Synthesis of Unsaturated 5-Hydroxy- and 7-Oxo-acids by Addition of Unsaturated Carboxylic Acid Dienolates to Carbonyl Compounds

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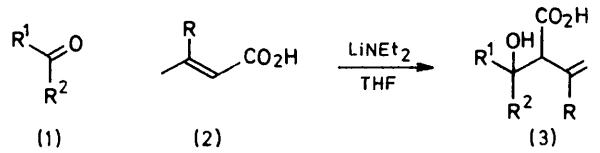
Alkylation of dienolates derived from crotonic and dimethylacrylic acids (2) by saturated or aromatic aldehydes and ketones (1) at low temperature affords 2-substituted-3-hydroxy-acids (3). The dianionic species of these isomerize on heating to (*E*)- and (*Z*)-unsaturated-5-hydroxy-acids (4) and (5), for crotonic and dimethylacrylic acids, respectively. Unsaturated ketones (6) suffer 1,4-addition through γ-alkylation, leading to (*E*)-unsaturated-7-oxo-acids (8) for both crotonic and dimethylacrylic acids. Unsaturated 5-hydroxy- and 7-oxo-carboxylic acids are readily prepared by the procedure here established.

γ-ALKYLATION of unsaturated carbonyl compounds, an attractive route to isoprenoid structure possessing a terminal oxygen function, has been the subject of a number of recent publications.[1-4] Although exclusive γ-addition of crotonic acid to some carbonyl compounds in the presence of lithium diethylamide was claimed by both Watanabe[5] and Chakravarti,[6] Pfeffer[7] and Cainelli[8] found alkylation to occur at both α- and γ-carbons for the same, or similar, reaction conditions and reagents. Here we report our studies on the influence of structure, temperature, and reaction time on yield, regioselectivity, and stereoselectivity for the addition of lithium dienolates derived from crotonic and dimethylacrylic acids to a variety of carbonyl compounds.

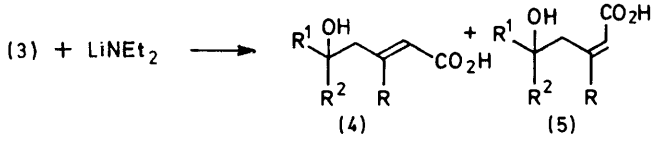
The addition of crotonic acid to cyclohexanone was studied first. Lithium diethylamide prepared from lithium naphthalide and diethylamine in tetrahydrofuran was used as base, although no substantial differences were found on substitution of the naphthalide by n-butyl-lithium. Yields were established for the total crude acid fractions, once unchanged starting acids had been removed. Mixtures of free acids were qualitatively studied by chromatography on acidified silica-gel plates, while compositions were determined by g.l.c. analysis and n.m.r. spectroscopy of the methyl esters resulting from diazomethane esterification. Best yields were obtained for experiments carried out for 5—10 min at −70 °C (solid CO_2–acetone bath), when complete and almost exclusive conversion into the hydroxy-acid [**3**; $R^1R^2 = (CH_2)_5$, R = H] occurred. Although temperatures up to 20 °C for 2 h reaction periods, or 40—50 °C (bath temperature) for shorter periods (5—15 min), did not noticeably modify the regioselectivity, some self-condensation products were obtained (n.m.r.) and product yields were lower. Prolonged heating at 40—50 °C (or under reflux) afforded the hydroxy-acid [**4**; $R^1R^2 = (CH_2)_5$, R = H], best yields being obtained when both ionization of the acid and addition of the ketone were carried out at −70 °C. G.l.c. analysis of

