A Facile Synthesis of Dialkoxycarbonylketene-, Dicyanoketene-, and Alkoxycarbonyl(cyano)ketene Ethylene Acetals

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In reverence to and grateful remembrance of the late David Ginsburg, Department of Chemistry, TECHNION, Haifa, Israel.

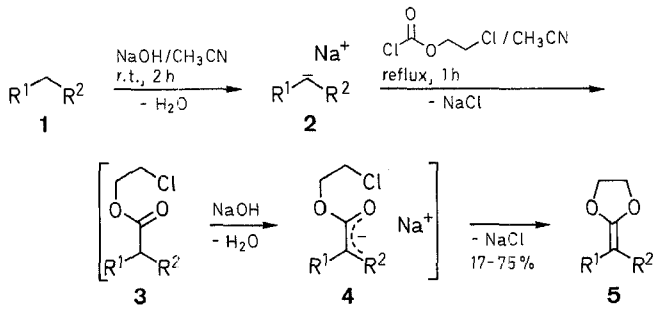
Dicyanoketene-, dialkoxycarbonylketene- and alkoxycarbonyl(cyano) ketene ethylene acetals can be conveniently prepared by reaction of malononitrile, dialkyl malonates and alkyl cyanoacetates with 2-chloroethyl chloroformate.

2-Alkylidene-1,3-dioxolanes **5** bearing cyano and/or alkoxycarbonyl groups at the exocyclic carbon atom are as cyclic ketene acetals very useful synthons for the preparation of diverse heterocyclic compounds.[2] Their great synthetical potential is due to a masked ketene functionality as well as to the presence of easily convertible cyano and ester groups.

With the exception of 2-dicyanomethylene-1,3-dioxolane **(5e)** which was obtained by the reaction of tetracyanoethylene with ethylene glycol,[3,4] these compounds have not been known so far. The parent ketenes, except from dicyanoketene[5–8] and bis(ethoxycarbonyl)ketene,[9,10] are also unknown. Analogous cyclic ketene dithioacetals have been known for the last 25 years.

They were prepared by the reaction of carbon disulfide with the appropriate active methylene compounds in the presence of a base and subsequent cyclization of the resulting products with 1,2-dibromoethane.[11] 2-(Dicyanomethylene)-1,3-dioxolane (**5e**) and the sulfur analogues of **5** have already been applied in heterocyclic synthesis.[12,13]

We report here a simple and efficient procedure for the preparation of the title compounds **5** from the respective methylene compounds **1** and 2-chloroethyl chloroformate in acetonitrile using solid sodium hydroxide as base. Detailed studies of the reaction between malononitrile salts and chloroformates as well as structural investigations of the resulting alkali salts of dicyanoacetates[12] suggest that the formation of **5** proceeds via sodium salts **4** which need to be isolated in reaction workings.



1–5	R^1	R^2	1–5	R^1	R^2
a	CN	CO_2Me	**e**	CN	CN
b	CN	CO_2Et	**f**	CO_2Me	CO_2Me
c	CN	CO_2Bu-*t*	**g**	CO_2Et	CO_2Et
d	CN	CO_2Bu-*n*	**h**	CO_2Me	CO_2Bu-*t*

Table 1. Cyclic Ketene Acetals **5** from Active Methylene Compounds **1**

Product 5	Purification Method	Yield[a] (%)	mp (°C)[b] (solvent)
a	A	63	148 (MeOH)
b	A	69	133 (EtOH)
c	B	75	124 ($CHCl_3/Et_2O$)
d	B	17	59 (Et_2O/*n*-hexane)[c]
e	A	75	113 (EtOH)
f	A	59	130 (MeOH)
g	A[d]	62	38 (EtOH)
h	B[d,e]	41	oil

[a] Yield of isolated, pure product **5** based on **1**.
[b] Uncorrected, determined on a Reichert hot stage microscope.
[c] The product was precipitated by cooling in an dry ice/acetone bath.
[d] After removal of CH_3CN the unreacted starting methylene compound **1** was removed by a vacuum distillation.
[e] Additionally purified by column chromatography (silica gel, $CHCl_3$/MeOH, 9:1).

Methyl Cyano(1,3-dioxolan-2-yliden)acetate (5a); Typical Procedure:
To a solution of methyl cyanoacetate (9.9 g, 100 mmol) in CH_3CN (200 mL) finely powdered NaOH (8.0 g, 200 mmol) is added. The resulting suspension is stirred at room temperature for 2 h. During this time, the sodium salt of **1** separates as a fine white precipitate. Then, a solution of 2-chloroethyl chloroformate (14.3 g, 100 mmol) in CH_3CN (20 mL) is added dropwise over a period of 15 min with stirring and cooling in an ice/water bath. When the addition is complete, the ice/water bath is removed, and the mixture is heated with stirring under reflux for 1 h. After cooling to room temperature and filtration of NaCl, CH_3CN is removed under reduced pressure. Recrystallization of the residue (Method A) with MeOH gives **5a** as white crystals; yield: 10.65 g (63%); mp 148°C.

