Communications

Thallium in Organic Synthesis. 46. Oxidative Coupling of Aromatic Compounds Using Thallium(III) Trifluoroacetate. Synthesis of Biaryls[1]
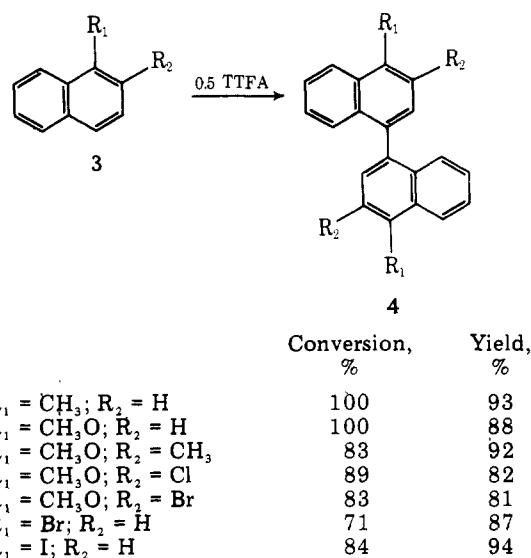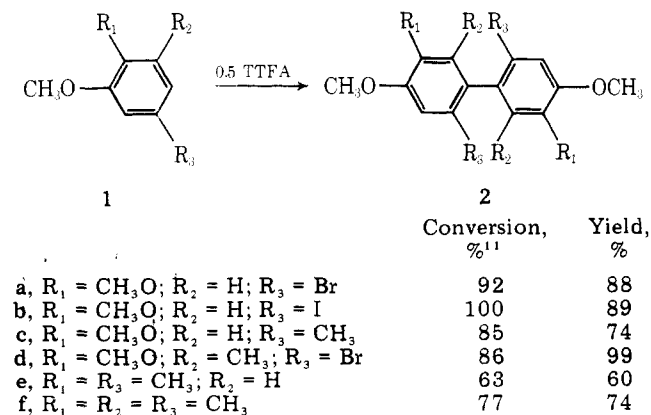
Summary: Treatment of a variety of aromatic compounds with thallium(III) trifluoroacetate in trifluoroacetic acid, carbon tetrachloride, or acetonitrile results in oxidative coupling to give symmetrical biaryls in good to excellent yield.

Sir: There are few preparatively useful procedures for the synthesis of biaryls. The most important, and commonly used, methods are the Ullmann reaction,[2] the Gomberg reaction,[3] the thermal decomposition of aroyl peroxides,[4] and various Kharasch-type reactions in which an aromatic Grignard reagent is treated with an organic halide in the presence of a metal halide.[5] More recent methods which have not yet been widely utilized include the reaction of aromatic Grignard reagents with thallium(I) bromide,[6] treatment of aryllead(IV) triacetates with trifluoroacetic acid in the presence of activated hydrocarbons,[7] reaction of diaryltellurium(IV) dihalides with Raney nickel at 200 °C,[8] treatment of aryl halides with zerovalent nickel complexes,[9] and the coupling of arylmercury(II) salts with copper metal and a catalytic amount of palladium(II) chloride in the presence of pyridine.[10] The requirement that the starting material possess a substituent group which must eventually be lost in the coupling process is the common denominator in *all* of the above biaryl syntheses.[11]

We now report that treatment of a variety of aromatic substrates with thallium(III) trifluoroacetate (TTFA) in trifluoroacetic acid (TFA), or in carbon tetrachloride or acetonitrile containing boron trifluoride etherate results in smooth, rapid, and direct oxidative coupling to give symmetrical biaryls in good to excellent yield.

Thus, reaction of 4-bromoveratrole **1a** (1 equiv) with TTFA (0.5 equiv) in TFA is complete within a few minutes; pure 2,2'-dibromo-4,4',5,5'-tetramethoxybiphenyl **2a** is obtained in 88% yield (92% conversion[12]) after recrystallization from toluene/petroleum ether (bp 100–120 °C).[13] The anisole derivatives **1b–f** react analogously to give the biaryls **2b–f**, and the naphthalene derivatives **3a–g** are smoothly converted into the binaphthyls **4a–g**.[14]
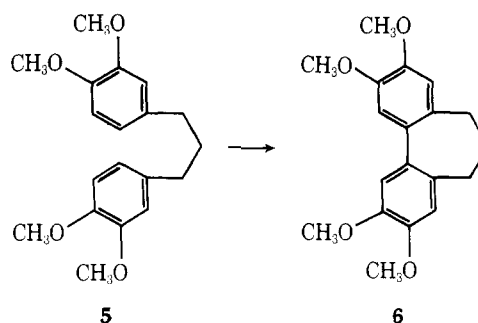
Thus, this method constitutes a simple, effective procedure for the preparation of a variety of highly substituted biaryls in which the ring substituents are either electron-donating or mildly electron-withdrawing groups. Aromatic substrates

