systems for the tumor-inhibitory activity of related compounds,[11,12] investigations are in progress to determine the significance of various structural features in relation to the biological activity of liatrin.

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Thallium in Organic Synthesis. XXVI. Direct Conversion of Oximes into Aldehydes and Ketones with Thallium(III) Nitrate (TTN)[1]

Sir:

There has been considerable recent interest in the development of mild techniques for the conversion of oximes and their derivatives into aldehydes and ketones.[2] A variety of hydrolytic, oxidative, and reductive procedures have been described, only one of which appears to be of general applicability.[3]

We wish to describe in this communication a new method for the direct conversion of oximes into aldehydes and ketones by treatment with thallium(III) nitrate (TTN).[4] The following general procedure illustrates the manipulative simplicity of the method. A solution of TTN in methanol was added to a stirred solution of an equimolar amount of the oxime in methanol at room temperature. Reaction was rapid and nonexothermic, and was complete within a few minutes. The precipitated thallium(I) nitrate was removed by filtration, and the filtrate was shaken with dilute sulfuric acid for a few minutes and then extracted with ether or chloroform. The extract was dried, concentrated, and filtered through a short column of alumina or silica, using benzene or chloroform as eluent. Evaporation of the solvent followed by distillation or crystallization gave the pure aldehyde or ketone. Representative conversions are summarized in Table I.

From an examination of the reactions of a wide range of oximes with TTN under a variety of conditions, the advantages and limitations of the present method can be summarized as follows. (1) Reaction proceeds on the free oxime and prior conversion into a derivative is unnecessary (*cf.* ref 2). (2) Reaction proceeds virtually instantaneously at room temperature, and yields of pure products are uniformly high. (3) Considerable variation in experimental conditions is possible, depending on the solubility characteristics of the starting oxime. Thus, deoximation occurs equally efficiently in aqueous solution, provided that a small amount of perchloric acid is added to stabilize the TTN. Alternatively, deoximation can be accomplished in high yield by stirring a solution of the oxime in benzene with a suspension of TTN. In the latter case the water of crystallization of TTN participates in the reaction.

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Table I. Conversion of Oximes into Aldehydes and Ketones with TTN

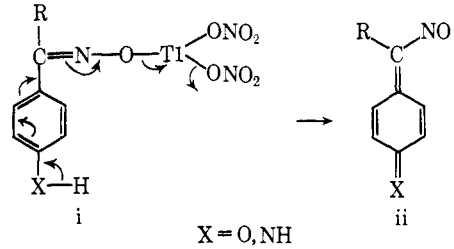
Ketone or aldehyde	Yield, %[a]
Ethyl methyl ketone	82
Pinacolone	74
Hexane-2,5-dione[b]	73
Cyclohexanone	92
2,2,6,6-Tetramethylcyclohexanone	78
n-Heptaldehyde	96
Furfuraldehyde	88
Benzaldehyde	88
Anisaldehyde	85
Mesitaldehyde	88
Cinnamaldehyde	88
Acetophenone	85
Benzophenone	86
4-Methoxybenzophenone	87
2,2′-Dithienyl ketone	72

[a] Calculated on pure recrystallized or redistilled material. [b] From hexane-2,5-dioxime.

(4) The procedure is unsuccessful when applied to aryl aldehydes or ketones which contain ortho or para substituted phenolic OH or aromatic NH_2 groups due to concomitant oxidation of the aromatic ring to quinone derivatives.[5] This limitation is, however, trivial and can be eliminated by acetylation of the OH or NH_2 group prior to formation of the oximes. (5) Treatment of monooximes of α-dicarbonyl compounds with TTN results in the formation of only 50–60% of the corresponding α-dicarbonyl compound. The remainder of the product consists of (as yet) unidentified products. (6) Oxythallation of α,β-unsaturated ketones is slow compared with isolated C=C bonds;[6] consequently, deoximation proceeds smoothly with α,β-unsaturated aldoximes and ketoximes. With oximes which contain an isolated C=C bond, however (*e.g.*, 1,2,5,6-tetrahydrobenzaldoxime), both deoximation and oxidative rearrangement[4] of the C=C bond occur, leading to mixtures of products.

Semicarbazone and phenylhydrazone derivatives of carbonyl compounds react analogously with TTN. Thus, treatment of the semicarbazone derivatives of cyclohexanone, acetophenone, and benzophenone at room temperature with TTN in methanol resulted in formation of the corresponding ketones in yields of 95, 86, and 82%, respectively. These reactions were slightly slower than those of the corresponding oximes, however, and required 1–5 min for completion. Regeneration of cyclohexanone and benzophenone from the corresponding phenylhydrazone derivatives was

(5) A. McKillop, B. P. Swann, and E. C. Taylor, *Tetrahedron*, **26**, 4031 (1970). Failure of the reaction in these cases is due to rapid and preferential oxidation to a quinone methide (*i.e.* i → ii).

