Tetrahedron Letters,Vol.27,No.41,pp 4953-4956,1986 0040-4039/86 $3.00 + .00
Printed in Great Britain Pergamon Journals Ltd.

SYNTHESIS OF DIOSPHENOL ETHERS BY MEANS OF ALKOXYTRIMETHYLSILANES

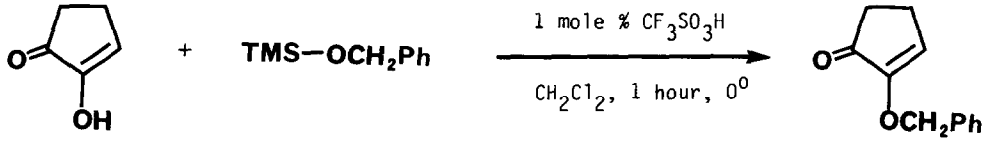
A.A. Ponaras* and Md. Younus Meah

Department of Chemistry
The Catholic University of America
Washington, DC 20064

ABSTRACT: α-Diketones may be O-alkylated with a variety of alkoxytrimethylsilanes.

Diosphenol ethers (α-alkoxy-α,β-unsaturated ketones) are not only structural units in a number of physiologically-active substances[1] but are also important synthons for carbonyl transposition,[2] various photochemical transformations,[3] carbocation rearrangements[4] and Claisen rearrangements.[5] In connection with the last, we needed a reliable method for preparing enol ethers from 1,2-dicarbonyl compounds and various allylic and propargylic alcohols. The usual method for effecting this etherification (treatment of diosphenols with alcohols and a strong acid catalyst at elevated temperature)[6] is incompatible with sensitive functionality and often gives low yields. In order to overcome these problems we have developed a milder method involving the well-known strategy[7] of replacing hydrogen by silicon in reagents which attack carbonyl groups.

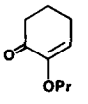
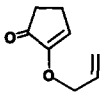
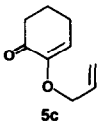
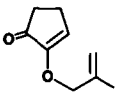
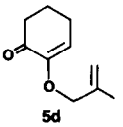
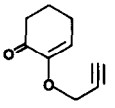
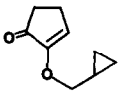
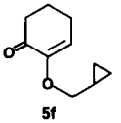
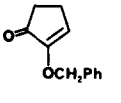
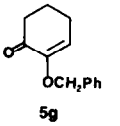
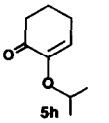
The utility of our procedure can be illustrated in the preparation of diosphenol benzyl ethers. Treatment of an ice-cold solution of 10 mmoles of 1,2-cyclopentanedione 1 and 20 mmoles of benzyl trimethylsilyl ether 3g in 10 mL of dry methylene chloride with 11 uL (0.1 mmole) of triflic acid,[8] followed by stirring at 0^0 for one hour, washing with sodium bicarbonate solution, and rapid chromatography gives 4g in 73% yield. By contrast, the conventional procedure[6a] gives mainly dibenzyl ether and only about 30% yield of diosphenol ether.



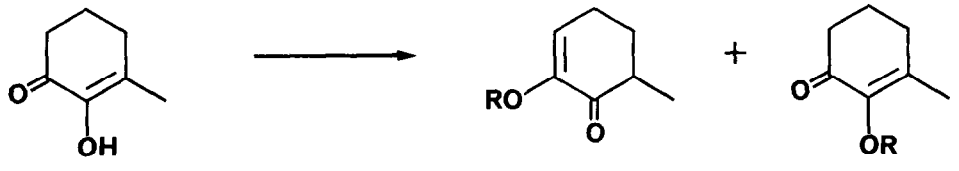
1 3g 4g

In reactions of 1,2-cyclohexanedione 2 with alkoxytrimethylsilanes at 0°, the dione monoketal is the major initial product. Keeping the reaction mixture at room temperature for several hours causes virtually complete conversion to the diosphenol ether.

Below are tabulated isolated yields and selected spectral data[9] of a variety of diosphenol ethers prepared from 1 and 2 by our method.

