

atoms, while all hydrogen atoms were located from a difference Fourier synthesis. The structure was refined to an R value of 0.040 with anisotropic thermal parameters assigned to the carbon and oxygen atoms, and fixed isotropic temperature factors assigned to the hydrogen atoms. A stereoscopic view of the acetate (oxygen atoms shaded) summarising the X-ray results to be discussed in detail elsewhere,³ is given in Fig. 1.

The absolute configuration of the new thunberganoid (1*S*,4*S*,8*R*,11*S*,12*R*) was inferred from the CD-curves of the corresponding 11-*O*-benzoate and 11-*O*-*p*-nitrobenzoate. These displayed positive 1L_a bands at 227 (MeOH, $\Delta\epsilon_{227} \approx 0.1$) and 260 nm (MeOH, $\Delta\epsilon_{260} \approx 0.2$), respectively, in compliance with the fact that C(12), which is vicinal to the benzyloxyated C(11) and carries the ether oxygen, occurs in a positive sector when a Dreiding model of the benzoate possessing the stereostructure and conformation shown in Fig. 1 is aligned according to the benzoate sector rule.^{4,5}

Since the new compound (*1*) possesses the expected 1*S*-configuration and the chirality at C(4) is *S*, it is likely to be derived from the known tobacco diol (*3*) (cf. Scheme 1). Similar to other ether bridged tobacco thunberganoids of established absolute configuration, whose formation can be viewed as a result of an oxidative attack on the 11,12-double bond from the α -side of the appropriate 4,8-diols and anchimeric assistance by the 8-hydroxy-group in the formation of the 8,11-ether bridge, it can be inferred from the 11-*S*,12-*R*-configuration of *1* that it is formed in a corresponding manner involving the 11*S*,12-*S*-epoxide (*4*) or related species as intermediate.

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Alkylation of Enamines. A Convenient Route to 1,4-Dicarbonyl Compounds

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Methods for preparation of 1,4-dicarbonyl compounds are of current interest, and have been subject to a recent review.¹ Alkylation of enamines with α -halocarbonyl compounds have been reported previously, although these reports deal with enamines derived from cyclic ketones and aldehydes.²⁻⁵

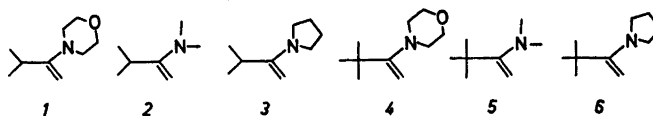
In the present investigation we have studied the reactions of enamines derived from acyclic aliphatic ketones towards several α -bromocarbonyl compounds, as a possible route to acyclic 1,4-dicarbonyl compounds. The enamines used were the morpholino, dimethylamino and pyrrolidino derivatives of methyl isopropyl ketone and methyl *tert*-butyl ketone (pinacolone), respectively. The α -bromocarbonyl compounds used were bromomethyl isopropyl ketone,⁶ bromomethyl *tert*-butyl ketone,⁷ bromomethyl phenyl ketone,⁸ and ethyl bromoacetate. The reactions were carried out using equimolar amounts or excess of enamine, without any solvent present.

Results and discussion. The yields of the 1,4-dicarbonyl compounds obtained in the reactions of α -bromocarbonyl compounds with the enamines are summarized in Table 1 (calculated from ^1H NMR spectra). Physical data are summarized in Table 2. The reaction mechanism is under consideration and will be reported later.

Experimental. The IR spectra were obtained on neat samples using a Perkin Elmer 257 spectrometer, the ^1H NMR spectra were recorded on a JEOL C60-HL spectrometer and the ^{13}C NMR spectra were recorded on a JEOL PFT-60HL spectrometer. TMS was used as internal standard. Deuteriochloroform (^1H NMR) was used as solvent, and the sample concentrations were ca. 1 M. ^{13}C NMR spectra were obtained using neat samples and a D_2O capillary. Probe temperature 23 °C.

Alkylation of enamines. A typical procedure was: Bromomethyl *tert*-butyl ketone, 1.90 g (10.6 mmol), was placed in an Erlenmeyer flask equipped with a magnetic stirrer, dropping funnel and reflux condenser fitted with a CaCl_2 drying tube. 2-Dimethylamino-3-methyl-1-butene, 6.3 g (56 mmol, excess), was added in portions to the stirred bromoketone, the stirring being continued for 0.5 h to ensure complete reaction. The precipitated ketoimmonium salt was hydrolyzed with 20 ml of acidulated (HCl) water and stirred for an additional 0.5 h. The aqueous phase was extracted with 2×50 ml of ether, and the combined ethereal layers were treated with 10 ml

Table 1. Yields (%) of 1,4-dicarbonyl compounds. Without asterisk: excess enamine; with asterisk: equimolar amounts of bromoketone and enamine.



