(E)-4-LITHIO-4-TOSYLBUTENONE DIMETHYL KETAL: A NEW B-ACYLVINYL

ANION EQUIVALENT

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<u>Summary</u>: (<u>E</u>)-4-Lithio-4-tosylbutenone dimethyl ketal is regio and stereoselectively prepared by direct lithiation of the corresponding precursor with methyl-lithium at -20^oC; the reaction of this β -acylvinyl anion equivalent with different electrophilic reagents (H₂O, D₂O, Me₃SiCl, Me₂S₂, Mel, CH₂=CHCH₂Br, BuⁱCHO, PhCHO, PhCOCl, Ac₂O) affords the corresponding functionalized compounds.

β-Acylvinyl anion equivalents **1** are versatile synthons to provide α, β-unsaturated functionality in organic synthesis¹ and should be consider as sp²-hybridized homoenolates.² The corresponding organolithium derivatives can be prepared starting directly from β-functionalized α,β-unsaturated carbonyl compounds or their derivatives through two ways: (a) a kinetic β-deprotonation to afford intermediates of the type **2** $[X = R_2N, {}^3 RO, {}^{4,5} RS, {}^5 Br, {}^6$ ArSO; ⁷ $Z = CO_2Li, {}^5 CO_2R, {}^{3-5} CONR_2, {}^{3,4} CN, {}^{3,4} CH(OR')_2 {}^{6,7}]$; (b) a bromine-lithium exchange reaction to give the unsubstituted derivatives **2** $(i.e. X = H, Z = CO_2Li), {}^8 3, {}^9$ or **4**.⁶ All these intermediates have to be prepared at low temperature (below -78°C) to avoid either rearrangements to the thermodinamically more stable α-anion, {}^{3-5} or by-processes. In this paper we describe the preparation of a very stable new β-functionalized acylvinyl anion equivalent **6** derived from methyl vinyl ketone following a defensive strategy. ^{1b}



The reaction of the (\underline{E})-isomer of methyl 2-tosylvinyl ketone dimethyl ketal **5** (obtained from methyl vinyl ketone by a tandem iodosulphonylation-dehydroiodination reaction¹⁰ followed by ketalization with trimethyl orthoformate¹¹ in 75% overall yield; m.p. 99-100^oC) with methyl-lithium¹² at -20^oC led regio and stereospecifically to the vinyl anion **6**

Product ^a	E ⁺	Y	Yield (१) ^b	m.p. (^o C) ^c
5 ^d	н ₂ о	н	95	99-100
7a	D ₂ O	D	93	98-99
7Ь	Me ₃ SiCI	Me ₃ Si	85	135
8	Me ₂ S ₂	-	88	oil ^e
7d	Mel	Me	96	36-38
7e	CH ₂ = CHCH ₂ Br	CH ₂ =CHCH ₂	81	oil ^f
7f	Ви ^і СНО	Ви ^і СНОН	84	oila
7g	РҺСНО	PhCHOH	80	90-91
7h	PhCOCI	PhCO	90	112-113
7i	Ac ₂ O	Ac	78	oil ^h

Table 1. Reaction of the β -sulphonyl acylvinyl anion equivalent **6** with electrophiles. Preparation of compounds **7** and **8**.

^aAll compounds gave satisfactory spectral data (i.r., ¹H and ¹³C n.m.r., and mass spectra).

^bBased on compound **5**. Yields of isolated products.

^CFrom hexane-carbon tetrachloride.

d_{Prepared via} intermediate **6**.

^eAfter silica gel column chromatography the corresponding deprotected ketone was isolated.

 $f_{\underline{R}} = 0.33$ (hexane-ether:1-1).

⁹<u>R</u>=0.30 (hexane-ether:1-2).

 $h_{\underline{R}_{f}} = 0.35$ (hexane-ether:1-1).

with <u>E</u>-configuration. The treatment of this intermediate with a variety of electrophiles yielded the products **7** (Scheme 1 and Table 1). When dimethyl disulphide was used as electrophilic reagent, product **8** was obtained due to the addition of the <u>in situ</u> generated lithium methyl sulphide to the initially formed compound **7c** (Y = MeS). When the intermediate **6** was hydrolysed ($E^+=H_2O$), the starting compound **5** was exclusively isolated; this result corroborates the asigned stereochemistry in the products **7**. So, the tandem lithiation-electrophilic substitution occurs with total retention in the configuration of the starting material.



