Notes

Preparation of 4-Alkyl and 4-Aryl Derivatives of 6-(Acetoxymethyl)isochroman-3-one

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Received September 30, 1986

3-Isochromanones are increasing in importance as precursors in organic synthesis. Spangler,[2] for example, has shown that gas-phase pyrolysis of these lactones provides a convenient and efficient method for the generation of synthetically useful *o*-quinodimethane intermediates.[3] These intermediates so formed have been cyclized to benzocyclobutenes[3] or have served as dienes that have been trapped intramolecularly[4] or intermolecularly[5-7] by dienophiles to form Diels–Alder adducts. 3-Isochromanones have also been converted by nonpyrolytic methods to derivatives of isoquinoline,[8] thioisoquinoline,[9] and epoxyethanophenanthrene.[10]

Most of the previously mentioned syntheses utilized 3-isochromanones with methoxy substituent(s) on the aromatic ring. These derivatives are usually prepared by (a) the hydrolysis and cyclization of aromatic compounds possessing appropriately substituted ortho side chains[11-13] and (b) by making use of a heteroatom-directed metalation reactions.[14,15] Recently, 4,4-disubstituted 3-isochromanones have been prepared by tandem electrocyclic–sigmatropic reaction of 1-acyl-1-alkylbenzocyclobutenones.[16] 4-Alkylisochroman-3-ones, which have been little studied, are prepared by alkylation of the corresponding isochroman-3-one enolate.[16,17] These alkylations are accompanied frequently by dialkylation, yielding mixtures that occasionally are difficult to separate.[17] 4-Arylisochroman-3-ones were unknown prior to this report.

We report a new synthesis of 4-alkyl- and 4-aryl derivatives of 6-(acetoxymethyl)isochroman-3-ones in which the key step involves an aryne reaction. Impetus for the present work came from a previous study in which 2-bromo-1,4-dimethylbenzene was found to yield α-alkyl-2,5-dimethylphenylacetonitriles in good yields via the symmetrical 3,6-dimethylbenzyne intermediate.[18] By analogy the reaction of the symmetrical aryne, 3,6-bis(methoxymethyl)benzyne (**4**), generated from 2-bromo-1,4-bis(methoxymethyl)benzene (**3**) with the anions of aliphatic and aromatic nitriles yielded α-alkyl- and α-aryl-2,5-bis(methoxymethyl)phenylacetonitriles (**5a–d, 5e–k**). Subsequent hydrolysis and cyclization of nitriles afforded the corresponding isochroman-3-ones in much the same way as nitriles with the same ortho difunctionality have been lactonized previously.[13]

Table I

$1 + RCH_2CN \rightarrow ArCH(R)CN$

entry	nitrile	time, h	nitrile product (% yield)
1	acetonitrile	2	**5a** (31)
2	propionitrile	2	**5b** (79)
3	butyronitrile	2	**5c** (47)
4	valeronitrile	2	**5d** (57)
5	phenylacetonitrile	3	**5e** (35)
6	3-methoxyphenylacetonitrile	3	**5f** (55)
7	3,4-dimethoxyphenylacetonitrile	4	**5g** (60)
8	3,4,5-trimethoxyphenylacetonitrile	4	**5h** (58)
9	4-fluorophenylacetonitrile	2	**5i** (57)
10	3-fluorophenylacetonitrile	2	**5j** (40)
11	2-furfurylacetonitrile	2	**5k** (37)

Results and Discussion

Synthesis of 2-Bromo-1,4-bis(methoxymethyl)benzene (3). Haloarene **3** was prepared by the photoinitiated bromination (*N*-bromosuccinimide) of 2-bromo-1,4-dimethylbenzene (**1**) and subsequent methanolysis of the α,α',2-tribromo intermediate (**2**) in overall yields of 60–65%. An attempt to prepare **3** by directly brominating 1,4-bis(methoxymethyl)benzene was unsuccessful.

Preparation of α-Alkyl- and α-Aryl-2,5-bis(methoxymethyl)phenylacetonitriles (5a–d, 5e–k). The reaction of haloarene **3** with various nitriles and sodamide in liquid ammonia yield the corresponding α-alkyl- and α-aryl-2,5-bis(methoxymethyl)phenylacetonitriles **5a–d** and **5e–k**, respectively, via the symmetrical aryne 3,6-bis(methoxymethyl)benzyne (**4**), in good yields (eq 1). A small undetermined quantity of 2,5-bis(methoxymethyl)-aniline (**6**) was isolated from each of these reactions. The results are listed in Table I. Nitriles studied included straight-chain aliphatic nitrile homologues ranging from acetonitrile to valeronitrile; aromatic nitriles, including the

(1) Robert Welch Postdoctoral Fellow.

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(3) For reviews see: (a) Kametani, T.; Fukumoto, K. *Heterocycles* **1975**, *3*, 29. Kunalt, I. L. *Chem. Rev.* **1970**, *70*, 471. Oppolzer, W. *Synthesis* **1978**, 793. Funk, R. L.; Vollhardt, K. P. C. *Chem. Soc. Rev.* **1980**, *9*, 41.

