2a,3a-Dihydro-2,3-benztriptycene (8). 2,3-Benztriptycene[17] (0.25 g) was reduced with lithium according to the general procedure with *t*-BuOH as the proton source. This was a difficult reaction to carry out cleanly, but the use of somewhat lesser amounts of lithium (1.1 equiv) afforded a product consisting primarily of 8 together with unreacted starting material. Recrystallization from acetone–hexane provided 8: mp 209 °C; NMR ($CDCl_3$) δ 6.9 (m, 10), 5.7 (br s, 2), 5.2 (s, 2), 3.2 (br s, 4).

Anal. Calcd for $C_{24}H_{18}$: C, 94.08; H, 5.92. Found: C, 93.87; H, 5.90.

1,4-Dihydro-2,3-benztriptycene (9). When the above reaction was quenched with H_2O instead of *t*-BuOH, 8 and 9 were formed in a ratio of 1:2 together with ~30% unreacted starting material. Purification of 9 was not possible, and the NMR spectrum was determined by subtracting out those of 7 and 8: NMR ($CDCl_3$) δ 6.9 (m, 12), 4.75 (s, 2), 3.5 (s, 4).

9-(2-Naphthyl)-9,10-dihydroanthracene. 1,2-Benztriptycene[17] (0.75 g, 2.5 mmol) was reacted with lithium metal (6.2 mmol) as usual with a *t*-BuOH quench. Recrystallization of the crude product from ethanol gave white crystals of 12: mp 128–129 °C (0.4 g, 53%); NMR ($CDCl_3$) δ 7.2 (m, 15), 5.35 (s, 1), 4.0 (br s, 2).

Anal. Calcd for $C_{24}H_{18}$: C, 94.08; H, 5.92. Found: C, 93.84; H, 6.07.

(17) Hurd, C. D.; Juel, L. H. *J. Am. Chem. Soc.* **1955**, *77*, 601.

Dehydrogenation of 12 (0.2 g) with 5% Pd/C (0.12 g) at 350 °C for 1.5 h provided 9-(2-naphthyl)anthracene, mp 200–202 °C.[18]

5,8-Dihydro-1,2-benztriptycene (15). When the above reaction was carried out by using sodium metal at −78 °C, a mixture of 15 and 16 resulted. Two recrystallizations from ethanol provided 15 in 40% yield: mp 211–213 °C; NMR ($CDCl_3$) δ 7.0 (m, 10), 5.8 (br s, 2), 5.5 (br s, 1), 5.25 (s, 1), 3.4 (m, 4).

Anal. Calcd for $C_{24}H_{18}$: C, 94.08; H, 5.92. Found: C, 93.79; H, 6.15.

1,4-Dihydro-1,2-benztriptycene (16). This compound could not be obtained free from 15, but the NMR spectrum was determined by subtracting out the spectrum of 15: NMR ($CDCl_3$) δ 7.0 (m, 12), 5.9 (br s, 1), 5.0 (br s, 1), 4.8 (s, 1), 3.1 (br s, 3).

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Registry No. 1, 2734-13-6; 2, 5675-64-9; 3, 477-75-8; 5, 71870-39-8; 6, 71870-40-1; 7, 13395-89-6; 8, 71870-41-2; 9, 71870-42-3; 10, 69096-77-1; 12, 71870-43-4; 13, 7424-72-8; 15, 71870-44-5; 16, 71870-45-6; 22, 71870-46-7.

(18) Vingiello, F. A.; Borkovec, A.; Zajac, W., Jr. *J. Am. Chem. Soc.* **1958**, *80*, 1714.

Alkylations and Acylations of α-Aryl-4-morpholineacetonitriles (Masked Acyl Anion Equivalents) and Their Use in 1,4-Additions

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The anions of α-aryl-4-morpholineacetonitriles are alkylated with ethyl bromoacetate, epichlorohydrin, or allyl chloride and displace halogen on benzene derivatives containing electron-withdrawing groups to give benzophenones. These anions are acylated with ethyl chloroformate and benzoyl chlorides and add to ethyl acrylate and acrylonitrile to give good yields of 1,4-addition products.

Discussion

The use of masked functional groups such as masked acyl anion equivalents in the formation of carbon–carbon bonds has proved to be a powerful strategy in the development of new synthetic methods.[1] Stetter has studied the addition of aryl aldehydes to α,β-unsaturated esters, ketones, and nitriles by the use of anions from intermediate cyanohydrins.[2] The utility of O-alkylated cyanohydrins[3,4] and O-silylated cyanohydrins[5] in the synthesis of ketones has been reported. Related masked acyl anion equivalents are those derived from α-aryl-α-(dialkylamino)acetonitriles.[6] Alkylations with benzyl halides have been studied[6a,7] and Leete reported[8] the 1,4-addition of α-(3-pyridyl)-4-morpholineacetonitrile to acrylonitrile.

We have found that diverse α-aryl-4-morpholineacetonitriles add to acrylonitrile and ethyl acrylate to give good yields of 1,4-addition products.[9] With ethyl acrylate the yields are superior to those obtained from aryl-aldehyde cyanohydrins,[2,6] and with acrylonitrile yields are at least equivalent. The addition of α-aryl-4-morpholineacetonitriles to ethyl acrylate followed by hydrolysis of the masked acyl function is a useful high-yield route to ethyl 3-aroylpropionates[10] and 3-aroylpropionitriles (see Table III).

(1) (a) Seebach, D. *Angew. Chem., Int. Ed. Engl.* **1969**, *8*, 639. (b) Seebach, D.; Kolb, M. *Chem. Ind. (London)* **1974**, 687. (c) Lever, O. W., Jr. *Tetrahedron* **1976**, *32*, 1943. (d) Seebach, D.; Burstinghaus, R. *Angew. Chem., Int. Ed. Engl.* **1975**, *14*, 57. (e) Stetter, H.; Kuhlmann, H. *Ibid.* **1974**, *13*, 539. Stork, G.; Ozorio, A. A.; Leong, A. Y. W. *Tetrahedron Lett.* **1978**, 5175.

(2) Stetter, H. *Angew. Chem., Int. Ed. Engl.* **1976**, *15*, 639 and references therein.

(3) Stork, G.; Maldonado, L. *J. Am. Chem. Soc.* **1971**, *93*, 5286.

(4) Kalir, A.; Balderman, D. *Synthesis* **1973**, 358.

(5) Hunig, S.; Wehner, G. *Synthesis* **1974**, 180.