[1] J. A. Katzenellenbogen and A. L. Crumrine, *J. Amer. Chem. Soc.*, 1976, **98**, 4925.
[2] B. M. Trost and L. S. Melvin, jun., *J. Amer. Chem. Soc.*, 1976, **98**, 1204.
[3] W. E. Parham and D. W. Boykin, *J. Org. Chem.*, 1977, **42**, 260.
[4] H. H. Meyer, *Tetrahedron Letters*, 1975, 3221.
[5] K. Suga, S. Watanabe, and T. Fujita, *Austral. J. Chem.*, 1972, **25**, 2393.
[6] Y. Gopichand and K. K. Chakravarti, *Tetrahedron Letters*, 1974, 3851.
[7] P. E. Pfeffer, L. S. Silbert, and E. Kinsel, *Tetrahedron Letters*, 1973, 1163.
[8] G. Cainelli, G. Cardillo, M. Contento, G. Trapani, and A. Umani Ronchi, *J.C.S. Perkin I*, 1973, 400; G. Cainelli, G. Cardillo, M. Contento, P. Grasselli, and A. Umani Ronchi, *Gazzetta*, 1973, **103**, 117; G. Cainelli, G. Cardillo, M. Contento, and A. Umani Ronchi, *ibid.*, 1974, **104**, 625; G. Cardillo, M. Orena, and S. Sandri, *Tetrahedron*, 1976, **32**, 107.

samples taken from the reaction mixture showed that the initially formed hydroxy-acid (3) was transformed completely in 10—15 h into a mixture of the (*E*)- and



(1) (2) (3)

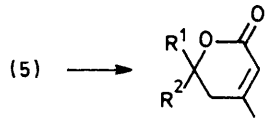


(4) (5)

(*Z*)-unsaturated hydroxy-acids (4) and (5), the same stereoselectivity ratio for these (95 : 5) being maintained essentially throughout the heating period. A similar result was obtained when a mixture of the hydroxy-acid (3) and 2 equivalents of lithium diethylamide were allowed to react for the same period of time. The hydroxy-acid (4; R^1 = Me, R^2 = Bu^i, R = H) was observed (n.m.r.) among the components of the reaction mixture when the above isomerization was carried out in the presence of isobutyl methyl ketone as the competing carbonyl compound. A similar isomerization experiment starting from the hydroxy-acid [4, $R^1R^2 = (CH_2)_5$; R = H] failed to give observable quantities of either the acid (3) or the isobutyl methyl ketone derived from the hydroxy-acid (4).

These observations agree with expectation [2] and contribute to a better understanding of the results described by Watanabe,[5] Pfeffer,[7] and Cainelli.[8] They also indicate a fast α-alkylation and a slow isomerization through retroaddition and recombination to the more stable γ-alkoxide. Yield dependence on initiation temperature can be understood as due to Michael-type addition of the dienolate to mono-ionized crotonic acid as a competing process. Ionization of the acid to the dienolate seems to proceed fast, but at a lesser extent, since *ca.* 50% isomerization of crotonic acid to but-3-enoic acid occurred on treatment with lithium diethylamide (2 equivalents) for 5 min at −70 °C, but very little deuterium incorporation was observed (n.m.r.) on quenching with deuterium oxide. Higher ionization temperatures gave a similar isomerization mixture, along with large amounts of self-condensation products. A small equilibrium concentration of the dienolate is not surprising, since ethyl crotonate is just partially ionized under similar conditions.[9] Strong temperature dependence for the Michael self-condensation, along with fast addition and slow retro-addition of the dienolate to the carbonyl group at low temperature, would then account for the absence of the undesirable high molecular-weight products when both ionization and ketone addition are carried out at low temperature. On the other hand, the same fast addition to the carbonyl compound would ensure a low concentration of the mono-ionized crotonic acid for the α- to γ-alkylation isomerization, self-condensation being this way minimized for experiments started at −70 °C and continued at 40—50 °C.

