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THALLIUM IN ORGANIC SYNTHESIS. 54. REACTIONS OF REISSERT COMPOUNDS WITH THALLIUM(III) NITRATE (TTN)[1,2]

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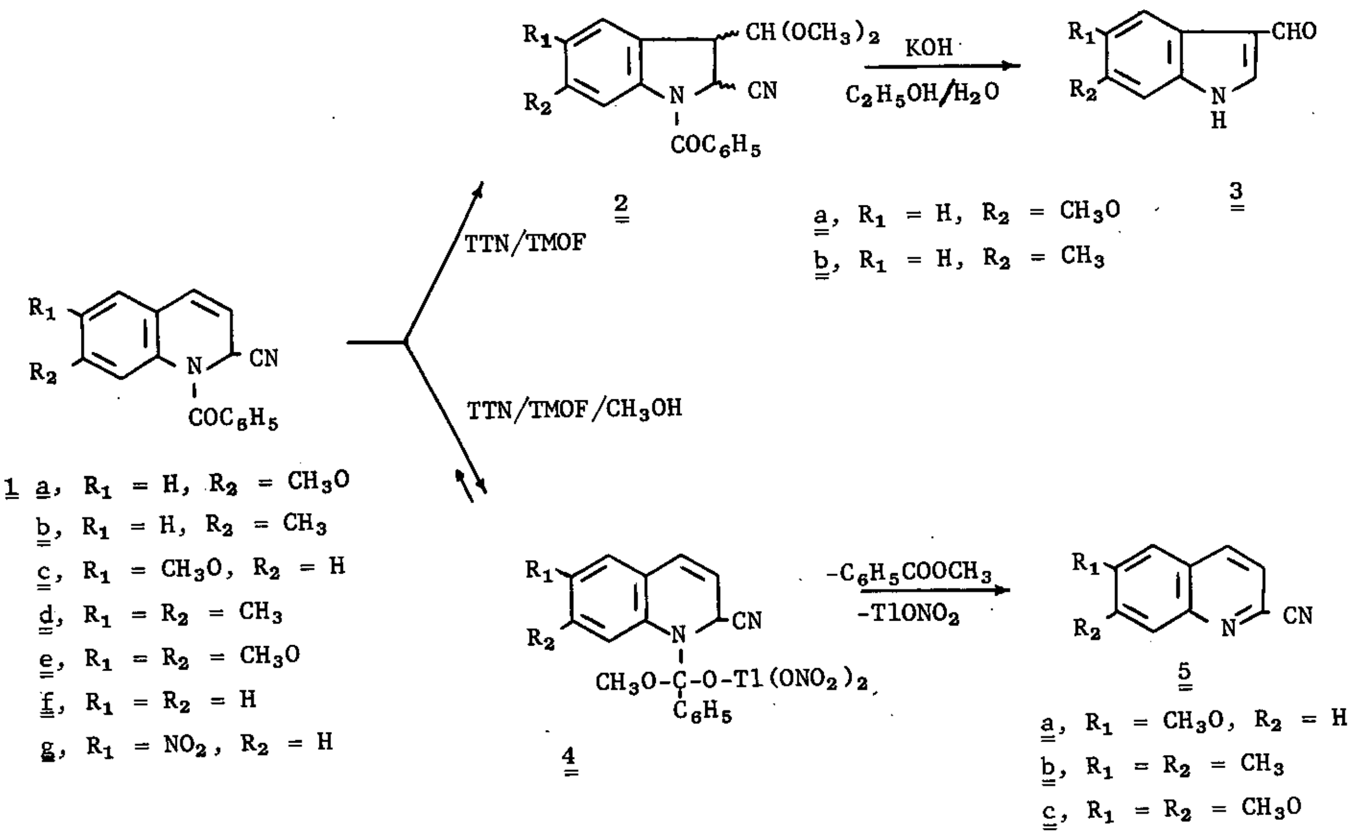
Treatment of the Reissert compounds derived from substituted quinolines with thallium(III) nitrate (TTN) results either in ring contraction to dihydroindole derivatives or oxidative debenzoylation and formation of 2-cyanoquinolines, depending on the nature and postion of the substituent groups in the aromatic ring. Reissert compounds derived from isoquinolines give tetrahydroisoquinoline derivatives under the same conditions.

