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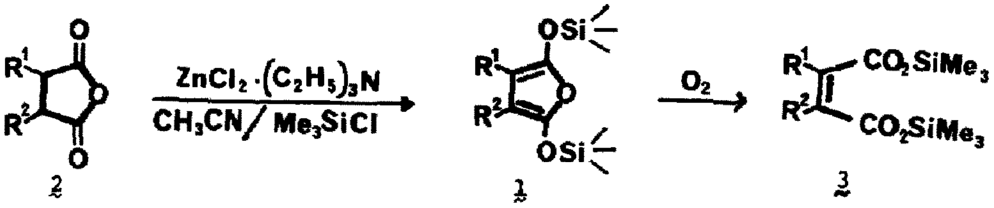
CHEMISTRY OF 2,5-BIS(TRIMETHYLSILOXY)FURANS[1]. I: PREPARATION AND DIELS-ALDER REACTIONS

Peter Brownbridge and Tak-Hang Chan*

Department of Chemistry, McGill University,
Montreal, Quebec, Canada, H3A 2K6.

Summary: A number of substituted 2,5-bis(trimethylsiloxy)furans were prepared from the corresponding succinic anhydrides, and were found to be reactive dienes for the Diels-Alder reaction with electron - withdrawing dienophiles, giving p-quinones and hydroquinones.

It will be evident from this and the following communications that 2,5-bis (trimethylsiloxy)furans (1 a-e) are useful intermediates for the synthesis of lignans, butenolides, hydroquinones and p-quinones. As part of our program on the chemistry of enol silyl ethers[1], we became interested in the preparation of 1. We found that simply by treating succinic anhydrides 2 with triethylamine, zinc chloride and trimethylchlorosilane in acetonitrile as solvent[2], 1 can be obtained in essentially quantitative yield.

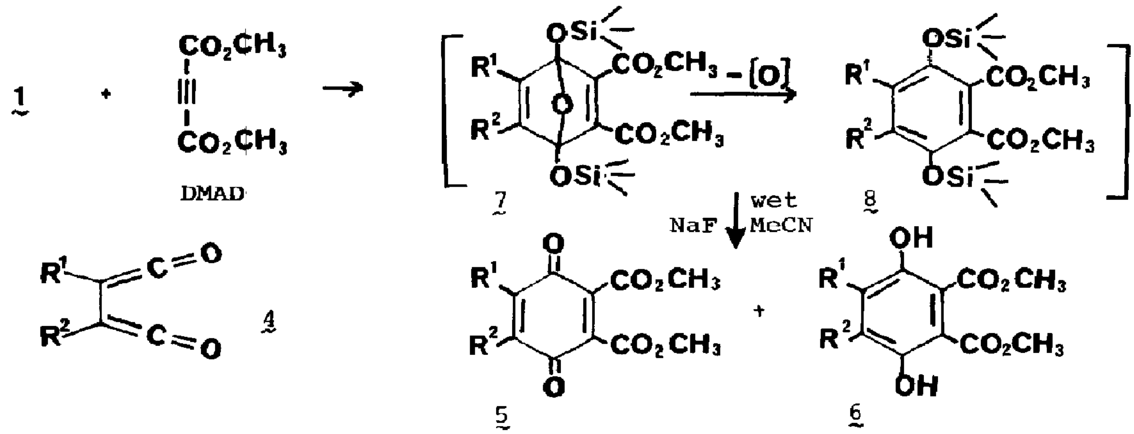


a; $R^1=R^2=H$, b; $R^1=Me$, $R^2=H$, c; $R^1=Ph$, $R^2=H$, d; $R^1,R^2=(CH_2)_4$, e; $R^1,R^2=CH_2CH=CHCH_2$