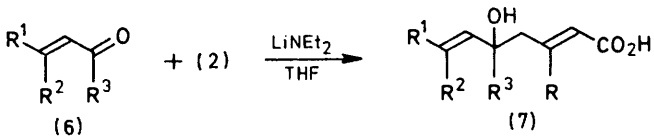
The study was extended both to aldehydes and other ketones and to dimethylacrylic acid, in order to confirm the above conclusions and to explore the scope and synthetic utility of the method. Yields, regioselectivities, and stereoselectivities are given in Tables 1 and 2. α-Alkylation of dienolates is shown to be favoured, in general, by low temperatures, and by substituents of small volume attached to the carbonyl group. α : γ-Regioselectivity ratios are, generally, higher for dimethylacrylic acid than for crotonic acid for low-temperature runs, while the reverse seems to be true for additions carried at higher temperature. These trends can be understood in terms of destabilization by steric crowding of the alkoxides derived from α-alkylation. Different heating time is required for each ketone–dienolate pair in order to obtain a high γ-regioselectivity; unsaturated 5-hydroxy-acids (4) and (5) can thus be conveniently



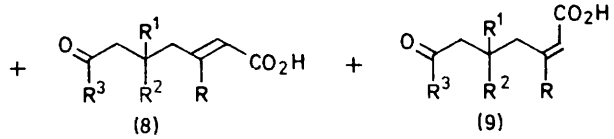
(10)

prepared, since yields do not greatly decrease on heating once reactions have been initiated at low temperature. The *Z*-unsaturated acids (5; R = Me) derived from dimethylacrylic acid cyclize to the lactones (10; R = Me) during working up or when set aside.

Unsaturated ketones afforded complex mixtures of α- and γ-alkylation and 1,2- and 1,4-addition products in the cold, but almost exclusively γ-alkylation and Michael addition giving 7-oxo-acids (8) on heating. No α-alkylation compound could be isolated, the hydroxy-acid (7; $R^1 = R^2 = R^3$ = Me, R = H) being the only 1,2-addition derivative obtained. These and other results to be published show that 7-oxo-acids (8) are readily obtained by this procedure.



(6) (7)



(8) (9)

As for stereoselectivity, crotonic acid leads to (*E*)-unsaturated acids (4) and (8), while dimethylacrylic acid affords (*Z*)-derivatives on 1,2-addition, and (*E*)-unsaturated acids (8) on 1,4-addition. A small amount of (*Z*)-unsaturated oxo-acid (9) has been obtained however

[9] M. W. Rathke and D. Sullivan, *Tetrahedron Letters*, 1972, 4249.

from the addition of dimethylacrylic acid to isophorone.

Stereoselectivities for γ-alkylations of α,β-unsaturated carboxylic acids by carbonyl compounds and by halides have been discussed by Cainelli [8] and by Katzenellenbogen.[1] Some of our results parallel those found by Cainelli and Cardillo,[8] who also obtained *Z*-hydroxy-acids by addition of dimethylacrylic acid to aldehydes in the presence of HMPTA. Although a firm rationalization for the observed stereoselectivities cannot be substantiated at the present state of our work, the different stereochemistry shown by crotonic and dimethylacrylic derivatives might be due to equilibration of the alkoxides derived from the latter by intra- or intermolecular proton loss from the free methyl group. The driving force for this isomerization would probably be an eight-membered cyclic proton or lithium ion bond. This interpretation would agree with the preferred *E* configuration for Michael addition oxo-acids derived from the same acid, when no such proton bond is possible. Crotonic acid derivatives on the other hand would not possess an equivalent isomerization mechanism, and found *E* : *Z* ratios would result from equilibria for free dienolates.

TABLE 1

Addition of unsaturated carboxy-dienolates to saturated and aromatic aldehydes and ketones