(6) (a) Hauser, C. R.; Taylor, H. M.; Ledford, T. G. *J. Am. Chem. Soc.* **1960**, *82*, 1786. Morris, G. F.; Hauser, C. R. *J. Org. Chem.* **1961**, *26*, 4741. Hauser, C. R.; Morris, G. F. *Ibid.* **1961**, *26*, 4740. (b) Bennett, D. J.; Kirby, G. W.; Moss, V. A. *Chem. Commun.* **1967**, 218; *J. Chem. Soc. C* **1970**, 2049.

(7) Dyke, S. F.; Tiley, E. P.; White, A. W. C.; Gale, D. P. *Tetrahedron* **1975**, *31*, 1219.

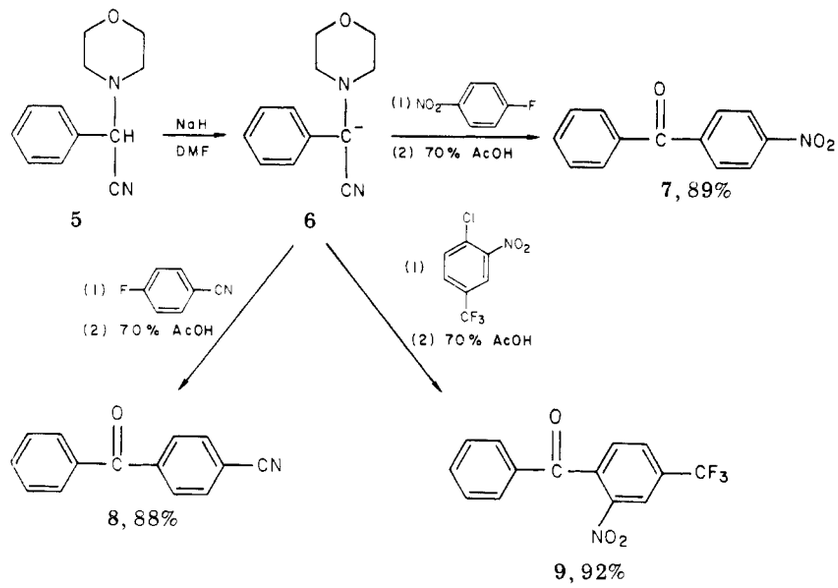
(8) (a) Leete, E.; Chedekel, M. P.; Boden, G. B. *J. Org. Chem.* **1972**, *37*, 4465. (b) Leete, E.; Boden, G. B. *J. Am. Chem. Soc.* **1976**, *98*, 6321.

(9) Albright, J. D.; McEvoy, F. J.; Moran, D. B. *J. Heterocycl. Chem.* **1978**, *15*, 881.

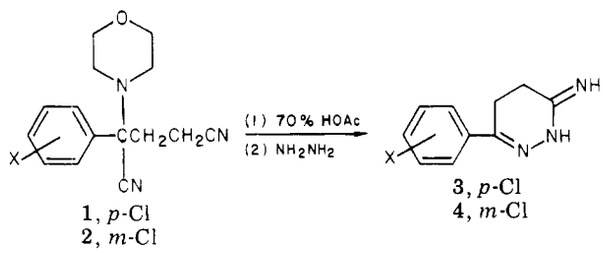
(10) McEvoy, F. J.; Allen, G. R. *J. Org. Chem.* **1973**, *38*, 4044.

0022-3263/79/1944-4597$01.00/0

Scheme I



We report on some reactions of α-aryl-4-morpholineacetonitriles **1** which extend the utility of these derivatives in organic synthesis. The 1,4-addition products **1** and **2** react directly with hydrazine to give imino derivatives **3** and **4**, respectively. The reaction of anion **6** with 4-fluoronitrobenzene, 4-chloro-3-nitro-1-(trifluoromethyl)-benzene, or 4-fluorobenzonitrile followed by hydrolysis of the intermediates gave high yields of benzophenone derivatives **7–9** (Scheme I).

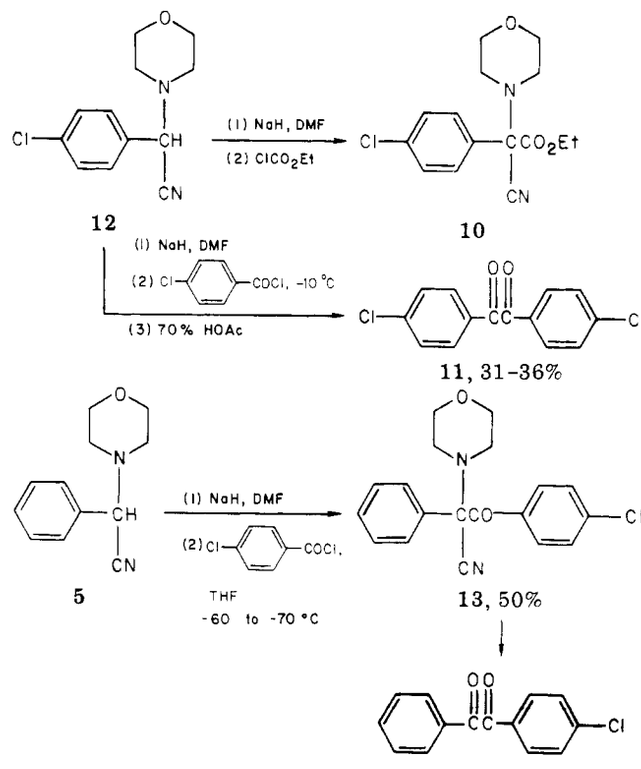


The anions of α-aryl-4-morpholineacetonitriles can also be acylated. For example, reaction of ethyl chloroformate with the anion of **12** gave **10** (94% crude yield) while *p*-chlorobenzoyl chloride gave benzil **11**, after hydrolysis to free the masked carbonyl function. The original acylation studies were conducted at −10 to −20 °C. However, later work showed that superior results are obtained at −60 to −70 °C. By this acylation procedure, unsymmetrical benzils can be conveniently prepared in moderate yields (ca. 50%.) (Scheme II).

