

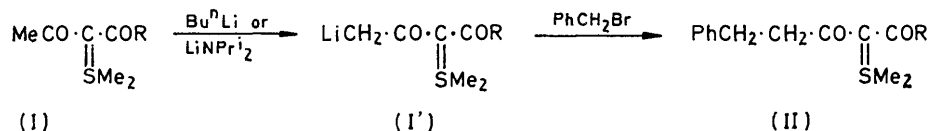
Syntheses with Carbanions derived from Carbonyl-stabilized Sulphonium Ylides: a Novel Route to Furan-3(2H)-ones

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The sulphonium $\alpha\alpha'$ -dicarbonylmethylides (I) were acylated at the β -position in the presence of *n*-butyl-lithium or lithium di-isopropylamide. These acylated sulphonium ylides underwent thermal elimination of dimethyl sulphide to give alkyl- and aryl-substituted furan-3(2H)-ones (3-hydroxyfurans). The mechanism of furanone formation is discussed.

CARBONYL-STABILIZED sulphonium ylides, such as sulphonium phenacylides, react with alkyl halides,¹ sulphonyl chloride,² and acid anhydrides³ at the ylide carbon atom. In contrast, bis-carbonyl-stabilized sulphonium ylides do not exhibit similar reactivity, owing

ated with *n*-butyl-lithium or lithium di-isopropylamide in tetrahydrofuran (THF) or dimethoxyethane (DME) at -10 to -15 °C under nitrogen. The product (I'a), obtained as a white precipitate above -25 °C, is stable below 0 °C for several hours under nitrogen, but was not



a; R = Me b; R = OEt

to the possibility of further delocalization of the negative charge. I recently reported that dimethylsulphonium diacetylmethylide (Ia) was easily lithiated at the acetyl methyl position.⁴ This suggests that the ylide group acts in this case as a carbonyl-protecting group. It is also known that dimethylsulphonio-derivatives having appropriately placed acidic C-H bonds easily eliminate dimethyl sulphide to form a cyclic product.^{5,6}

On the basis of the above facts, it was considered that introduction of an active methylene group into a bis-carbonyl-stabilized sulphonium ylide, as in (I), would make it possible to form a furanone, and we now report the β -acylation of sulphonium $\alpha\alpha'$ -dicarbonylmethylides, and the cyclization of the products to furanones.

Dimethylsulphonium diacetylmethylide (Ia) was lithi-

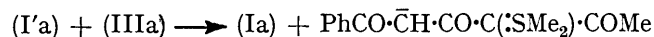
† From the n.m.r. spectrum it was considered that (IIIa) contained its isomer (V; R = Me, R' = Ph) (ratio *ca.* 1 : 1). Compound (IIIc) showed the same behaviour. Compounds (IIIa and c) are unstable at room temperature, and are readily converted into the furanones (IVa and c).

¹ K. W. Ratts and A. N. Yao, *J. Org. Chem.*, 1966, **31**, 1689.

² H. Nozaki, M. Takaku, Y. Hayashi, and K. Kondo, *Tetrahedron*, 1968, **24**, 6563.

formed below -30 °C, and above 30 °C it gradually decomposes.

The formation of (I'a) was shown by its alkylation reactions, *e.g.* treatment with 1 mol. equiv. of benzyl bromide gave dimethylsulphonium acetyl-(3-phenylpropionyl)methylide (IIa) in 73% yield.⁴ The lithiated sulphonium ylide (I'b) was also alkylated with benzyl bromide to give (IIb) in 55% yield, and the ylide (I'a) reacted with benzoyl chloride to give the benzoylated sulphonium ylide (IIIa) in 69% yield.† The molar ratio of (I') and benzoyl chloride used was 2 : 1, because lithium-hydrogen exchange was assumed to occur in solution:



The benzoylated sulphonium ylide (IIIa) was also formed

³ A. W. Johnson and R. T. Amel, *J. Org. Chem.*, 1969, **34**, 1240.

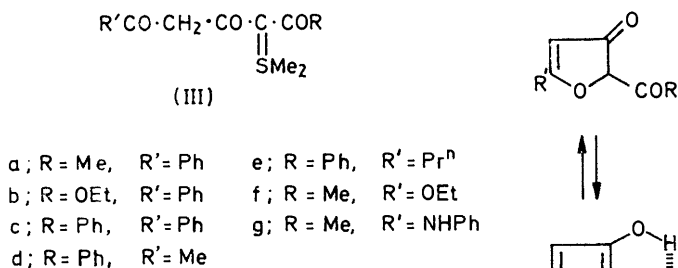
⁴ M. Yamamoto, *J.C.S. Chem. Comm.*, 1975, 289.

