A Convenient Synthesis of Dialkyl (*E*)-2,3-Dicyanobutendioates

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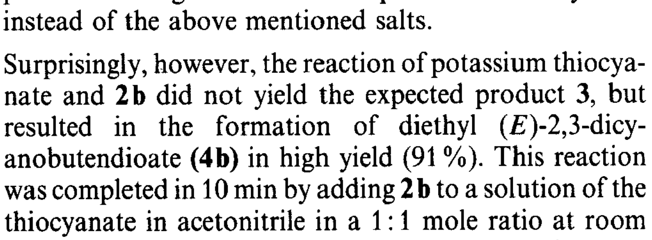
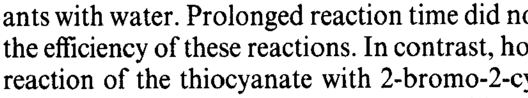
Dialkyl (*E*)-2,3-dicyanobutendioates **4**, potentially useful intermediates for the synthesis of a wide variety of heterocyclic compounds, are conveniently prepared by the reaction of alkyl bromocyanoacetates **2** with potassium thiocyanate in acetonitrile followed by treatment with water. The starting alkyl bromocyanoacetates are prepared by the photochemical reaction of the appropriate alkyl cyanoacetate with bromine in carbon tetrachloride.

The main product in the reaction of ethyl bromocyanoacetate (**2b**) with various nucleophiles[1-10] is triethyl *trans*-1,2,3-tricyanocyclopropane-1,2,3-tricarboxylate (**3**), and this was found to be independent of the nucleophile used. The cyclopropane triester **3** was also obtained by the reaction of **2b** with potassium *tert*-butoxide[11] or with other potassium salts[12] such as cyanate, cyanide, fluoride, or iodide. We attempted to prepare **3** starting from **2b** and potassium thiocyanate instead of the above mentioned salts.

Surprisingly, however, the reaction of potassium thiocyanate and **2b** did not yield the expected product **3**, but resulted in the formation of diethyl (*E*)-2,3-dicyanobutendioate (**4b**) in high yield (91 %). This reaction was completed in 10 min by adding **2b** to a solution of the thiocyanate in acetonitrile in a 1 : 1 mole ratio at room temperature, and subsequently treating the crude reactants with water. Prolonged reaction time did not improve the efficiency of these reactions. In contrast, however, the reaction of the thiocyanate with 2-bromo-2-cyano-*N*,*N*-dimethylacetamide (**5**) gave the nucleophilic substitution product, 2-cyano-2-thiocyanato-*N*,*N*-dimethylacetamide (**6**) in 77 % yield.

The ester **4b** thus obtained is a potentially useful intermediate in the preparation of heterocyclic compounds.





1, 2, 4	R	1, 2, 4	R	1, 2, 4	R
a	Me	d	*i*-Pr	g	*s*-Bu
b	Et	e	Bu	h	$C_{12}H_{25}$
c	Pr	f	*i*-Bu	i	*c*-C_6H_{11}

We investigated further the behavior of the thiocyanate with other alkyl bromocyanoacetates **2a,c–i** (Table 1). Interestingly, enough, these esters were also transformed under the same reaction conditions into the corresponding alkoxycarbonylethylenes **4a,c–i** in excellent yields (67–93 %) (Tables 2 and 3).

Three different procedures have been reported[4,13,14] for the synthesis of compound **4b**, but the yields were very low (10–14 %). Compound **4b** was also obtained by the reaction of ethyl cyanoacetate with thionyl chloride in 64 % yield,[15] if the reaction was allowed to proceed for 3 h at high temperatures. This method, however, is relatively limited as drastic reaction conditions are required, and the difficulty in obtaining reproducible yields. Furthermore, this method could not be applied to the synthesis of the other alkoxycarbonylethylenes **4** possessing alkyl groups higher than ethyl, because the desired ethylenes **4** are obtained in very low yields with considerable decomposition, as exemplified in the cases of propyl- and *iso*butyl cyanoacetates. Consequently, the significantly higher yields of alkoxycarbonylethylenes **4a–i** under the mild and simple reaction conditions as compared to the literature show the advantages of the present method.

All the synthesized compounds **4a–i** are identified by their microanalyses, IR, ^1H- and ^{13}C-NMR, and mass spectral data. The IR spectra show no absorption band attributable to the nitrile group, but the ester carbonyl appears at $\nu = 1727–1743\ cm^{-1}$. Mass spectra are, at first sight, very similar. For all compounds the expected molecular ion peak was not observed, but the $M^+ + 1$ ion peak was detected usually of medium intensity. The geometry of double bond in compounds **4a,b** is specified as (*E*)-configuration on the basis of the literature.[15] The new compounds **4c–i** are also assigned (*E*)-stereochemistry, by comparing the mass and ^{13}C-NMR spectral data with those of several known (*E*)- and (*Z*)-butendioic esters.[16,17].