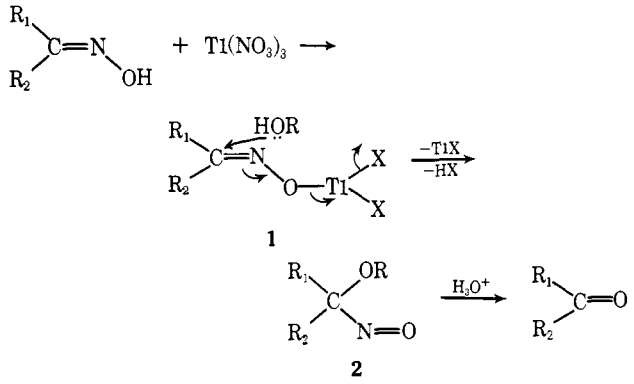


(6) A. McKillop, B. P. Swann, and E. C. Taylor, *Tetrahedron Lett.*, 5281 (1970).

slower still; after treatment with TTN at room temperature for 1 hr the ketones were obtained in 65 and 55% yield, respectively.[7] 2,4-Dinitrophenylhydrazone derivatives were unaffected by TTN even after several days at reflux temperature.

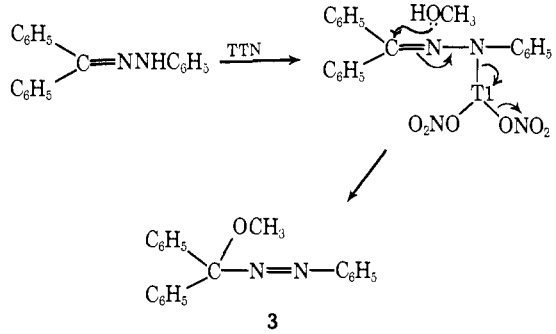
The above deoximation process can be explained in terms of the reactions outlined in Scheme I (X = ONO_2).

Scheme I



Compound **1** ($R_1 = R_2 = X = CH_3$) has been prepared[8] by treatment of acetoxime with trimethylthallium, and shown to give acetone on hydrolysis. Compounds of the type **2** (R = H) have been proposed as intermediates in the Nef reaction;[9] compounds of the type **2** ($R = CH_3CO$) have been isolated and identified as intermediates in the oxidation of oximes with lead(IV) acetate.[10-12] In the present study we have been unsuccessful in attempts to isolate intermediates analogous to **1** or **2**, but were able to obtain the azo ether **3**[13] (Scheme II) in 57% yield by treatment of benzophenone

Scheme II



phenylhydrazone with TTN in anhydrous methanol. The ether **3** presumably arises, as shown, by a mechanism similar to that suggested in Scheme I for oximes.

While the reactions summarized in Scheme I appear to account adequately for the deoximation process, a one-electron transfer pathway may also be operative under certain conditions. Thus, examination of the reaction of benzophenone oxime with TTN in benzene by esr spectroscopy showed clearly the formation of the corresponding iminoxy radical (triplet, $a_N = 31.6$ G, $a_H = 1.4$ G).[14] Iminoxy radicals were detected similarly for a variety of oximes and it appears that, as is the case with lead(IV) acetate,[10,11] oxidation of oximes with TTN may proceed by at least two different reaction pathways.

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Thallium in Organic Synthesis. XXVII. A Simple One-Step Conversion of Acetophenones into Methyl Phenylacetates Using Thallium(III) Nitrate (TTN)[1]

Sir:

The Willgerodt–Kindler reaction is a unique transformation whereby readily accessible alkyl aryl ketones are converted into ω-arylalkanoic acid derivatives.[2,3] The synthetic utility of the reaction is, however, limited by (a) the conditions of high temperature and, frequently, high pressure, under which the reaction is conducted; (b) a tedious and rather complicated isolation technique; and (c) the modest yields of products which are obtained in many cases.

We wish to describe in this communication a novel procedure for the direct conversion of acetophenones into methyl arylacetates using thallium(III) nitrate (TTN)[4] in acidic methanol. Thus, 0.01 mol of the acetophenone was added to a solution of 0.011 mol of TTN in 25 ml of methanol containing 5 ml of 70% perchloric acid and the reaction mixture was stirred at room temperature for 2–18 hr. The thallium(I) nitrate which precipitated was removed by filtration, the filtrate was diluted with water, and the product was extracted with chloroform. The organic extract was washed with water, dried, concentrated, and filtered through a short column of alumina using benzene as eluent. Evaporation of the eluate followed by distillation or crystallization gave the pure methyl arylacetate. Experimental data for representative conversions are summarized in Table I.

(7) Treatment of phenylhydrazone derivatives of α,β-unsaturated ketones does not result in regeneration of the parent carbonyl compound, but leads to 1-phenylpyrazoles. Thus, oxidation of chalcone phenylhydrazone with TTN in methanol gave 1,3,5-triphenylpyrazole in 40% yield.

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