α -Bromocarbonyl compound	1	2	3	4	5	6
Bromoethyl isopropyl ketone	58	85	75	trace	29*	59*
Bromomethyl <i>t</i> -butyl ketone	trace	87	40	—*	trace	51*
Bromomethyl phenyl ketone	73	59*	—*	—*	35*	72*
Ethyl bromoacetate	—	40	44	—*	63	88

Table 2. Physical data of 1,4-dicarbonyl compounds formed.

Compound	IR (cm ⁻¹)	¹³ C NMR (ppm)	¹ H NMR (δ)
(CH ₃) ₂ CHCOCH ₂ CH ₂ COCH(CH ₃) ₂	1709 (C=O)	211.1 (C=O)	1.1 (d, 12 H, <i>J</i> = 7 Hz), 2.8 (s, 4 H) 2.7 (sept, 2 H, <i>J</i> = 7 Hz, part. overlapped)
(CH ₃) ₂ CHCOCH ₂ CH ₂ COC(CH ₃) ₃	1707 (C=O)	212.4 (<i>t</i> -BuCO) 211.1 (<i>i</i> -PrCO)	1.1 (d, 6 H, <i>J</i> = 7 Hz), 2.8 (s, 4 H) 2.7 (sept, 1 H, <i>J</i> = 7 Hz, part. overlapped) 1.2 (s, 9 H)
(CH ₃) ₃ CCOCH ₂ CH ₂ COC(CH ₃) ₃	1706 (C=O)	212.7 (C=O)	1.2 (s, 18 H), 2.8 (s, 4 H)
C ₆ H ₅ COCH ₂ CH ₂ COCH(CH ₃) ₂	1710 (<i>i</i> -PrCO) 1687 (PhCO)	211.9 (<i>i</i> -PrCO) 198.0 (PhCO)	1.1 (d, 6 H, <i>J</i> = 7 Hz), 3.0 (m, 4 H) 2.7 (sept, 1 H, <i>J</i> = 7 Hz, part. overlapped) 8.1–7.9 (m, 2 H) 7.6–7.3 (m, 3 H)
C ₆ H ₅ COCH ₂ CH ₂ COC(CH ₃) ₃	1702 (<i>t</i> -BuCO) 1686 (PhCO)	213.0 (<i>t</i> -BuCO) 197.8 (PhCO)	1.2 (s, 9 H), 3.1 (m, 4 H) 8.1–7.9 (m, 2 H), 7.6–7.3 (m, 3 H)
CH ₃ CH ₂ O ₂ CCH ₂ CH ₂ COCH(CH ₃) ₂	1714 (<i>i</i> -PrCO) 1737 (R-COO)	211.3 (<i>i</i> -PrCO) 172.4 (R-COO)	1.2 (d, 6 H, <i>J</i> = 6.5 Hz), 2.7 (m, 4 H) 1.3 (t, 3 H, <i>J</i> = 7 Hz) 2.5 (sept, 1 H, <i>J</i> = 6.5 Hz, part. overlapped) 4.2 (quart, 2 H, <i>J</i> = 7 Hz)
CH ₃ CH ₂ O ₂ CCH ₂ CH ₂ COC(CH ₃) ₃	1708 (<i>t</i> -BuCO) 1736 (R-COO)	212.5 (<i>t</i> -BuCO) 172.3 (R-COO)	1.2 (s, 9 H), 2.7 (m, 4 H) 1.3 (t, 3 H, <i>J</i> = 6.5 Hz) 4.1 (quart, 2 H, <i>J</i> = 6.5 Hz)

of 2% NaHCO₃ solution and washed with 3 × 10 ml of water. The organic layer was dried (MgSO₄) and the ether evaporated *in vacuo*, yielding 1.70 g (87%) of 2,2,7-trimethyl-3,6-octanedione (calculated from ¹H NMR spectra).

For preparative scale: 2-Dimethylamino-3-methyl-1-butene, 13.0 g (0.12 mol), was added in portions to bromomethyl phenyl ketone 19.9 g (0.10 mol) with stirring followed by the procedure given above. The yield obtained after distillation (119–120 °C/0.3 mmHg) was 12.0 g (59%) of 1-phenyl-5-methyl-1,4-hexanedione.

The haloketones were prepared according to methods described in the literature.^{6–8} Com-

mercially available ethyl bromoacetate was used. The enamines were prepared according to White and Weingarten.⁹

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The Crystal Structure of Succinylcholine Chloride Dihydrate

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The crystal structures of three different succinylcholine salts have earlier been determined.¹⁻⁴ Succinylcholine chloride is the only choline ester salt known to crystallize as a

hydrate. It was therefore found worth-while to examine the crystal structure as part of solid state studies of choline ester salts, in which hydrogen bonding of the choline ester ion cannot *a priori* be excluded.