Oxidative rearrangement of olefins by thallium(III) nitrate (TTN) is a versatile synthetic procedure for the preparation of aldehydes and ketones,[3] and one which has been widely applied to both ring expansion and ring contraction of carbocyclic olefins.[4] There are few reports, however, of the application of this type of reaction to heterocyclic substrates,[5] and we have therefore undertaken a systematic study of the TTN-mediated oxidative rearrangement of representative heterocyclic systems. We now describe the reactions of a variety of quinoline- and isoquinoline-derived Reissert compounds with TTN.

Reaction of 1-benzoyl-2-cyano-7-methoxy- and -7-methyl-1,2-dihydroquinoline, 1a and 1b, with one equivalent of TTN in trimethyl orthoformate (TMOF) at 25°C resulted in smooth oxidative rearrangement and formation of 1-benzoyl-2-cyano-3-(dimethoxymethyl)-6-methoxy- and -6-methyl-2,3-dihydroindole, 2a and 2b, in 76 and 73% yield respectively (Scheme 1). Analytical and spectroscopic data were fully consistent with the assigned structures; treatment with potassium hydroxide in ethanol gave the known indole-3-carboxaldehydes 3a and 3b. As far as we are aware, these transformations represent only the second example of ring contraction of Reissert compounds to indole derivatives.[6]

Oxidation of the Reissert compounds 1c-e proceeded slowly, and the reactions were complete only after 24 hr at 50°C. Ring contraction was not observed in these cases; instead, oxidative debenzoylation occurred, and the 2-cyanoquinolines 5a-c were isolated in moderate (45, 35, 39%) yield (Scheme 1).[7] Treatment of the Reissert compounds 1f and 1g with TTN resulted in extensive decomposition, and no identifiable products could be isolated.

The results summarized in Scheme 1 can readily be explained. TTN can coordinate with the Reissert compounds at either or both of the nucleophilic centers, namely the C=C bond of the dihydroquinoline or the O atom of the 1-benzoyl group. Electron releasing substituents at the 7-position (i.e., as in 1a and 1b) should facilitate reaction at the C=C bond, and oxidative ring contraction therefore occurs. Electron releasing substituents at the 6-position, on



1 a, $R_1 = H$, $R_2 = CH_3O$
b, $R_1 = H$, $R_2 = CH_3$
c, $R_1 = CH_3O$, $R_2 = H$
d, $R_1 = R_2 = CH_3$
e, $R_1 = R_2 = CH_3O$
f, $R_1 = R_2 = H$
g, $R_1 = NO_2$, $R_2 = H$

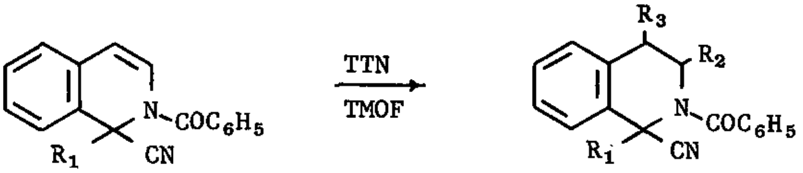
2, 3
a, $R_1 = H$, $R_2 = CH_3O$
b, $R_1 = H$, $R_2 = CH_3$

5
a, $R_1 = CH_3O$, $R_2 = H$
b, $R_1 = R_2 = CH_3$
c, $R_1 = R_2 = CH_3O$

Scheme 1

the other hand, should facilitate elimination of methyl benzoate and thallium(I) nitrate from the intermediate 4; in keeping with this hypothesis, oxidative debenzoylation is observed with 1c-e.

Oxidation of the isoquinoline-derived Reissert compounds 6a and 6b with TTN in either TMOF or methanol proceeded smoothly to give excellent yields (78 and 80%) of products derived by overall addition of CH_3O and ONO_2 to the 3,4-C=C bond. Analytical and spectroscopic (ir, mass, ^1H and ^{13}C nmr) data for these adducts are, however, fully consistent with either of the possible isomeric structures 7a,b and 8a,b (Scheme 2); attempts to establish structure by chemical degradation were unsuccessful and led to the formation of tarry, unidentifiable products. Moreover, reasonable mechanisms can be drawn for the formation of either 7a,b or 8a,b, and we do not believe that a choice between these isomers can be made on the basis of mechanistic considerations. A single crystal X-ray study is presently in progress to answer this question.