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(13) (a) Khanapure, S. P.; Bhawal, B. M.; Hazra, B. G. *Indian J. Chem., Sect. B* **1982**, *21B*, 889. (b) Khanapure, S. P.; Bhawal, B. M.; Das, K. G. *Synth. Commun.* **1984**, *14*, 1205.

(14) (a) Narsimhan, N. S.; Mali, R. S.; Kulkarni, B. K. *Tetrahedron* **1983**, *39*, 1975. (b) Mali, R. S.; Patil, S. D.; Patil, S. L. *Tetrahedron* **1986**, *42*, 2075.

(15) Shishido, K.; Shitara, E.; Fukumoto, K.; Kametani, T. *J. Am. Chem. Soc.* **1985**, *107*, 5810.

(16) Oppolzer, W. *Heterocycles* **1980**, *14*, 1615.

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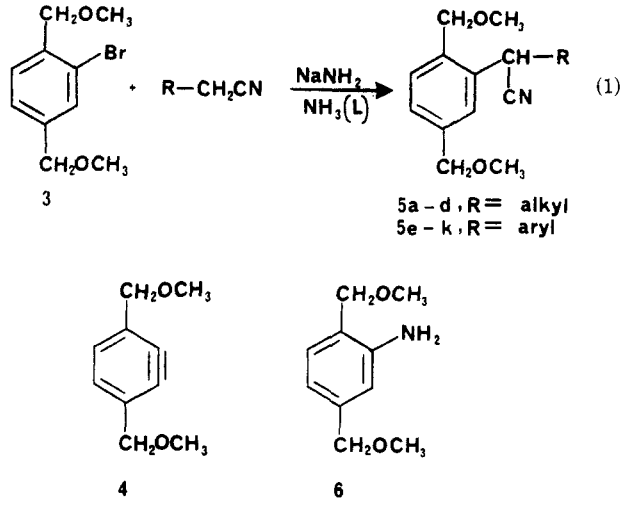
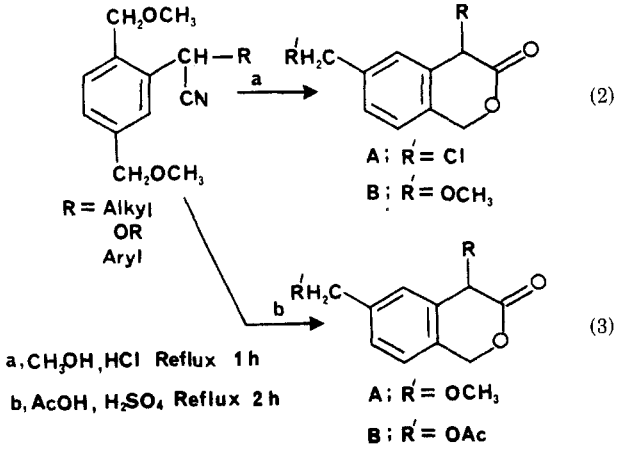


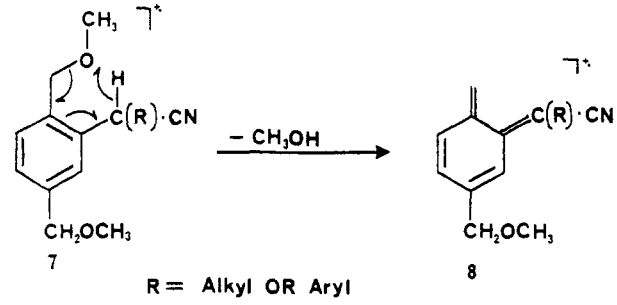
unsubstituted phenylacetonitrile and its methoxy, dimethoxy, trimethoxy, and fluoro derivatives; and 2-furfurylacetonitrile.

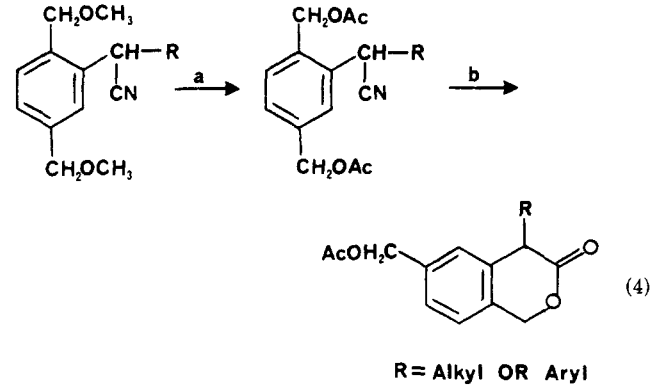
The ^1H NMR, ^{13}C NMR, IR, and mass spectra of these nitriles were consistent with proposed structures. For example, each showed the characteristic IR absorption for the nitrile stretch at 2240–2250 cm^{-1} and typical ^1H NMR AMX pattern of a 1,2,4-trisubstituted benzene ring. The mass spectrum of most of these nitriles exhibited a base peak of m/z P – 32, corresponding to the loss of methanol from the parent ion. Such a loss most likely occurs via a 6-membered transition state **7** to form the cyano-*o*-quinodimethane ion **8** (Scheme I). The structure of α-(3,4,5-trimethoxyphenyl)-2,5-bis(methoxymethyl)phenylacetonitrile (**5h**) was further substantiated by X-ray crystallography.[19]