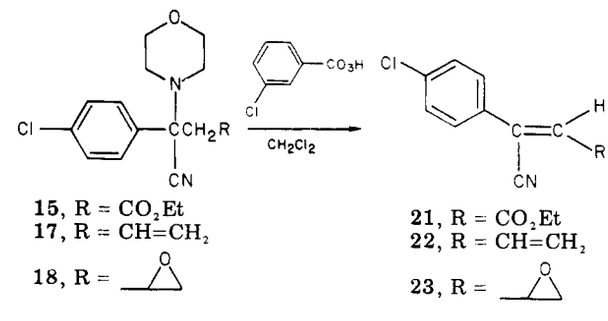
Alkylation of the anion of **5** or **12** with ethyl bromoacetate, epichlorohydrin, or allyl chloride gave derivatives **15–18**. Better yields were obtained when alkylations with ethyl bromoacetate were carried out at −60 to −70 °C. Of special interest is the reactivity of epoxide **18**. Hydrolysis of **18** in 70% acetic acid or stirring with a sulfonic acid resin gave 2-(*p*-chlorophenyl)furan (82%) (**19**). Reaction with ammonium acetate gave 2-(*p*-chlorophenyl)pyrrole (**20**). Thus the overall reaction sequence of alkylation of an α-aryl-4-morpholineacetonitrile with epichlorohydrin and hydrolysis under appropriate conditions is a potentially useful method for the preparation of 2-arylfurans and -pyrroles (Scheme III).

The products **15**, **17**, and **18** were reacted with *m*-chloroperbenzoic acid to give unsaturated nitrile derivatives. Three to four moles of peracid (analytically assayed for peracid content) was required to completely consume

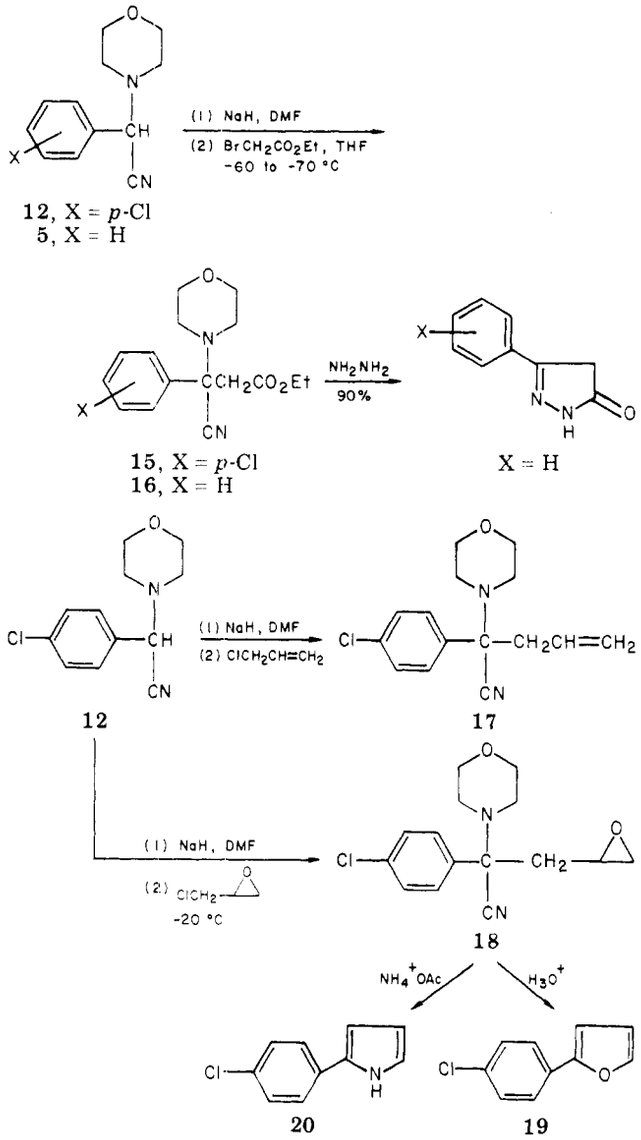
Scheme II



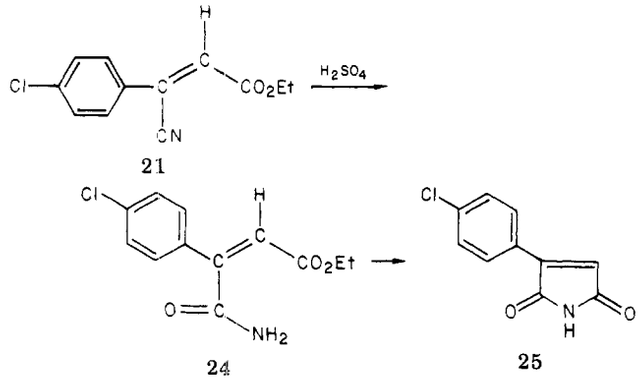
starting material and give the best yields (40–70%). The requirement for excess peracid is not understood since the mechanism is visualized as *N*-oxide formation followed by elimination of morpholine *N*-oxide to introduce the double bond.



Scheme III



The cis relationship of the R group and the cyano function was established for derivative **21** by hydrolysis and ring closure to the known derivative **25**.[11]



Of interest was the preparation of the *N*-oxide derivatives **26** and **27** as potential synthetic substrates. α-(*p*-Chlorophenyl)-4-morpholineacetonitrile and α-[3,4-(methylenedioxy)phenyl]-4-morpholineacetonitrile with *m*-chloroperbenzoic acid gave *N*-oxides **26** and **27**. However, reaction of **26** with sodium hydride followed by ethyl bromoacetate failed. The anions of **26** and **27** are unstable and rearrange to the amides **28** and **29** (Scheme IV). Hydrolysis of **27** with aqueous acetic acid gave 3,4-(methylenedioxy)benzoic acid (**30**). The overall consequence of the *N*-oxide rearrangement is the oxidization of the aldehyde function to an acid.

Scheme IV

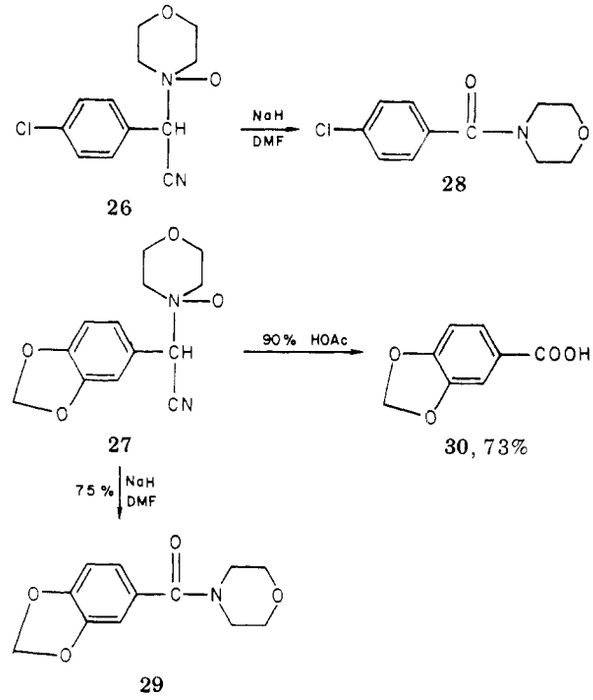
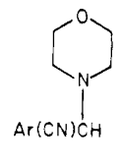
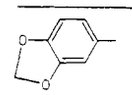
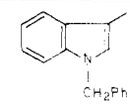
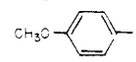
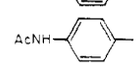


