

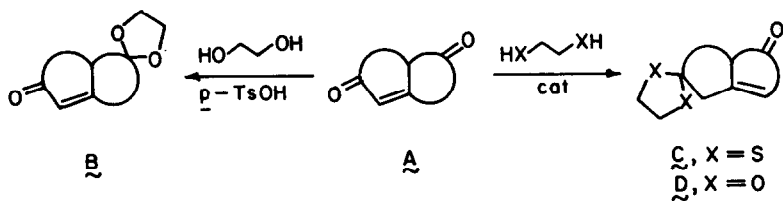
CHEMOSELECTIVE ETHYLENE ACETALIZATION OF α,β -UNSATURATED
 vis-à-vis SATURATED CARBONYL GROUPS

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Summary: The difficulties which in the past have precluded controlled acetalization of an α,β -unsaturated ketone functionality in the presence of a saturated carbonyl group can be overcome simply by making recourse to 2,4,6-collidinium *p*-toluenesulfonate as catalyst.

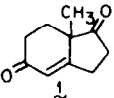
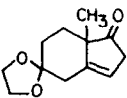
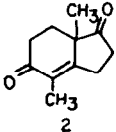
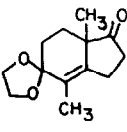
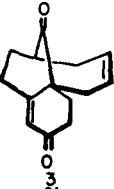
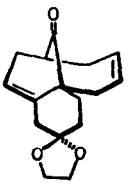
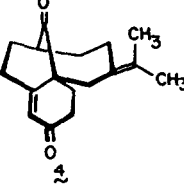
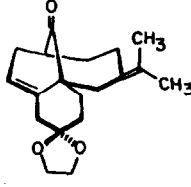
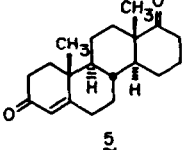
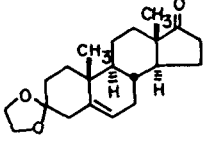
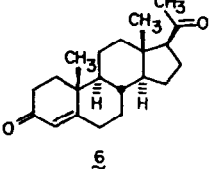
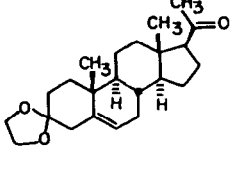
The use of dioxolane-type acetals as carbonyl protective groups has become a widespread and integral part of synthetic practice. Chemists have often availed themselves of the proclivity of ethylene glycol to enter selectively into reaction with a saturated carbonyl partner while disregarding an α,β -unsaturated functionality ($A \rightarrow B$).¹ The reversed mode of protection (e.g., $A \rightarrow C$) has been almost uniformly achieved by making recourse to ethane-1,2-dithiol.² In connection with one of our proposed routes to isoingenol,³



the latter sequence could not be utilized because of impending oxidation reactions where divalent sulfur atoms would surely interfere. Consequently, we have sought to remove the long-standing restriction associated with conversions of the general type $A \rightarrow C$ and herein report the development of a satisfactorily simple one-step procedure.

The answer to the chemoselectivity question was found to reside in the proper selection of catalyst. Our process relies on the special advantages offered by a hindered pyridinium salt. Studies involving 2,4,6-collidinium *p*-toluenesulfonate (CTPS) with a range of substrates have led to a reasonably clear definition of the scope and selectivity of this useful procedure (Table I). The corresponding 2,6-lutidinium salt (LPTS) is almost equally effective. In all

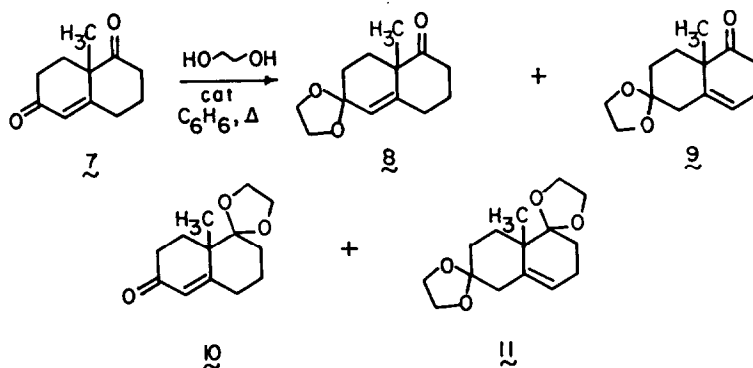
Table I. Enone Selective Acetalizations Promoted by CPTS.^a