Preparation of 4-Alkyl and 4-Aryl Derivatives of 6-(Acetoxymethyl)isochroman-3-ones 10a–d and 10e–k. We attempted initially to transform nitriles **5a–j** to isochroman-3-ones by treatment with hydrochloric acid in water or methanol and with acetic acid in the presence of sulfuric acid. Lactonization occurred under each set of conditions; however, the methoxymethyl group not engaged in cyclization underwent competing conversion to chloromethyl (even in methanol) and acetoxymethyl, respectively, giving rise to mixtures of 3-isochromanones (eq 2 and 3). This problem was overcome by first transforming these nitriles with acetic acid and acetic anhydride in the presence of sulfuric acid to bis(acetoxymethyl) nitriles (**9a–j**), which were then cyclized to the 6-(acetoxymethyl)-4-alkyl- and 6-(acetoxymethyl)-4-aryl-3-isochromanones (**10a–d, 10e–j**) by refluxing in aqueous acetic acid in the presence of sulfuric acid (eq 4). The results are summarized in Table II.



Scheme I





Isochromanones **10a–j** were characterized on the basis of their ^1H NMR, ^{13}C NMR, IR, and mass spectra (see the Experimental Section). The mass spectra of most of the 3-isochromanones exhibit a base peak at m/z P – 44 corresponding to a loss of carbon dioxide. Similar fragmentation patterns of other isochroman-3-ones have been reported.[2] The introduction of substituents at C-4 renders the two methylene hydrogens at C-1 nonequivalent, and as a result each appears as a doublet in the ^1H NMR spectra.

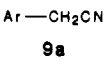
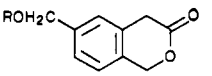
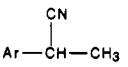
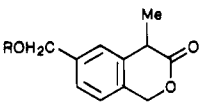
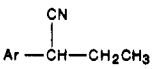
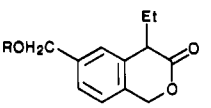
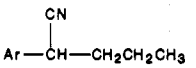
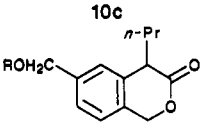
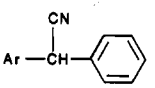
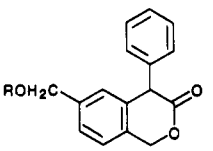
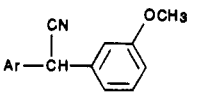
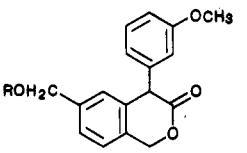
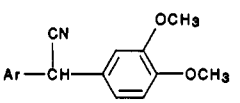
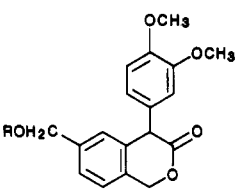
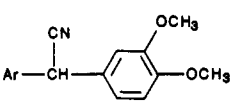
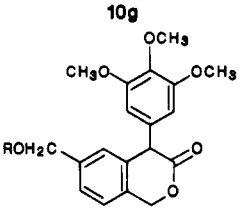
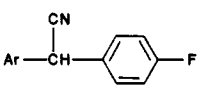
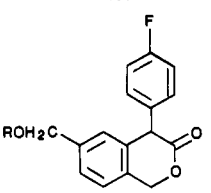
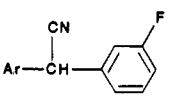
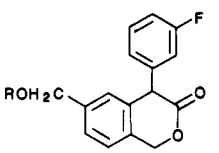
The data listed in Tables I and II indicate that the conversion of bromoarene **3** to isochromanones **10a–j** proceeds in good overall yields, thus providing a convenient method for introducing a 4-alkyl and 4-aryl substituent into the isochromanone ring system. This method complements those previously used for preparing 4-alkyl-3-isochromanones and is the method of choice for synthesizing 4-aryl-3-isochromanones, which were unknown prior to this study. We presently are extending this method to include the synthesis of other aromatic lactones and studying the thermal reaction of 4-substituted isochroman-3-ones with various dienophiles.

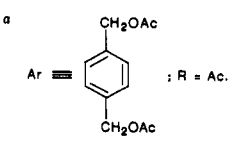
Experimental Section

General Aspects. Proton nuclear magnetic spectra (^1H NMR) were measured in $CDCl_3$ solution on a Perkin-Elmer R-32 spectrometer at 90 MHz or on a WP 200-SY Bruker spectrometer. Carbon NMR spectra (^{13}C NMR) were recorded on a WP 200-SY Bruker spectrometer. All chemical shifts are reported in parts per million downfield from internal tetramethylsilane. Infrared spectra (IR) were recorded on a Perkin-Elmer 283 grating spectrometer as a liquid film or in a solution cell. Chromatographic analysis and mass spectra (70 eV) were obtained on a Hewlett-Packard Model 5988A chromatograph/mass spectrometer equipped with a 12-m height × 0.2-mm i.d. capillary column containing cross-linked methyl silicone of 0.33-μm film thickness.

