

DIRECT OXIDATION OF ALCOHOLS AND DIOLS VIA HYDRIDE ABSTRACTION

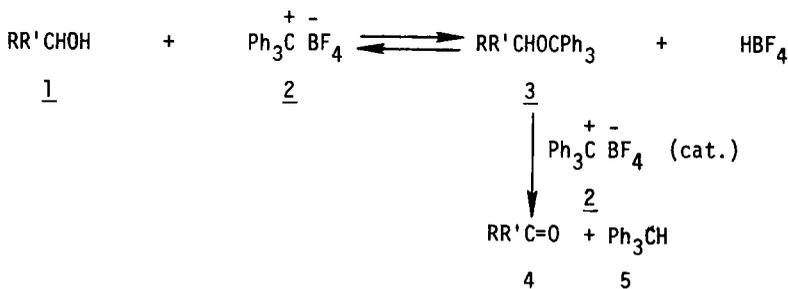
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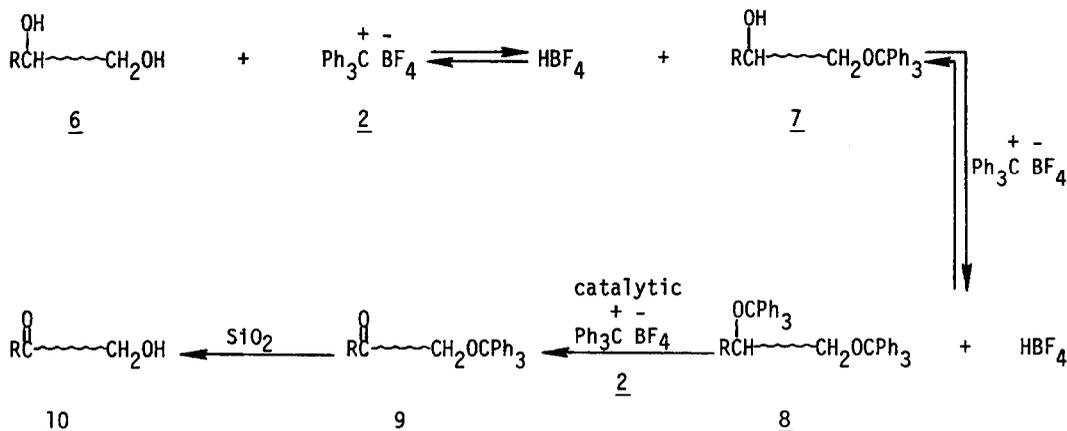
Recently we reported the oxidation of various ether derivatives of alcohols - trimethylsilyl ethers,¹ *tert*-butyl and trityl ethers,² trimethylsilyl enol ethers³ - to the corresponding ketones and enones by triphenylcarbenium (trityl) tetrafluoroborate. The use of the bis-trityl ethers of primary, secondary diols permitted selective oxidation at the secondary position in preference to the primary one.² We now wish to report the direct oxidation of unprotected secondary alcohols to ketones and the selective oxidation of primary, secondary diols at the secondary position by treatment with trityl tetrafluoroborate.

It was reasoned that treatment of a secondary alcohol 1 with one equivalent of trityl tetrafluoroborate 2 would generate an equilibrium mixture of the starting materials and the trityl ether 3 and fluoroboric acid. If additional trityl salt 2 was added, one would expect the secondary trityl ether to be rapidly oxidized to the corresponding ketone 4 with the concomitant formation of triphenylmethane 5. The additional trityl salt need be present only in catalytic quantities,⁴ although the use of more than a catalytic amount would ensure a much faster conversion in this bimolecular oxidation process. This theory indeed proved to be the case.