Typical experimental procedure for the preparation of 1b serves as an illustration: dry Et_3N (16 g) and $ZnCl_2$ (0.5 g) were stirred vigorously under N_2 for 1 h, giving a fine suspension. Methylsuccinic anhydride (5.7 g) in dry CH_3CN (40 ml) was added, followed after 5 minutes by Me_3SiCl (18 ml)[3]. The mixture was stirred overnight, 200 ml dry ether added, filtered, concentrated. The residue was diluted with dry hexane (300 ml), cooled to precipitate remaining solids, filtered and concentrated (finally under high vacuum) giving 1b as a slightly yellowish oil (12.2 g) containing about 5% of 3b as the only impurity according to nmr and g.c. ^{1}H nmr (CDCl$_3$): **1a** δ 0.18 (18H, s), 4.83 (2H, s); **1b** 0.23 (18H, s), 1.73 (3H, s), 4.80 (1H, s); **1c** 0.36 (18H, s), 5.33 (1H, s), 7.1-7.6 (5H, m); **1d** 0.28 (18H, s), 1.5-1.9 (4H, m), 2.1-2.5 (4H, m); **1e** 0.34 (18H, s), 2.97 (4H, br s), 5.78 (2H, br s); ^{13}C nmr of **1a** δ (CDCl$_3$) -0.3(q), 84.0(d) and 147.4(s). The ir and mass spectra also agree with structures **1**.

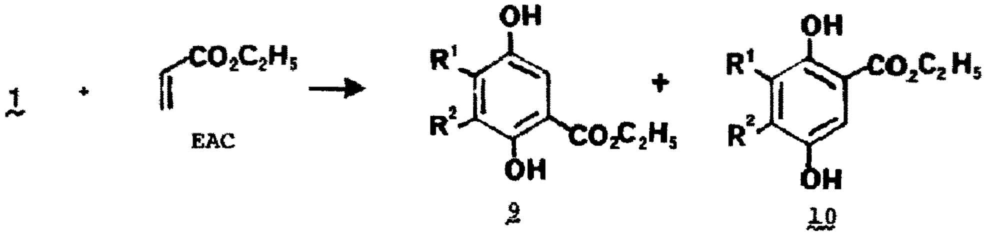
Compounds **1** are very sensitive to moisture and air: with water they are rapidly hydrolysed to succinic acids (e.g. **1b** reacts with D$_2$O to give 2,3-dideuteriomethylsuccinic acid); in the presence of oxygen they are converted to the corresponding bis(trimethylsilyl) maleates **3**. We have no information on the mechanism of this oxidation, except that its rate increases with increasing substitution of **1** (a<b<c<d≈e). This suggests that a radical reaction is occuring. The susceptibility of compounds **1** to oxidation is also evident in their reactions with halogens. Both bromine (-78°) and iodine (0° convert **1b** to citraconic anhydride.

Diels-Alder reactions. The use of various oxygenated butadienes in a Diels-Alder reaction to fashion phenolic compounds is a subject to much current activity[4]. In particular, those dienes which are 1,1-dioxygenated can be considered as formal equivalents of vinylketenes[5]. We have found the 2,5-bis (trimethysiloxy)furans to be reactive dienes, undergoing cycloaddition with dienophiles to give *p*-quinones and hydroquinones. Thus **1** act as synthetic equivalents of the inaccessible diketenes **4**.



Thus dimethyl acetylenedicarboxylate (DMAD) readily cycloadded to **1**. The products obtained, after hydrolytic workup to remove the trimethylsilyl group were the quinones **5** and/or the hydroquinones **6**, their relative ratio dependin critically on the reaction conditions and on the substitution of **1** (see Table For instance, at 50° in CCl$_4$ **1b** and DMAD gave only the quinone **5b**, but on raising the temperature to 80°, deoxygenation occurred and **6b** became the maj product. It was possible to observe both **7b** and **8b** directly in the nmr of th reaction mixture. With **1a** this deoxygenation took place at a lower temperatu as at 50° a 5:4 mixture of 5a and 6a was formed. Such a deoxygenation has been observed on similar bicyclic compounds by Paquette at al[6]. The reaction however may not be a simple cycloreversion with extrusion of oxygen, because we find that the ratio of 5a to 6a was not affected by adding benzyl methyl sulfide or cyclohexene to the reaction mixture. Nor was any sulfoxide or cyclohexene oxide formed.

