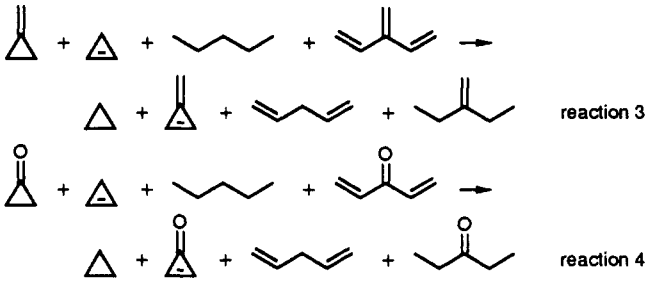
to measure such quantities as RE and RSE. This reaction conserves groups as defined by Benson and gives a reaction that minimizes the structural differences between reactant and product. Possible group equivalent reactions to obtain the RE of **1** and **2** are given in reactions 3 and 4, respectively. Unfortunately, these reactions involve fairly sizable



molecules that will tax most computational resources. However, if care is excercised in utilizing simple reactions and one corrects for nonconservation of chemical groups, quite reasonable estimates of RE can be readily calculated.

Registry No. **1a**, 4095-06-1; **2a**, 2961-80-0.

A New Synthetic Route to 1,1,2,2-Tetracyanocyclopropanes

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Received February 13, 1990

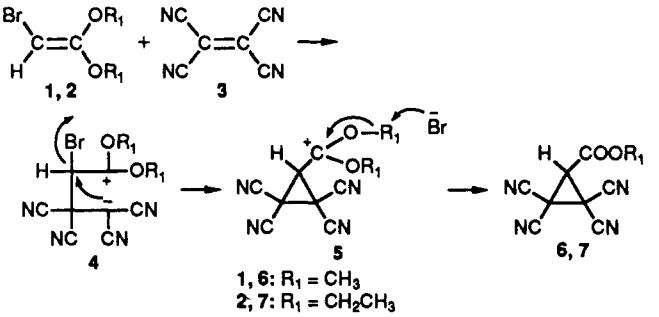
1,1,2,2-Tetracyanocyclopropane can be prepared rather easily by reaction of aqueous formaldehyde and malononitrile[1] or tetracyanoethylene with diazomethane.[2] A large number of substituted 1,1,2,2-tetracyanocyclopropanes are available by the Wideqvist reaction,[3,4] in which a carbonyl compound reacts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

In a previous report, we described the rather unexpected 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 was 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 yields a cyclopropane derivative as a reaction product.[8]

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

Results and Discussion

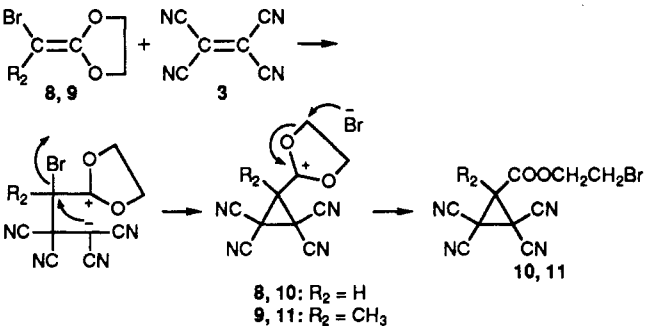
1,1-Dialkoxy-2-bromoethylenes **1** or **2** react with tetracyanoethylene (TCNE, **3**) at −10 °C to form methyl or ethyl 2,2,3,3-tetracyanocyclopropanecarboxylate (**6** or **7**), respectively. In analogy to the α-cyanoacrylate case,[7] the following mechanism is proposed. The initially formed



1,4-zwitterion **4** undergoes intramolecular elimination of bromide to form the dialkoxy cation **5**, which in turn undergoes dealkylation to form cyclopropane (**6**, **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 a 1,4-zwitterion in the course of reaction, which can initiate 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**) reacts with TCNE, a high yield of 2-bromoethyl 2,2,3,3-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**. In this case, the extra methyl



group on the double bond of the ketene acetal did not reduce the reactivity significantly.

All 2,2,3,3-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

Melting points were obtained on a Thomas-Hoover capillary melting point apparatus. ^1H NMR and ^{13}C NMR spectra were taken on a Bruker WM 250 nuclear magnetic resonance spec-

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0022-3263/90/1955-4963$02.50/0

trometer at 250 MHz. Infrared spectra were recorded on a Perkin-Elmer 983 spectrometer. Elemental analyses were performed by Desert Analytics, Tucson, AZ.

Tetrahydrofuran was purified by distillation from $LiAlH_4$. Tetracyanoethylene (3) was purchased from Aldrich and was purified by two recrystallizations from chlorobenzene followed by two sublimations through a layer of charcoal (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] Dibromo acetal 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 according to a similar procedure as for 1,1-dimethoxy-2-bromoethylene (1).