⁵ J. W. Batty, P. D. Howes, and C. J. M. Stirling, *Chem. Comm.*, 1971, 534.

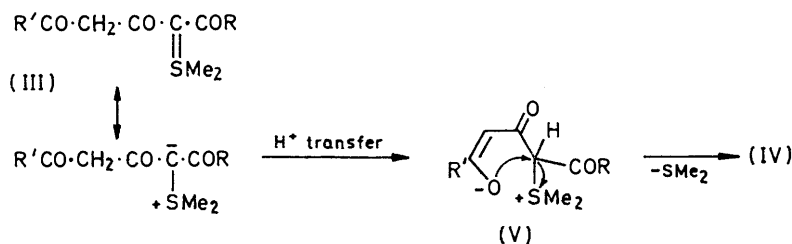
⁶ J. Gosselck, L. Beress, H. Schenck, and G. Schmidt, *Angew. Chem. Internat. Edn.*, 1965, **4**, 1080.

by the reaction of (I'a) with methyl benzoate or benzoic anhydride (41 and 46% yield, respectively).

Heating the ylide (IIIa) in refluxing benzene for 1 h afforded 2-acetyl-5-phenylfuran-3(2H)-one (IVa) quantitatively. The n.m.r. spectrum of compound (IVa) in



CDCl₃ shows signals at δ 2.42 (Ac), 6.50 (H-4), 7.30—7.44 and 7.64—7.78 (ArH), and 7.28—7.52 (enolic OH), indicating the predominance of the enol tautomer; similar behaviour was exhibited by all the other furanones prepared.



SCHEME

Similarly, the ylides (Ib and c) reacted with benzoyl chloride to form (IIIb and c), which underwent thermal elimination of dimethyl sulphide to give the furanones (IVb and c) (see Table). The furanones (IVd and e)

		Synthesis of furanones			
		(III)	(IV)		
R	R'	Yield (%)	Solvent ^a	Time (h)	Yield (%)
a; Me	Ph	69	B	1	95
		41 ^b			
		46 ^c			
b; OEt	Ph	65	T	2	74
c; Ph	Ph	76 ^d	B	1	94
d; Ph	Me	26	B	2	86
e; Ph	Pr ⁿ	28 ^d	B	2	80

^a B, benzene; T, toluene. ^b Methyl benzoate was used. ^c Benzoic anhydride was used. ^d Lithium di-isopropylamide was used as base.

were synthesized similarly from the ylide (I'c) and the corresponding acyl chlorides. The relatively low yields of (IIId and e) were ascribed to α -methyl or -methylene protons of the newly formed acyl group quenching the starting ylide (I'c).

The ylides (IIIf and g), synthesized from (I'a) with ethyl chloroformate and phenyl isocyanate, respectively,

⁷ R. Oda and Y. Hayashi, *Nippon Kagaku Zasshi*, 1966, **87**, 1110.

were also examined for cyclization to furanones. The ylide (IIIf) did not give the desired product, but the ylide (IIIg) gave the furanone (IVg) after refluxing in toluene for 2 h.

The mechanism of the reaction (III) \rightarrow (IV) (see Scheme) is considered to involve initial proton transfer from the active methylene group to the ylide carbon atom, followed by attack of the resulting enolate anion. Dimethyl sulphide is then displaced concertedly.

EXPERIMENTAL

The bis-carbonyl-stabilized sulphonium ylides (Ia—c) were synthesized by the reactions of the corresponding β -dicarbonyl compounds with dimethyl sulphoxide and acetic anhydride.⁷

Dimethylsulphonium diacetylmethylide (Ia) had m.p. 165—167 °C (lit.,⁷ 167—169 °C). Dimethylsulphonium acetyl(ethoxycarbonyl)methylide (Ib) had m.p. 64—66 °C (lit.,⁷ 66—67 °C). Dimethylsulphonium acetyl(benzoyl)-methylide (Ic) had m.p. 108—109 °C (lit.,⁸ 109 °C).

General Procedure (A) for Synthesis of the Ylides (II) and (III).—The sulphonium ylide (I) (10 mmol) and dry THF (60 ml; distilled from LiAlH₄) were mixed under nitrogen, and the suspension was cooled to -15 to -20 °C in an

ice-salt bath. *n*-Butyl-lithium (20% in hexane; 6.3 ml, 10.5 mmol) was added dropwise within 10—15 min. After 1 h stirring at -15 °C, the electrophile (10 mmol) in dry THF (5 ml) was added dropwise and stirring was continued for 1 h at -10 to -15 °C under nitrogen. The mixture was quenched with brine (50 ml) and ether (50 ml), and acidified with dilute hydrochloric acid. The organic layer was separated and washed with brine (30 ml). The aqueous layer was extracted with chloroform (50 ml) and the extract washed with brine (30 ml). The organic layers were dried (Na₂SO₄) and concentrated. The combined residue was purified by silica gel (Merck 7734; 70—230 mesh) column chromatography with benzene-acetone.