Table I[a-c]



Ar	% yield	mp, °C	Ar	% yield	mp, °C
	90	118-120		88	142-144[a]
	84	77-19		85	98-99[a]
	93	152-154		83	73-74[a]

[a] Analytical values (C, H, N) for compounds were submitted for review and were within ± 0.4% of calculated values; unmarked compounds were not analyzed. [b] ^{1}H NMR spectra were determined on all compounds and chemical shifts (δ) were as expected. [c] Compounds were prepared according to procedure 1 in the Experimental Section.

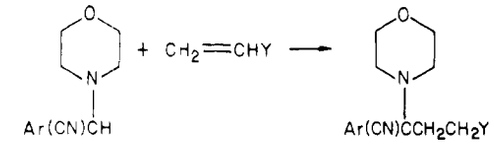
Experimental Section

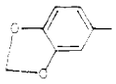
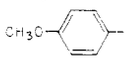
All melting points were taken on a Mel-Temp apparatus and are uncorrected. Samples for analysis were dried in vacuo 18 h at 50 °C. Infrared spectra were determined on a Perkin-Elmer spectrophotometer (Model 21). ^{1}H NMR spectra were determined on all compounds reported with a Varian HR-100 spectrometer and chemical shifts (δ) were as expected.

Procedure 1. 9-Ethyl-α-morpholino-3-carbazoleacetonitrile. To a solution of 44.6 g (0.20 mol) of *N*-ethylcarbazole-

(11) Umio, S.; Kariyone, K.; Nakamura, H. Japanese Patent 68 29950; *Chem. Abstr.* **1969**, *70*, 67956.

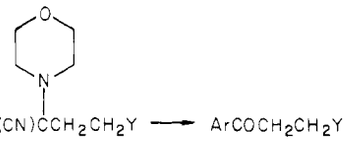
Table II[a-c]

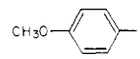
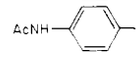
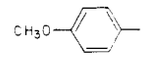


Ar	Y	% yield	mp, °C
	CN	65	gum
	CN	100	gum
	CN	100	109–111[a]
	CO_2Et	90	79–81
	CO_2Et	95	gum
	CO_2Et	68	94–95[a]

[a] Analytical values (C, H, N) for compounds were submitted for review and were within ±0.4% of calculated values; unmarked compounds were not analyzed. [b] ^1H NMR spectra were determined on all compounds and chemical shifts (δ) were as expected. [c] Compounds were prepared according to procedure 2 in the Experimental Section. When Y is CO_2Et, ethyl acrylate was used in place of acrylonitrile in procedure 2.

Table III[b-d]



Ar	Y	% yield	mp, °C
	CN	61[a]	92–93[b]
	CN	87	185–189
	CO_2Et	54[a]	52–53[b]
	CN	90	67–68[b]
	CN	29[a]	49–52
	CO_2Et	74	162–164[b]
	CO_2Et	75	134–136[b]
	CO_2Et	59	137–138[b]

[a] Yields are for two steps: reaction of the aryl-4-morpholineacetonitrile with acrylonitrile followed by hydrolysis with 70% acetic acid. A similar procedure for the preparation of 3-aroylpropionitriles has been reported.[19] [b] Analytical values (C, H, N, Cl) for compounds were submitted for review and were within ±0.4% of calculated values; unmarked compounds were not analyzed. [c] ^1H NMR spectra were determined on all compounds and chemical shifts (δ) were as expected. [d] Compounds were prepared by hydrolysis in refluxing 70% acetic acid for 1 h.

3-carboxaldehyde was added 34.8 mL (0.40 mol) of morpholine and 40 g (0.21 mol) of *p*-toluenesulfonic acid. To the mixture was added 13 g (0.20 mol) of potassium cyanide in 10 mL of water. The mixture was refluxed for 1 h and poured into 920 mL of a 10% potassium carbonate solution. The mixture was extracted with CH_2Cl_2 and the extract washed with 10% $NaHSO_3$ solution. The extract was dried ($MgSO_4$) and the solvent removed to give a viscous oil which was crystallized from petroleum ether (bp 30–60 °C) to give 59.6 g (93%) of tan crystals. Recrystallization from ethanol gave 46.1 g (72%) of tan crystals, mp 142–143° C. A 30-g sample was recrystallized from ethanol with the aid of activated carbon to give 24.4 g of white crystals, mp 143–144 °C.

Anal. Calcd for $C_{20}H_{21}N_3O$: C, 75.2; H, 6.6; N, 13.2. Found: C, 75.2; H, 6.9; N, 13.2.

Procedure 2. 4-Methyl-2-morpholine-2-phenylglutaronitrile. To a solution of 40.4 g (0.2 mol) of α-phenyl-4-morpholineacetonitrile in 400 mL of tetrahydrofuran was added 10 mL of 30% KOH in ethanol. To the solution was added dropwise 21 mL (0.25 mol) of methacrylonitrile (exotherm, 16 → 26 °C). After 18 h of stirring, the solvent was removed and ether added. Acetone was added until the crystals dissolved. The mixture was filtered and the filtrate concentrated. The residue was triturated with hexane to give 51.1 g (95%) of off-white crystals, mp 93–98 °C. A sample (0.5 g) recrystallized twice from methanol–water gave 0.29 g of 4-methyl-2-morpholine-2-phenylglutaronitrile as white crystals, mp 105–112 °C.

Anal. Calcd for $C_{16}H_{19}ON_3$: C, 71.3; H, 7.1; N, 15.6. Found: C, 71.3; H, 7.3; N, 15.6.

3-Benzoyl-2-methylpropionic Acid. A mixture of 5.0 g (0.0186 mol) of 4-methyl-2-morpholine-2-phenylglutaronitrile and 50 mL of 6 N HCl was refluxed for 1 h. The mixture was chilled and filtered, and the solid was washed with water to give 3.11 g (87%) of white crystals, mp 142–144 °C. Recrystallization from acetone–hexane gave 2.4 g of crystals, mp 145–146 °C (lit.[17] mp 139–141 °C).