The starting methyl and ethyl bromocyanoacetates **2a** and **2b** are generally obtained by direct bromination of the corresponding ester with bromine at about 130 °C. Higher alkyl bromocyanoacetates, however, are difficult to synthesize by this procedure, because large quantities of dibromocyanoacetates are simultaneously formed, which are difficult to separate by distillation. Similar phenomena are also encountered in the synthesis of **2a** and **b**, and both esters are not obtained in a satisfactorily yield. We present herein a favorable alternative method for the synthesis of alkyl bromocyanoacetates **2a–i**. This method uses the photochemical reaction of the appropriate cyanoacetate with bromine in carbon tetrachloride, and appears to be quite general for lower and higher esters **2a–i**. It should be noted that the pure bromoesters **2a–i** on exposure to light are gradually converted into the corresponding dibromoacetates.

Melting points and boiling points are uncorrected. Microanalyses were obtained using a Perkin-Elmer Model 240 element analyser. ^{1}H-NMR spectra were recorded on either a JEOL C-60 HL (60 MHz) or a Varian VXR-300 (300 MHz) instrument. ^{13}C-NMR spectra were taken on a Varian VXR-300 (74.45 MHz) instrument.

IR spectra were recorded on a Perkin–Elmer 283 spectrophotometer. High resolution mass spectra were obtained with a Hitachi M-80 mass spectrometer (EI: 70 eV). *s*-Butyl, cyclohexyl, and dodecyl cyanoacetate used were prepared according to literature.[18] Their boiling points and melting points agreed with the literature values.[16,19,20] All other cyanoacetates and 2-bromo-2-cyano-*N*,*N*-dimethylacetamide were purchased from Tokyo Kasei Co., and distilled before use. The acetamide was used without purification. Column chromatography was performed on silica gel Merck 60 (70–230 mesh). All solvents were dried under standard conditions, if necessary.

Alkyl Bromocyanoacetates 2; General Procedure:
To a Pyrex photochemical reaction vessel are added the appropriate cyanoacetate (0.22 mol) and CCl_4 (100 mL), and the mixture is magnetically stirred and thermostated at 100 °C. Br_2 (46 g, 0.287 mol) is added dropwise under irradiation with a high pressure mercury lamp UVL 100 W (Riko Science Co.) to the well-stirred CCl_4 solution over a period of 1 h. The Br_2 is decolorized immediately and gaseous HBr is vigorously evolved. The irradiation is

Table 1. Alkyl Bromocyanoacetates **2** Prepared

Product	Yield (%)	bp (°C)/mbar	Molecular Formula[a] or Lit. bp (°C)/mbar	MS *m*/*z* (%)
2a	61	85–89/5	49–63/0.4[21]	180 (M^+ + 3,35), 178 (M^+ + 1,36), 135 (100), 133 (100), 114 (77), 113 (60), 100 (38), 72 (83)
2b	94	69–71/3.5	135/40[22]	194 (M^+ + 3, 100), 192 (M^+ + 1, 99), 175 (23)
2c	78	92–95/5	$C_6H_8BrNO_2$ (206.0)	208 (M^+ + 3, 88), 206 (M^+ + 1, 93), 170 (41), 168 (45), 128 (100)
2d	70	75–77/5.5	$C_6H_8BrNO_2$ (206.0)	208 (M^+ + 3, 51), 206 (M^+ + 1, 53), 148 (48), 146 (48), 128 (66), 86 (33), 68 (85), 45 (38), 43 (100), 41 (48)
2e	75	101–103/5	$C_7H_{10}BrNO_2$ (220.1)	222 (M^+ + 3, 100), 220 (M^+ + 1, 100), 198 (74), 142 (65), 57 (69), 56 (32)
2f	63	76–77/3	$C_7H_{10}BrNO_2$ (220.1)	222 (M^+ + 3, 82), 220 (M^+ + 1, 86), 198 (100), 142 (65), 57 (86), 56 (30)
2g	65	72–73/2	$C_7H_{10}BrNO_2$ (220.1)	222 (M^+ + 3, 51), 220 (M^+ + 1, 53), 148 (58), 146 (59), 142 (76), 68 (97), 57 (100), 56 (40), 45 (38), 41 (54)
2h	44	163–170/3.5	$C_{15}H_{26}BrNO_2$ (332.3)	334 (M^+ + 3, 7), 332 (M^+ + 1, 17), 252 (44), 169 (100), 111 (89), 99 (40), 98 (44), 97 (98), 85 (83), 84 (63), 83 (98), 71 (82), 70 (71), 69 (93), 57 (88), 55 (78)
2i	79	108–115/2.5	$C_9H_{12}BrNO_2$ (246.1)	248 (M^+ + 3, 78), 246 (M^+ + 1, 81), 168 (47), 83 (100), 82 (72), 81 (48), 67 (76)