Dimethylsulphonium Acetyl-(3-phenylpropionyl)methylide (IIa).—By general procedure (A), (Ia) (3.20 g, 20 mmol) and benzyl bromide (3.42 g, 20 mmol) gave the ylide (IIa) (3.65 g, 73%), ν_{max} (film) 1 605, 1 575, 1 495, and 700 cm⁻¹; λ_{max} (EtOH) 236 and 274 nm; δ (CDCl₃) 2.28 (3 H, s), 2.76 (6 H, s), 2.92 (4 H, s), and 7.12 (5 H, s); *m/e* 250 (*M*⁺), 235, 189, and 145. Compound (IIa) was hard to crystallize, so it was converted into the corresponding β -diketone as follows. Compound (IIa) (300 mg) and zinc dust (2.0 g) in dioxan (10 ml) were stirred at room temperature.⁴ Acetic acid was added dropwise (total 1 ml) and stirring was continued for 2 h. The residual zinc was filtered off and

⁸ H. Nozaki, M. Takaku, Y. Yamamoto, and K. Kondo, *Nippon Kagaku Zasshi*, 1967, **88**, 1.

washed with chloroform (20 ml) and acetone (20 ml). The filtrate was concentrated and the residue was mixed with water (30 ml) and neutralized with dilute sodium hydrogen carbonate solution. The aqueous solution was extracted with chloroform (2 × 20 ml) and the extracts were washed with water (20 ml), dried (Na_2SO_4), and concentrated. The residue gave pure 6-phenylhexane-2,4-dione, δ (CCl_4) 1.92 (3 H, s), 2.48 (2 H, t), 2.88 (2 H, t), 3.32 (0.5 H, s), 5.30 (1 H, s), and 7.10 (5 H, s). The copper chelate, m.p. 160–161 °C, was identical with an authentic sample.⁹

Dimethylsulphonium Acetyl-(3-oxo-3-phenylpropionyl)methylide (IIIa).—(i) *By use of benzoyl chloride.* By general procedure (A), (Ia) (2.24 g, 14 mmol) and benzoyl chloride (984 mg, 7 mmol) gave an orange viscous oil (IIIa) (1.27 g, 69%); δ (CDCl_3) 2.26 (1.5 H, s), 2.38 (1.5 H, s), 2.92 (3 H, s), 2.94 (3 H, s), 4.36 (1 H, s), 7.30 (0.5 H, s), 7.30–7.50 (3 H, m), and 7.70–8.00 (2 H, m).

(ii) *By use of methyl benzoate.* The ylide (Ia) (1.60 g, 10 mmol) and methyl benzoate (680 mg, 5 mmol) by general procedure (A) gave (IIIa) (541 mg, 41%).

(iii) *By use of benzoic anhydride.* By general procedure (A), (IIIa) (485 mg, 46%) was synthesized from (Ia) (1.28 g, 8 mmol) and benzoic anhydride (904 mg, 4 mmol).

General Procedure (B) for Synthesis of Furanones (IV).—Compound (IIIa) (1.00 g) was dissolved in benzene (50 ml); the mixture was heated to reflux for 1 h, and evaporated, and the residue was crystallized from acetone to give 2-acetyl-5-phenylfuran-3(2H)-one (620 mg), m.p. 200–201 °C. The mother liquor was concentrated and the residue crystallized from acetone-ether (2 : 1) to give a further 107 mg (total 95%); ν_{max} (KBr) 1 610, 1 590, 1 555, and 1 525 cm^{-1} ; λ_{max} (EtOH) 227 (ϵ 13 500), 233 (14 100), 244 (13 000), and 329 nm (ϵ 25 100); m/e 202 (M^+) and 187 (Found: C, 71.5; H, 5.0. $\text{C}_{12}\text{H}_{10}\text{O}_3$ requires C, 71.3; H, 5.0%).

