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PYRIDINIUM p-TOLUENESULFONYLMETHYLIDE AS A FORMYL ANION EQUIVALENT

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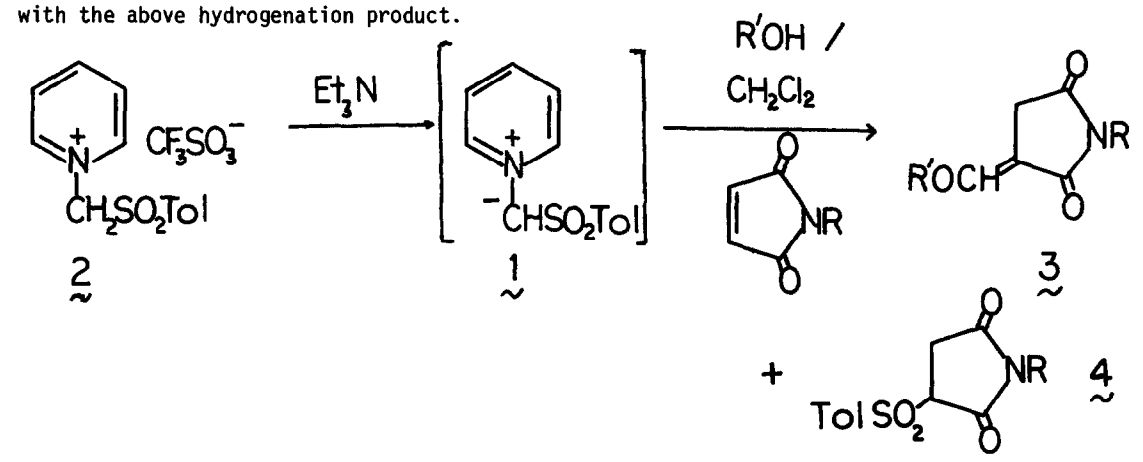
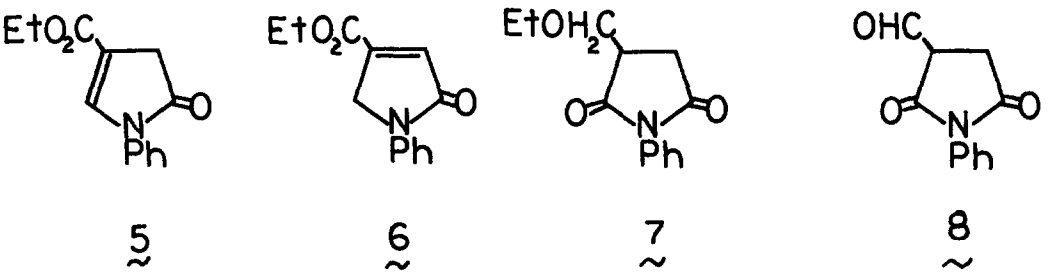
Abstract. Pyridinium p-toluenesulfonylmethylide serves as a formyl anion equivalent and, in the presence of an alcohol, undergoes 1,4-addition to N-substituted maleimides to give alkoxy- (or aryloxy)-methylene-succinimides. The protected aldehyde group can be liberated readily.

Formyl anion equivalents have recently been receiving considerable attention in synthetic methodology,[3] and some interesting work has been carried out to achieve 1,4-addition to enones.[4] We now report a novel one carbon donor, namely pyridinium p-toluenesulfonylmethylide (1), which adds 1,4 to N-substituted maleimides and leads to the formation of enol ethers 3.

The ylides (1 and substituted derivatives thereof) react with activated acetylenes[5] and with maleic anhydride in the presence of alcohols[6] to give indolizine derivatives. In the latter case, yields are very low when the pyridine ring does not bear an electron-withdrawing substituent. Reaction of 1-p-toluenesulfonylmethylpyridinium triflate (2) with N-phenylmaleimide in the presence of triethylamine in chloroform-ethanol (5:1 v/v)[7] did not yield a cycloadduct. Instead, a product $C_{13}H_{13}NO_3$ (3), m/e 217, mp 178-179°C, was isolated (62% yield) together with 3-p-toluenesulfonyl-N-phenylsuccinimide (4; R = Ph) (5%), mp 176-177°C.[8] Compound 3 exhibited C=O stretching bands at 1700 and 1666 cm^{-1} and the NMR spectrum showed the presence of an OC_2H_5 group, a 2H (doublet) (J = 2Hz) at δ 3.3, and a six proton multiplet at δ 7.3 (5 aromatic protons and one deshielded vinylic proton). These data rule out all possible structures except 3 (R = Ph, R' = OC_2H_5) and 5 (or a tautomer 6). Structure 5 was ruled out by comparison of the product with an authentic sample of 5 prepared from diethyl phenylaminomethylenesuccinate.[9] Catalytic reduction of 3 (10% Pd-C) in ethyl acetate gave 7[8] (100%), mp 81-82°C [NMR ($CDCl_3$) δ 7.3 (m, 5H, aromatic), 3.5 (m, 4H), 2.8 (m, 3H), 1.1 (t, 3H, Et)], different from the