(19) de Meester, P.; Khanapure, S. P.; Chu, S. S. C.; Biehl, E. R. *Acta Crystallogr.*, in press.

Table II. Preparation of 4-Alkyl- and 4-Aryl-6-(acetoxymethyl)isochroman-3-ones via 2-(α-Cyanoalkyl)- and 2-(α-Cyanoaryl)-1,4-bis(acetoxymethyl)benzenes

entry	cyano compd	diacetate[a]	yield, %	lactone	yield, %
1	**5a**	 **9a**	73	 **10a**	60
2	**5b**	 **9b**	72	 **10b**	62
3	**5c**	 **9c**	74	 **10c**	58
4	**5d**	 **9d**	81	 **10d**	55
5	**5e**	 **9e**	76	 **10e**	49
6	**5f**	 **9f**	70	 **10f**	43
7	**5g**	 **9g**	71	 **10g**	60
8	**5h**	 **9h**	74	 **10h**	36
9	**5i**	 **9i**	90	 **10i**	85
10	**5j**	 **9j**	90	 **10j**	77

[a] 

Data reported are the m/z values for the most abundant peaks. E. Merck silica gel 9385 (230–400 mesh) was used for flash chromatography. All reagents and solvents were purified and distilled according to standard methods. Reported boiling points are uncorrected; melting points were determined on an electrothermal apparatus and are uncorrected. All reactions were carried out in flame-dried flasks under nitrogen atmosphere. Since the reactions performed are all similar in many respects, typical reactions will be described as specific examples.

Starting Materials. The nitriles and 2-bromo-*p*-xylene were obtained from Aldrich Chemical Co. The alkyl nitriles were dried and distilled over calcium hydride and stored over 4-Å molecular sieves prior to use. The *N*-bromosuccinimide was recrystallized from boiling water and dried in a vacuum desiccator.

2-Bromo-1,4-bis(methoxymethyl)benzene (3). *N*-Bromosuccinimide (118 g, 0.6 mol) was added in several lots over 6 h to a refluxing solution of 2-bromo-*p*-xylene (48 g, 0.26 mol) in dry carbon tetrachloride (500 mL) containing 2 g of benzoyl peroxide under nitrogen atmosphere, in the presence of light (photolamp). After the addition of NBS, the resulting slurry was refluxed for 1 h more, cooled, and filtered to remove the solid material. The filtrate was concentrated under reduced pressure to give α,α'-dibromo-2-bromo-*p*-xylene, which, without further purification, was dissolved in benzene (200 mL), and the solution was added to a stirred solution of sodium methoxide prepared from sodium (18 g, 0.78 mol) in methanol (300 mL). The reaction mixture was refluxed with stirring for 2 h, cooled, and filtered to remove any solid material, and the filtrate was concentrated under reduced pressure. It was then diluted with cold water, acidified with diluted HCl, and extracted with methylene chloride. The methylene chloride extract was washed with water and brine, dried (Na_2SO_4), and evaporated to give an oil that was distilled at 100–105 °C (2 mm) to give pure 2-bromo-1,4-bis(methoxymethyl)benzene: yield 42 g (60–65%); ^{1}H NMR ($CDCl_3$) δ 3.40 (s, 3 H), 3.50 (s, 3 H), 4.43 (s, 2 H), 4.53 (s, 2 H), 7.3–7.6 (m, 3 H); ^{13}C NMR ($CDCl_3$) δ 139.36, 136.70, 131.43, 128.42, 122.60, 73.62, 73.47, 58.44, 58.11; MS, m/z 244 (M^+), 246 (M + 2).

General Procedure for the Aryne Reactions with Alkyl and Aryl Nitriles. Sodium amide (0.2 mol) was prepared from 4.6 g (0.2 mol) of sodium in liquid ammonia (150 mL) containing 0.01 g of ferric nitrate. After the discharge of the initial blue solution to gray, indicating the conversion of sodium to sodium amide, the appropriate nitrile was added slowly over a period of 5 min. After the addition was complete, the mixture was stirred for 15 min and 2-bromo-1,4-bis(methoxymethyl)benzene (0.05 mol) was added over a period of 5 min. The mixture then was stirred for 2–4 h and quenched with ammonium chloride and the ammonia evaporated. The residue was extracted with methylene chloride (3 × 25 mL), and the combined extracts were washed with brine, dried (Na_2SO_4), and concentrated under reduced pressure to provide an oil that consisted of a mixture of nitrile products and minor amount of 1,4-bis(methoxymethyl)aniline (**6**). Purification of the nitrile products was accomplished by flash column chromatography using a mixture of hexane/EtOAc [9:1 or 4:1, depending on the polarity of the nitrile product] as an eluent. The yields are given in Table I.

2,5-Bis(methoxymethyl)phenylacetonitrile (5a): colorless viscous oil; ^{1}H NMR ($CDCl_3$) δ 3.42 (s, 3 H), 3.47 (s, 3 H), 3.91 (s, 2 H), 4.54 (split s, 4 H), 7.37–7.50 (m, 3 H); IR (neat) 2990, 2930, 2820, 2250, 1620, 1580, 1450, 1420, 1380, 1290, 1100, 950 cm^{-1}; MS, m/z 205 (M^+), 173; m/z (M^+) for $C_{12}H_{15}NO_2$, calcd 205.1103, found 205.1082.

