Thallium in Organic Synthesis. XXXVII. A New Synthesis of Arylnitroso Compounds[1]

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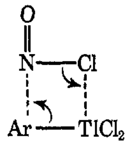
Previous papers in this series have demonstrated the effectiveness of thallium(III) trifluoroacetate (TTFA) as a thallating agent for aromatic compounds,[2,3] and have described procedures for the facile conversion of the resulting arylthallium ditrifluoroacetates into aryl iodides,[4,5] arylnitriles,[6] aryl isothiocyanates,[7] phenols,[6] thiophenols,[8] biaryls,[9] and deuterated aromatic compounds.[10] We now describe a simple method for the conversion of arylthallium ditrifluoroacetates into arylnitroso compounds by treatment with nitrosyl chloride (eq 1 and 2).[11]

$$\mathrm{ArTl(OOCCF_3)_2 + 2HCl \longrightarrow ArTlCl_2 + 2CF_3COOH} \quad (1)$$

$$\mathrm{ArTlCl_2 + NOCl \longrightarrow ArNO + TlCl_3} \quad (2)$$

Thus, the organothallium intermediate is suspended in chloroform containing 1.5 equiv of *n*-propyl nitrite, and hydrochloric acid is added. The nitrosyl chloride generated *in situ* reacts with the arylthallium dichloride (formed from the arylthallium ditrifluoroacetate and HCl) to give the arylnitroso compound. Yields are moderate to good (Table I). Since the arylthallium ditrifluoroacetates can be recrystallized to isomeric purity, this reaction constitutes a novel and general method for the direct introduction of nitrogen functionalities into aromatic nuclei, with all of the orientation control potential inherent in the initial thallation process.[3,12]

Our previously described[6] synthesis of phenols from arylthallium ditrifluoroacetates, lead tetratrifluoroacetate, and trifluoroacetic acid in all probability involves (in the initial step of the overall conversion) electrophilic attack by lead(IV) on the aryl–thallium bond[13] to give an aryllead tris(trifluoroacetate), which then undergoes spontaneous decomposition to an aryl trifluoroacetate (which gives the phenol by hydrolysis). We suggest that the reaction of arylthallium ditrifluoroacetates with nitrosyl chloride is another example of electrophilic displacement of Tl(III) from the aromatic nucleus [the formation of Tl(III) rather than Tl(I) in this reaction was confirmed experimentally], and that it may proceed through a four-centered transition state arising from initial complexation of nitrosyl chloride with the organothallium substrate.[14] Indeed, electrophilic substitution on the carbon–thallium bond of $\mathrm{ArTlX_2}$ compounds may be a general process[16] provided only that initial complexation of the $\mathrm{ArTlX_2}$ substrate precedes or accompanies attack by the electrophile. We are currently exploring this potentially new and versatile method for the introduction of electrophiles into aromatic systems.



Experimental Section

General Procedure for the Conversion of Arylthallium Ditrifluoroacetates to Arylnitroso Compounds.—*n*-Propyl nitrite (0.015 mol) was added to a suspension of the arylthallium ditrifluoroacetate (0.01 mol) in 100 ml of chloroform at room temperature. A solution of 12 *N* hydrochloric acid (4 ml) and glacial acetic acid (6 ml) was added with vigorous stirring.[18] The white precipitate which immediately formed (arylthallium dichloride) dissolved within minutes to give a green solution. After 10 min of stirring, 50 ml of 1.2 *N* hydrochloric acid was added, the mixture was stirred for 10 min, and the green chloroform layer was separated and extracted with 0.1 *N* hydrochloric acid (to remove

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[1] Part XXXVI: E. C. Taylor, R. L. Robey, and A. McKillop, *J. Org. Chem.*, **37**, 2797 (1972).

[2] A. McKillop, J. S. Fowler, M. J. Zelesko, J. D. Hunt, E. C. Taylor, and G. McGillivray, *Tetrahedron Lett.*, 2423 (1969).

[3] E. C. Taylor, F. Kienzle, R. L. Robey, A. McKillop, and J. D. Hunt, *J. Amer. Chem. Soc.*, **93**, 4845 (1971).

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[6] E. C. Taylor, H. W. Altland, R. H. Danforth, G. McGillivray, and A. McKillop, *ibid.*, **92**, 3250 (1970).