Compound (1)		(2)	Temp. (°C)		Time	Yield	Regio-selectivity	Stereo-selectivity
R^1	R^2	R	Start	Reaction	(h)	(%)	α : γ	γ-*E* : *Z*
H	Ph	H	−70	45	2	82.5	7 : 3	
		Me	−70	0	2	67.5	9 : 1	0 : 10
			−70	45	2	69	9 : 1	0 : 10
			−70	Reflux	2	65	6 : 4	0 : 10
H	Et	Me	−20	−20	0.1		8 : 2	0 : 10
			−20	45	2		8 : 2	0 : 10
			−20	45	4		8 : 2	0 : 10
$-(CH_2)_5-$		H	−70	−70	0.1	67	9 : 1	
			−70	0	2	90	9 : 1	
			−70	45	2		6 : 4	9 : 1
			−70	45	10	88	1 : 9	9 : 1
			−70	45	15		0 : 10	9 : 1
			−20	−20	0.1	52	8 : 2	
			−20	−20	2	48.5	8 : 2	
			−20	45	2	42	6 : 4	
		Me	−70	0	2	87	9 : 1	0 : 10
			−70	45	2	78	0 : 10	1 : 9
Me	Bu^i	Me	−20	−20	0.1		6 : 4	0 : 10
			−20	45	2		1 : 9	0 : 10
Me	Ph	H	−70	−70	0.1	45	4 : 6	10 : 0
			−70	45	2	63	0 : 10	10 : 0
		Me	−70	−70	0.1	81.5	6 : 4	0 : 10
			−70	45	2	80	0 : 10	0 : 10
Ph	Ph	H	−70	−70	0.1	73.5	0 : 10	10 : 0
			−70	45	2	63	0 : 10	10 : 0
		Me	−70	−70	0.1	72.5	0 : 10	0 : 10
			−70	45	2	70	0 : 10	0 : 10

TABLE 2

Addition of unsaturated carboxy-dienolates to unsaturated ketones

Compound (6)			(2)	Temp. (°C)		Time	Yield	Regioselectivity		Stereo-selectivity
R^1	R^2	R^3	R	Start	Reaction	(h)	(%)	α : γ	1,2 : 1,4	γ-*E* : *Z*
Me	Me	Me	H	−70	20	2	54	1 : 9	2 : 8	10 : 0
				−70	45	2	44	1 : 9	2 : 8	10 : 0
Me	$CH_2CMe_2CH_2$		H	−70	0	2	69	0 : 10	0 : 10	10 : 0
				−70	45	2	53.5	0 : 10	0 : 10	10 : 0
			Me	−70	0	2	69	7 : 3	3 : 7	9 : 1
				−70	45	2	64	0 : 10	1 : 9	9 : 1
H	Ph	Me	H	−70	−70	0.1	42	0 : 10	5 : 5	10 : 0
				−70	45	2	59	0 : 10	1 : 9	10 : 0
			Me	−70	−70	0.1	68	6 : 4	10 : 0	10 : 0
				−70	45	2	67	1 : 9	1 : 9	

EXPERIMENTAL

Thin layer chromatography was performed on silica gel HF_{254} (Merck) plates. Acid silica-gel plates were prepared from slurries of silica gel acidified to *ca.* pH 1 by diluted sulphuric acid. Unless otherwise stated, hexane–diethyl ether (2 : 1) was used as eluant. G.l.c. was performed under isothermal conditions for nitrogen as carrier gas on SE-30 columns, with a Carlo Erba Fractovap 2350 flame detector chromatograph. M.p.s were determined with a Büchi SMP 20 apparatus, and are uncorrected. I.r. spectral data were obtained for liquid film or potassium bromide discs with Unicam SP 1000 or Beckman 4250 spectrophotometers. 60 and 90 MHz n.m.r. spectra were recorded for CCl_4 or $CDCl_3$ solutions, with $SiMe_4$ as internal reference, with Perkin-Elmer R 12B, R 24A, or R 32

spectrometers. Elemental analyses were determined by Servicio de Semimicroanálisis del Instituto de Química Orgánica de Barcelona. Esterifications were performed by treatment of carboxylic acids with diazomethane.

