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METAL REAGENTS IN ORGANIC REACTIONS : PART V - REACTIONS OF COUMARINS WITH THALLIUM (III) SALTS[1]

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Abstract - The reactions of several coumarins with thallium (III) salts have been investigated. The compounds isolated were usually oxidation products derived from initially formed organometallics.

INTRODUCTION

Though the organic chemistry of thallium (III) compounds is an established branch of research, a considerable amount of work still remains to be done on the reactions of the thallium (III) species with heterocyclic compounds. Previously, we have reported the reactions of these salts with indoles[2]. The present paper describes our investigations on coumarins.

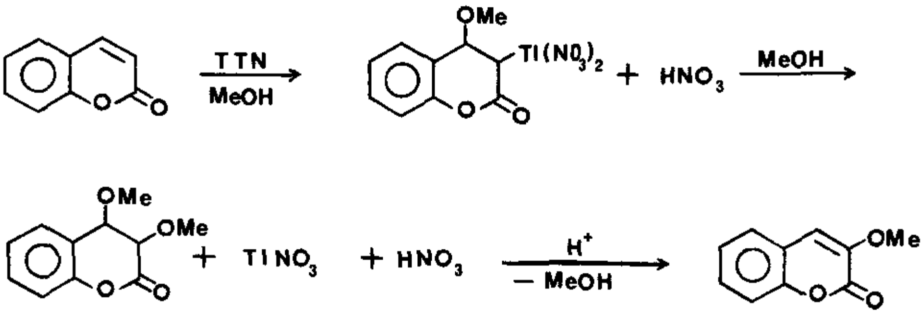
RESULTS AND DISCUSSIONS

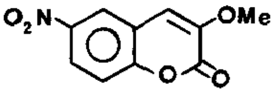
Coumarin reacted slowly with thallium (III) nitrate (TTN) in dry methanol to yield (I), mp 176°C, after 7 days. Its IR (KBr) spectrum showed absorption bands for the coumarin carbonyl (1720 cm^{-1}), nitro-group (1520, 1345, 896 cm^{-1}) and 1,2,4-trisubstituted benzene moiety (822, 802 cm^{-1}). Its 80 MHz ^1H-NMR showed a downfield C_4-H (δ 8.32, s), a methoxyl (δ 3.95, s) and three aromatic protons of an 1,2,4-trisubstituted benzene ring (δ 8.89, d, J = 2.3 Hz, C_5-H; δ 8.22, dd, J = 2.3, 9.3 Hz, C_7-H; δ 7.56, d, J = 9.3 Hz, C_8-H). This was in conformity with the presence of a 6-nitro group. The 3-methoxylation can be explained by the addition - elimination mechanism outlined in Scheme I. The first oxythallation step is necessarily slow because of the inert nature of the 3,4-double bond. Nitric acid, produced during the oxythallation process is responsible for the observed nitration, whose exact stage of occurrence is not clear.

3-Hydroxycoumarin when treated with TTN in dry methanol furnished 4-methoxy-3-hydroxycoumarin (II), mp 165°C. This compound showed hydroxyl and lactonic bands at 3300 (br) and 1708 cm^{-1} in its IR($CHCl_3$)spectrum. Its 80 MHz ^1H-NMR spectrum showed peaks for a methoxyl group (δ 4.34, s), an exchangeable hydroxyl (δ 5.73, s) and a low field aromatic proton (C_5-H at δ 7.78, dd, J= 7.9, 2.2 Hz). It lacked the C_4-H singlet at $\sim\delta$ 7.02. The EI-MS lacked the M^+ peak, the highest peak being observed at m/z 163 (M-HCO). The fragmentation pattern was commensurate with the assigned structure. The probable mechanism involves thallation at the activated C-4 position followed by nucleophilic displacement of thallium by a methoxyl group and tautomerisation (Scheme II).

The oxidation of 4-hydroxycoumarin by TTN proceeded in a different manner by way of a novel dimerisation to give the product (III), mp 148-50°C.Its IR spectrum($CHCl_3$)showed peaks for hydroxyl and lactonic carbonyl groups (broad peak at 3000-3300 cm^{-1} and 1710 cm^{-1}) and was very similar to that of the parent compound. The ^1H-NMR spectrum was also similar to that of 4-hydroxycoumarin but lacked the C_3-H singlet at $\sim\delta$ 5.56. The product could therefore be formulated as the dimer (III)[5] or its tautomer (III'), whose probable genesis has been outlined in Scheme III, involving the attack of one molecule of the substrate on the initially thallated species of the other. The EI-MS lacked the M^+ peak, the highest peak being observed at m/z 138 corresponding to the fragmentation shown.