product of hydrogenation of 5, thus ruling out structure 6. Authentic 7 was prepared from 3-ethoxymethylsuccinic anhydride[8] (bp 80°C at 0.1 mm) by treatment with aniline in ether and then heating the product with Ac_2O/AcONa at 80°C for 2 hr, and was identical with the above hydrogenation product.





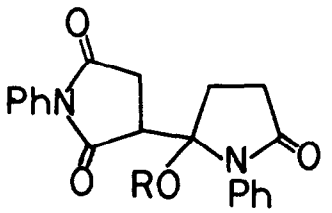
The formation of alkoxy- (or aryloxy)-methylenesuccinimides (3) appears to be quite general and some examples are collected in Table I.

The protected aldehyde group in 3 (R = Ph; R' = $CH_2C_6H_4$-p-OMe) could be cleaved with HBr in CH_2Cl_2 at room temperature to give the formyl derivative 8, (40% yield) mp 162-162.5°C (hydrazone, mp 226-227°C: semicarbazone, mp 198-199°C).[10] All attempts to formylate N-phenylsuccinimide by conventional means (e.g. ethyl formate/NaH; Vilsmeier

TABLE I. Synthesis of 3 from Maleimides

R	R'	Yield of 3 (%)	mp(°C)
Ph	Me	54	179-180
	Et	62	178-179
	n-Pr	37	101-102
	Ph	32	169-170
Me	Me	80	133
	$PhCH_2$	63	113
	p-$MeOC_6H_4CH_2$	54	127
m-$NO_2C_6H_4$	Me	67	238-240
	$PhCH_2$	59	124-126
	p-$MeOC_6H_4CH_2$	74	157-159
3-Cl-4-FC_6H_3	Et	34	174-175

reagent/LDA) failed. Treatment with dimethylformamide and LDA gave, instead, the dimer 9 (R = H), mp 158.5-159.5°C,[11] which could not be dehydrated but gave a stable tertiary tosylate (R = Tos), mp 174-174.5°C.



9

Studies of the scope of using 1 as a formyl anion equivalent are continuing.

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7. Subsequent experiments were carried out in methylene chloride in which the nature and quantity of alcohol could be better controlled since commercial $CHCl_3$ contains ethanol as a stabilizer.

8. All new compounds exhibited the expected spectral data (ir, NMR, mass spec.) and gave correct C,H microanalyses.

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10. I.R. (KBr) 3200 (v br), 1710 cm^{-1} (br). N.M.R. (acetone-d_6) δ 8.0 (S, 1, =CH-O). 7.67 (s, 5, ArH), 3.49 (S, 2, CH_2). Mass spectrum m/e (rel. intensity) 203 (61) ($M^{+\cdot}$), 175 (20), 146 (20), 119 (100) ($PhNCO^+$), 93 (33), 77 (26), 55 (61). The compound appears to exist mainly in the enol form.

11. I.R. (KBr) 3300 (v br), 1700, 1685 cm^{-1}. N.M.R. (acetone-d_6) δ 7.7-7.0 (m, 10, ArH), 3.5-3.1 (m, 4), 2.85-2.6 (m, 4) (OH proton appears to be buried under the multiplet centered at δ 3.3). The tosylate exhibited the following spectral data: I.R. (KBr) 1700 (sh), 1665, 1362, 1180 cm^{-1}; N.M.R. ($CDCl_3$) δ 7.9 (d, 2, H ortho to SO_2), 7.6-7.1 (m, 12, ArH), 3.4 (m, 5, $COCH_2$ and -COCH-), 2.7 (d, 2, CH_2), 2.45 (s, 3, CH_3).

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