Anal. Calcd for $C_{11}H_{12}O_3$: C, 68.7; H, 6.3. Found: C, 69.0; H, 6.5.

3-(*p*-Chlorophenyl)-1,4,5,6-tetrahydro-6-iminopyridazine (3).[18] A mixture of 10.4 g of 3-(*p*-chlorobenzoyl)propionitrile, 4.5 g of hydrazine hydrate, 1.8 g of glacial acetic acid, and 50 mL of ethanol was refluxed for 1 h. The mixture was cooled and filtered to give 6.7 g (60%) of crystals, mp 224–226 °C.

Anal. Calcd for $C_{10}H_{10}ClN_3$: C, 57.84; H, 4.85; N, 20.24; Cl, 17.07. Found: C, 57.79; H, 4.67; N, 20.36; Cl, 17.01.

3-(*m*-Chlorophenyl)-1,4,5,6-tetrahydro-6-iminopyridazine (4).[18] A mixture of 3.54 g of 3-(*m*-chlorobenzoyl)propionitrile, 1.5 g of hydrazine hydrate, 1.8 g of glacial acetic acid, and 25 mL of ethanol was refluxed for 2 h. (A precipitate formed after 15 min.) After cooling, the mixture was filtered to give 2.5 g (66%) of crystals, mp 213–214 °C.

Anal. Calcd for $C_{10}H_{10}ClN_3$: C, H, 4.9; N, 20.2; Cl, 17.1. Found: C, 57.7; H, 4.8; N, 20.3; Cl, 17.0.

***p*-Benzoylbenzonitrile (8).** A sample of 1.15 g (0.025 mol) of NaH (50% in oil) was washed with hexane. To the hydride was added 50 mL of dry *N,N*-dimethylformamide and 4.04 g (0.020 mol) of α-phenyl-4-morpholineacetonitrile. The mixture was stirred 2 h and 2.42 g (0.020 mol) of *p*-fluorobenzonitrile in 10 mL of DMF was added dropwise (moderate exotherm). The mixture was stirred at room temperature for 1 h and heated on a steam bath for 1 h. The mixture was poured onto ice containing

(12) (a) "Dictionary of Organic Compounds"; Oxford University Press Inc.: New York, 1965; Vol. I, p 357. (b) *Ibid.*, p 961. (c) *Beilstein 19*, 629.
(13) Ayres, D. C.; Smith, J. R. *J. Chem. Soc. C* **1968**, 2737.
(14) Thompson, T. W. *Chem. Commun.* **1968**, 532.
(15) Kasztreiner, E.; Brosy, J.; Vargha, L. *Biochem. Pharmacol.* **1962**, *11*, 651.
(16) Farnum, D. G.; Yates, P. *J. Am. Chem. Soc.* **1962**, *84*, 1399.
(17) Alexander, E. R.; Mudrak, A. *J. Am. Chem. Soc.* **1950**, *72*, 3194. Harnik, M. *Isr. J. Chem.* **1965**, *3*, 1. From the literature procedure (Friedel–Crafts acylation of benzene with methylsuccinic anhydride), it is not clear whether significant amounts of isomeric 3-benzoyl-3-methylpropionic acid are formed.
(18) Prepared by J. P. Dusza.
(19) Reutrakul, V.; Nimgirawath, S.; Panickanun, S.; Ratananukul, P. *Chem. Lett.* **1979**, 339.

3 mL of acetic acid and filtered. The solid in 100 mL of 70% acetic acid was refluxed for 30 min. The mixture was chilled, poured onto ice, and filtered to give 3.65 g (88%) of yellow crystals, mp 110–114 °C (lit.[12a] mp 107–108 °C).

Anal. Calcd for $C_{14}H_9NO$: C, 81.1; H, 4.4; N, 6.8. Found: C, 80.7; H, 4.5; N, 6.8.

α-Phenyl-α-(α,α,α-trifluoro-2-nitro-*p*-tolyl)-4-morpholineacetonitrile and 2-Nitro-4-(trifluoromethyl)-benzophenone (9). A 1.15-g sample (0.025 mol) of sodium hydride (50% in oil) was washed with hexane. To the hydride was added 50 mL of *N,N*-dimethylformamide and 4.04 g (0.020 mol) of α-phenyl-4-morpholineacetonitrile. After 1 h of stirring under argon, the mixture was chilled to 0 °C and 4.50 g (0.020 mol) of 4-chloro-3-nitro-1-(trifluoromethyl)benzene in 10 mL of DMF was added dropwise over 30 min. The ice bath was removed, and the mixture was stirred 30 min and poured onto ice containing 3 mL of acetic acid. After the mixture was allowed to stand, the solid was filtered and washed with water to give 7.45 g (95%) of yellow crystals, mp 173–177 °C. The solid was dissolved in 75 mL of hot $CHCl_3$–EtOH (2:1), and the mixture was diluted with ethanol and chilled. The crystals were filtered and washed with ethanol to give 6.12 g of yellow crystals, mp 188–192 °C.

Anal. Calcd for $C_{19}H_{16}F_3N_3O_3$: C, 58.3; H, 4.1; N, 10.7; F, 14.6. Found: C, 57.8; H, 4.1; N, 10.6; F, 14.7.

A 2.0-g sample of α-phenyl-α-(α,α,α-trifluoro-2-nitro-*p*-tolyl)-4-morpholineacetonitrile in 50 mL of 70% acetic acid was refluxed for 30 min. The mixture was chilled, diluted with ice water, and filtered to give 1.47 g (97%) of tan crystals, mp 79–81 °C (lit.[4] mp 79–82 °C).

Anal. Calcd for $C_{14}H_8F_3NO_3$: C, 57.0; H, 2.7; N, 4.7; F, 19.3. Found: C, 56.8; H, 2.8; N, 4.8; F, 19.7.

4-Nitrobenzophenone (7). A 1.15-g (0.025 mol) sample of NaH (50% in oil) was washed with hexane. To the hydride was added 50 mL of dry *N,N*-dimethylformamide and 4.04 g (0.020 mol) of α-phenyl-4-morpholineacetonitrile. The mixture was stirred under argon for 45 min and chilled in ice bath, and 2.82 g (0.020 mol) of *p*-fluoronitrobenzene in 10 mL of DMF was added dropwise over 15 min. The mixture was stirred for 1.5 h and poured onto ice containing 5 mL of acetic acid. The mixture was filtered and the damp solid, in 100 mL of 70% acetic acid, was refluxed for 30 min. The mixture was chilled, diluted with ice water, and filtered. The solid was washed with water to give 4.05 g (89%) of yellow crystals, mp 134–137 °C (lit.[4] mp 135–136 °C).