[7] E. C. Taylor, F. Kienzle, and A. McKillop, *Synthesis*, 38 (1972).

[8] E. C. Taylor and A. McKillop, *Accounts Chem. Res.*, **3**, 338 (1970).

[9] E. C. Taylor, F. Kienzle, and A. McKillop, *J. Amer. Chem. Soc.*, **92**, 6088 (1970).

[10] M. J. Zelesko, Ph.D. Thesis, Princeton University, 1970.

[11] Arylmercury [L. I. Smith and F. L. Taylor, *J. Amer. Chem. Soc.* **57**, 2460 (1935)], -magnesium [B. Oddo, *Gazz. Chim. Ital.*, **39**, I, 659 (1909)], and -tin [E. H. Bartlett, C. Eaborn, and D. R. M. Walton, *J. Chem. Soc. C*, 1717 (1970)] compounds react analogously with nitrosyl chloride.

[12] E. C. Taylor, F. Kienzle, R. L. Robey, and A. McKillop, *J. Amer. Chem. Soc.*, **92**, 2175 (1970).

[13] Trans metalation reactions of this type have been viewed as an electrophilic substitution reaction on the original aryl–metal bond: R. Criegee, P. Dimroth, and R. Schempf, *Chem. Ber.*, **90**, 1337 (1957).

[14] Thallium is known to be capable of expansion of its coordination sphere; complexes with halide and cyanide ions are well known.[15]

[15] A. G. Lee, "The Chemistry of Thallium," Elsevier, Amsterdam, 1971.

[16] Protodethallation[15,17] is still a further example of an electrophilic "displacement" of Tl(III) from the aromatic ring.

[17] A. N. Nesmeyanov and K. A. Kocheshkov, "Methods of Elemento-Organic Chemistry. Vol. 4. The Organic Compounds of Boron, Aluminium, Gallium, Indium, and Thallium," North-Holland Publishing Co., Amsterdam, 1967.

[18] 12 *N* hydrochloric acid alone was used with arylthallium ditrifluoroacetates derived from less reactive aromatic substrates (*i.e.*, chlorobenzene).

TABLE I
SYNTHESIS OF ARYLNITROSO COMPOUNDS FROM ARYLTHALLIUM DITRIFLUOROACETATES
$ArTl(OOCCF_3)_2 \longrightarrow ArNO$

Registry no.	Product[a]	Registry no.[l]	Yield, %
1516-21-8	4-Nitrosoanisole	28688-23-5	59[b]
586-96-9	Nitrosobenzene	23586-54-1	43[c]
932-98-9	4-Nitrosochlorobenzene	23586-58-5	50[d]
38899-21-7	Nitrosodurene	38899-26-2	93[e]
1196-12-9	Nitrosomesitylene	23586-57-4	93[f]
22955-65-3	4-Nitrosoethylbenzene	35322-30-6	88[g]
623-11-0	4-Nitrosotoluene	23586-55-2	88[h]
38899-22-8	4-Nitroso-1,2-dimethylbenzene	23586-56-3	91[i]
38974-06-0	4-Nitroso-1,3-dimethylbenzene	34202-98-7	90[j]
17075-25-1	2-Nitroso-1,4-dimethylbenzene	34202-99-8	93[k]

[a] The use of isomerically pure arylthallium ditrifluoroacetates led to the formation of isomerically pure arylnitroso compounds; otherwise, mixtures of isomeric arylnitroso compounds were obtained whose isomeric distribution matched that of the starting material (see Experimental Section). [b] A. Baeyer and E. Knorr, *Ber.*, **35,** 3034 (1902); mp 32–34°. [c] "Organic Syntheses," Collect. Vol. III, Wiley, New York, N. Y., 1955, p 668; mp 64–67°. [d] R. E. Lutz and M. R. Lytton, *J. Org. Chem.*, **2,** 68 (1937); mp 89.5°. [e] L. I. Smith and F. L. Taylor, *J. Amer. Chem. Soc.*, **57,** 2460 (1935); mp 160° dec. [f] E. Bamberger and A. Rising, *Ber.*, **33,** 3623 (1900); mp 122°. [g] See footnote *d;* mp 22°. [h] E. Bamberger, *Ber.*, **28,** 245 (1895); mp 48.5°. [i] E. Bamberger and A. Rising, *Justus Liebigs Ann. Chem.*, **316,** 257 (1901); mp 44–45°. [j] See footnote *i;* mp 41.5°. [k] See footnote *i;* mp 101.5°. [l] Of starting material.

