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New Synthesis Route for 1,1,2,2-Tetracyanocyclopropanes

by

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1,1-Dimethoxy-2-bromoethylene 1 reacts with tetracyanoethylene (TCNE, 3) at -10° C to form methyl 2,2,3,3-tetracyanocyclopropanecarboxylate 6 in high yield. A similar reaction occurs with 1,1-diethoxy-2-bromoethylene 2 to yield ethyl 2,2,3,3-tetracyanocyclopropanecarboxylate 7. Further, β-bromoethyl 2,2,3,3-tetracyano-1-methylcyclopropanecarboxylate 10 and β-bromoethyl 2,2,3,3-tetracyano-1-ethylcyclopropanecarboxylate 11 were obtained by reacting TCNE with 2-bromomethyl-1-ene 8 and 2-bromoethylidene-1,3-dioxolane 9, respectively. A reaction mechanism via a zwitterion and intra-molecular displacement of bromide is proposed.

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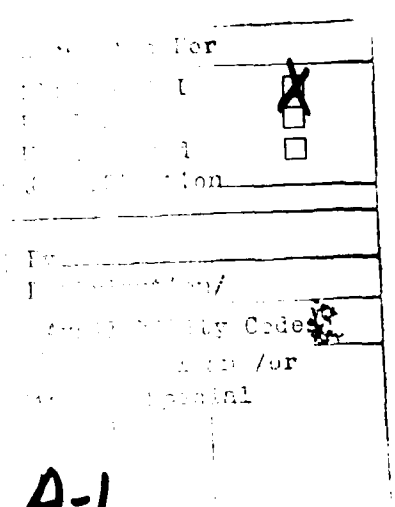


Abstract

1,1-Dimethoxy-2-bromoethylene 1 reacts with tetracyanoethylene (TCNE, 3) at -10°C to form methyl 2,2,3,3-tetracyanocyclopropanecarboxylate 6 in high yield. A similar reaction occurs with 1,1-diethoxy-2-bromoethylene 2 to yield ethyl 2,2,3,3-tetracyanocyclopropanecarboxylate 7. Further, β-bromoethyl 2,2,3,3-tetracyano-1-methylcyclopropanecarboxylate 10 and β-bromoethyl 2,2,3,3-tetracyano-1-ethylcyclopropanecarboxylate 11 were obtained by reacting TCNE with 2-bromomethylidene 8 and 2-bromoethylidene-1,3-dioxolane 9, respectively. A reaction mechanism via a zwitterion and intra-molecular displacement of bromide is proposed.

Introduction

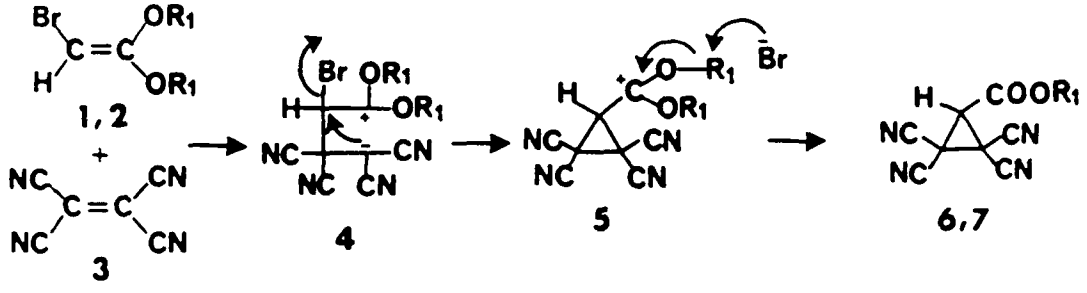
1,1,2,2-Tetracyanocyclopropane can be prepared rather easily by reaction of aqueous formaldehyde and malononitrile[1] or tetracyanoethylene with diazomethane[2]. A large number of substituted 1,1,2,2-tetracyanocyclopropanes are available by the Wideqvist reaction[3,4], in which a carbonyl compound is reacted with two equivalents of bromomalononitrile. A similar cyclopropanation procedure was reported by Hart[5,6].

