

VINYLOGUES AND HETEROCYCLIC ANALOGUES OF BENZYLIDENEMALONALDEHYDES

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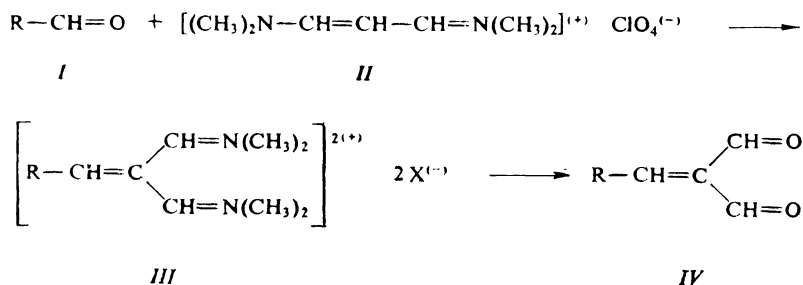
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Nine analogues of benzylidenemalonaldhyde (*IV*) were prepared by condensation of bis(dimethylamino)trimethinium perchlorate with two vinylogues of benzaldehyde and a series of heterocyclic aldehydes. The reaction intermediate was isolated and shown by ^1H NMR spectroscopy to be the bis-iminium salt *III*. The conformation of 3-phenylprop-2-enylidenemalonaldhyde (*IVa*), determined by its ^1H NMR spectrum, may serve as a more general model of arylmethylenemalonaldhydes.

In the preceding communication we described a two-step synthesis of benzylidenemalonaldhydes¹⁻³. This approach, successfully applied to a series of substituted benzaldehydes, has been now extended to vinylogues of benzaldehyde and heterocyclic aldehydes. At the same time, this extension led to elaboration of conditions enabling work with more sensitive compounds, confirmed our previous mechanistic considerations and afforded information on some conformational aspects of the obtained products (Scheme 1).

Both benzaldehyde vinylogues, 3-phenylprop-2-enal and 5-phenylpenta-2,4-dienal, react smoothly under conditions used for substituted benzaldehydes, *i.e.* in acetic



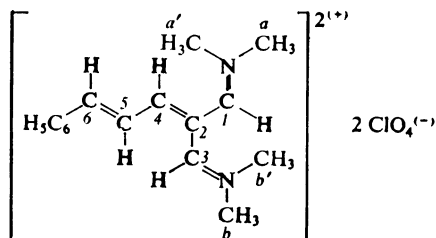
R: *a* $\text{C}_6\text{H}_5\text{CH}=\text{CH}$; *b* $\text{C}_6\text{H}_5(\text{CH}=\text{CH})_2$; *c* 2-furyl; *d* 5-methyl-2-furyl; *e* 5-brom-2-furyl; *f* 5-nitro-2-furyl; *g* 2-thienyl; *h* 3-thienyl; *i* ferrocenyl

SCHEME 1

anhydride, and particularly the former gives high yield of the product (Table I). On the other hand, furan derivatives partially decompose under analogous conditions. In the preparation of such sensitive starting compounds including thiophene derivatives, the reaction medium of choice proved to be a 1 : 1 mixture of acetic anhydride and acetic acid containing boron trifluoride etherate or zinc chloride. Instead of the 5-nitrofuryl derivative or some other compounds the reaction was performed with the corresponding acylal without a serious decrease of yield. This finding, which agrees with the suggested mechanism of the condensation reaction³, may be also of preparative significance.

The method of preparation of the dialdehydes, together with their spectral and other data, is given in Tables I–III. As seen from the Tables, we synthesized two vinylogues of benzylidenemalonaldehyde (*IVa,b*) four furan derivatives *IVc–f* and two isomeric thienylmethylenemalonaldehydes *IVg,h*. Ferrocenecarboxaldehyde was included as a representative of less common types of aldehydes; its reaction afforded the corresponding ferrocenylmethylenemalonaldehyde (*IVi*) in a modest yield (47%). The dialdehydes *IV*, described in this communication, are yellow to red crystalline compounds which can be stored at low temperature (–20°C) for several months, with the exception of 5-bromo-2-furylmethylenemalonaldehyde which decomposes even at low temperatures during several hours.