General Procedure for Addition of Crotonic and Dimethylacrylic Acids to Carbonyl Compounds.—A mixture of lithium (1.12 g, 160 mg-atom), naphthalene (10.24 g, 80 mmol), and THF (80 ml) was stirred under nitrogen at room temperature for 2 h. Diethylamine (11.7 g; 160 mmol) was added dropwise with water cooling during 10 min. The solution was cooled (−70 or −20 °C) after being stirred for 1 h, and crotonic acid or dimethylacrylic acid (65 mmol) in THF (20 ml) and then the ketone (65 mmol), either in the same solvent or without solvent, were added during 30 or 15 min, respectively. The mixture was stirred at the temperature and for the time stated in each case, and ammonium chloride (200—500 mmol) and then 1M-sodium hydroxide were added. The solvent was partially evaporated, and the aqueous mixture washed with diethyl ether (+4), acidified by slow addition of concentrated hydrochloric acid with ice–water cooling, and then extracted several times with diethyl ether. The combined organic layers were washed with water (×2) and dried. Evaporation of the solvent afforded the crude mixture of hydroxy- and (or) oxo-acids.

2-(1-*Hydroxycyclohexyl*)*but*-3-*enoic Acid* [3; $R^1R^2 = (CH_2)_5$, R = H].—This compound was obtained according to the general procedure from crotonic acid (5.6 g) and cyclohexanone (6.4 g) at −70 °C, and 2 h stirring at 0 °C, as a syrup (8.8 g), which crystallized from benzene as white prisms, m.p. 96—97 °C (Found: C, 65.3; H, 8.55. $C_{10}H_{16}O_3$ requires C, 65.2; H 8.7%); $\nu_{max.}$ 3 350 (OH), 3 100 (=C–H), 1 710 (C=O), 1 635 (C=C), and 955 and 935 cm^{-1} (CH=CH_2). The methyl ester was obtained as an oil on esterification of the above hydroxy-acid; R_F 0.7; $\nu_{max.}$ 3 520 (OH), 3 080 (=C–H), 1.720 (C=O), 1 635 (C=C), and 980 and 920 cm^{-1} (CH=CH_2); τ 4.04 (3 × d, *J* 17, 10, and 9 Hz, CH=C), 4.8 (2 × d, *J* 10 and 2 Hz, C=CH), 4.86 (2 + d, *J* 17 and 2 Hz, C=CH), 6.32 (s, OMe), 7.05 (d, *J* 9 Hz, CH–CO), 7.11 (s, OH), and 8.53br (s, C_6H_{10}).

(E)-4-(1-*Hydroxycyclohexyl*)-*but*-2-*enoic Acid* [4; $R^1R^2 = (CH_2)_5$, R = H].—The crude acid was obtained as a syrup (5.28 g) from crotonic acid (2.8 g) and cyclohexanone (3.2 g); addition was carried out at −70 °C and heating at 40—50 °C for 10 h. An ethereal solution of the syrup yielded white prisms, m.p. 128—129 °C, of the hydroxy-acid (lit.,[6,9] m.p. 132—133 °C, m.p. 127—128.5 °C); $\nu_{max.}$ 3 100 (OH), 1 690 (C=O), 1 630 (C=C), and 960 cm^{-1} (*trans*-CH=CH).

Methyl ester. This compound was obtained as an oil; R_F 0.4; $\nu_{max.}$ 3 450 (OH), 1 710 (C=O), 1 650 (C=C), and 970 cm^{-1} (*trans*-CH=CH); τ 2.92 (d, t, *J* 16 and 8 Hz, CH=C–CO), 4.1 (d, *J* 16 Hz, C=CH–CO), 6.3 (s, OMe), 7.2 (s, OH), 7.65 (d, *J* 8 Hz, CH_2–C=C), and 8.5br (s, C_6H_{10}).

(*Z*)-4-(1-*Hydroxycyclohexyl*)*but*-2-*enoic Acid* [5; $R^1R^2 = (CH_2)_5$, R = H].—The methyl ester of this acid resulted from esterification of the mother liquors of crystallization of the above *E*-isomeric hydroxy-acid; on column chromatographic separation it was obtained as an oil, R_F 0.5; $\nu_{max.}$ 3 450 (OH), 1 720 (C=O), and 1 640 cm^{-1} (C=C); τ 3.45 (d, t, *J* 12 and 8 Hz, CH=C–CO), 4.01 (d, *J* 12 Hz, C=CH–CO), 6.29 (s, OMe), 7.2 (d, *J* 8 Hz, CH_2–C=C), 7.58 (s, OH), and 8.5br (s, C_6H_{10}).