Dimethylsulphonium Ethoxycarbonyl-(3-phenylpropionyl)methylide (IIb).—The ylide (Ib) contained water of crystallization,⁸ this was removed as follows. Sodium hydride (50% in oil; 580 mg, 12 mmol) was washed with dry n-hexane (3 × 5 ml) (to remove oil) and flushed with nitrogen, then dry THF (20 ml) was added. To the suspension the ylide (Ib) (2.00 g, 10 mmol) in dry THF (10 ml) was added dropwise. Hydrogen was evolved, and after the addition the mixture was stirred for 20 min at room temperature, warmed at 50 °C for 10 min, then cooled. The supernatant was transferred by microsyringe to another flask and the general procedure (A) was carried out. From (Ib) (10 mmol) and benzyl bromide (1.71 g, 10 mmol), the ylide (IIb) (1.55 g, 55%), m.p. 82–83 °C, was obtained as crystals (from ether); ν_{max} (KBr) 1 670, 1 570, and 700 cm^{-1} ; λ_{max} (EtOH) 228 (ϵ 7 740) and 261 nm (13 100); δ (CCl_4) 1.28 (3 H, t), 2.87 (6 H, s), 3.10 (4 H, m), 4.02 (2 H, q), and 7.00–7.26 (5 H, m) (Found: C, 64.5; H, 7.2. $\text{C}_{15}\text{H}_{20}\text{O}_3\text{S}$ requires C, 64.3; H, 7.2%); m/e 280 (M^+), 219, 145, 105, and 91.

Dimethylsulphonium Ethoxycarbonyl-(3-oxo-3-phenylpropionyl)methylide (IIIb).—Before benzylation, crystalline (Ib) was treated with sodium hydride as described above. By general procedure (A), (Ib) (2.66 g, 14 mmol) and benzoyl chloride (984 mg, 7 mmol) gave (IIIb) (1.34 g, 65%) as an orange oil, δ (CCl_4) 1.29 (3 H, t), 2.92 (6 H, s), 4.04 (2 H, q), 4.32 (2 H, s), 7.26–7.56 (3 H, m), and 7.70–7.96 (2 H, m).

Ethyl 2,3-Dihydro-3-oxo-5-phenylfuran-2-carboxylate (IVb).—By general procedure (B), with toluene as solvent, the furan (IVb) (705 mg, 74%) was obtained from (IIIb)

(1.20 g) as needles, m.p. 71–73 °C [from n-hexane-ether (2 : 1)]; ν_{max} (KBr): 1 680, 1 620, 1 600, 1 495, and 690 cm^{-1} ; λ_{max} (EtOH) 223 (ϵ 15 400), 242 (7 100), and 310 nm (23 000); δ (CCl_4) 1.40 (3 H, t), 4.36 (2 H, q), 6.46 (1 H, s), 7.26–7.48 (3 H, m), 7.62–7.80 (2 H, m), and 7.90br (1 H); m/e 232 (M^+), 204, 187, and 160 (Found: C, 67.4; H, 5.2. $\text{C}_{13}\text{H}_{12}\text{O}_4$ requires C, 67.2; H, 5.2%).

Dimethylsulphonium Benzoyl-(3-oxo-3-phenylpropionyl)methylide (IIIc).—(i) *By use of butyl-lithium.* By general procedure (A), (Ic) (1.11 g, 5 mmol) and benzoyl chloride (355 mg, 2.5 mmol) gave the ylide (IIIc) (320 mg, 39%); δ (CCl_4) 2.2–2.9br (6 H), 4.20 (0.3 H, s), 6.22 (0.45 H, s), 6.46 (0.45 H, s), and 7.04–8.16 (10 H, m).

(ii) *By use of lithium di-isopropylamide.* Dry THF (10 ml) and di-isopropylamine (0.85 ml, 606 mg, 6 mmol) were cooled in an ice-salt bath at –10 to –15 °C under nitrogen. n-Butyl-lithium (20% in hexane; 4.0 ml, 5.5 mmol) was added dropwise within 10 min. After stirring for 30 min, the solution was transferred to another flask, which contained (Ic) (1.11 g, 5 mmol) in dry THF (10 ml). General procedure (A) afforded the ylide (IIIc) (617 mg, 76%).

2-Benzoyl-5-phenylfuran-3(2H)-one (IVc).—By general procedure (B), (IIIc) (650 mg) gave the furan (IVc) as yellow needles (495 mg, 94%), m.p. 113.5–114.5 °C [from ether-n-hexane (3 : 1)]; ν_{max} (KBr) 1 605, 1 600, 1 580, and 1 540 cm^{-1} ; λ_{max} (EtOH) 261 (ϵ 18 500) and 358 nm (21 900); δ (CCl_4) 6.40 (1 H, s), 7.16–7.60 (8 H, m), 8.02–8.18 (2 H, m), and 10.18br (1 H) (Found: C, 77.5; H, 4.35. $\text{C}_{17}\text{H}_{12}\text{O}_3$ requires C, 77.3; H, 4.6%).