α-Methyl-2,5-bis(methoxymethyl)phenylacetonitrile (5b): colorless oil; bp 136–138 °C (0.25 mm); ^{1}H NMR ($CDCl_3$) δ 1.52 (d, 3 H, J = 7.5 Hz), 3.27 (s, 3 H), 3.32 (s, 3 H), 4.24 (q, 1 H, J = 7.5 Hz), 4.42 (s, 4 H), 7.25–7.50 (m, 3 H); IR (neat) 2990, 2930, 2825, 2240, 1615, 1580, 1450, 1385, 1145, 1100, 960, 910 cm^{-1}; MS, m/z 219 (M^+), 187, 172; m/z (M – CH_3) for $C_{12}H_{14}NO_2$, calcd 204.1016, found 204.1052.

α-Ethyl-2,5-bis(methoxymethyl)phenylacetonitrile (5c): colorless viscous oil; bp 142–144 °C (0.3 mm); ^{1}H NMR ($CDCl_3$) δ 1.13 (t, 3 H, J = 7.5 Hz), 1.94 (m, 2 H), 3.36 (s, 3 H), 3.42 (s, 3 H), 4.14 (t, 1 H, J = 7.5 Hz), 4.50 (s, 4 H), 7.33–7.52 (m, 3 H); IR (neat) 2980, 2940, 2880, 2725, 2240, 1460, 1385, 1195, 1100 cm^{-1}; MS, m/z 233 (M^+), 201; m/z (M^+) for $C_{14}H_{19}NO_2$, calcd 233.1416, found 233.1411.

α-Propyl-2,5-bis(methoxymethyl)phenylacetonitrile (5d): pale yellow oil; ^{1}H NMR ($CDCl_3$) δ 1.1 (t, J = 8 Hz, 3 H), 1.3–1.8 (m, 4 H), 3.42 (s, 3 H), 3.46 (s, 3 H), 4.3 (br t, 1 H), 4.6 (s, 1 H), 7.45–7.65 (m, 3 H); IR (Nujol) 2900, 2850, 2240, 1470, 1380, 1200, 1100 cm^{-1}; MS, m/z 247 (M^+), 215 (M – CH_3OH).

α-Phenyl-2,5-bis(methoxymethyl)phenylacetonitrile (5e): colorless viscous oil; ^{1}H NMR ($CDCl_3$) δ 3.35 (s, 3 H), 3.40 (s, 3 H), 4.43 (s, 2 H), 4.47 (s, 2 H), 5.74 (s, 1 H), 7.35–7.44 (m, 3 H); IR (neat) 2995, 2930, 2240, 1605, 1500, 1455, 1385, 1200, 1100 cm^{-1}; MS, m/z 271 (M^+).

α-(3-Methoxyphenyl)-2,5-bis(methoxymethyl)phenylacetonitrile (5f): colorless thick oil: ^{1}H NMR ($CDCl_3$) δ 3.42 (s, 3 H), 3.45 (s, 3 H), 3.83 (s, 3 H), 4.52 (s, 4 H), 5.77 (s, 1 H), 6.9–7.15 (m, 4 H), 7.3–7.65 (m, 3 H); ^{13}C NMR ($CDCl_3$) δ 159.91, 139.33, 136.64, 134.62, 130.29, 129.88, 128.10, 127.24, 119.52, 113.71, 113.30, 113.20, 73.73, 73.52, 58.00, 57.81, 58.03, 38.11; IR (neat) 2930, 2240, 1600, 1585, 1490, 1450, 1265, 1195, 1100, 1050 cm^{-1}; MS, m/z 279 (M – CH_3OH); m/z (M^+) for $C_{19}H_{21}NO_3$, calcd 311.1516, found 311.1512.

α-(3,4-Dimethoxyphenyl)-2,5-bis(methoxymethyl)-phenylacetonitrile (5g): white needles (from hexane); mp 77 °C; ^{1}H NMR ($CDCl_3$) δ 3.39 (s, 3 H), 3.42 (s, 3 H), 3.87 (s, 3 H), 3.92 (s, 3 H), 4.51 (s, 4 H), 5.72 (s, 1 H), 6.94 (s, 3 H), 7.42–7.53 (m, 3 H); ^{13}C NMR ($CDCl_3$) δ 149.20, 148.72, 139.25, 134.88, 134.44, 130.30, 128.00, 127.67, 127.42, 127.20, 120.00, 119.73, 111.43, 111.21, 110.92, 73.91, 73.76, 72.55, 58.03, 57.85, 55.72, 55.53, 37.71; IR (Nujol) 2240, 1600, 1100 cm^{-1}; MS, m/z 341 (M^+), 309, 278. Anal. Calcd for $C_{20}H_{23}O_4N$: C, 70.36; H, 6.79; N, 4.10. Found: C, 70.06; H, 6.78; N, 4.22.