In a previous report, we described the novel formation of a cyclopropane ring in the reaction of 1,1-diethoxy-2-bromoethylene with ethyl α-cyanoacrylate.[7] A zwitterionic tetramethylene is formed by reaction of the electron-rich olefin with the electron-poor olefin. The expected cyclobutane cycloadduct is not formed. Instead, elimination of the bromide anion takes place with formation of a cyclopropane ring. Dealkylation of the dialkoxycarbocation by Br^- leads to an ester substituent. A similar reaction has been described by Scheeren: β,β-dicyanostyrene with 1,1-diethoxy-2-chloroethylene also yield a cyclopropane derivative as reaction product[8].

In the present work, we react bromoketene acetals with tetracyanoethylene to lead to tetracyanocyclopropanecarboxylates.

Results and Discussion

1,1-Dialkoxy-2-bromoethylenes (1 or 2) react with tetracyanoethylene (TCNE 3) at -10°C to form methyl (6) or ethyl 1,1,2,2-tetracyanocyclopropane carboxylate (7), respectively. In analogy to the α-cyanoacrylate case, the following mechanism is proposed:

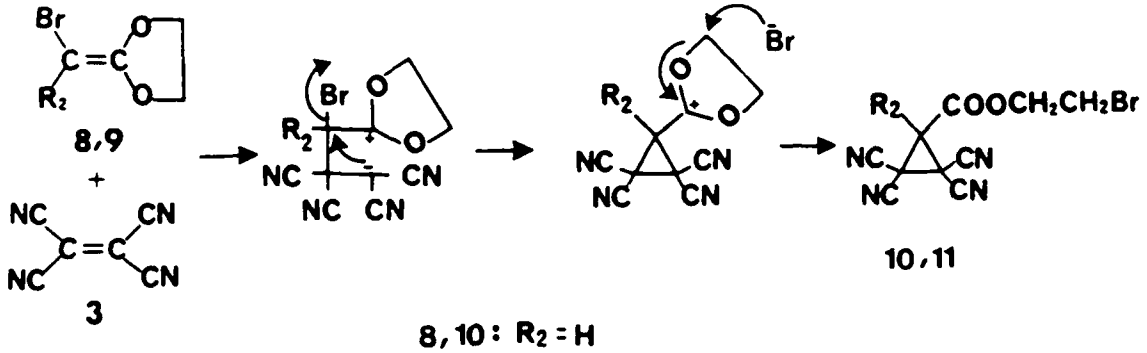


1,6 : $R_1 = CH_3$
2,7 : $R_1 = CH_2CH_3$

The initially formed 1,4-zwitterion 4 undergoes intramolecular elimination of bromide to form the dialkoxycation 5, which in turn undergoes dealkylation to form cyclopropane 6 or 7 and alkyl bromide. When the reaction is carried out in THF as solvent, a large quantity of poly-THF is formed together with the desired cyclopropane. This is additional evidence for the formation of 1,4-zwitterion in the course of reaction, which can initiates the cationic polymerization of THF[9].

1,1-Diethoxy-2-bromopropene was much less reactive than 1,1-diethoxy-2-bromoethylene. Even at room temperature, no reaction occurred when 1,1-diethoxy-2-bromopropene was mixed with TCNE in a 1:1 molar ratio in THF.

Cyclic ketene acetals also undergo the reaction. When 2-(bromomethylidene)-1,3-dioxolane (8) or 2-(bromoethylidene)-1,3-dioxolane (9) is reacted with TCNE, a high yield of 2-bromoethyl 1,1,2,2-tetracyanocyclopropanecarboxylate 10 or 11 is obtained. The cyclic ketene acetal 8 has a tendency to undergo spontaneous cationic polymerization and the cyclopropane was always contaminated by the homopolymer of 8.