We have suggested already previously^{1–3} that in the synthesis of benzylidenemalonaldehydes the key intermediate is a bis-iminium salt which, however, was not characterized owing to its high sensitivity towards hydrolysis. We have now isolated and characterized by analysis and NMR spectra the diperchlorates *IIIa* and *IIIb*,



IIIa

obtained as intermediates in the reaction of 3-phenylprop-2-enal and 5-nitrofuran, respectively. Their ¹H NMR spectra were measured in sulfur dioxide in which both diperchlorates are well soluble and the hydrolysis is prevented. The ¹H NMR spectrum of the salt *IIIa* showed the presence of two N,N-dimethyliminium groupings and mutual *trans*-orientation of both C=C double bonds. Under assumption of at least approximate planarity, the structure can be described by the formula *IIIa*. Since the spectrum of *IIIb* is analogous, we assume that both salts are structurally similar.

The structure of the obtained dialdehydes *Va–IVf* is confirmed also by their ^1H NMR spectra. The compound *IVa* deserves a more detailed study because

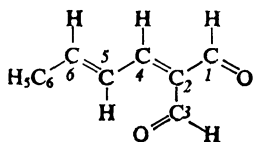
*IVa*

TABLE I
Method of preparation, yields, melting points and elemental analyses of dialdehydes *IV*

Compound Method	Reaction time, h yield, %	M.p., °C	Formula (mol.wt.)	Calculated/Found		
				% C	% H	% X
<i>IVa</i>	20	79–80 ^a	C ₁₂ H ₁₀ O ₂	77.40	5.41	—
<i>A</i>	86		(186.2)	77.30	5.45	—
<i>IVb</i>	24	111–112 ^b	C ₁₄ H ₁₂ O ₂	79.23	5.70	—
<i>A</i>	42		(212.2)	78.98	5.86	—
<i>IVc</i>	24	51–54 ^a	C ₈ H ₆ O ₃	64.00	4.03	—
<i>B</i>	90		(150.1)	63.67	4.01	—
<i>IVd</i>	24	116–117.5 ^b	C ₉ H ₈ O ₃	65.85	4.91	—
<i>B</i>	85		(164.2)	65.58	4.88	—
<i>IVe</i>	48	75–83 ^c	C ₈ H ₅ BrO ₃	41.95	2.20	34.89 Br
<i>A</i>	72		(229.0)	41.61	2.35	34.50 Br
<i>IVf</i>	—	129–133 ^a	C ₈ H ₅ NO ₅	49.24	2.58	7.18 N
—	—		(195.1)	49.19	2.20	7.15 N
<i>IVg</i>	24	96–97 ^b	C ₈ H ₆ O ₂ S	57.82	3.64	19.29 S
<i>B</i>	86		(166.2)	57.59	3.42	19.01 S
<i>IVh</i>	20	56–58.5 ^b	C ₈ H ₆ O ₂ S	57.82	3.64	19.29 S
<i>B</i>	75		(166.2)	57.68	3.98	19.31 S
<i>IVi</i>	24	67–72 ^d	C ₁₄ H ₁₂ FeO ₂	62.72	4.51	^e
	43		(268.1)			

^a Purified by sublimation; ^b from tetrachloromethane; ^c the intermediate *IIIe*, precipitated with ether, was rapidly dried and hydrolyzed with water, the separated compound was filtered, washed with water, dried *in vacuo* and crystallized from tetrachloromethane; ^d purified by chromatography on silica gel in dichloromethane crystallized from *n*-hexane; ^e mass spectrum: M^+ 268.

of its relation to the salt *IIIa* and, particularly, because it can afford information on the more general problem of detailed spatial arrangement of unsaturated dialdehydes studied in the preceding³, present and next⁴ communications. A characteristic feature of ¹H NMR spectrum of the dialdehyde *IVa* is the coupling ⁴ $J_{H^3, H^4} = 2.2$ Hz indicating *trans*-relation between the less shielded aldehyde group at C₍₃₎ and the H⁴ proton on the C₍₂₎=C₍₄₎ bond and thus *cis*-relation towards the rest of the molecule. Also the chemical shift of the H⁵ proton ($\delta = 8.24$) agrees with the suggested conformation in which this proton is deshielded by the anisotropic formyl group. No similar effect on the proton H⁵ can occur in *IIIa*. In benzyli-