6 a, R_1 = H
b, R_1 = $C_6H_5CH_2$

7 a, R_1 = H, R_2 = ONO_2, R_3 = CH_3O
b, R_1 = $C_6H_5CH_2$, R_2 = ONO_2, R_3 = CH_3O

8 a, R_1 = H, R_2 = CH_3O, R_3 = ONO_2
b, R_1 = $C_6H_5CH_2$, R_2 = CH_3O, R_3 = ONO_2

Scheme 2

EXPERIMENTAL[8]

Oxidative Rearrangement of 1a and 1b to 2a and 2b with TTN/TMOF. A solution of the Reissert compound (0.005 mol) and TTN (2.22 g, 0.005 mol) in TMOF (40 ml) was stirred at room temperature for 4 hr. Chloroform (150 ml) was added and the mixture was cooled to 0°C and filtered to remove thallium(I) nitrate. The filtrate was washed with saturated sodium chloride solution, saturated sodium bicarbonate solution, dried ($MgSO_4$), and the solvent removed by distillation under reduced pressure. The residual oil was triturated with methanol (10-20 ml), the solution was cooled, and the solid which crystallized was collected by filtration and recrystallized from methanol.

2a: mp 103-104°C.

Anal. Calcd for $C_{20}H_{20}N_2O_4$: C, 68.17; H, 5.72; N, 7.95. Found: C, 68.40; H, 5.49; N, 8.18.
Ir (KBr), cm^{-1}: $_{C=N}$ 2240 (w); $_{C=O}$ 1634 (s). Nmr ($CDCl_3$): 3.35 (3H, s); 3.43 (3H, s); 3.60 (3H, s); 3.67 (1H, m); 4.35 (1H, d, J = 5.5 Hz); 5.30 (1H, d, J = 2.5 Hz); 6.57 (2H, m); 7.23 (1H, d, J = 8.5 Hz); 7.55 (5H, s). M^+ 352.

2b: mp 170-171°C.

Anal. Calcd for $C_{20}H_{20}N_2O_3$: C, 71.41; H, 5.99; N, 8.33. Found: C, 71.13; H, 6.20; N, 8.27.
Ir (KBr), cm^{-1}: $_{C=N}$ 2240 (w); $_{C=O}$ 1633 (s). Nmr ($CDCl_3$): 2.16 (3H, s); 3.30 (3H, s); 3.40 (3H, s); 3.67 (1H, m); 4.35 (1H, d, J = 5 Hz); 5.23 (1H, d, J = 2Hz); 6.6-7.4 (8H, m). M^+ 336.

Hydrolysis of 2a and 2b was accomplished by stirring a solution of the appropriate substrate in aqueous ethanol containing excess potassium hydroxide for 24 hr at room temperature. This gave 6-methoxyindole-3-carboxaldehyde 3a, mp 183-184°C (lit[9] mp 185°C) and 6-methylindole-3-carboxaldehyde 3b, mp 190-191°C (lit[10] mp 190-192°C).

Oxidative Debenzoylation of **1c**-**e** to **5a**-**c** with TTN/TMOF.

A solution of the Reissert compound (0.005 mol) and TTN (2.22 g, 0.005 mol) in TMOF (50 ml) was stirred and heated at 50°C (water bath) for 24 hr. The 2-cyanoquinolines were isolated as described above.

Oxidation of **6a** and **6b** to **7a** and **7b** or **8a** and **8b** with TTN/TMOF.

A solution of the Reissert compound (0.005 mol) and TTN (2.22 g, 0.005 mol) in TMOF (50 ml) was stirred at room temperature for 2-3 hr. The products were isolated as described above.

7a or **8a**: mp 176-177°C (dec).

Anal. Calcd for $C_{18}H_{15}N_3O_5$: C, 61.19; H, 4.28: N, 11.89. Found: C, 61.31; H, 4.06; N, 11.63.
Ir (KBr), cm^{-1}: 1660, 1635, 1380, 1327, 1309, 1268, 1085, 850, Nmr ($CDCl_3$): 3.40 (3H,s); 5.42 (1H, broad s); 5.96 (1H, d, *J* = 2 Hz); 6.25 (1H, s); 8.47 (9H, s).

7b or **8b**: mp 180-181°C

Anal. Calcd for $C_{25}H_{21}N_3O_5$: C, 67.71; H, 4.77; N, 9.18. Found: C, 67.81; H, 4.92; N, 9.18.
Ir (KBr), cm^{-1}: 1665, 1630, 1447, 1385, 1360, 1312, 1265, 1078, 898, 835, 760, 700. Nmr ($CDCl_3$): 3.23 (3H, s); 4.05 (2H, dd); 5.28 (1H, d, *J* = 2.5 Hz); 5.72 (1H, d, *J* = 2.5 Hz); 6.50 (2H, m); 6.7-8.0 (14 H, m).

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