8,10 : $R_2 = H$
9,11 : $R_2 = CH_3$

In these cases, the extra methyl group on the double bond of the ketene acetal did not reduce the reactivity significantly.

All 1,1,2,2-tetracyanocyclopropanecarboxylates (6,7,10,11) were very sensitive to base or nucleophile. Saponification to carboxylic acid has failed so far. Even weak bases such as silver acetate, attacked the ring or the cyano groups. We were unable to obtain the vinyl ester derivatives in attempted dehydrobrominations of 10 and 11.

Experimental Section

Instrumentation. All melting points were obtained from a Thomas-Hoover capillary melting point apparatus. ^{1}H-NMR and ^{13}C-NMR spectra were taken on a Bruker WM 250 nuclear magnetic resonance spectrometer at 250 MHz. Infrared spectra were recorded on a Perkin-Elmer 983 spectrometer. Elemental analyses were performed by Desert Analytics, Tucson, AZ.

Materials. Tetrahydrofuran was purified by refluxing with $LiAH_4$ and distilled. Tetracyanoethylene (3) was purchased from Aldrich and was purified by two successive recrystallizations from chlorobenzene and sublimations (125°C, 0.5 mmHg). 1,1-Dimethoxy-2-bromoethylene (1) was obtained by dehydrobromination of 1,1-dibromo-2,2-dimethoxyethane according to a literature procedure[10]. Dibromoacetal was synthesized by bromination of 2-bromo-1,1-dimethoxyethane with bromine and calcium carbonate in dry diethyl ether.

1,1-Diethoxy-2-bromoethylene (2) was prepared following a similar procedure as for 1,1-dimethoxy-2-bromoethylene (1).

Methyl 1,1,2,2-tetracyanocyclopropane carboxylate (6). TCNE (2.56 g, 20 mmole) was dissolved in 30 ml of tetrahydrofuran. The solution under nitrogen was cooled to -10°C in dry ice-ethanol-water. Freshly distilled 1,1-dimethoxy-2-bromoethylene (4.18g, 25 mmole) was added slowly with stirring, and the reaction mixture was stirred for 1 hour. Solvent and methyl bromide were then evaporated by rotary evaporator. The obtained crude product was washed with n-hexane and purified by column chromatography (column size: 4.0 cm/40 cm, diameter/height, adsorbent: Silica Gel, 70-230 mesh, 60Å, eluent: ethylacetate/n-hexane, 40/60, V/V). Yield: 3.52 g (88%). Mp = 175° - 176°C (dec.). IR (KBr): 3051 (CH, cyclopropane), 2261 (CN), 1752 (ester); ^{1}H-NMR (acetone-d_6): δ 3.93 (s, $-COOCH_3$) 4.55 (s, CHCOO-). Anal. Calcd for $C_9H_4N_4O_2$: C, 53.89; H, 2.00; N, 27.94. Found: C, 53.66; H, 1.95; N, 27.86.

Ethyl 1,1,2,2-tetracyanocyclopropane carboxylate (7) was synthesized using a similar procedure as for cyclopropane 6 from TCNE and 1,1-diethoxy-2-bromoethylene. Yield: 3.62 g (85%). Mp = 158°-159°C (dec.). IR (KBr): 3057 (CH, cyclopropane), 2263 (CN), 1753 (ester); ^{1}H-NMR (acetone-d_6): δ 1.33 (t, $-CH_3$), 4.38 (q, $-CH_2-$), 4.52 (s, CHCOO-); ^{13}C-NMR (acetone-d_6): δ 14.2 (s, $-CH_3$), 22.3 (s, >CH<), 38.5 (s, >CH-), 64.5 (s, $-OCH_2-$), 108.6 (s, cis-CN) 110.8 (s, trans-CN), 161.7 -COO-(s,

-COO-). Anal. Calcd for $C_{10}H_6N_4O_2$: C, 56.08; H, 2.82; N, 26.16. Found: C, 56.03; H, 2.67; N, 26.14.