Substrate	CPTS, equiv	Ethylene glycol, equiv	Time, h	Products (%) ^b
	0.125	1.2	72	 (77)
	0.125	1.5	96	 (39) ^c
	0.125	1.2	72	 (70)
	0.50	1.5	18	 (88)
	0.125	1.2	60	 (39) ^d
	0.125	1.2	96	 (44) ^e

^aAll reactions were conducted in refluxing benzene with azeotropic removal of water. ^bProduct yields which are given have been corrected for small amounts of recovered starting material in the case of **2** and **6**. The products were isolated in isomerically pure condition for all entries except **4** where a small amount of α,β -unsaturated isomer was spectroscopically detectable. ^cAlso isolated was the diacetal (8%) and isomeric monoacetal (7%). ^dThe diacetal (16%) and isomeric monoacetal (10%) were also produced. ^eThe diacetal (23%) and isomeric monoacetal (10%) were also obtained.

cases investigated, separation of the desired ketal was achieved readily by medium pressure liquid chromatography. All structural assignments are based on analysis of IR and 300 MHz ^1H NMR spectra,⁴ and where possible comparison with literature data.

The behavior of Wieland-Mischer ketone (ζ) toward various pyridinium tosylates, including the well known PPTS,⁵ was probed most exhaustively. For this substrate, the α,β -unsaturated acetal ξ is formed most rapidly in the presence of CPTS (Table II). Only more slowly does the double bond in ξ migrate to the thermodynamically more favored β,γ environment to produce η .



Consequently, these reactions are not mediated by dienolether intermediates,⁶ in agreement with selected earlier mechanistic conclusions.^{4b,7} The effectiveness of CPTS and LPTS in providing synthetically useful amounts of η is to be contrasted with the inability of PPTS to discriminate effectively between the different carbonyl groups. Evidently, steric shielding of the proton in these salts and its consequences on acidity exert an influence suitably conducive to chemoselectivity.

In summary, CPTS is a conveniently prepared reagent (mp 128-130°C) which promotes the favored formation of dioxolane-type acetals with α,β -unsaturated ketones in the presence of saturated carbonyl systems. The method complements the reactivity profile observed when *p*-toluenesulfonic acid is employed as catalyst.

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Table II. Ethylene Acetalization of Wieland-Mischer Ketone (γ).^{a,b}

Catalyst	(equiv)	reflux time, h	Composition of reaction mixture; %				
			γ	δ	ρ	λ	μ
CPTS	0.125	0.5	86.1	13.9	0	0	0
		1.0	66.4	30.9	1.4	1.2	0
		1.5	52.1	42.6	2.5	2.7	0
		3.5	28.1	52.9	16.1	2.8	0
		8.0	15.1	48.0	29.4	1.6	5.9
		15.5	2.7	20.4	59.5	0.8	16.6
		22.0	0.9	13.4	65.4	0.2	19.9
		32	4	0	80	3	8 ^c
CPTS	0.250	36	5	0	67	12	3 ^c
LPTS	0.250	34	5	0	76	5	11 ^c
PPTS	0.250	20	6	0	35	34	14 ^c

^aBenzene was employed as the solvent. The amount of ethylene glycol ranged from 1.5 in the first group of experiments to 1.2 in the last triad. ^bThe first seven data points represent one run which was followed by capillary VPC. The percentage compositions were derived by machine integration of the peaks. ^cIn the last four entries, the product distributions are based upon the actual amounts of material isolated following MPLC on silica gel.

References and Notes

- (1) For representative examples, see: (a) Corey, E. J.; Ohno, M.; Mitra, R. B.; Vatakencherry, P. A. *J. Am. Chem. Soc.* **1964**, *86*, 478. (b) Kitahara, Y.; Yoshikoshi, A.; Oida, S. *Tetrahedron Lett.* **1964**, 1763. (c) Bauduin, G.; Pietrasanta, Y. *Tetrahedron* **1973**, *29*, 4225. (d) Bauduin, G.; Pietrasanta, Y.; Pucci, B. *Tetrahedron Lett.* **1975**, 2889. (e) Andon-Jimenez, A.; Halsall, T. G. *J. Chem. Soc., Perkin I* **1978**, 1461. (f) Trost, B. M.; Nishimura, Y.; Yamamoto, K. *J. Am. Chem. Soc.* **1979**, *101*, 1328. (g) Devreese, A. A.; DeClercq, P. J.; Vandewalle, M. *Tetrahedron Lett.* **1980**, 4767. (h) McMurry, J. E.; Andrus, A.; Ksander, G. M.; Musser, J. H.; Johnson, M. A. *Tetrahedron Suppl. No. 1* **1981**, *37*, 319.
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