TABLE II
¹H NMR spectra of dialdehydes *IV*

R	CH=O	CH=	Other signals	
<i>IVa</i>	10.30 d, 1 H(H ³) $J = 2.2$ Hz 9.83 s, 1 H(H ¹)	7.42 m, 1 H(H ⁴) $J_{H^3, H^4} = 2.2$ $J_{H^4, H^5} = 11.5$	8.24 dd, 1 H(H ⁵) ^a 7.36 d, 1 H(H ⁶)	7.39–7.69 m, 5 H (C ₆ H ₅)
<i>IVb</i>	10.23 d, 1 H $J = 2$ Hz 9.77 s, 1 H		6.95–8.03 m, 10 H	
<i>IVc</i>	10.70 s, 1 H 10.08 s, 1 H	7.66 s, 1 H	7.80 d, 1 H	7.50 d, 1 H 6.68 dd, 1 H
<i>IVd</i>	10.67 s, 1 H 10.03 s, 1 H	7.58 s, 1 H	7.48 d, 1 H $J = 4$ Hz	6.35 d, 1 H ^b $J = 4$ Hz
<i>IVe</i>	10.60 s, 1 H 10.03 s, 1 H	7.52 s, 1 H	7.57 d, 1 H $J = 4$ Hz	6.63 d, 1 H $J = 4$ Hz
<i>IVf</i>	10.63 s, 1 H 10.03 s, 1 H	7.57 s, 1 H	7.73 d, 1 H $J = 4$ Hz	7.47 d, 1 H $J = 4$ Hz
<i>IVg</i>	10.36 d, 1 H $J = 1.5$ Hz 9.92 s, 1 H	7.86 bs	7.98–7.17 m, 3 H	
<i>IVh</i>	10.14 d, 1 H $J = 1$ Hz 9.94 s, 1 H	7.81 s, 1 H	8.36–8.46 m, 1 H	7.39–7.61 m, 2 H
<i>IVi</i>	10.23 bs, 1 H 9.90 s, 1 H	7.87 s, 1 H	4.80–5.00 m, 4 H	4.00–4.36 m, 5 H

^a $J_{H^5, H^6} = 15.5$; Hz; $J_{H^5, H^4} = 11.5$ Hz; ^b 2.45 s, 3 H(CH₃).

denemalonaldehydes containing an aromatic nucleus bonded to the C₍₄₎ carbon atom an analogous structure, manifested by coupling across four bonds, is obviously less stable because of steric interaction between the aromatic nucleus and oxygen atom of the corresponding formyl group. This problem will be dealt with in a separate communication⁵.

EXPERIMENTAL

Melting points were determined on a Kofler block. Analytical samples were dried over phosphorus pentoxide at 25°/27 Pa for 24 h. IR Spectra were taken on a Zeiss UR 20 spectrometer, ¹H NMR spectra on Varian HA-100 (100 MHz) and Tesla BS 467 (60 MHz) instruments in deuteriochloroform with tetramethylsilane as internal standard (unless stated otherwise).

TABLE III
IR Spectra of dialdehydes *IV* in chloroform

Dialdehyde	C—H(CH=O)	(C=O)	(C=C)	Ring
<i>IVa</i>	2 733 w	1 752 w, br	1 580 vs	1 603 vs
	2 760 w	1 716 w, sh	1 572 vs, sh	1 493 vw
	2 784 w	1 695 vs, sh	1 554 s	1 452 m
	2 871 w	1 681 vs 1 666 s, sh		
<i>IVb</i>	2 750 vw, br	1 749 w, sh, br	1 615 m, sh	1 599 m
		1 715 w, sh	1 576 vs	1 576
		1 694 s, sh	1 556 s	1 450 w
		1 679 s	1 539 m, sh	
<i>IVe^a</i>		1 694 m, sh	1 601 s	—
		1 675 m, br	1 585 m, sh	—
<i>IVg</i>	2 720 w	1 696 s, sh	1 575 vs	1 426 m, sh
	2 744 w	1 680 vs	1 550 m	1 410 s
	2 765 w	1 662 m, sh		1 368 w 1 363 w
<i>IVh</i>	2 792	1 714 m, sh	1 587 vs	1 508 m
	2 775 w, sh	1 701 s, sh		1 411 w
		1 682 vs		1 484 m
<i>IVi</i>	2 764 vw	1 667 s	1 571 s	1 413 w
		1 680 s, sh	1 556 m, sh	1 110 w
		1 695 m, sh		

^a Values in CCl₄: (C=O) 1 697 w, sh, 1 688 m, 1 678 w; (C=C) 1604 w, 1 585 w.