[a] Satisfactory microanalyses obtained: C ±0.25, H ±0.07, N ±0.10.

Table 2. Dialkyl (*E*)-2,3-Dicyanobutendioates **4** Prepared

Product	Yield (%)	mp (°C)[a]	Molecular Formula[b] or Lit. mp (°C)	IR (KBr) ν(cm^{-1})	MS *m*/*z* (%)
4a	90	177–178.5	176–177[17]	1738	195 (M^+ + 1, 18), 164 (100), 163 (94), 91 (61), 59 (65)
4b	91	117.5–118.5	115–116[15]	1728	223 (M^+ + 1, 89), 195 (68), 177 (100), 167 (47), 150 (79), 106 (47), 77 (74)
4c	93	115–116	$C_{12}H_{14}N_2O_4$ (250.3)	1730	251 (M^+ + 1, 18), 209 (45), 167 (100), 43 (100), 42 (51)
4d	93	126–127	$C_{12}H_{14}N_2O_4$ (250.3)	1727	251 (M^+ + 1, 22), 209 (38), 191 (57), 167 (39), 150 (46), 57 (87), 56 (100)
4e	87	93–94	$C_{14}H_{18}N_2O_4$ (278.3)	1730	279 (M^+ + 1, 21), 223 (52), 167 (42), 150 (46), 57 (100), 56 (100)
4f	91	113.5–114	$C_{14}H_{18}N_2O_4$ (278.3)	1743	279 (M^+ + 1, 12), 223 (56), 150 (100), 57 (100), 56 (100), 43 (46), 41 (61)
4g	73	87–88	$C_{14}H_{18}N_2O_4$ (278.3)	1727	279 (M^+ + 1, 44), 223 (100), 205 (99), 193 (100), 167 (60), 150 (47), 149 (74), 57 (100), 56 (95)
4h	88	92.5–93	$C_{30}H_{50}N_2O_4$ (502.7)	1739	503 (M^+ + 1, 11), 334 (100), 168 (62), 111 (64), 97 (76), 83 (57), 69 (55), 57 (48)
4j	67	106–107	$C_{18}H_{22}N_2O_4$ (330.4)	1727	331 (M^+ + 1, 18), 168 (75), 99 (55), 83 (100), 82 (100), 81 (62), 67 (100), 55 (86), 41 (46)

[a] Compound **4a** is recrystallized from CH_3CN, the rest from EtOH.
[b] Satisfactory microanalyses obtained: C ±0.25, H ±0.06, N ±0.10.

