

UTILISATION OF α -SULFONYL CARBANIONS FOR THE PREPARATION OF 1,4-DIKETONES

B.KOUBEK, L.PAVLÍČKOVÁ and M.SOUČEK

*Institute of Organic Chemistry and Biochemistry,
Czechoslovak Academy of Sciences, 166 10 Prague 6*

Received April 12th, 1973

A three-step synthesis of 1,4-diketones is described where carboxylic acid esters served as starting material and dioxo sulfones as intermediates. For the alkylation of α -sulfonyl carbanion with α -halo ketones the method of extraction of ionic pairs utilising tetrabutylammonium hydroxide as a base was used in addition to the classical procedure. From the reaction of 2-(methanesulfonyl)propiofenone with bromoacetophenone 1,2,3-tribenzoylcyclopropane was isolated as the main product.

1,4-Diketones are important intermediates in the preparation of cyclic and heterocyclic compounds, especially cyclopentenones and furan derivatives. Present methods of preparation of 1,4-diketones usually have no general validity, either from the point of view of the choice of substituents on both carbonyl groups, or that of the difficult preparation of starting compounds.

Electrolysis of the salts of β -oxo acids¹, syntheses utilising dimerisation of α -diazoketones with cupric oxide² or α -bromo ketones with nickel carbonyl³, photochemical dimerisation of ketones⁴, and the synthesis of γ -diketones from aroyl tricarbonyl nickelates and substituted acetylenes⁵ are limited to the preparation of symmetrical products. The methods based on acetoacetate synthesis⁶ or the condensation of acetylacetone with α -halo ketones and subsequent hydrolysis of the triketone formed⁷ are limited to the preparation of compounds with a terminal $\text{CH}_3\text{—CO}$ -group, and in a number of cases their modifications^{8,9} cannot be applied due to considerable difficulties in the preparation of starting α -oxo esters. A similar disadvantage is also met with in catalytic hydrogenolysis of 1-furyl-3-alkanols¹⁰, directed hydration of acetylenes¹¹, acylation of conjugated enones¹², and the reaction of α -diazoketones with 2-acetoxypropene¹³.

We tried to elaborate a more general synthesis of 1,4-diketones which would not require a symmetrical product or the presence of at least one acetylene group, from relatively easily accessible starting material. It is known that β -oxo sulfoxides^{14,15} and β -oxo sulfones¹⁶, prepared on reaction of methanesulfinyl- or methanesulfonyl carbanion with carboxylic acids esters, may be mono- and dialkylated on the carbon atom between a carbonyl and a sulfoxide (sulfonyl) group. As alkylation agents some primary halo compounds^{17,18} were used. We based our own synthesis of 1,4-diketones on both these reactions. Reactive α -halo ketones served as alkylating com-

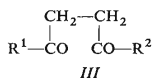
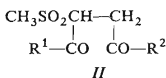
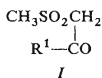
ponents. Already during preliminary experiments we observed that the course of alkylation of oxo sulfoxides is more complex than expected. We were able to isolate the required dioxo sulfoxides from the reaction mixture only in low yields. Therefore we concentrated our attention on the relatively little studied alkylation of β -oxo sulfones which due to symmetry and a higher resonance energy¹⁹ should display a higher chemical stability.

Oxosulfonyl carbanions were first prepared from corresponding neutral particles by reacting oxosulfone with sodium hydride in dimethyl sulfoxide. However, the results of this reaction was dependent on the amount of the occluded water in the reaction system and on the quality of sodium hydride. Therefore we used the method of extraction of ionic pairs²⁰ in subsequent experiments. Oxosulfonyl carbanion generated with lipophilic tetrabutylammonium hydroxide was extracted with chloroform as a separated ionic pair. Its alkylation with ω -bromoacetophenones took place with good yields even at room temperature. In contrast to the classical procedure this method is advantageous mainly because of its simplicity, while the yields achieved by this method are usually better (Table I). During the reaction of oxosulfonyl carbanions with bromoacetone under standard conditions the autocondensation of bromoacetone took place more rapidly than alkylation. In order to obtain the required diketone the reaction had to be carried out at a lower temperature. In the last step of the synthesis the sulfonyl group was eliminated by reductive cleavage with zinc in acetic acid. The yields of this operation were practically quantitative (Table III).

TABLE I
Dioxosulfones II

Compound	Procedure	Yield %	M.p., °C	Composition (mol.w.)	Calculated/Found		
					% C	% H	% S
IIa	A	65	147–148	C ₁₇ H ₁₆ O ₄ S	64.54	5.09	10.13
	B	80		(316.4)	64.70	4.83	10.22
IIb	A	62	183–184	C ₂₅ H ₂₄ O ₆ S	66.35	5.34	7.09
	B	70		(452.5)	66.38	5.32	7.09
IIc	A	70	98–99	C ₁₂ H ₁₄ O ₄ S	56.68	5.55	12.61
	B	81		(254.3)	56.42	5.49	12.65
IIc	A	65	166–167	C ₁₇ H ₁₅ BrO ₄ S	51.65	3.82	8.11
	B	63		(395.3)	51.39	3.90	8.19
IIe	A	58	126–127	C ₃₃ H ₃₂ O ₈ S	67.33	5.47	5.44
	B	73		(588.7)	67.63	5.39	5.51

The attempt at alkylation of the tertiary anion *IV* prepared from 2-methanesulfonyl-propiofenone with sodium hydride had an anomalous course. If ω -bromoacetophenone was used as alkylating agent 1,*c*-2,*t*-3-tribenzoylcyclopropane (*V*) was isolated as the sole product. The high yield of cyclopropane *V* indicates that the nucleophilicity of carbanion *IV* is appreciably increased by the presence of the methyl group and that the carbanion only functions as a base. An analogous reaction was observed when potassium tert-butylylate reacted with 4-bromo-2,2-dimethyl-3-butanone²¹.