Scheme 1. <u>Reagents and conditions</u>: i, MeLi~LiBr, -20° C; ii, E⁺=H₂O, D₂O, Me₃SiCl, Me₂S₂, Mel, CH₂=CHCH₂Br, Bu¹CHO, PhCHO, PhCOCl, Ac₂O; iii, HCl-H₂O.

In a <u>typical reaction</u>, to a solution of methyl 2-tosylvinyl ketone dimethyl ketal **5** (2.0 mmol) and lithium bromide (2.2 mmol) in tetrahydrofuran (10 ml) was dropwise added a solution of methyl-lithium (2.2 mmol) in ether at -20° C under argon. After 10 min stirring the corresponding electrophile (2.2 mmol)[†] was added and the mixture was stirred 30 min at -20° C and then at room temperature for 30 min. The resulting solution was hydrolysed with water and 1 N aqueous hydrochloric acid, extracted with dichloromethane, and the organic layer was washed with a saturated solution of sodium hydrogen carbonate and water, dried with sodium sulphate, and evaporated (15 mmHg) to afford the crude products 7, which were purified by recrystallization or by column chromatography on silica gel.¹⁵

[†] When water or deuterium oxide were used as electrophilic regent, a large excess (<u>ca</u>. 10 mmol) was used.

References and Notes

- (a) J. C. Stowell, <u>Chem. Rev.</u>, **1984**, <u>84</u>, 409; (b) D. Hoppe, <u>Angew. Chem. Int. Ed.</u> Eng., **1984**, 23, 932.
- For the corresponding sp³-derivatives see, for instance: (a) J. Barluenga, C. Rubiera, J. R. Fernandez, and M. Yus, <u>J. Chem. Soc., Chem. Commun</u>., **1987**, 425; (b) J. C. Carretero, S. De Lombaert, and L. Ghosez, <u>Tetrahedron Lett.</u>, **1987**, 2135 and literature cited therein.
- 3. R. R. Schmidt and J. Talbiersky, <u>Angew. Chem. Int. Ed. Eng</u>., **1976**, <u>15</u>, 171; **1977**, <u>16</u>, 853; **1978**, <u>17</u>, 204.
- 4. R. R. Schmidt, J. Talbierky, and P. Russegger, Tetrahedron Lett., 1979, 4273.
- 5. N. C. Barua, K. Evertz, G. Huttner, and R. R. Schmidt, <u>Chem. Ber</u>., **1987**, <u>120</u>, 213 and references cited therein.
- 6. A. I. Meyers and R. F. Spohn, J. Org. Chem., 1985, 50, 4872.
- 7. G. Solladie and G. Moine, <u>J. Am. Chem. Soc</u>., **1984**, <u>106</u>, 6097.
- 8. D. Caine and A. S. Frobese, Tetrahedron Lett., 1978, 5167.
- 9. W. R. Baker and R. M. Coates, J. Org. Chem., 1979, 44, 1022.
- 10. C. Najera, B. Baldo, and M. Yus, J. Chem. Soc., Perkin Trans. 1, in the press.
- C. Giordano, G. Castaldi, F. Casagrande, and A. Belli, <u>J. Chem. Soc., Perkin Trans. 1</u> 1982, 2575.
- 12. The lithiation of vinylic sulphones by means of methyl-lithium at $-95^{\circ}C^{13}$ or <u>n</u>-butyl-lithium at $-78^{\circ}C^{-14}$ has been described.
- 13. J. J. Eisch and J. E. Galle, J. Org. Chem., 1979, 44, 3277 and 3279.
- 14. N. S. Simpkins, Tetrahedron Lett., 1987, 989.
- 15. We thank Professor José Barluenga, Departamento de Química Organometálica, Facultad de Química, Universidad de Oviedo for financial assistance.

(Received in UK 30 October 1987)