Silyl Ether[10]	Product from 1	Comments	Product from 2	Comments
MeO—SiMe$_3$ **3a**	 **4a**	81% Yield. NMR: 2.0-2.6, m, 4H; 3.70, s, 3H; 6.51, t, J = 3, 1H. IR: 1711, 1627 Spectra are consistent with those reported[3b]	 **5a**	88% Yield. NMR: 1.6-2.2, m, 2H; 2.2-2.7, m, 4H; 3.55, s, 3H; 5.88, t, J = 4.5, 1H. IR: 1687, 1626 Spectra are consistent with those reported[3b]
n-PrO—SiMe$_3$ **3b**			 **5b**	80% Yield. NMR: 0.96, t, J = 7, 3H; 1.3-2.2, m, 4H; 2.3-2.6, m, 4H; 3.60, t, J = 6.5, 2H; 5.78, t, J = 4.5, 1H. IR: 1688, 1624
O—SiMe$_3$ **3c**	 **4c**	82% Yield. NMR: 2.2-2.8, m, 4H; 4.40, d, J = 6, 2H; 5.0-5.6, m, 2H; 5.6-6.4, m, 1H; 6.48, t, J = 2.5, 1H. IR: 1715, 1625	 **5c**	83% Yield. Reported[3d] yield by Method A is 74% NMR: 1.6-2.2, m, 2H; 2.2-2.6, m, 4H; 4.26, d, J = 5.5, 2H; 5.0-5.5, m, 2H; 5.5-6.4, m, 2H. IR: 1692, 1624 Spectra are consistent with those reported[3d]
O—SiMe$_3$ **3d**	 **4d**	70% Yield. NMR: 1.74, s, 3H; 2.2-2.6, m, 4H; 4.25, s, 2H; 4.93, "d," 2H; 6.31, t, J = 3, 1H. IR: 1714, 1626	 **5d**	64% Yield. Reported[3d] yield by Method A is 34%. NMR: 1.76, s, 3H; 1.5-2.7, m, 6H; 4.16, s, 2H; 4.93, "d," 2H; 5.91, t, J = 4, 1H. IR: 1693, 1626 Spectra are consistent with those reported[3d]
O—SiMe$_3$ **3e**			 **5e**	68% Yield. Method A gives 22% yield. Method B gives 9% yield. NMR: 1.8-2.8, m, 7H; 4.43, d, J = 2.5, 2H; 6.03, t, J = 4.5, 1 H. IR: 1687, 1628
O—SiMe$_3$ **3f**	 **4f**	67% Yield. Method A gives 22% yield; Method B gives 10% yield. NMR: 0.1-0.7, m, 4H; 0.7-1.5, m, 1H; 2.42, *narr m*, 4H; 3.62, *d*, J = 7, 2H; 6.24, t, J = 3, 1H. IR: 1714, 1623	 **5f**	70% Yield. Method A gives 27% yield. Method B gives 10% yield. NMR: 0.1-0.7, m, 4H; 0.9-1.5, m, 1H; 1.5-2.2, m, 4H; 2.2-2.6, m, 2H; 3.46, d, J = 7, 2H; 5.76, t, J = 4.5, 1H. IR: 1688, 1623
PhCH$_2$O—SiMe$_3$ **3g**	 **4g**	73% Yield. Method B gives 30% yield. NMR: 2.37, s, 4H; 4.87, s, 2H; 6.28, t, J = 3, 1H; 7.25, s, 5H. IR: 1714, 1625 m.p. 62-63°	 **5g**	62% Yield. Method A gives 35% yield. Method B gives <10% yield. NMR: 1.6-2.1, m, 2H; 2.1-2.7, m, 4H; 4.76, s, 2H; 5.83, t, J = 4.5, 1H; 7.24, s, 5H. IR: 1687, 1626 m.p. 53-55°; Lit.[11] 55-56°
O—SiMe$_3$ **3h**			 **5h**	66% Yield. NMR: 1.22, d, J = 6, 6H; 1.5-2.7, m, 6H; 4.22, septet, J = 6, 1H; 5.93, t, J = 4.5, 1H. IR: 1687, 1621

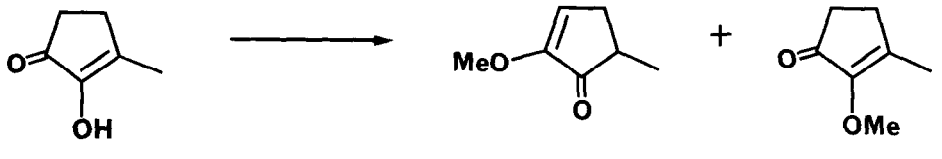
With 3-substituted-1,2-cyclohexanediones the less-substituted enol ether is the major product. For example, treatment of 3-methyl-1,2-cyclohexanedione 6 with two equivalents of methoxytrimethylsilane 3a at room temperature for one half hour gives 7a and 8a in the ratio of 9:1 (67% yield). Similarly, using allyloxytrimethylsilane, 7c and 8c are obtained in the same ratio (65% yield). This selectivity contrasts with that found using equilibrating procedures[6] where the more-substituted enol ether is the (exclusive) product.