Ia; R¹ = C₆H₅

Ib; R¹ = 3-CH₃O-4-C₆H₅CH₂O-C₆H₃

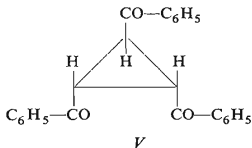
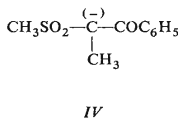
IIa, IIIa; R¹ = R² = C₆H₅

IIb, IIIb; R¹ = C₆H₅, R² = 3-CH₃O-4-C₆H₅CH₂O-C₆H₃

IIc, IIIc; R¹ = C₆H₅, R² = CH₃

IIId, IIIId; R¹ = C₆H₅, R² = 4-Br-C₆H₄

IIe, IIIe; R¹ = R² = 3-CH₃O-4-C₆H₅CH₂O-C₆H₃



EXPERIMENTAL

The melting points were determined on a Kofler block and they are not corrected. The samples for analysis were dried at room temperature and 0.1 Torr for 8 hours.

ω -Methanesulfonyl-3-methoxy-4-benzyloxyacetophenone (*Ib*)

Oxo sulfone *Ib* was prepared according to House and Larson¹⁶ in a 75% yield by condensation of methyl 3-methoxy-4-benzyloxybenzoate with dimethyl sulfone. After crystallisation from a mixture of ethyl acetate and light petroleum it had m.p. 165–166°C. For C₁₇H₁₈O₅S (334.4) calculated: 61.06% C, 5.43% H, 9.58% S; found: 61.05% C, 5.29% H, 9.53% S.

ω -Methanesulfonylacetophenone (*Ia*) was prepared in the same manner in 80% yield. M.p. 107–108°C (lit.²² gives 107.5–108°C).

TABLE II
1,4-Diketones III

Compound	Yield, %	M.p., °C (lit.)	Composition (mol.w.)	Calculated/Found	
				% C	% H
<i>IIIa</i>	98	144–145 (144–145) ²³	—	—	—
<i>IIIb</i>	98	111–112 —	C ₂₄ H ₂₂ O ₄ (374.4)	77.00 77.37	5.92 6.35
<i>IIIc</i>	96	161 ^a —	C ₁₁ H ₁₂ O ₂ (176.2)	74.95 74.90	6.86 6.72
<i>III d</i>	97	112–113 (116) ²⁵	—	—	—
<i>IIIe</i>	97	184–185 —	C ₃₂ H ₃₀ O ₆ (510.6)	75.28 74.89	5.92 6.08

^a B.p./12 Torr.

1,4-Diphenyl-2-(methanesulfonyl)-1,4-butanedione (*IIa*)

A) A mixture of oxo sulfones *Ia* (1.98 g), sodium hydride (0.24 g), and dimethyl sulfoxide (15 ml) was stirred at 20°C under nitrogen for 45 minutes. A solution of ω -bromoacetophenone (1.99 g) in tetrahydrofuran (20 ml) was then added dropwise and after 2 hours' stirring at 20°C the mixture was poured into an icecold 0.5M-HCl solution (150 ml). Dioxosulfone *IIa* was extracted with chloroform (6 \times 50 ml) and the extract worked up in the usual manner.

B) Tetrabutylammonium bromide (3.22 g) was added to a cold solution of sodium hydroxide (0.40 g) in water (8 ml) and the quaternary base solution obtained was then added dropwise to a stirred solution of oxo sulfone *Ia* (1.98 g) in chloroform (17 ml). After 30 minutes stirring at 20°C the chloroform layer was separated, dried over anhydrous magnesium sulfate and filtered. The filtrate was added with phenacyl bromide (1.99 g) dissolved in chloroform (5 ml) and the mixture allowed to stand for 40 minutes. Chloroform was evaporated under reduced pressure and the residue extracted with ether (4 \times 20 ml). The ethereal extract was worked up in the conventional manner. Parallely compounds *I Ib–I Ie* were prepared by both procedures, and they were crystallised from ethyl acetate–light petroleum. Yields, melting points, and analyses of all substances prepared are listed in Table I.

Reduction of Dioxo Sulfones *II* to 1,4-Diketones *III*

A solution of dioxo sulfone *II* (1 mmol) in a mixture of ethyl acetate (3 ml) ethanol (1 ml), and acetic acid (1 ml) was refluxed in the presence of zinc dust (0.52 g). The reaction course was followed by thin-layer chromatography in light petroleum–ether (1 : 1). When the reduction was complete the solution was filtered and the filtrate worked up in the conventional manner. The yields, physical constants, and elemental analyses are given in Table II.

Reaction of ω -Bromoacetophenone with 2-(Methanesulfonyl)propiophenone and Sodium Hydride

A mixture of 2-(methanesulfonyl)propiophenone (2.12 g) and sodium hydride (0.24 g) in dimethyl sulfoxide (5 ml) was stirred under nitrogen at 20°C for 45 minutes. A solution of ω -bromoacetophenone (1.99 g) in tetrahydrofuran (20 ml) was added dropwise to the reaction mixture containing carbanion *IV* and diluted with tetrahydrofuran (5 ml). After 4 hours' stirring at 20°C the reaction mixture was poured into ice-cold 0.5M-HCl (200 ml) and extracted with chloroform. After the usual work-up of the extract 1, *c*-2, *t*-3-tribenzoylcyclopropane was obtained in 75% yield, m.p. 216–217°C (lit.²⁴ gives 215°C).

For the elemental analyses we thank Mrs V. Rusová and Mrs E. Šípová of the analytical department of our Institute (head Dr J. Horáček).

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Translated by Ž. Procházka.