α-(3,4,5-Trimethoxyphenyl)-2,5-bis(methoxymethyl)-phenylacetonitrile (5h): white crystals (from EtOAc); mp 80 °C; ^{1}H NMR ($CDCl_3$) δ 3.35 (s, 3 H), 3.36 (s, 3 H), 3.79 (s, 6 H), 3.82 (s, 3 H), 4.44 (s, 2 H), 4.45 (s, 2 H), 5.64 (s, 1 H), 6.54 (s, 2 H), 7.31–7.40 (m, 3 H); ^{13}C NMR ($CDCl_3$) δ 153.40, 139.34, 137.59, 134.68, 134.43, 130.58, 130.43, 128.00, 127.34, 119.57, 104.97, 73.73, 72.61, 60.64, 58.02, 57.89, 55.97, 38.14; IR (Nujol) 2240, 1600, 1120 cm^{-1}; MS, m/z 371 (M^+). Anal. Calcd for $C_{21}H_{25}O_5N$: C, 67.72, H, 6.76; N, 3.76. Found: C, 67.74; H, 6.85; N, 3.79.

α-(4-Fluorophenyl)-2,5-bis(methoxymethyl)phenylacetonitrile (5i): pale yellow thick oil; ^{1}H NMR ($CDCl_3$) δ 3.33 (s, 3 H), 3.38 (s, 3 H), 4.41 (split s, 4 H), 5.72 (s, 1 H), 7.03 (m, 4 H), 7.32–7.40 (m, 3 H); ^{13}C NMR ($CDCl_3$) δ 164.58, 159.67, 139.44, 134.57, 131.13, 130.39, 129.47, 129.29, 127.96, 127.31, 119.41, 115.97, 115.53, 73.63, 73.51, 58.01, 57.73, 37.40; IR (neat) 2850, 2240, 1610, 1450, 1425, 1390, 1240, 1200, 1160, 1100 cm^{-1}; MS m/z 299 (M^+), 267 (M – 32), 235, 222; m/z (M – MeOH) for $C_{17}H_{14}NOF$, calcd 267.1064, found 267.1061.

α-(3-Fluorophenyl)-2,5-bis(methoxymethyl)phenylacetonitrile (5j): pale yellow thick oil; ^{1}H NMR ($CDCl_3$) δ 3.35 (s, 3 H), 3.40 (s, 3 H), 4.46 (br s, 4 H), 5.74 (s, 1 H), 7.03–7.2 (m, 4 H), 7.34–7.41 (m, 3 H); IR (neat) 2850, 2240, 1610, 1450 cm^{-1}; MS, m/z 299 (M^+), 267 (M – MeOH).

α-2-Furfuryl-2,5-bis(methoxymethyl)phenylacetonitrile (5k): pale yellow oil; ^{1}H NMR ($CDCl_3$) δ 3.33 (s, 3 H), 3.38 (s, 3 H), 4.45 (s, 4 H), 5.77 (s, 1 H), 6.26 (m, 2 H), 7.31–7.49 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 147.39, 143.17, 139.41, 134.45, 132.27, 130.29, 127.89, 127.57, 117.64, 110.56, 108.52, 73.73, 72.51, 58.10, 57.82, 32.73; IR (neat) 2850, 2245, 1500, 1450, 1380, 1200, 1100 cm^{-1}; MS, m/z 239 (M –CH_3OH).

General Procedure for the Preparation of 2-(α-Cyanoalkyl)- or 2-(α-Cyanoaryl)-1,4-bis(acetoxymethyl)benzenes (9a–j). A solution of the appropriate nitrile (**5a–j**; 0.1 mol) in acetic acid (20 mL), acetic anhydride (20 mL), and 0.2 mL of H_2SO_4 was refluxed for 1 h. The acetic acid solution was cooled to room temperature, diluted with water (100 mL), and extracted with methylene chloride (2 × 100 mL). The combined methylene chloride extracts were successively washed with water (2 × 100 mL), saturated $NaHCO_3$ (2 × 100 mL), and brine (2 × 50 mL) and then dried (Na_2SO_4) and filtered, and the filtrate on evaporation gave the corresponding diacetate nitriles **9a–j**. The products were dissolved in methylene chloride, treated with charcoal, and then filtered through a small column of silica gel to give pure **9a–j**.[20]

(20) All the products were characterized by ^{1}H NMR, ^{13}C NMR, and mass spectra.

General Procedure for the Preparation of 4-Alkyl- or 4-Aryl-Substituted Derivatives of 6-(Acetoxymethyl)isochroman-3-one (10a-j). A solution of the appropriate cyano compound (**9a-j**; 0.005 mol) in acetic acid (10 mL), water (1 mL), and H_2SO_4 (0.25 mL) was refluxed for 1 h. The reaction mixture was then cooled, diluted with water (100 mL), and extracted with methylene chloride (2 × 100 mL). The combined methylene chloride extracts were successively washed with water (2 × 100 mL), saturated $NaHCO_3$ (2 × 75 mL), and brine (2 × 75 mL) and then dried (Na_2SO_4), filtered, and concentrated under reduced pressure to give the corresponding lactone product (**10a-j**). All the lactone products (**10a-j**) were purified by flash column chromatography (EtOAc:hexane = 1:9) to give pure **10a-j**. The yields are given in Table II.