Ethyl α-(*p*-Chlorophenyl)-α-cyano-4-morpholineacetate (10). A sample of 2.9 g (0.072 mol) of sodium hydride (57% in oil) was washed with hexane under argon. *N,N*-Dimethylformamide (100 mL) was added followed by 14.2 g (0.060 mol) of α-(*p*-chlorophenyl)-4-morpholineacetonitrile. The mixture was stirred 30 min and chilled to 0 °C, and 5.73 mL (0.060 mol) of ethyl chloroformate was added. The mixture was stirred for 30 min, poured into ice, and filtered to give 16.7 g (94%) of orange crystals. Recrystallization from ethanol–hexane gave 11.7 g (61%) of yellow-orange crystals, mp 82–85 °C.

Anal. Calcd for $C_{15}H_{17}N_2O_3Cl$: C, 58.4; H, 5.6; N, 9.1; Cl, 11.5. Found: C, 58.0; H, 5.5; N, 9.0; Cl, 11.5.

α-(*p*-Chlorobenzoyl)-α-phenyl-4-morpholineacetonitrile (13). A 1.15-g (0.025 mol) sample of NaH (50% in oil) was washed with hexane under argon. To the hydride were added 40 mL of DMF and 4.04 g (0.020 mol) of α-phenyl-4-morpholineacetonitrile. The mixture was stirred for 2 h and then chilled in a dry ice–acetone bath. To the almost solidified mixture was added 3.50 g (0.020 mol) of *p*-chlorobenzoyl chloride over 5 min. The bath was removed and the mixture stirred for 45 min. To the mixture was added 1 mL of acetic acid and, while the mixture was cooled, water was added. The supernatant was decanted from the gummy solid and the solid dissolved in ethanol. Chilling and filtering gave 3.45 g of white crystals, mp 124–127 °C. Recrystallization from hexane–acetone gave 2.0 g of white crystals, mp 128–131 °C.

Anal. Calcd for $C_{19}H_{17}N_2O_2Cl$: C, 67.0; H, 5.0; N, 8.2; Cl, 10.4. Found: C, 66.6; H, 5.0; N, 7.8; Cl, 11.2.

4,4'-Dichlorobenzil (11). A sample of 1.15 g (0.025 mol) of NaH (50% in oil) was washed with hexane. To the hydride were added 40 mL of *N,N*-dimethylformamide and 4.73 g (0.020 mol) of α-(*p*-chlorophenyl)-4-morpholineacetonitrile. The mixture was stirred under argon for 1 h and 3.50 g (0.020 mol) of *p*-chlorobenzoyl chloride was added all at once (exothermic). After 20 min, the mixture was poured into ice. After the mixture was allowed to stand, it was filtered and the solid in 80 mL of 70% acetic acid was refluxed for 30 min. The mixture was chilled, poured onto ice, and filtered, and the solid was washed with water, ethanol, and ether to give 1.7 g (31%) of yellow crystals, mp 195–197 °C (lit.[12b] mp 199 °C).

A similar run in *N,N*-dimethylacetamide gave a 36% yield of product. Chilling the reaction mixture (DMF solvent) at −5 °C with addition of the *p*-chlorobenzoyl chloride dropwise over 5 min gave a 32% yield of product.

Ethyl β-Cyano-β-phenyl-4-morpholinepropionate (16). A 1.15-g (0.025 mol) sample of NaH (50% in oil) was washed with hexane under argon. Dry DMF (40 mL) and 4.04 g (0.020 mol) of α-phenyl-4-morpholineacetonitrile were added. The mixture was stirred for 1.5 h and then chilled in a dry ice–acetone bath. To the viscous mass was added dropwise 2.2 mL (0.020 mol) of ethyl bromoacetate over ca. 2 min. The mixture was stirred for 5 min and the bath removed. After 30 min, 1 mL of acetic acid was added and, while cooling, water was added slowly, the mixture was filtered and the solid was washed with water to give 4.65 g (80%) of white crystals, mp 114–115 °C. Recrystallization of a sample from hexane–acetone gave white crystals, mp 114–116 °C.

Anal. Calcd for $C_{16}H_{20}N_2O_3$: C, 66.6; H, 7.0; N, 9.7. Found: C, 66.8; H, 7.2; N, 9.7.

A mixture of 1 g of ethyl β-cyano-β-phenyl-4-morpholinepropionate in 25 mL of ethanol and 1.0 mL of hydrazine hydrate was refluxed for 18 h and the solvent removed. To the residue was added 7 mL of 70% acetic acid. The mixture was filtered and the solid washed with water to give 0.50 g (90%) of 3-phenyl-2-pyrazolin-5-one as white crystals, mp 238–240 °C (lit.[16] mp 239–240 °C).

Ethyl β-Cyano-β-(*p*-chlorophenyl)-4-morpholinepropionate (15). A 1.76-g (0.044 mol) sample of NaH (60% in oil) was washed with hexane under argon. Dry DMF (30 mL) was added and 9.48 g (0.04 mol) of α-(*p*-chlorophenyl)-4-morpholineacetonitrile in 30 mL of DMF was added dropwise. The mixture was stirred for 1 h and chilled to −18 °C (CCl_4–dry ice), and 4.4 mL (0.04 mol) of ethyl bromoacetate was added all at once (mixture warmed to +10 °C). After 30 min in a cooling bath, the mixture was poured into ice and water. The mixture was extracted with ether and the extract washed with water and saturated NaCl solution. After the mixture was dried ($MgSO_4$), the solvent was removed to give 12.0 g of a gum. Trituration with hexane plus a trace of ether gave 8.6 g of gummy off-white crystals. Recrystallization from ethanol gave 4.5 g (34%) of white crystals, mp 80–81 °C.

Anal. Calcd for $C_{16}H_{19}N_2O_3Cl$: C, 59.5; H, 5.9; N, 8.7; Cl, 11.0. Found: C, 59.6; H, 6.2; N, 8.7; Cl, 11.1.