Bond lengths and angles calculated from the final parameters (Table 1) are shown in Fig. 1 and are in general agreement with accepted values. The conformations of the succinylcholine ions in the present crystal structure (the torsion angles are given in the legend to Fig. 1) and in the crystals of succinylcholine perchlorate⁵ are approximately the same. A stereo view of the crystal packing is given in Fig. 2. The water oxygen atom is donor for two hydrogen bonds O11-H111...Cl⁻_{x, -y, 1-z} and O11-H112...Cl⁻. The O...Cl⁻ distances are 3.300(4) and 3.255(4) Å, respectively, and the O-H...Cl⁻ angles are 170(3) and 172°(5), respectively. No hydrogen bonding involves the ester oxygen atoms O3 and O4. The ability of choline ester ions to be acceptors for hydrogen bonds seems to be low, as the same situation now has been found in several choline ester salts: Acetylcholine β -resorcyate,⁵ acetylcholine (+)-bitartrate⁶ (both of which have two formula units in the asymmetric unit), γ -aminobutyric acid choline ester diiodide and (\pm)-tartrate,⁷ lactoylcholine iodide,⁸ and the present structure.

Experimental. Succinylcholine chloride dihydrate appears as a white microcrystalline material. Several attempts to grow single crystals from a variety of solvents using different techniques have been unsuccessful. Finally a few transparent crystals were found among the microcrystalline material obtained by slow evaporation of an aqueous solution.

Crystal data. Succinylcholine chloride dihydrate, C₁₄H₃₄N₂O₆Cl₂, $M = 397.34$, m.p. 190–191 °C. Space group $P\bar{1}$, $a = 8.941(4)$, $b =$

Table 1. Final positional and thermal parameters. The estimated standard deviations, referring to the last figure, are given in parentheses. Thermal parameters are $\times 10^3$. The temperature factor is defined by:

$$\exp [-2\pi^2(U_{11}h^2a^{*2} + \dots + 2U_{12}hka^*b^* + \dots)]$$

ATOM	x/B	y/A	z/C	U11	U22	U33	U12	U13	U23
C 1	.0895(4)	.5084(5)	.5768(3)	2.4(1)	4.5(2)	2.4(1)	0.6(1)	1.0(1)	1.1(1)
C 2	.2318(4)	.4385(4)	.5416(3)	2.5(1)	3.8(2)	2.6(2)	0.5(1)	0.8(1)	1.3(1)
O 3	.2157(3)	.3876(4)	.4108(3)	3.3(1)	6.3(1)	3.0(1)	1.2(1)	1.5(1)	1.5(1)
O 4	.3865(3)	.4383(4)	.6777(3)	2.4(1)	6.0(1)	2.9(1)	1.1(1)	1.0(1)	1.8(1)
C 5	.5245(4)	.3509(6)	.6498(4)	3.2(2)	7.1(2)	3.8(2)	1.4(2)	1.9(1)	2.6(2)
C 6	.6563(4)	.3760(5)	.8088(4)	2.6(2)	5.2(2)	4.0(2)	0.5(1)	1.5(1)	1.9(1)
N 7	.7170(3)	.2245(4)	.8963(3)	2.3(1)	3.5(1)	2.5(1)	0.6(1)	1.1(1)	0.8(1)
C 8	.5963(4)	.2570(6)	.9590(4)	3.1(2)	6.0(2)	4.1(2)	1.3(1)	2.2(1)	2.2(2)
C 9	.6908(5)	.0041(6)	.7949(5)	4.0(2)	4.2(2)	3.8(2)	0.5(1)	1.2(2)	0.0(1)
C 10	.9047(4)	.2669(5)	1.0390(4)	2.4(1)	4.7(2)	3.3(2)	0.3(1)	1.0(1)	0.7(1)
O11	-.2375(4)	.0587(5)	.4630(4)	4.0(2)	9.6(2)	4.8(2)	-0.7(1)	1.9(1)	0.3(2)
Cl-	-.1331(1)	.1470(1)	.8119(1)	4.35(5)	5.12(5)	3.72(5)	-0.04(3)	2.03(4)	1.20(3)

ATOM	x/A	y/B	z/C	ATOM	x/A	y/B	z/C
H 11	.121(5)	.647(6)	.643(5)	H 91	.571(5)	-.026(5)	.717(5)
H 12	.085(5)	.427(5)	.638(5)	H 92	.767(5)	-.009(6)	.757(5)
H 51	.492(5)	.188(6)	.587(4)	H 93	.714(5)	-.082(6)	.800(5)
H 52	.548(5)	.439(5)	.600(5)	H101	.977(5)	.242(5)	.994(4)
H 61	.792(5)	.359(5)	.787(4)	H102	.916(5)	.414(6)	1.102(5)
H 62	.711(5)	.525(6)	.887(4)	H103	.914(5)	.176(6)	1.097(5)
H 81	.623(5)	.405(6)	1.030(5)	H111	-.200(5)	.015(6)	.407(5)
H 82	.472(5)	.224(5)	.864(5)	H112	-.149(6)	.070(6)	.538(5)
H 83	.614(5)	.170(6)	1.020(5)				