1 704, 1 645, 1 614, 1 582, 1 522, 1 350, 1 307, 1 234, 1 205, 1 140, 906 and 781 cm^{-1}. UV: λ_{max} 245 (ϵ 16 600), 332 (25 800) and 380 nm (11 900). ^{1}H-NMR: δ (ppm) 8.26 (d, 1 H, $J = 1.7$ Hz, H-4), 8.05 (q, 2 H, H-2′, 6′), 7.91 (d, 1 H, $J = 1.7$ Hz, H-6), 7.50 (m, 3 H, H-3′, 4′, 5′) and 7.03 (s, 1 H, =CH—). MS: *m*/e 281 (M^+), 280 (100%), 234 and 133. High resolution MS: Found M^+, 281.0691. $C_{16}H_{11}NO_4$ requires *M*, 281.0688.

(Z)-2-[(2-nitro-4,5-dimethoxyphenyl)methylene]-5-methyl-7-nitro-3(2H)-benzofuranone (**3b**)

Thallium(III) nitrate (0.45 g, 2.0 mol equiv.) was added to a stirred suspension of 1-(2-hydroxy-3-nitro-5-methylphenyl)-3-(2-nitro-4,5-dimethoxyphrenyl)propen-1-one (**2b**) (0.2 g) in methanol (100 ml) and the reaction was worked up after 3 days as described above to give **3b**; thin yellow needles (19%), mp 300 °C (*Me*OH).

IR: 1 707, 1 648, 1 620, 1 586, 1 526, 1 480, 1 290, 1 235, 1 145, 1 072 and 779 cm^{-1}. UV: (CH_2Cl_2) 254, 318 (inf.), 368 and 406 nm. ^{1}H-NMR (*TFA*): 8.48-7.88 (5 H, *Ar*-H and =CH—), 4.28 and 4.11 (each s, each 3 H, —OCH_3) and 2.60 (s, 3 H, —CH_3). MS: *m*/e 386 (M^+), 340, 207, 164 (100%) and 136. High resolution MS: Found M^+, 386.07303. $C_{18}H_{14}N_2O_8$ requires *M*, 386.0750.

(Z)-2-[(2,4-dimethylphenyl)methylene]-5-methyl-7-nitro-3(2H)-benzofuranone (**3c**)

Thallium(III) nitrate (0.45 g, 2.0 mol equiv.) was added to a solution of 1-(2-hydroxy-3-nitro-5-methylphenyl)-3(2,4-dimethylphenyl)propen-1-one (**2c**) (0.16 g) in methanol (50 ml) and the whole was stirred at 20-22 °C. After 10 h, precipitated thallium(I) nitrate was filtered, methanol removed *in vacuo* and water (50 ml) was added to the residue. The organic products were extracted with methylene chloride (3 × 40 ml), washed with water, dried ($MgSO_4$) and the solution was passed though a small column of basic alumina to give *2-(α-methoxybenzyl)-benzofuranone* derivative **4** (80%), mp 145-155 °C (ether-hexane).

IR: 1 737, 1 630, 1 584, 1 527, 1 480, 1 350, 1 285, 1 230, 1 195, 889, 840, 772 and 761 cm^{-1}. ^{1}H-NMR: 8.22 (d, 1 H, $J = 2$ Hz, H-4), 7.78 (d, 1 H, $J = 2$ Hz, H-6), 7.51 (d, 1 H, $J = 8$ Hz, H-6′), 7.15 (dd, $J = 2$ and 8 Hz, H-5′), 7.02 (d, 1 H,

$J = 2$ Hz, H-3′), 5.09 (d, 1 H, $J = 2.5$ Hz, —CH), 4.75 (d, 1 H, $J = 2.5$ Hz, —CH), 3.11 (s, 3 H, —OCH_3), 2.46, 2.39 and 2.34 (each s, each 3 H, —CH_3).

4, on refluxing with 10% methanolic hydrochloric acid for 4 h or on treatment with 10% aq. KOH at 20 °C gave immediately yellow needles (92%) of **3 c**, mp 227-228 °C (*Me*OH).

IR: 1 709, 1 644, 1 622, 1 603, 1 583, 1 520, 1 474, 1 206, 1 155, 829, 778 and 774 cm^{-1}. UV: 249 (ϵ 18 000), 344 (20 900) and 388 nm (16 550). ^{1}H-NMR: 8.37 (d, 1 H, $J = 8$ Hz, H-6′), 8.24 (d, 1 H, $J = 1.5$ Hz, H-4), 7.90 (d, 1 H, $J = 1.5$ Hz, H-6), 7.25-7.08 (3 H, H-3′, 5′ and =CH—), 2.50, 2.49 and 2.37 (each s, each 3 H, —CH_3). MS: *m*/e 309 (M^+), 294, 262 and 180 (100%). High resolution MS: Found M^+, 309.09931. $C_{18}H_{15}NO_4$ requires *M*, 309.10010.

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