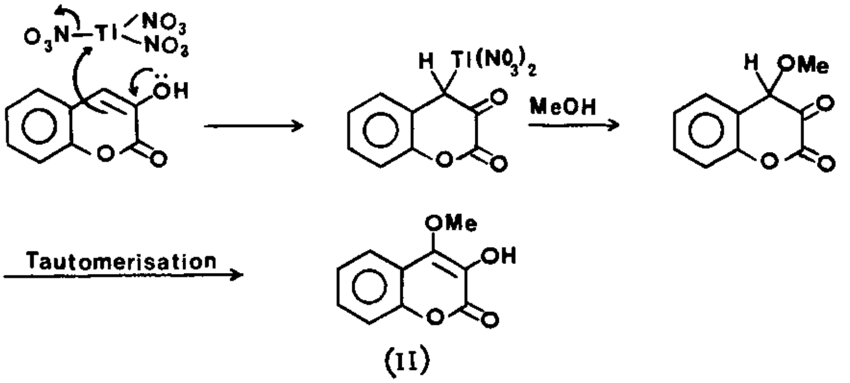
Scheme I



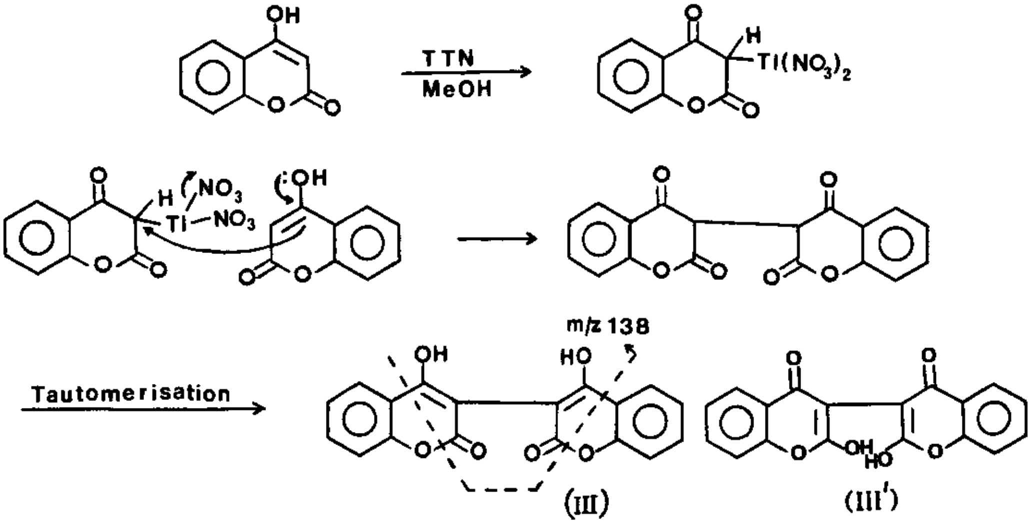


(I)

Scheme II

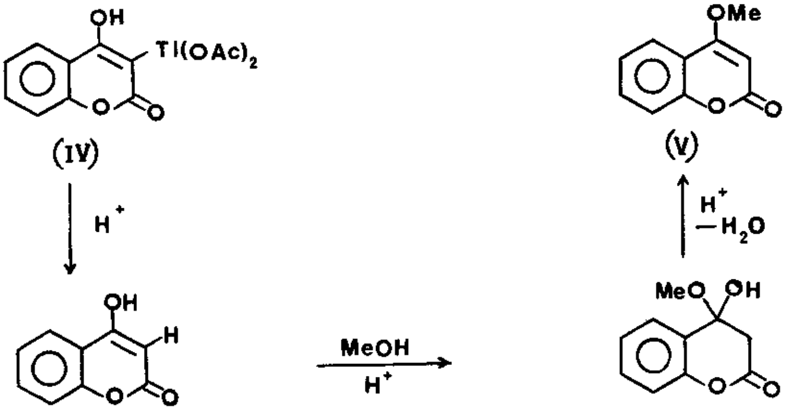


Scheme III

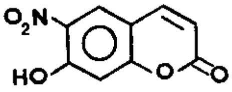


The reaction of 4-hydroxycoumarin was repeated with thallium (III) acetate (TTA) as the reagent when the thallated compound (IV) was obtained. This lacked the C_3-H signal in the ^{1}H-NMR but instead showed a singlet at δ 1.58 for the $-Tl(OAc)_2$ grouping. Presumably, the lower leaving group capability of $-Tl(OAc)_2$ as opposed to $-Tl(NO_3)_2$ prevents the formation of the dimer. Treatment of (IV) with sodium perchlorate and perchloric acid in methanol, in an attempt to prepare dimer (III), led to dethallation and replacement of the 4-hydroxy group by a methoxyl to give (V)[6], $C_{10}H_8O_3$, mp 124°C. The probable mechanism is shown in Scheme IV. (V) was also obtained on treatment of 4-hydroxycoumarin with acidified methanol.