6-(Acetoxymethyl)isochroman-3-one (10a): colorless thick liquid; ^1H NMR ($CDCl_3$) δ 2.12 (s, 3 H), 3.73 (s, 2 H), 5.12 (s, 2 H), 5.32 (s, 2 H), 7.25-7.30 (m, 3 H); ^{13}C NMR ($CDCl_3$) δ 170.40, 170.04, 136.74, 131.27, 131.19, 127.07, 126.61, 124.67, 69.53, 65.31, 30.84, 20.62; IR ($CHCl_3$) 1740 cm^{-1} (>C=O); MS, m/z 220 (M^+), 188, 186; m/z (M^+) for $C_{12}H_{12}O_4$, calcd 220.0735, found 220.0736.

4-Methyl-6-(acetoxymethyl)isochroman-3-one (10b): white crystals (from ethyl acetate); mp 76 °C; ^1H NMR ($CDCl_3$) δ 1.65 (d, J = 7 Hz, 3 H), 2.11 (s, 3 H), 3.64 (q, J = 7.5 Hz, 1 H), 5.12 (s, 2 H), 5.28 (s, 1 H), 5.31 (s, 1 H), 7.23-7.32 (m, 3 H); IR ($CHCl_3$) 1740, 1460, 1380 cm^{-1}; MS, m/z 234 (M^+), 190 ($M - CO_2$). Anal. Calcd for $C_{13}H_{14}O_4$: C, 66.64; H, 6.02. Found: C, 66.71; H, 6.06.

4-Ethyl-6-(acetoxymethyl)isochroman-3-one (10c): colorless thick liquid; ^1H NMR ($CDCl_3$) δ 1.09 (t, J = 7.5 Hz, 3 H), 1.75-2.0 (m, 2 H), 2.12 (s, 3 H), 3.56 (t, J = 7 Hz, 1 H), 5.13 (s, 2 H), 5.05 (d, J = 10 Hz, 1 H), 5.37 (d, J = 10 Hz, 1 H), 7.21-7.30 (m, 3 H); IR ($CHCl_3$) 1740, 1460, 1380, 1230 cm^{-1}; MS, m/z 248 (M^+), 204 ($M - CO_2$); m/z (M^+) for $C_{14}H_{16}O_4$, calcd 248.1044, found 248.1051.

4-*n*-Propyl-6-(acetoxymethyl)isochroman-3-one (10d): colorless thick liquid; ^1H NMR ($CDCl_3$) δ 0.9 (t, 3 H, J = 8 Hz), 1.2-1.9 (m, 4 H), 2.1 (s, 3 H), 3.6 (br t, 1 H), 5.3 (s, 2 H), 5.4 (s, 2 H), 7.25-7.4 (m, 3 H); IR ($CHCl_3$) 1740, 1465, 1380 cm^{-1}; MS, m/z 362 (M^+), 320, 318.

4-Phenyl-6-(acetoxymethyl)isochroman-3-one (10e): colorless thick liquid; ^1H NMR ($CDCl_3$) δ 2.11 (s, 3 H), 5.04 (s, 1 H), 5.12 (s, 2 H), 5.25 (s, 2 H), 7.15-7.38 (m, 8 H); IR ($CHCl_3$) 1740, 1600, 1460, 1380, 1240 cm^{-1}; MS, m/z (M^+) for $C_{18}H_{16}O_4$, calcd 296.1044, found 296.1042.

4-(3-Methoxyphenyl)-6-(acetoxymethyl)isochroman-3-one (10f): colorless thick liquid; ^1H NMR ($CDCl_3$) δ 2.03 (s, 3 H), 3.78 (s, 3 H), 5.01 (s, 1 H), 5.12 (s, 2 H), 5.23 (split s, 2 H), 6.76-6.89 (m, 3 H), 7.27-7.40 (m, 4 H); IR ($CHCl_3$) 1740, 1595, 1510, 1380, 1250, 1140 cm^{-1}; MS, m/z 326 (M^+); m/z (M^+) for $C_{19}H_{18}O_5$, calcd 326.1149, found 326.1160.

4-(3,4-Dimethoxyphenyl)-6-(acetoxymethyl)isochroman-3-one (10g): colorless thick liquid; ^1H NMR ($CDCl_3$) δ 2.10 (s, 3 H), 3.78 (s, 3 H), 3.86 (s, 3 H), 4.95 (s, 1 H), 5.13 (s, 2 H), 5.27 (s, 2 H), 6.37 (s, 2 H), 7.16-7.43 (m, 4 H); IR ($CHCl_3$) 1740, 1595, 1510, 1380, 1250, 1140 cm^{-1}; MS, m/z 356 (M^+); m/z (M^+), calcd 356.1254, found 356.1263.