	Conversion, %[11]	Yield, %
a, $R_1 = CH_3O$; $R_2 = H$; $R_3 = Br$	92	88
b, $R_1 = CH_3O$; $R_2 = H$; $R_3 = I$	100	89
c, $R_1 = CH_3O$; $R_2 = H$; $R_3 = CH_3$	85	74
d, $R_1 = CH_3O$; $R_2 = CH_3$; $R_3 = Br$	86	99
e, $R_1 = R_3 = CH_3$; $R_2 = H$	63	60
f, $R_1 = R_2 = R_3 = CH_3$	77	74

	Conversion, %	Yield, %
a, $R_1 = CH_3$; $R_2 = H$	100	93
b, $R_1 = CH_3O$; $R_2 = H$	100	88
c, $R_1 = CH_3O$; $R_2 = CH_3$	83	92
d, $R_1 = CH_3O$; $R_2 = Cl$	89	82
e, $R_1 = CH_3O$; $R_2 = Br$	83	81
f, $R_1 = Br$; $R_2 = H$	71	87
g, $R_1 = I$; $R_2 = H$	84	94

which contain powerful electron-withdrawing groups (COOR, CN, NO₂) fail to couple under the above conditions. Consequently, the TTFA method is complementary to the Ullmann reaction since the latter procedure usually gives satisfactory yields of biaryls only when the aromatic halides contain powerful electron-withdrawing groups, and is normally an inefficient reaction for the preparation of binaphthyls.

Another important aspect of the present procedure is the facility with which 2,2',6,6'-tetrasubstituted biaryls can be prepared in good yields. Gibson and Bailey, for example, reported recently that both the Ullmann reaction of the benzyl ether of 2,3,5-trimethyl-4-iodophenol and the Kharasch-type reaction of the corresponding Grignard reagent with cupric chloride failed to yield any biaryl.[15] Treatment of the benzyl ether of 2,3,5-trimethylphenol with TTFA in acetonitrile containing boron trifluoride, however, gives 2,2',3,3',6,6'-hexamethyl-4,4'-dibenzyloxybiphenyl in 39% yield (51% conversion) in 10 min.

The effectiveness of this procedure for *intra*molecular coupling is illustrated by the conversion of 1,3-bis(3,4-di-

methoxyphenyl)propane (**5**) to the bridged biphenyl **6** in 81% yield (100% conversion).[16] Applications to the construction of aporphine and homoaporphine alkaloids[17] from 1-benzyl- and 1-phenethyl-1,2,3,4-tetrahydroisoquinolines are under investigation.

The detailed mechanism of this coupling reaction is not yet known, but the available evidence is compatible with the sequence (a) reaction of TTFA with the aromatic substrate and generation of the radical cation Ar·⁺; (b) reaction of this

electrophile with the aromatic substrate; and (c) oxidative aromatization of the intermediate thus produced by TTFA. Formation of arene radical cations in the reactions of certain alkyl benzenes with TTFA in TFA has been demonstrated by Elson and Kochi,[18] while formation of small amounts of biaryls during electrophilic aromatic thallation using TTFA and other thallium(III) salts has been noted on several occasions.[19] Moreover, treatment of durene with TTFA in TFA gives the heptamethyldiphenylmethane 7 (~15% yield), which

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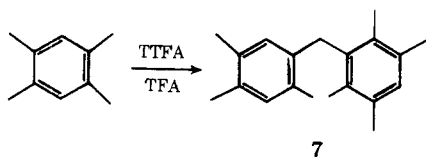
is also one of the products formed by electrochemical oxidation of durene, a process known to proceed via the radical cation.[20] An important consequence of the radical cation mechanism is that the oxidation potential of an aromatic substrate should be one of the major factors governing the particular reaction course which will be followed when that aromatic substrate is treated with TTFA, i.e., electrophilic aromatic thallation or oxidative coupling. Studies to establish this point and to define more rigorously the scope and limitations of this new biaryl synthesis are currently in progress.