α-(*p*-Chlorophenyl)-α-(2,3-epoxypropyl)-4-morpholineacetonitrile (18). A 1.76-g (0.044 mol) sample of NaH (60% in oil) was washed with hexane under argon. Dry DMF (30 mL) was added and 9.48 g (0.040 mol) of α-(*p*-chlorophenyl)-4-morpholineacetonitrile in 30 mL of DMF was added dropwise. The mixture was stirred at room temperature for 2 h and cooled to 5° in an ice bath. To the mixture was added dropwise 3.44 mL (0.04 mol) of epibromohydrin in 10 mL of DMF. The mixture was stirred for 1 h at 5–10 °C and poured into ice and water. The mixture was extracted with ether, and the extracts were washed with water and saturated NaCl solution. After the mixture was dried ($MgSO_4$), the solvent was removed to give 11.2 g (96%) of a colorless gum. A similar run (0.10 mol) using epichlorohydrin (0.10 mol) gave 23.1 g (79%) of an amber gum. A 20-g sample was chromatographed over silica gel with CCl_4 as eluent to give 13.6 g of a clear gum which yielded one spot by TLC (silica gel, CH_2Cl_2). Trituration of a sample with hexane and recrystallization from methanol–water gave white crystals, mp 82–84 °C.

Anal. Calcd for $C_{15}H_{17}N_2O_2Cl$: C, 61.5; H, 5.9; N, 9.6; Cl, 12.1. Found: C, 61.3; H, 6.2; N, 9.5; Cl, 12.0.

α-[3,4-(Methylenedioxy)phenyl]-α-(2,3-epoxypropyl)-4-morpholineacetonitrile. A sample of 8.8 g (0.22 mol) of NaH (60% in oil) was washed with hexane under argon. Dry DMF (10 mL) and 49.2 g (0.20 mol) of α-[3,4-(methylenedioxy)phenyl]-4-morpholineacetonitrile in 200 mL of DMF were added, and the mixture was heated at 60 °C for 3 h. The mixture was chilled and 17.2 mL (0.22 mol) of epichlorohydrin in 24 mL of DMF was

added dropwise (exotherm). After 18 h of stirring at room temperature, the mixture was poured into ice and water. The mixture was extracted with ether and the extracts were washed with water and NaCl solution. After the mixture was dried ($MgSO_4$), the solvent was removed to give 51 g of a dark gum. The gum was chromatographed over silica gel with CH_2Cl_2–ether (1:1) as eluent. The first two cuts were combined to give 23.7 g (40%) of a gum which yielded one spot by TLC [silica gel, CH_2Cl_2–Et_2O (1:1)].

α-Allyl-α-(*p*-chlorophenyl)-4-morpholinacetonitrile (17). A 4.4-g (0.11 mol) sample of NaH (60% in oil) was washed with hexane under argon. Dry DMF (75 mL) was added and 23.7 g (0.10 mol) of α-(*p*-chlorophenyl)-4-morpholineacetonitrile in 75 mL of DMF was added dropwise. The mixture was stirred at room temperature for 2 h and 7.9 mL (0.11 mol) of allyl chloride was added dropwise. The mixture was stirred 18 h and filtered, and the filtrate was poured into 600 mL of ice and water. The mixture was extracted with ether and the extracts were washed with water and saturated NaCl solution. After the mixture was dried ($MgSO_4$), the solvent was removed to give 20.4 g (74%) of an amber oil. Trituration with hexane gave 13.7 g (50%) of white crystals, mp 80–84 °C. A sample was recrystallized from acetone–hexane to give white crystals, mp 84–86 °C.

Anal. Calcd for $C_{15}H_{17}N_2OCl$: C, 65.1; H, 6.2; N, 10.1; Cl, 12.8. Found: C, 65.1; H, 6.1; N, 10.0; Cl, 12.9.

2-(4-Chlorophenyl)furan (19). A 2-g sample of sulfonic acid resin (in the Na^+ form) was slurried with 25 mL of 1 N HCl and the solvent decanted. The resin was washed with water until the supernatant was neutral. The wet resin was added to a solution of 1.0 g (3 mmol) of α-(*p*-chlorophenyl)-α-(2,3-epoxypropyl)-4-morpholineacetonitrile in 20 mL of tetrahydrofuran. The mixture was refluxed for 18 h and filtered, and the filtrate was concentrated to dryness. Toluene was added and the solvent removed. The residue crystallized to give 0.50 g (82%) of product, mp 65–66 °C. In a similar run, hydrolysis of a sample (30 mmol) with 90% acetic acid (reflux 2 h) gave 0.98 g of white crystals (after silica gel chromatography with CH_2Cl_2 as eluent). Recrystallization from methanol–water gave 0.37 g (7%) of white crystals, mp 66–68 °C (lit.[13] mp 66 °C).

Anal. Calcd for $C_{10}H_7OCl$: C, 67.2; H, 4.0; Cl, 19.9. Found: C, 67.4; H, 4.3; Cl, 19.5.

2-(*p*-Chlorophenyl)pyrrole (20). A mixture of 1.0 g (3 mmol) of α-(*p*-chlorophenyl)-α-(2,3-epoxypropyl)-4-morpholineacetonitrile and 2.0 g of ammonium acetate was heated at 135 °C for 2 h. The cooled mixture was diluted with water and extracted with dichloromethane, and the extracts were washed with water and dried ($MgSO_4$). The solvent was removed and the residue (0.49 g) chromatographed on silica gel (CH_2Cl_2). The first cut gave 0.24 g (40%) of crystals. Recrystallizations from methanol–water gave 45 mg of white crystals mp 126–129 °C (lit.[14] mp 137–139 °C), which darkened on standing.

Anal. Calcd for $C_{10}H_8NCl$: C, 67.6; H, 4.5; N, 7.9, Cl, 20.0. Found: C, 67.4; H, 4.5; N, 6.8; Cl, 20.0.

Ethyl *p*-Chloro-β-cyanocinnamate (21). To a solution of 0.969 g (0.003 mol) of ethyl β-cyano-β-(*p*-chlorophenyl)-4-morpholinepropionate in 10 mL of CH_2Cl_2 was added 2.40 g (0.009 mol) of *m*-chloroperbenzoic acid (65%) in 40 mL of CH_2Cl_2 (exotherm, 17 → 31 °C). The mixture was stirred at room temperature for 18 h, chilled, and filtered. The filtrate was washed with 10% sodium sulfite, saturated $NaHCO_3$ solution, and NaCl solution. After the mixture was dried ($MgSO_4$), the solvent was removed to give 0.9 g of an amber oil which crystallized. The solid was dissolved in MeOH (6 mL), and water was added until the solution was turbid. Chilling and filtering gave 0.44 g (62%) of white needles, mp 76–77 °C.