Alternatively, the crude product can be adsorbed on silica gel (0.063–0.200 mm, 30 g) and extracted continuously with $CHCl_3$ in a Soxhlett apparatus (Method B). After removal of the solvent analytically pure **5a** is obtained. The yields are in both cases nearly identical.

Table 2. Spectral Data of Compounds **3a–h**

Compound 5	Molecular Formula[a] or Lit. mp (°C)	IR[b] (KBr/film)[c] ν (cm^{-1})	UV/VIS[d] (CH_3CN) λ_{max} (nm) (log ε)	^{1}H-NMR[e] (DMSO-d_6/$CDCl_3$)[f] δ, J (Hz)	^{13}C-NMR[g] (DMSO-d_6) δ	MS (100 eV)[h] *m/z* (%)
a	$C_7H_7NO_4$ (169.1)	2220, 1740, 1585	240 (4.24)	3.64 (s, 3H); 4.70–4.78 (m, 2H); 4.83–4.91 (m, 2H)	51.32 (q); 58.56 (s); 68.98 (t); 71.46 (t); 115.78 (s); 162.84 (s); 175.72 (s)	169 (M^+, 37); 138 (100)
b	$C_8H_9NO_4$ (183.2)	2220, 1730, 1580	240 (4.25)	1.20 (t, 3H, J = 7.0); 4.11 (q, 2H, J = 7.0); 4.70–4.78 (m, 2H); 4.83–4.91 (m, 2H)	14.23 (q); 58.79 (s); 59.90 (t); 68.93 (t); 71.44 (t); 115.81 (s); 162.40 (s); 175.75 (s)	183 (M^+, 34); 138 (100)
c	$C_{10}H_{13}NO_4$ (211.2)	2220, 1715, 1600	240 (4.25)	1.50 (s, 9H); 4.65–4.74 (m, 2H); 4.80–4.88 (m, 2H)	27.79 (q); 59.89 (s); 68.61 (t); 71.15 (t); 80.14 (s); 115.93 (s); 161.60 (s); 175.45 (s)	211 (M^+, 18); 155 (100)
d	$C_{10}H_{13}NO_4$ (211.2)	2220, 1725, 1575	240 (4.27)	0.96 (t, 3H, J = 7.0); 1.42 (sext, 2H, J = 7.5); 1.66 (quint, 2H, J = 7.5); 4.18 (t, 2H, J = 6.5); 4.70–4.78 (m, 2H); 4.82–4.90 (m, 2H)	13.44 (q); 18.50 (t); 30.26 (t); 58.74 (s); 63.49 (t); 68.91 (t); 71.41 (t); 115.73 (s); 162.40 (s); 175.69 (s)	211 (M^+, 17); 138 (100)
e	115–116.5[14]	2230, 1590	235 (4.20)	4.88 (s, 4H)	37.13 (s); 71.86 (t); 112.83 (s); 178.71 (s)	136 (M^+, 39); 43 (100)
f	$C_8H_{10}O_6$ (202.2)	1730, 1575	240 (4.18)	3.76 (s, 6H); 4.63 (s, 4H)	51.09 (q); 68.32 (t); 78.41 (s); 164.72 (s); 170.21 (s)	202 (M^+, 35); 171 (100)
g	$C_{10}H_{14}O_6$ (230.2)	1710, 1610	240 (4.21)	1.17 (t, 6H, J = 6.5); 4.05 (q, 4H, J = 6.5); 4.61 (s, 4H)	14.06 (q); 59.42 (t); 68.19 (t); 79.01 (s); 164.26 (s); 169.86 (s)	230 (M^+, 22); 185 (100)
h	$C_{11}H_{16}O_6$ (244.2)	1730, 1710, 1620	240 (3.98)	1.39 (s, 9H); 3.58 (s, 3H); 4.59 (s, 4H)	27.90 (q); 51.25 (q); 68.33 (t); 68.43 (t); 79.65 (s); 163.90 (s); 165.0 (s); 169.95 (s)	244 (M^+, 2); 103 (100)

[a] Microanalyses were performed on a Heraeus automatical C,H,N-analyser; satisfactory microanalyses obtained: C ±0.33, H ±0.12, N ±0.33, except from **3h** which was characterized by mass spectrometry (peak matching).
[b] Recorded on a Perkin Elmer 325 Spectrophotometer.
[c] KBr disc for **3a**, **3b**, **3c**, **3d**, **3e**, **3f**; film for **3g**, **3h**.
[d] Recorded on a Carl Zeiss DMR 4 Spectrophotometer.
[e] Recorded on a Bruker WM-250 Spectrometer at 250.13 MHz.
[f] DMSO-d_6 for **3a**, **3b**, **3g**, **3h**, $CDCl_3$ for **3c**, **3d**, **3f**.
[g] Recorded on a Bruker WM-250 Spectrometer at 62.89 MHz.
[h] Recorded on a Varian MAT 311 A Instrument.

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