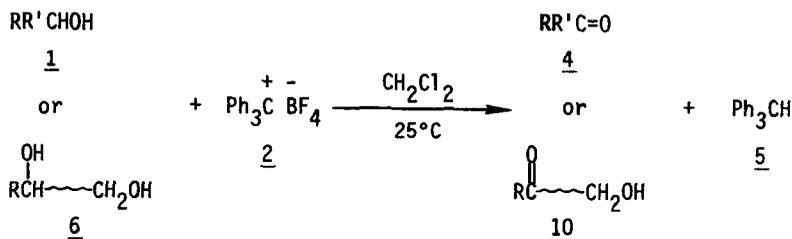
Treatment of the secondary alcohols 1a-d with 2.0 equivalents of trityl tetrafluoroborate 2 in dichloromethane under nitrogen for 10-13.5 hr followed by the usual aqueous workup afforded the corresponding ketones 4a-d in good yields (Table). Conducting the reaction for a shorter period of time resulted in the recovery of some unreacted alcohol, while longer reaction times afforded greater amounts of side products, mainly products of acid-catalyzed aldol condensations. Primary alcohols are not oxidized to any great extent under these conditions.

The above results implied that treatment of a primary, secondary diol 6 with two equivalents of the trityl salt 2 would generate an equilibrium mixture of the mono-trityl ether 7 and the bis-trityl ether 8 along with fluoroboric acid. Since we had already shown that primary trityl ethers are oxidized very slowly compared to secondary ones,² it was anticipated that the use of a slight excess of trityl salt 2 would afford oxidation only at the secondary center to afford the keto trityl ether 9. Hydrolysis would then furnish the hydroxy ketone 10. Our results bear out this contention.



When diols 6a-c are treated with 2.1-2.2 equivalents of trityl tetrafluoroborate 2 in dichloromethane at 25°C under nitrogen for 8-12.5 hr, worked up in the normal fashion, and passed down a Davison silica gel column (to hydrolyze the primary trityl ether), good yields of the corresponding hydroxy ketones 10a-c are obtained (Table). In the case of the cycloalkanone products 10b-c, the yields are lowered probably because of acid-catalyzed aldol condensation due to the presence of fluoroboric acid. Therefore, it is still preferable to preform the bis-trityl ethers 8 of cyclic diols and oxidize them in a separate step as described earlier² rather than utilize this direct one-step procedure. However for simple alcohols and acyclic diols, this one-step procedure works well.

TABLE
OXIDATION OF ALCOHOLS AND DIOLS WITH TRITYL FLUOROBORATE



<u>Compound</u>	<u>Alcohol/Diol</u>	<u>Compound</u>	<u>Ketone</u>	<u>Reaction Time (hr)</u>	<u>Yield (%)^a</u>
<u>1a</u>		<u>4a</u>		10.5	82
<u>1b</u>		<u>4b</u>		10	84
<u>1c</u>		<u>4c</u>		13.5	66
<u>1d</u>		<u>4d</u>		12	68
<u>6a</u>		<u>10a</u>		12.5	80
<u>6b</u>		<u>10b</u>		9	59
<u>6c</u>		<u>10c</u>		8	53

a. All yields are for isolated purified materials.

There are some limitations to this simplified oxidation method. Very sterically hindered alcohols are not oxidized by this procedure. For example, menthol, 2,2-dimethyl-1,3-butanediol, and 2-ethyl-1,3-hexanediol were recovered unchanged after treating for several hours with the trityl salt 2 followed by mild hydrolysis. No oxidation at the secondary center was observed.

This simple one-step oxidation process forms a useful alternative to the other known methods for selective oxidation of primary, secondary diols.^{5,6,7}

A typical experimental procedure follows: 1,6-heptanediol 6a (0.4960 g, 3.752 mmol) was allowed to stir for 8 hours with triphenylcarbenium tetrafluoroborate 2 (2.4883 g, 7.537 mmol)⁸ in 40 ml dichloromethane at 25°C under nitrogen. The reaction mixture was poured into dilute aqueous sodium bicarbonate solution and stirred for 15 minutes. The layers were separated and the aqueous layer extracted with 25 ml dichloromethane. The organic layer was dried (sodium sulfate) and concentrated in vacuo, dissolved in a small volume of dry benzene and applied to a dry column of Davison 56 silica gel (30 g). The column was developed and allowed to stand at 25°C overnight. Elution with benzene yielded triphenylmethane and triphenylmethanol. Further elution with ethyl acetate yielded the product, 7-hydroxy-2-heptanone 10a (0.3907 g, 3.005 mmol). Yield 80%. For the alcohols 1a-d, distillation proved more efficient than chromatography as a means of purification.

References and Notes

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7. For other selective oxidation methods, see Reference 2.
8. Commercially available from Cationics, Inc.