2-(*Hydroxycyclohexyl*)-3-*methylbut*-3-*enoic acid* [3; $R^1R^2 = (CH_2)_5$, R = Me].—This compound was obtained from cyclohexanone (3.2 g) and dimethylacrylic acid (3.25 g) at −70 °C and 2 h at 0 °C, as a syrup (5.6 g). The *hydroxy-acid* crystallized from benzene as white prisms, m.p. 95—96 °C (Found: C, 66.55; H, 9.0. $C_{11}H_{18}O_3$ requires C, 66.65; H, 9.1%), $\nu_{max.}$ 3 100 (OH), 1 695 (C=O), 1 635 (C=C), and 895 cm^{-1} (C=CH_2).

Methyl ester. Esterification of the acid with diazomethane afforded the methyl ester as white prisms, m.p. 44—45 °C; R_F 0.7 (Found: C, 67.9; H, 9.7. $C_{12}H_{20}O_3$ requires C, 67.9; H, 9.45%); $\nu_{max.}$ 3 450 (OH), 1 700 (C=O), 1 630 (C=C), and 900 cm^{-1} (C=CH_2); τ 5.1br (s, C=CH_2), 6.35 (s, OMe), 6.7 (s, OH), 7.03 (s, CH–CO), 8.15 (s, C=C–Me), and 8.5br (s, C_6H_{10}).

(Z)-4-(1-*Hydroxycyclohexyl*)-3-*methylbut*-2-*enoic Acid* [5; $R^1R^2 = (CH_2)$, R = Me].—This acid was obtained from cyclohexanone (1.7 g) and dimethylacrylic acid (1.6 g); addition was at −70° followed by heating for 2h at 45°. Esterification of an aliquot (0.5 g) of the crude acid (2.5 g), and column chromatography gave the methyl ester as an oil (0.3 g); R_F 0.3 (Found: C, 68.15; H, 9.7. $C_{12}H_{20}O_3$ requires C, 67.9; H, 9.45%), $\nu_{max.}$ 3 480 (OH), 1 695 (C=O), and 1 630 cm^{-1} (C=C); τ 4.22 (s, C=CH–CO), 6.37 (s, OMe), 6.95 (s, OH), 7.3 (s, CH_2–C=C), 8.02 (s, Me–C=C), and 8.52br (s, C_6H_{10}).

Reaction of Crotonic Acid with Mesityl Oxide.—Crotonic acid (5.6 g) and mesityl oxide (6.32 g) were mixed at −70 °C and then stirred for 2 h at 0 °C to give a syrup (6.5 g); this was esterified and chromatographed to give the *methyl ester* of (*E*)-5,5-dimethyl-7-oxo-oct-2-enoic acid (8; $R^1 = R^2 = R^3$ = Me; R = H) as a syrup, R_F (hexane–ether 3 : 1) 0.5 (Found: C, 66.35; H, 9.7. $C_{11}H_{18}O_3$ requires C, 66.65; H, 10.0%); $\nu_{max.}$ 1 720 (C=O), 1 655 (C=C), and 985 cm^{-1} (*trans*-CH=CH); τ 3.05 (d, t, *J* 15 and 8 Hz, CH=C–CO), 4.18 (d, *J* 15 Hz, C=CH–CO), 6.3 (s, OMe), 7.65 (s, CO–CH_2), 7.72 (d, *J* 8 Hz, CH_2C=C), 7.9 (s, MeCO), and 8.98 (s, 2 × Me).

Further elution of the column afforded a syrup of the methyl ester of (*E*)-5-hydroxy-5,7-dimethylocta-2,6-dienoic acid (7; $R^1 = R^2 = R^3$ = Me, R = H), R_F (hexane–diethyl ether 3 : 1) 0.4; $\nu_{max.}$ 3 450 (OH), 1 710 (C=O), 1 650 (C=C), and 980 cm^{-1} (*trans*-CH=CH); τ 3.1 (d, t, *J* 16 and 8 Hz, CH=C–CO), 4.28 (d, *J* 16 Hz, C=CH–CO), 4.8 (s, C=CH–C), 6.35 (s, OMe), 7.55 (s, OH), 7.61 (d, *J* 8 Hz, CH_2–C=C), 8.17 (s, Me–C=C), 8.31 (s, Me–C=C), and 8.72 (s, Me–C).