2-(Bromomethylydene)-1,3-dioxolane (8) was obtained by dehydrobromination of 2-(dibromomethyl)-1,3-dioxolane as described by McElvain[11]. 2-(Dibromomethyl)-1,3-dioxolane was prepared by an alcohol exchange between 1,1-dibromo-2,2-diethoxythane and glycol[10].

2-(Bromoethylydene)-1,3-dioxolane (9) was synthesized using a procedure similar to that for 2-(bromomethylidene)-1,3-dioxolane (8) from 2-(β,β-dibromoethyl)-1,3-dioxolane which was obtained from propionaldehyde by two successive bromination and alcohol exchange reaction. The total yield of the reactions was 66%. Bp = 59°-60°C/0.5 mmHg. This compound crystallized in the refrigerator. IR (neat): 2968 (CH), 1644 (C=C); ^{1}H-NMR ($CDCl_3$): δ 2.10 (s, $-CH_3$), 4.32 (m, $-CH_2-CH_2-$). Anal. Calcd. for $C_5H_7BrO_2$: C, 33.52; H, 3.91; Br, 44.69. Found: C, 33.39; H, 3.88; Br, 44.48.

Bromoethyl 1,1,2,2-tetracyanocyclopropanecarboxylate (10). TCNE (3.84 g, 30 mmole) was dissolved in 30 ml of tetrahydrofuran. The solution under nitrogen atmosphere was cooled in ice bath. 2-(Bromomethylidene)-1,3-dioxolane (6.6 g, 40 mmole) was added slowly with stirring under nitrogen, and the reaction mixture was stirred for 2 hr. Homopolymer of 2-(bromomethylidene)-1,3-dioxolane was separated by filtration and the resulting filtrate was concentrated by rotary evaporator. The obtained crude product was washed with n-hexane and purified by column chromatography. After washing with cold diethyl ether, the white crystals were dried under vacuum. Yield: 6.32 g (72%). Mp = 152°-153°C. IR (KBr): 3051 (CH, cyclopropane), 2265 (CN), 1746 (ester); ^{1}H-NMR (acetone-d_6): δ 3.72 (t, $-CH_2Br$), 4.67 (t, $-COOCH_2-$); ^{13}C-NMR (acetone-d_6): δ 22.5 (s, >C<), 29.2 (s, $-CH_2Br$), 38.2 (s, >CH-), 67.9 (s, $-OCH_2-$), 108.5 (s, cis-CN), 110.7 (s, trans-CN), 161.9 (s, -COO-).

Anal. Calcd for $C_{10}H_5BrN_4O_2$: C, 40.96; H, 1.70; Br, 27.30; N, 19.11. Found: C, 41.05; H, 1.65; Br, 27.18; N, 19.16.

Bromoethyl 1,1,2,2-tetracyano-3-methylcyclopropanecarboxylate (11) was synthesized according to a procedure similar to that of bromoethyl 1,1,2,2-tetracyanocyclopropanecarboxylate (10) from TCNE (3.84 g, 30 mmole) and 2-(bromoethylidene)-1,3-dioxolane (7.17 g, 40 mmole). Yield: 8.3 g (90%). Mp=179°-180°C (dec). IR (KBr): 2964 (CH), 2257 (CN), 1745 (ester); ^{1}H-NMR (DMSO-d_6): δ 1.77 (s, $-CH_3$), 3.71 (t, $-CH_2Br$), 4.54 (t, $-COOCH_2-$); ^{13}C-NMR (DMSO-d_6): δ 16.4 (s, $-CH_3$), 27.5(s, $>C(CN)_2$) 29.2 (s, $-CH_2Br$), 43.8 (s, >C<), 68.2 (s, $-OCH_2$), 109.1 (s, cis-CN), 110.2 (s, trans-CN), 163.3 (s, -COO-). Anal. Calcd for $C_{11}H_7BrN_4O_2$: C, 42.99; H, 2.28; Br, 26.05; N, 18.24. Found: C, 43.12; H, 2.26; Br, 26.00; N, 18.14.

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