References and Notes

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(12) Conversion data are based on the amount of starting material which is recovered, while yield data are based on the amount of starting material which is consumed. Starting material was recovered from all but three of the reactions; in the other cases use of excess TTFA did result in complete oxidation of the starting materials but led to substantially lower yields of biaryls. This is due to competitive reactions in which the starting material and product are oxidized by TTFA to highly colored, polymeric materials.
(13) The following procedure for the preparation of 2,2'-dibromo-4,4',5,5'-tetramethoxybiphenyl illustrates the general experimental method. 4-Bromoveratrole (4.34 g, 0.02 mol) was added in one portion to a solution of TTFA (5.50 g, 0.01 mol) in TFA (25 ml) at room temperature. The solution immediately turned deep red in color and became warm, and a colorless solid precipitated within a few minutes. The mixture was stirred for 10 min then poured into water and the resulting mixture extracted with chloroform. The chloroform solution was passed through a short column of basic alumina using petroleum ether (bp 40–60 °C)/chloroform (1:1) as eluent to remove highly colored polymeric materials. Evaporation of the eluent under reduced pressure followed by crystallization of the residual solid thus obtained from petroleum ether (bp 100–120 °C)/toluene gave 3.48 g of pure 2,2'-dibromo-4,4',5,5'-tetramethoxybiphenyl as colorless needles, mp 159–160 °C [lit.,mp 160 °C: W. Baker, J. W. Barton, J. F. W. McOmie, R. J. Penneck, and M. L. Watts, *J. Chem. Soc.*, 3986 (1961)]. Concentration of the mother liquors gave 0.35 g (8% recovery) of 4-bromoveratrole. The yield of biaryl based on 92% conversion of the starting material is 88%.
(14) Yields are calculated from percentage conversions as indicated above, and refer to pure recrystallized materials. Satisfactory spectroscopic and microanalytical data were obtained for all new compounds.
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Sulfuranes. The Use of Tetraoxysulfuranes in the Formation of Olefins and Ethers from Alcohols

Summary: Phenylene orthosulfite synthesized from SF₄ and the dilithium salt of catechol reacts with alcohols to form olefins probably by means of a cyclic elimination route.

Sir: Interest in alkoxysulfuranes has been stimulated by reports of their utility as dehydrating reagents.[1-6] The dialkoxysulfurane $[C_6H_5C(CF_3)_2O]_2S(C_6H_5)_2$ reacts with primary alcohols to form unsymmetrical ethers of the type $C_6H_5C(CF_3)_2OR$ and with secondary alcohols to form olefins preferentially by trans coplanar elimination.[1]

We report results indicating that considerable control over the stereochemistry of elimination and the products formed from primary alcohols may be possible by a judicious choice of the sulfurane reagent.

Tetraoxysulfurane **1** reacts rapidly with cyclohexanol in $CDCl_3$ solution at room temperature to provide cyclohexene.
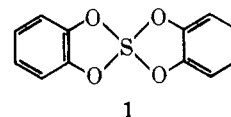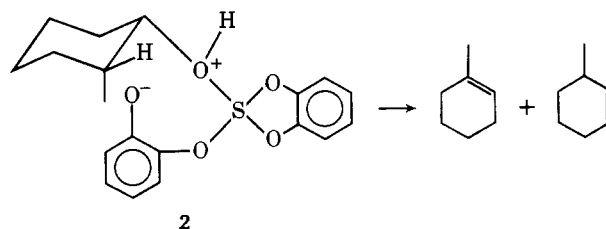

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Both the cis and trans isomers of 2-methylcyclohexanol provide a 1:1 mixture of 1-methyl- and 3-methylcyclohexene together with *o*-phenylene sulfite. The sulfite is incapable of effecting the dehydration, and the olefins are stable under the reaction conditions.

This result is inconsistent with expectations for either an E1 or E2 elimination route. A trans coplanar elimination of the trans isomer could produce only 3-methylcyclohexene. By analogy with the phosphoric acid catalyzed dehydration of the isomeric 2-*tert*-butylcyclohexanols,[7] the trans isomer of 2-methylcyclohexanol would be expected to give a mixture of 1- and 3-methylcyclohexene but the cis alcohol should give mainly 1-methylcyclohexene. The observed result is consistent with a cyclic elimination mechanism similar to that found for amine oxide pyrolyses.[8]

In this mechanism the sulfurane undergoes ligand exchange with the alcohol to form **2** with the sulfurane group occupying the equatorial position of the cyclohexane ring by virtue of its

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