6 7 8

9 : 1

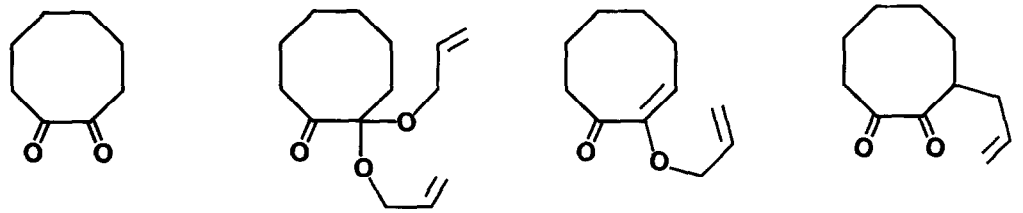
With 3-substituted-1,2-cyclopentanediones selectivity is lower:



9 10 11

2 : 1

As expected,[12] acyclic or medium-ring α-diketones give by our method the monoketal and not the enol ether (even after prolonged reaction at room temperature). Thus, for example, 1,2-cyclooctanedione 12 and 3c give 13 in 72% yield. Heating the ketal with a trace of potassium bisulfate for twenty minutes at 140° followed by vacuum distillation gives 3-allyl-1,2-cyclooctanedione 15 (77% yield) presumably via Claisen rearrangement of the intermediate diosphenol ether 14:



12 13 14 15

Further investigation of these reactions, with particular concern for improving chemoselectivity with non-symmetrical diosphenols and development of reagents for preparing difficultly-accessible diosphenol ethers (e.g., those of tertiary alcohols), is now underway.

ACKNOWLEDGEMENT. We thank the National Science Foundation for their support of this work. FT-NMR and FT-IR spectra were run at the CUA Chemical Instrumentation Center.

NOTES AND REFERENCES

[1]Examples: bruceantin, elatericin B, sinomenine, cepharamine and the cephalotaxus alkaloids.

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[5]a. Ponaras, A.A. J. Org. Chem. 1983, 47, 3866 and references therein.
b. Koreeda, M.; Luengo, J.I. J. Amer. Chem. Soc. 1985, 107, 5572.

[6]a. Method A: A benzene solution of diosphenol, excess alcohol and a few mole % of p-TsOH is heated under a Dean-Stark trap, usually for several hours (cf. ref. 2a).

b. Method B: A 1 M alcoholic solution of the diosphenol is treated, at 65°- 100° (as needed to consume starting materials within several hours), with 0.1 eq. of triflic acid (cf. ref. 2b and 2c where MeOH/BF_3 and MeOH/HCl, respectively, are employed).

c. We have found the ketalization procedure of Taylor and Chiang using acidic Montmorillonite clay K-10 and trimethyl orthoformate to be ineffective for the preparation of diosphenol methyl ethers (cf. Taylor, E.C.; Chiang, C.-S. Synthesis 1977, 467).

[7]a. Selin, T.G. U.S. Patent 3 621 060, 1971; Chem. Abstr. 1972, 76, 45,258a.
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c. Tsunoda, T.; Suzuki, M.; Noyori, R. Tetrahedron Lett. 1980, 21, 1357.

[8]Trimethylsilyl triflate and other acids catalyze the reaction less efficiently.

[9]NMR spectra were measured in deuteriochloroform at 60 or 90 MHz; IR spectra were taken of thin films. HRMS were obtained for all new compounds.

[10]These silyl ethers are all known compounds, prepared in high yield from the corresponding alcohol. For a compendium of procedures, see Pierce, A. Silylation of Organic Compounds; Pierce: Rockford, Illinois, 1976.

[11]Gibson, M.S. J. Chem. Soc. 1962, 681.

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(Received in USA 1 July 1986)