The hydroquinones 6 were also obtained in good yield by reaction of 3 with dimethyl maleate (Table). While furan cycloadds only with doubly activated dienophiles under normal conditions[7], we find that the 2,5-bis (trimethylsiloxy)furans are somewhat more reactive. Thus they react with ethyl acrylate (EAC) to give substituted gentisic esters 9 and 10 in excellent yield. With 1b or 1c as diene, regioisomers are possible. In both cases (Table), the regioisomer derived from the para-orientation predominates, as expected both empirically[8] and on the basis of frontier orbitals[9].



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References and Notes

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3. In the preparation of 1c, the Me_3SiCl must be added before the anhydride to prevent polymerization.
4. For a summary of the Diels-Alder reactions of oxygenated butadienes see G.M. Rubottom in "Organometallic Chemistry Reviews: annual surveys: silicon, germanium, tin lead (1977)", D. Seyferth and R.B. King, eds., Elsevier, Amsterdam, 1979.
5. For vinylketene equivalents, see M. Gillard, C. T'kint, E. Sonbeaux and L. Ghosez, J. Am. Chem. Soc., 101, 5837 (1979) and references therein.
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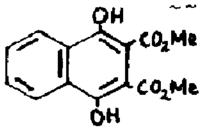
Table

Furan	Conditions	products
3a	DMM, CCl_4, 70°	6a (72%)
	DMAD, C_6H_6, 80°	6a (50%) mp 138-9° (lit.[a] 141-2°)
	DMAD, CCl_4, 50°	5:4 mixture of 5a and 6a (~86%)
	DMAD, neat, RT	4:1 mixture of 5a and 6a; 5a (53%) mp 153-4° (lit.[b] 155.5-157°)
	EAC, CCl_4, 50°	9a (88%) mp 76.5-77° (lit.[d] 77°)
3b	DMAD, CCl_4, 80°	1:5 mixture of 5b and 6b; 6b (73%) mp 72-72.5°
	DMAD, CCl_4, 50°	5b (100%) mp 91-2° (lit.[b] 91-2°)
	DMAD, neat, RT	6:1 mixture of 5b and 6b (~100%)
	EAC, CCl_4, 60°	87% of a 4:1 mixture of 9b (para) (mp 104-5°)[g] and 10b (meta) (mp 92.5-93°)[g]
3c	EAC, neat, RT	9c (para) (90%, mp 95-6°) and 10c (meta) (7%, mp 88-9°)[h]
3d	DMM, CCl_4, 50°	6d (87%) mp 118-118.5°
	DMAD, CCl_4, 50°	5d (84%) oil[i]
	EAC, CCl_4, 50°	9d (91%) mp 99-100°
3e	EAC, CCl_4, 70°	9e (98%) mp 152.5-153°
	DMAD, neat, RT	5:2 mixture of 6e mp 143-143.5° (lit.[c] 142-3°)[i] and  mp[e] 102-102.5° (lit.[f] 112-3°)[i]

Isolated yields; DMAD = dimethyl acetylenedicarboxylate; DMM = dimethyl maleat
EAC = ethyl acrylate.

[a] B. Helferich, Ber., 54, 155 (1921); [b] M.F. Ansell, B.W. Nash and D.A. Wilson, J. Chem. Soc., 3028 (1963); [c] idem., ibid., 3012; [d] Dictionary of Organic Compounds 4th ed., Eyre and Spottiswoode, London, 1965, vol. 2, p. 1056. [e] corrected, to constant mp; [f] C.W. Bird, C.K. Wong, D.Y. Wong and F.L.K. Koh, Tetrahedron, 32, 269 (1976). [g] separated by fractional crystallization from toluene; [h] 10c obtained by t.l.c. of mother liquor (cyclohexane) from 9c; [i] purified by column chromatography on silica gel.

General procedure: a mixture of the furan (5 mmol), the dienophile (5 mmol) a CCl_4 (5 ml) was heated as stated under nitrogen. The reaction was followed by nmr . When no furan remained (usually 3-6d) the mixture was shaken overnight with wet acetonitrile containing excess NaF, diluted with water and extracted with chloroform. The extracts were dried (Na_2SO_4), evaporated and the crude product recrystallized.

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