Methyl 2,2,3,3-Tetracyanocyclopropanecarboxylate (6). TCNE (2.56 g, 20 mmol) 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 (4.18 g, 25 mmol) was added slowly with stirring, and the reaction mixture was stirred for 1 h. Solvent and methyl bromide were then evaporated on a rotary evaporator. The crude product obtained was washed with hexane and purified by column chromatography (column size 4.0 cm/40 cm diameter/height; adsorbent silica gel, 70–230 mesh, 60 Å; eluent ethyl acetate/*n*-hexane, 40/60, v/v). Yield: 3.52 g (88%). Mp = 175–176 °C dec. IR (KBr): 3051, 2261, 1752 cm^{-1}. ^1H 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 2,2,3,3-tetracyanocyclopropanecarboxylate (7) was synthesized according to 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, 2263, 1753 cm^{-1}. ^1H 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, >C<), 64.5 (s, $-OCH_2-$), 108.6 (s, cis-CN), 110.8 (s, trans-CN), 161.7 (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-(Bromomethylidene)-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-diethoxyethane and glycol.[10]

2-(Bromoethylidene)-1,3-dioxolane (9) was synthesized according to 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 reactions. The total yield of the reactions was 66%. Bp = 59–60 °C/0.5 mmHg. This compound crystallized in the refrigerator, approximate mp 14 °C. IR (neat): 2968, 1644 cm^{-1}. ^1H NMR ($CDCl_3$): δ 2.10 (s, CH_3), 4.32 (m, $-CH_2CH_2-$). 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 2,2,3,3-Tetracyanocyclopropanecarboxylate (10). TCNE (3.84 g, 30 mmol) was dissolved in 30 mL of tetrahydrofuran. The solution was cooled in an ice bath under a nitrogen atmosphere. 2-(Bromomethylidene)-1,3-dioxolane (6.6 g, 40 mmol) was added slowly with stirring under nitrogen, and the reaction mixture was stirred for 2 h. The 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 hexane and purified by column chromatography. After washing with cold ether, the white crystals were dried under vacuum. Yield: 6.32 g (72%). Mp 152–153 °C. IR (KBr): 3051, 2265, 1746 cm^{-1}. ^1H 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, >CH-), 29.2 (s, $-CH_2Br$), 38.2 (s, >C<), 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 2,2,3,3-tetracyano-3-methylcyclopropanecarboxylate (11) was synthesized according to a procedure similar to that of bromoethyl 2,2,3,3-tetracyanocyclopropanecarboxylate (10) from TCNE (3.84 g, 30 mmol) and 2-(bromoethylidene)-1,3-dioxolane (7.17 g, 40 mmol). Yield: 8.3 g (90%). Mp = 179–180 °C dec. IR (KBr): 2964, 2257, 1745 cm^{-1}. ^1H NMR (DMSO-d_6): δ 1.77 (s, CH_3), 3.71 (t, CH_2Br), 4.54 (t, $-COOCH_2-$). ^{13}C-NMR (acetone-d_6): δ 16.4 (s, CH_3), 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.

Acknowledgment. We are deeply indebted to the Office of Naval Research for financial support of this work and to Dr. Anne Padias for helpful discussions.

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Isobatzellines A, B, C, and D. Cytotoxic and Antifungal Pyrroloquinoline Alkaloids from the Marine Sponge *Batzella* sp.

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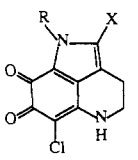
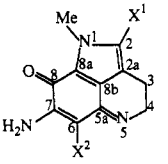
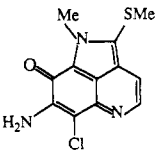
Received January 16, 1990

Recently we reported the isolation of three highly functionalized pyrroloquinoline alkaloids, batzellines A (1), B (2), and C (3), from the deep water Caribbean sponge







1 R = Me, X = SMe
2 R = H, X = SMe
3 R = Me, X = H

4 X^1 = SMe, X^2 = Cl
5 X^1 = SMe, X^2 = H
6 X^1 = H, X^2 = Cl
8 X^1 = H, X^2 = H

7

Batzella sp. (family Esperiopsidae, order Poecilosclerida). The structure of batzelline A was secured by X-ray analysis.[1] Further search for bioactive agents from *Batzella* has resulted in the discovery of four structurally related pyrroloquinolines, which we have named isobatzellines A (4), B (5), C (6), and D (7). The isobatzellines were found to exhibit in vitro cytotoxicity against P388 leukemia cell and moderate antifungal activity against *Candida albicans*.[2] The structures of the isobatzellines are described here and are based on spectral comparison with batzelline A and chemical interconversion.

Deep water sponge samples collected off the Grand Bahama Islands in June, 1984, and November, 1987, were frozen immediately and subsequently extracted with methanol–chloroform (2:1). Solvent partitioning of the extracts and centrifugal countercurrent chromatography of the resulting fractions yielded isobatzellines A (4), B (5), C (6), and D (7). The molecular formula of isobatzelline A (4) was determined to be $C_{12}H_{12}N_3OSCl$ by high-resolution FAB mass spectrometry. The ^1H and ^{13}C NMR data of 4, which are summarized in Table I, are similar to those of batzelline A. The presence of *S*-methyl, *N*-methyl, *N*-methylene, and an allylic methylene group including eight nonprotonated sp^2 carbons in 4 is consistent with the structural features of 1, but 4 contains one more nitrogen

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0022-3263/90/1955-4964$02.50/0