Preparation of Dialdehydes *IV*

A) 1,3-Bis(dimethylamino)trimethinium perchlorate^{6,7} (2.26 g; 10 mmol) was dissolved in acetic anhydride (25 ml) and freshly fused and ground zinc chloride (2.5 g) was added. The corresponding aldehyde (12 mmol) was then added under stirring and cooling with ice. The mixture was stirred for 2 h and set aside at room temperature for the time specified in Table I. Dry ether was added and the precipitated material was repeatedly washed with dry ether and hydrolyzed with water (200 ml) in the presence of a benzene-dichloromethane (5 : 1; 50 ml) mixture. After dissolution of the solid portion, the mixture was stirred for 1 h, the organic layer separated and the aqueous one twice extracted. The combined extracts were dried over anhydrous magnesium sulfate, the solvent was evaporated and the residue crystallized or sublimed (Table I).

B) Boron trifluoride etherate (2.5 ml), followed by the corresponding aldehyde (10 mmol), was added to a stirred and ice-cooled solution of 1,3-bis(dimethylamino)trimethinium perchlorate (2.26 g; 10 mmol) in a mixture of acetic anhydride (7.5 ml) and acetic acid (7.5 ml). Further processing was the same as described under *A*).

2-(3-Phenyl-2-propenylidene)propane-1,3-bis(ylidene-N,N-dimethyliminium) Dip perchlorate (*IIIa*)

Perchloric acid (70%, 1 ml), followed by the trimethinium salt *II* (2.26 g; 10 mmol) and 3-phenylprop-2-enal (1.5 ml; 10 mmol), was added with cooling to a mixture of acetic anhydride (5 ml) and acetic acid (5 ml). After 5 h the separated compound was filtered, washed with an acetic anhydride-acetic acid (1 : 1) mixture and dried; m.p. 186–190°C, yield of *IIIa* 1.9 g. For C₁₆H₂₂Cl₂N₂O₈ (441.3) calculated: 43.55% C, 5.03% H, 16.07% Cl, 6.35% N; found: 43.02% C, 4.93% H, 16.10% Cl, 6.32% N. ¹H NMR spectrum (SO₂, tetramethylsilane, δ): 9.05 bs (1 H; H³); 8.50 bs (1 H; H¹); 8.06 d (1 H; H⁴), ³J_{H⁴,H⁵} = 12.3 Hz; 7.99 d (1 H; H⁶), ³J_{H⁶,H⁵} = 14.7 Hz; 7.26 dd (1 H; H⁵), ³J = 12.3 and 14.7 Hz; 7.45–8 m (C₆H₅); 4.08 bs (3 H; N—CH₃; b') ⁴J_{N—CH₃,H³} = 1.2 Hz; 3.87 bs (3 H; N—CH₃; a'), ⁴J_{N—CH₃,H¹} = 1.1 Hz; 3.72 bs (6 H; N—CH₃; a, b).

2-(5-Nitro-2-furylmethylene)propane-1,3-bis(ylidene-N,N-dimethyliminium) Dip perchlorate (*IIIf*)

5-Nitrofural (0.28 g; 2 mmol) was added to a cooled and stirred solution of the trimethinium salt *II* (0.5 g; 2.25 mmol) and conc. perchloric acid (0.5 ml) in acetic anhydride (3 ml) and the stirring was continued for 3 h. After standing for 2 days, the solid was collected on a filter, washed with ether and dried, affording 0.34 g (37%) of the salt *IIIf*, m.p. 219–222°C. For C₁₂H₁₇Cl₂N₃O₁₁ (450.2) calculated: 32.02% C, 3.81% H, 15.75% Cl, 9.33% N; found: 31.64% C, 3.89% H, 15.98% Cl, 9.21% N. ¹H NMR spectrum (SO₂, tetramethylsilane, δ): 9.18 bs (1 H); 8.5 bs (1 H); 7.93 bs (1 H); 7.68–7.43 m (2 H); 4.18 bs (3 H); 3.9 bs (3 H); 3.75 bs (6 H).

5-Nitro-2-furylmethylenemalonaldehyde (*IVf*)

The salt *IIIf* (0.45 g; 1 mmol) was added into water (1 ml) under stirring. After 10 min the solid was filtered and sublimed, giving 0.15 g (77%) of the dialdehyde *IVf* (for m.p. and analysis see Table I).

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