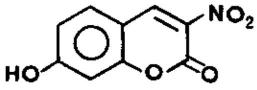
Scheme IV



Umbelliferone failed to yield any oxidation product even on prolonged treatment with TTN in methanol. The only two products obtained were the 3-nitro and 6-nitro derivatives, (VII) and (VI), arising from nitration by the nitric acid, generated during the formation of the thallium (III) salt of the phenolic group in umbelliferone as well as by some solvolysis of TTN. Both nitro-derivatives showed IR absorptions for the $-NO_2$, -OH and lactonic >C=O groups [1525, 1310, 1290; 3220; 1730 cm^{-1}—(VI); and 1560, 1370; 3210; 1730 cm^{-1}—(VII)] respectively . The ^{1}H-NMR spectra were compatible with the structures (VI) and (VII). The former exhibited the characteristic AB pattern for the coumarin 3- and 4-protons (δ 6.33 and δ 7.97, $J = 9.5$ Hz). (VII) lacked this characteristic doublet, but showed a downfield singlet at δ 9.10 which can be ascribed only to the C_4-proton. Action of dilute methanolic nitric acid on umbelliferone also gives (VI) and (VII) under similar conditions.



(VI)



(VII)

EXPERIMENTAL

Mps were recorded on a Kofler block and are uncorrected. ^{1}H-NMR spectra were recorded at 80 or at 100 MHz. IR and UV spectra were recorded on a Perkin-Elmer (Model 782) and Varian 634 S spectrometers respectively. Anhydrous Na_2SO_4 was used for drying extracts. Column and thin-layer chromatography were carried out using silica gel (60-120 mesh) and silica gel G, respectively. 3-Hydroxycoumarin[3] and 4-hydroxycoumarin[4] were prepared by literature methods.

Reaction of TTN and Coumarin - Coumarin (1.46 g, 10 mmol) in dry MeOH (20 ml)was treated with thallium (III) nitrate trihydrate (TTN) (5.00 g, 11 mmol) at room temperature. After 7 days, the solvent was removed and the residue chromatographed to give (I) (400 mg, 18%) mp 176°C(from benzene) in the petrol-benzene(1:1) eluate and unreacted coumarin (450 mg, 31%) in the benzene-EtOAc (6:1) eluates. (Found : C,54.12; H,3.09; N,6.21%, $C_{10}H_7NO_5$ requires C,54.30; H,3.19; N,6.33%). 70 eV MS m/z 221 (M^+), 190 (M-OMe), 175 ($M-NO_2$), 144 ($M-OMe-NO_2$).

Reaction of TTN and 3-Hydroxycoumarin - 3-Hydroxycoumarin (500 mg, 3 mmol) in dry MeOH (15 ml) was treated with TTN (1.32 g, 3 mmol) at room temperature. After keeping overnight, the precipitated thallium (I) nitrate was filtered and the solvent was removed. Chromatography of the residue yielded (II) (100 mg, 17%), mp 165°C,in the petrol-benzene (1:1) eluates. (Found : C,62.42; H,4.03; $C_{10}H_8O_4$ requires C,62.50; H,4.16%). EI-MS m/z 163 (M-HCO), 162 (M-HCHO), 134, 133 ($M-OCH_3-CO$), 127, 121, 120 ($M-C_3H_4O_2$), 105, 93, 92, 77 ($C_6H_5^+$).

Reaction of TTN and 4-Hydroxycoumarin - 4-Hydroxycoumarin (400 mg, 2 mmol) in dry MeOH (12 ml) was treated with TTN (1.00 g, 2 mmol) at room temperature and kept overnight. The precipitated thallium (I) nitrate was filtered off. After removal of the solvent, the residue was chromatographed to give(III/III')(150 mg, 19%), mp 148-50°C,in the petrol benzene (1:1) eluates. (Found : C,66.99; H,3.02; $C_{18}H_{10}O_6$ requires C,67.08; H,3.11%). UVλ_{max}^{EtOH} 298, 229 nm. EI-MS m/z 138, 120, 92.

Reaction of TTA and 4-Hydroxycoumarin - 4-Hydroxycoumarin (100 mg, 0.6 mmol) in the 1:2 mixture of glacial acetic acid and absolute ethanol (15 ml) was treated with TTA (230 mg, 0.6 mmol) at room temperature. After 5 days, the solvent was removed under reduced pressure, the residue treated with $CHCl_3$ and water. The residue from the aqueous portion after removal of water was extracted with anhydrous ethanol to give (IV) (200 mg, 67%), decomp. pt. 205°C.

Reaction of (IV) with Sodium Perchlorate and Perchloric Acid - The compound (IV) (150 mg, 0.3 mmol) in dry MeOH (10 ml) was treated with sodium perchlorate and perchloric acid at room temperature. After three days, the reaction-mixture was neutralised and then extracted with ether. Removal of the solvent gives (V), (20 mg, 37%) mp 124°C.(Found : C,68.05; H,4.22, $C_{10}H_8O_3$ requires C,68.18; H,4.54%).

Reaction of TTN and Umbelliferone - Umbelliferone (650 mg, 4 mmol) in dry MeOH (25 ml) was treated with TTN (2 g, 4 mmol) at room temperature. After 7 days,the precipitated thallium (I) salt was filtered off, the solvent was removed and the residue chromatographed to give (VI) (200 mg, 24%), mp 219°C,in the petrol - benzene (1:1) eluates and (VII) (100 mg, 12%), mp 260-62°C,in the benzene-ethylacetate (5:1) eluates. (Found: C,51.99; H,2.32; N,6.45, $C_9H_5NO_5$ requires C,52.17; H,2.41; N,6.71% - VI).

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