4-(3,4,5-Trimethoxyphenyl)-6-(acetoxymethyl)isochroman-3-one (10h): colorless thick oil; ^1H NMR ($CDCl_3$) δ 2.11 (s, 3 H), 3.84 (s, 6 H), 3.87 (s, 3 H), 4.97 (s, 1 H), 5.12 (s, 2 H), 5.25 (s, 2 H), 6.84 (s, 2 H), 7.28-7.46 (m, 3 H); IR ($CHCl_3$) 1740, 1595, 1460, 1380, 1230, 1180 cm^{-1}; MS, m/z for $C_{21}H_{22}O_7$, calcd 386.1359, found 386.1368.

4-(4-Fluorophenyl)-6-(acetoxymethyl)isochroman-3-one (10i): colorless thick liquid; ^1H NMR ($CDCl_3$) δ 2.08 (s, 3 H), 4.97 (s, 1 H), 5.09 (s, 2 H), 5.24 (s, 2 H), 7.07-7.28 (m, 4 H), 7.32-7.40 (m, 3 H); IR ($CHCl_3$) 1740, 1610, 1510, 1460, 1380, 1240, 1165 cm^{-1}; MS, m/z 314 (M^+), 270 ($M - CO_2$).

4-(3-Fluorophenyl)-6-(acetoxymethyl)isochroman-3-one (10j): colorless thick liquid; ^1H NMR ($CDCl_3$) δ 2.08 (s, 3 H), 4.99 (s, 1 H), 5.09 (s, 2 H), 5.23 (s, 2 H), 7.00-7.36 (m, 7 H); IR ($CHCl_3$) 1740, 1615, 1595, 1490, 1380, 1290, 1175 cm^{-1}; MS, m/z 314 (M^+), 270 ($M - CO_2$); m/z (M^+) for $C_{18}H_{15}O_4F$, calcd 314.0954, found 314.0944.

Acknowledgment. This work was sponsored in part by Grant N-118 from the Welch Foundation, Houston, TX. S.P.K. thanks the Robert Welch Foundation for the award of a postdoctoral fellowship. We thank Dr. J. Maguire for performing microanalysis. We are also grateful to the Midwest Center for Mass Spectrometry, a National Science Foundation Regional Instrumentation Facility (Grant No. CHE 8211164), for recording high-resolution mass spectra.

Registry No. **3**, 106520-26-7; **5a**, 106520-27-8; **5b**, 106520-28-9; **5c**, 106520-29-0; **5d**, 106520-30-3; **5e**, 106520-31-4; **5f**, 106520-32-5; **5g**, 106520-33-6; **5h**, 106542-90-9; **5i**, 106520-34-7; **5j**, 106520-35-8; **5k**, 106520-36-9; **6**, 106520-37-0; **9a**, 106520-38-1; **9b**, 106520-39-2; **9c**, 106520-40-5; **9d**, 106520-41-6; **9e**, 106520-42-7; **9f**, 106520-43-8; **9g**, 106520-44-9; **9h**, 106520-45-0; **9i**, 106520-46-1; **9j**, 106520-47-2; **10a**, 106520-48-3; **10b**, 106520-49-4; **10c**, 106520-50-7; **10d**, 106520-51-8; **10e**, 106520-52-9; **10f**, 106520-53-0; **10g**, 106520-54-1; **10h**, 106520-55-2; **10i**, 106520-56-3; **10j**, 106520-57-4; 3-fluorophenylacetonitrile, 501-00-8; 2-bromo-*p*-xylene, 553-94-6; α,α'-dibromo-2-bromo-*p*-xylene, 19900-52-8; 2-furfurylacetonitrile, 2745-25-7; acetonitrile, 75-05-8; propionitrile, 107-12-0; butyronitrile, 109-74-0; valeronitrile, 110-59-8; phenylacetonitrile, 140-29-4; 3-methoxyphenylacetonitrile, 19924-43-7; 3,4-dimethoxyphenylacetonitrile, 93-17-4; 3,4,5-trimethoxyphenylacetonitrile, 13338-63-1; 4-fluorophenylacetonitrile, 459-22-3; acetic acid, 64-19-7.

An Electrochemical "Switch" for Starting and Stopping the Energy-Releasing Conversion of Quadricyclanes to Norbornadienes

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Received September 2, 1986

Since its independent discovery by Hogeveen and Volger[1] and by Gassman et al.[2] in the mid sixties,[3] the catalytic conversion of quadricyclanes to norbornadienes[4] has attracted considerable attention because of its potential as a crucial component of a solar energy storage cell.[5-7] Both

(1) Hogeveen, H.; Volger, H. C. *J. Am. Chem. Soc.* **1967**, *89*, 2486.
(2) Gassman, P. G.; Aue, D. H.; Patton, D. S. *J. Am. Chem. Soc.* **1968**, *90*, 7271.
(3) The initial example of this type of isomerization was probably observed by Cristol and co-workers. However, the implications of their observations were not appreciated. Cristol, S. J.; Snell, R. L. *J. Am. Chem. Soc.* **1958**, *80*, 1950.
(4) Because of its common usage, the skeleton of 1 is referred to as the norbornadiene skeleton rather than as a bicyclo[2.2.1]hepta-2,5-diene, while 2 is classified as a quadricyclane instead of as a tetracyclo-[3.2.0.$0^{2,7}$.$0^{4,6}$]heptane derivative.
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