2-Benzoyl-5-methylfuran-3(2H)-one (IVd).—By procedure (A), the ylide (Ic) (1.11 g, 5 mmol) and acetyl chloride (0.4 ml, 440 mg, 5.5 mmol) gave the ylide (IIId) (346 mg, 26%), δ (CDCl_3) 2.18 (3 H, s), 2.91 (6 H, s), 3.83 (2 H, s), and 7.32 (5 H, s). By procedure (B), the ylide (IIId) (230 mg) gave the furan (IVd) (151 mg, 86%), δ (CCl_4) 2.35 (3 H, s), 6.00 (1 H, s), 7.36–7.64 (3 H, m), 8.16–8.36 (2 H, m), and 10.42br (1 H).

2-Benzoyl-5-propylfuran-3(2H)-one (IVe).—By procedure (A), the ylide (Ic) (2.77 g, 12.5 mmol) with butyryl chloride (0.65 ml, 670 mg, 6.25 mmol) gave the ylide (IIIE) (510 mg, 28%), δ (CCl_4) 0.96 (3 H, t), 1.40–1.82 (2 H, m), 2.56 (2 H, t), 3.04 (6 H, s), 3.86 (1.4 H, s), 5.92 (0.3 H, s), and 7.62 (5 H, s). By procedure (B), the ylide (IIIE) (350 mg) gave the furanone (IVe) (221 mg, 80%), δ (CCl_4) 0.98 (3 H, t), 1.51–1.90 (2 H, m), 2.60 (2 H, t), 6.00 (1 H, s), 7.36–7.56 (3 H, m), 8.14–8.33 (2 H, m), and 10.50 (1 H, s).

Dimethylsulphonium Acetyl(ethoxycarbonylacetyl)methylide (IIIf).—By procedure (A), the ylide (Ia) (1.28 g, 8 mmol) and ethyl chloroformate (436 mg, 4 mmol) gave the ylide (IIIff) (634 mg, 68%), m.p. 81–83 °C; ν_{max} (KBr) 1 730, 1 600, and 1 570 cm^{-1} ; λ_{max} (EtOH) 232 (ϵ 8 100) and 272 nm (11 400); δ (CDCl_3) 1.26 (3 H, t), 2.30 (3 H, s), 3.00 (6 H, s), 3.74 (2 H, s), and 4.14 (2 H, q). Compound (IIIff) underwent reductive elimination of dimethyl sulphide on treatment with zinc dust-acetic acid to give the corresponding dioxo-ester,⁴ identified by comparison (n.m.r.) with an authentic sample.¹⁰

Attempted Cyclization of the Ylide (IIIff).—The ylide (IIIff) (170 mg) was subjected to procedure (B) in benzene. The n.m.r. spectrum of the residue (168 mg) was almost the same as that of (IIIff). The residue in toluene (20 ml) was then subjected to general procedure (B). The reaction mixture

⁹ K. G. Hampton, T. M. Harris, and C. R. Hauser, *J. Org. Chem.*, 1965, **30**, 61.

¹⁰ S. N. Huckin and L. Weiler, *Tetrahedron Letters*, 1972, 2405.

contained some starting material (III_f) and decomposition products (n.m.r. spectrum and t.l.c.).

Dimethylsulphonium Acetyl(phenylcarbamoylacetyl)methylide (III_g).—By general procedure (A) the ylide (Ia) (2.24 g, 14 mmol) and phenyl isocyanate (840 mg, 7 mmol) gave the *ylide* (III_g) (898 mg, 46%) as crystals, m.p. 187–189 °C (from benzene);⁴ ν_{\max} (KBr) 1 685, 1 610, 1 565, and 1 555 cm^{-1} ; λ_{\max} (EtOH) 248 nm (ϵ 21 200); δ (CDCl₃) 2.30 (3 H, s), 2.92 (6 H, s), 3.81 (2 H, s), 6.84–7.28 (3 H, m), 7.40–7.60 (2 H, m), and 9.88br (1 H) (Found: C, 60.2; H, 6.15; N, 5.05. C₁₄H₁₇NO₃S requires C, 60.2; H, 6.15; N, 5.0%).

Cyclization of the Ylide (III_g).—By general procedure (B), the ylide (III_g) (200 mg) gave the furan (IV_g) (27 mg), an unknown compound (31 mg); 89 mg of the starting ylide (III_g) was recovered. The furan (IV_g) showed δ (CDCl₃) 2.16 (3 H, s), 5.55 (1 H, s), 7.00–7.56 (5 H, m), and 10.32br (1 H).

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