$TlCl_3$). The chloroform extract was dried ($MgSO_4$) and evaporated to give the crude arylnitroso compound, which was purified by Kugelrohr distillation (*in vacuo*).

Glc analysis of the arylnitroso compounds was frustrated by poor separation and, as a consequence, isomer distributions were determined by oxidation with pertrifluoroacetic acid to the arylnitro compounds, which were then satisfactorily analyzed by glc. As expected, the use as substrates of arylthallium ditrifluoroacetates which had not been recrystallized to isomeric purity led to a mixture of isomeric arylnitroso compounds whose isomeric distribution matched precisely that of the precursor arylthallium ditrifluoroacetates. Thus in this reaction, as in all previously investigated conversions of $ArTlX_2$ compounds to substituted aromatics, the new substituent group enters the ring at the position to which the thallium atom was originally attached.

Kinetic Evidence for an Enamine Mechanism in the Acid-Catalyzed Cleavage of β-Amino Alcohols[1]

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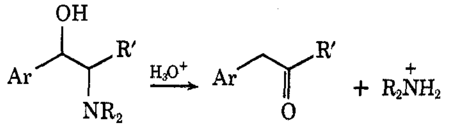
The reaction of α-aryl-β-amino alcohols with strong acids has been known for some time to cause cleavage to β-carbonyl compounds.[2-4] Two mechanisms have been proposed to account for the cleavage, one involving a glycol intermediate[2,3] and the other involving



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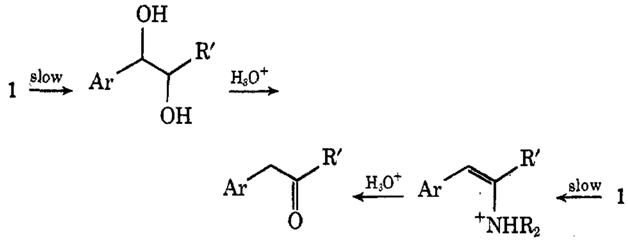

an enamine intermediate.[2,4] The details of these mechanisms have been reviewed recently.[5] In general there has been little convincing experimental evidence in favor of either mechanism, although recent work[5] has ruled out a glycol mechanism for the reaction of one amino alcohol with acid.

We have examined the acid-catalyzed reaction rates of 2-(*N*,*N*-diethylamino)-1-phenylethanol derivatives having from zero to three methyl groups on the aromatic rings. A large excess of 4 *N* hydrochloric acid at 100° was employed as the reaction medium, conditions which led to pseudo-first-order kinetics. Ultraviolet spectroscopy was used to monitor the disappearance of amino alcohols. The pseudo-first-order rate constants and relative rates are summarized in Table I.

TABLE I
GRAPHICALLY DETERMINED PSEUDO-FIRST-ORDER RATE CONSTANTS AND RELATIVE RATES FOR REACTION OF AMINO ALCOHOLS WITH 4 *N* HYDROCHLORIC ACID AT 100°

Registry no.	Amino alcohol	*k*, sec⁻¹	Relative rate
4249-64-3	$C_6H_5CHOHCH_2NEt_2$	2.63×10^{-7}	1.00
39008-11-2	*p*-$CH_3C_6H_4CHOHCH_2$-NEt_2	2.19×10^{-6}	8.33
39008-12-3	2,4-di-$CH_3C_6H_3CHOH$-CH_2NEt_2	1.61×10^{-5}	61.2
39008-13-4	2,4,6-tri-$CH_3C_6H_2CHOH$-CH_2NEt_2	8.14×10^{-5}	309

The rate constants are seen to increase with increasing methyl substitution on the ring, each increase by one methyl group leading to an increase in rate by a factor varying from approximately 5 to 8. A mech-

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(3) H. Auterhoff and H. J. Roth, *Arch. Pharm.* (*Weinheim*), **289,** 470 (1956).

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(5) S. A. Fine and R. L. Stern, *J. Org. Chem.*, **35,** 1857 (1970).