Table 3. NMR Data of Compounds **4**

Product	^{1}H-NMR ($CDCl_3$/TMS) δ, J(Hz)	^{13}C-NMR ($CDCl_3$/TMS) δ
4a	4.05 (s, CH_3)	55.1 (CH_3), 111.1 (CN), 125.8 (C=C), 158.0 (CO)
4b	1.44 (t, 6H, J = 7.1, CH_3), 4.49 (q, 4H, J = 7.1, CH_2)	13.8 (CH_3), 65.2 (CH_2), 111.3 (CN), 126.0 (C=C), 157.6 (CO)
4c	1.03 (t, 6H, J = 7.4, CH_3), 1.83 (tq, 4H, J = 7.4, 6.6, $\underline{CH_2}CH_3$), 4.39 (t, 4H, J = 6.6, OCH_2)	10.2 (CH_3), 21.7 ($\underline{C}H_2CH_3$), 70.5 (OCH_2), 111.3 (CN), 126.0 (C=C), 157.7 (CO)
4d	1.42 (d, 12H, J = 6.2, CH_3), 5.28 (sept, 2H, J = 6.2, CH)	21.4 (CH_3), 74.2 (CH), 111.3 (CN), 126.1 (C=C), 157.2 (CO)
4e	0.97 (t, 6H, J = 7.4, CH_3), 1.46 (sext, 4H, J = 7.4, $\underline{CH_2}CH_3$), 1.78 (tt, 4H, J = 7.4, 6.7, $\underline{CH_2}CH_2CH_3$), 4.43 (t, 4H, J = 6.7, OCH_2)	13.5 (CH_3), 18.9 ($\underline{C}H_2CH_3$), 30.1 ($CH_2CH_2CH_2$), 68.9 (OCH_2), 111.3 (CN), 125.9 (C=C), 157.7 (CO)
4f	1.03 (d, 12H, J = 6.7, CH_3), 2.11 (nonet, 2H, J = 6.7, CH), 4.21 (d, 4H, J = 6.7, OCH_2)	18.8 ($2CH_3$), 27.6 (CH), 74.8 (CH_2), 111.3 (CN), 125.9 (C=C), 157.6 (CO)
4g	0.98 (t, 6H, J = 7.5, $CH_2C\underline{H_3}$), 1.39 (d, 6H, J = 6.3, $CHC\underline{H_3}$), 1.68–1.87 (m, 4H, CH_2), 5.12 (sext, 2H, J = 6.3, CH)	9.5 ($CH_2\underline{C}H_3$), 19.3 ($CH\underline{C}H_3$), 28.4 (CH_2), 78.7 (CH), 111.4 (CN), 126.1 (C=C), 157.3 (CO)
4h	0.88 (t, 3H, J = 6.7, CH_3), 1.26 (br s, 18H, CH_2), 1.78 (tt, 4H, J = 6.8, 6.7, OCH_2CH_2), 4.41 (t, 4H, J = 6.7, OCH_2)	14.1 (CH_3), 22.7, 25.6, 28.2, 29.1, 29.4, 29.5, 29.6 ($9CH_2$), 31.9 (OCH_2CH_2), 69.2 (OCH_2), 111.3 (CN), 126.0 (C=C), 157.7 (CO)
4i	1.37–1.99 (several m, 20H, CH_2), 5.08 (tt, 2H, J = 8.7, 3.9, 2CH)	23.2 (C-3′), 25.0 (C-4′), 31.0 (C-2′), 78.6 (CH), 111.5 (CN), 126.1 (C=C), 157.2 (CO)

maintained for a further 1 h after completion of the Br_2 addition. The residual oil obtained after removal of the solvent is purified by careful fractional distillation under reduced pressure to give the desired bromocyanoacetate **2**. The exact purity of the distilled ester is determined by ^{1}H-NMR analysis before use for subsequent reaction. The resulting bromocyanoacetates are chromatographed on silica gel (eluent: hexane/EtOAc, 9:1) to give analytically pure esters (Table 1).

Dialkyl (*E*)-2,3-Dicyanobutendioates 4; General Procedure:

To a magnetically stirred solution of KSCN (0.48 g, 4.92 mmol) in CH_3CN (10 mL) is added dropwise a solution of the freshly distilled appropriate bromocyanoacetate **2** (4.92 mmol) in CH_3CN (2 mL) over a period of 5 min at r.t. The solution becomes immediately opaque and the reaction mixture is further stirred for an additional 5 min. The resulting mineral salts are filtered, and the filtrate is concentrated to dryness under reduced pressure. The slightly yellow oil thus obtained is poured into H_2O (500 mL) with vigorous stirring, and further stirred for 30 min. The H_2O layer becomes pale yellow, and almost colorless precipitate is formed. Pure compounds **4a–i** are obtained after recrystallization from CH_3CN or EtOH (Tables 2 and 3).

2-Cyano-2-thiocyanato-*N*,*N*-dimethylacetamide (6):

To a suspension of powdered KSCN (2.04 g, 21 mmol) in CH_3CN (30 mL) is added the 2-bromoacetamide **5** (4.0 g, 21 mmol), and stirring is continued at r.t. for 20 min. The inorganic salts begin to form immediately. The salts are filtered, and the solvent is removed under reduced pressure using a rotary evaporator. The residue is cooled and triturated with benzene (20 mL). The yellow solid thus formed is collected, washed with cold Et_2O (2 mL) and recrystallized from EtOH (20 mL); yield: 2.71 g (77%); mp 96.5–97.5 °C.

$C_6H_7N_3OS$	calc.	C 42.59	H 4.16	N 24.83
(169.2)	found	42.52	4.20	24.78

IR (KBr): ν = 2241, 2158, 1653, 1484, 1404, 1260, 1136, 1057, 769, 698, 591 cm^{-1}.

MS (70 eV): m/z (%) = 170 (M^+ + 1,3), 84 (9), 73 (100), 44 (9), 42 (18).

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