(E)-4-(1,5,5-*Trimethyl*-3-*oxocyclohexyl*)*but*-2-*enoic acid* (8; R^1 = Me, $R^2R^3 = CH_2CMe_2CH_2$, R = H).—The crude acid was obtained as a syrup (10.1 g) from crotonic acid 5.6 g) and isophorone (9.0 g), on addition at −70 °C and stirring for 2 h at 0 °C. The oxo-acid crystallized as white prisms from benzene, m.p. 98—99 °C (Found: C, 69.2; H, 9.3. $C_{13}H_{20}O_3$ requires C, 69.2; H, 8.9%); $\nu_{max.}$ 3 000 (OH), 1 700 (C=O), 1 665 (CO_2H), 1 635 (C=C), and 995 cm^{-1} (*trans*-CH=CH).

Methyl ester. This compound was obtained as an oil, R_F 0.5; $\nu_{max.}$ 1 715 (C=O), 1 650 (C=C), and 980 cm^{-1} (*trans*-CH=CH); τ 2.96 (d, t, *J* 16 and 8 Hz, CH=C–CO), 4.14 (d, *J* 16 Hz, C=CH–CO), 6.27 (s, OMe), 7.76 (d, *J* 8 Hz, CH_2–C=C), 7.8 (s, 2 × CH_2), 8.38 (s, CH_2–CO), and 8.93 (s, 3 × Me)

Reaction of Dimethylacrylic Acid with Isophorone.—Dimethylacrylic acid (6.5 g) and isophorone (9.0 g) were allowed to react at −70 °C and for 2 h at 40—50 °C to give a syrup (9.94 g). Column chromatography through acidified silica gel of an aliquot (1.5 g) gave white prisms of the oxo-acid (9; R^1 = Me, $R^2R^3 = CH_2CMe_2CH_2$, R = Me) (0.1 g), m.p. 83—86 °C; τ 1.2br (s, OH), 4.17 (s, C=CH–CO),

7.08 and 7.4 (2 × d, J 13 Hz, CH_2–C=C), 7.9 (s, 2 × CH_2), 8.03 (s, Me–C=C), 8.29 and 8.32 (2 × CH_2–CO), and 8.94 (s, 3 × Me). The methyl ester had R_F 0.6; $\nu_{max.}$ 1 710 (C=O) and 1 635 cm^{-1} (C=C); τ 4.22 (s, C=CH–CO), 6.37 (s, OMe), 7.01 and 7.44 (2 × d, J 13, CH_2–C=C), 7.9 (s, 2 × CH_2), 8.29 and 8.38 (2 × s, CH_2–CO), and 8.95 (s, 3 × Me).

Further elution gave white prisms of the oxo-acid (8; R^1 = Me, R^2R^3 = $CH_2CMe_2CH_2$, R = Me) (0.8 g), m.p. 51—54 °C; $\nu_{max.}$ 3 000 (OH), 1 710 (C=O), 1 690 (CO_2H), and 1 630 cm^{-1} (C=C); τ −0.5 (s, OH), 4.33 (s, C=CH–CO), 7.8 (s, Me–C=C, CH_2–C=C, 2 × CH_2), 8.37 (s, CH_2CO), and 8.92 (s, 3 + Me). The methyl ester had R_F 0.5; $\nu_{max.}$ 1 710 (C=O) and 1 640 cm^{-1} (C=C); τ 4.38 (s, C=CH–CO), 6.33 (s, OMe), 7.8 (s, Me–C–C, CH_2–C=C, 2 × CH_2), 8.37 (s, CH_2CO), and 8.92 (s, 3 × Me).

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