Anal. Calcd for $C_{12}H_{10}NO_2Cl$: C, 61.2; H, 4.3; N, 5.9; Cl, 15.1. Found: C, 61.2; H, 4.5; N, 6.0; Cl, 15.0.

A 50-mg sample was dissolved in concentrated sulfuric acid and the solution chilled in a refrigerator for 2 days. The solution was poured onto ice and filtered, and the solid was washed with water to give 51 mg of white crystals, mp 90–118 °C (resolidifies and melts at 181–184° C). The ^1H NMR spectrum (50 mg in $CDCl_3$–Me_2SO) showed the expected peaks for OCH_2CH_3, aromatic protons (5), and one olefinic proton. The solvent was removed under vacuum, and the residue was heated on a steam bath for 2 h and then under argon at 145 °C in an oil bath for 30 min. The crystalline residue was heated with 5 mL of toluene and filtered, and the filtrate was chilled and filtered to give 11 mg of yellow crystals of 2-(*p*-chlorophenyl)maleimide; mp 184–186 °C (lit.[11] 187–188 °C). Mass spectrum: *m/e* found, 207.0081 (M^+); calcd for $C_{10}H_6NO_2Cl$, 207.0087 (M^+).

2-(*p*-Chlorophenyl)-4,5-epoxy-2-pentenonitrile (23). To a solution of 21.0 g (0.0715 mol) of α-(*p*-chlorophenyl)-α-(2,3-epoxypropyl)-4-morpholineacetonitrile in 210 mL of CH_2Cl_2 was added 49.5 g (0.2443 mol) of *m*-chloroperbenzoic acid (85%) in 800 mL of CH_2Cl_2 (exotherm, 22 → 37 °C, moderated with a water bath). The mixture was stirred at room temperature for 18 h, chilled, and filtered. The filtrate was washed with 500 mL of 10% sodium sulfite and with saturated $NaHCO_3$ solution. After the mixture was dried ($MgSO_4$), the solvent was removed to give 14.5 g of an amber gum. The gum was chromatographed over a column of silica gel with CH_2Cl_2 as eluent (250-mL cuts). The first four cuts were combined and the solvent removed to give 9.8 g of gum. Trituration with hexane gave 8.73 g (63%) of crystals, mp 68–75 °C. A 6.7-g sample was recrystallized from methanol–water and from methanol to give 3.0 of off-white crystals, mp 83–84 °C. From a similar run (0.003 mol) the product was obtained as white needles, mp 81–82 °C.

Anal. Calcd for $C_{11}H_8NOCl$: C, 64.2; H, 3.9; N, 6.8; Cl, 17.2. Found: C, 64.6; H, 4.3; N, 6.7; Cl, 17.1.

Multiple runs (0.002-mol scale) showed that the best yields were obtained when 4 mol equiv of *m*-chloroperbenzoic acid was used.

2-(*p*-Chlorophenyl)-2,4-pentadienonitrile (22). To a solution of 161 g (0.79 mol) of *m*-chloroperbenzoic acid (85%) in 700 mL of dichloromethane was added dropwise a solution of 50 g (0.18 mol) of α-allyl-α-(*p*-chlorophenyl)-4-morpholineacetonitrile in 180 mL of CH_2Cl_2 (exotherm-controlled by chilling). The mixture was stirred at room temperature for 18 h, chilled, and filtered. The filtrate was washed with 10% sodium sulfite solution and saturated $NaHCO_3$ solution. The solvent was removed to give an oil. Trituration with hexane gave a semisolid. The hexane was decanted and the solvent removed to give 5.8 g of oil. The oil was chromatographed over silica gel (hexane–CH_2Cl_2 (1:1)) to give 1.6 g (4.6%) of crystals after trituration with petroleum ether. Several recrystallizations from methanol–water gave 0.25 g of crystals, mp 76–78 °C.

Anal. Calcd for $C_{11}H_8NCl$: C, 69.7; H, 4.3; N, 7.4; Cl, 18.7. Found: C, 69.4; H, 4.5; N, 7.4; Cl, 18.6.

The semisolid was chromatographed over silica gel (CH_2Cl_2) to give 21.1 g of a gummy solid after washing with hexane. Chromatography (basic alumina, CH_2Cl_2) of the hexane-soluble oil (8.1 g) gave 2.74 g (7.9%) of crystals, mp 76–78 °C. Chromatography of the 21.1 g of semisolid on basic alumina (CH_2Cl_2) gave 8.2 g (24%) of crystals, mp 76–78 °C.

α-(*p*-Chlorophenyl)-4-morpholineacetonitrile 4-Oxide (26). To a solution of 11.9 g of α-(*p*-chlorophenyl)-4-morpholineacetonitrile in 50 mL of dichloromethane was added a solution of 10.2 g of 85% *m*-chloroperbenzoic acid in 200 mL of dichloromethane (exotherm). The mixture was stirred at room temperature for 2 h, chilled, and filtered, and the filtrate was washed with 10% sodium sulfite solution and saturated sodium bicarbonate. The organic layer was dried ($MgSO_4$) and the solvent removed under vacuum. The residual gum was triturated with hexane and the crystals were filtered to give 9.6 g of tan solid. The solid in dichloromethane was passed through a column of silica gel. Evaporation of the first cut gave 8.7 g of a solid which was triturated with hexane to give 7.14 g (75%) of tan crystals, mp 85–89 °C. Recrystallization from methanol gave 5.5 g of white needles, mp 93–95 °C.

Anal. Calcd for $C_{12}H_{13}O_2N_2Cl$: C, 57.0; H, 5.2; N, 11.1; Cl, 14.0. Found: C, 57.2; H, 5.3; N, 10.2; Cl, 14.3.

4-(*p*-Chlorobenzoyl)morpholine (28). A 0.22-g (5.5 mmol) sample of NaH (60% in oil) was washed with hexane under argon. To the NaH was added 5 mL of DMF and 1.27 g (5.0 mmol) of α-(*p*-chlorophenyl)-4-morpholineacetonitrile 4-oxide in 10 mL of DMF. The mixture was stirred at room temperature for 4 h and poured into 40 mL of ice and water. The mixture was extracted with ether, and the ether extracts were washed with water, dried ($MgSO_4$), and concentrated to give 0.52 g of gum. Trituration with hexane gave 0.31 g of tan crystals, mp 71–73 °C (27%). Recrystallizations twice from CH_2Cl_2–hexane gave 84 mg of crystals, mp 76–77 °C.

Anal. Calcd for $C_{11}H_{12}ClNO_2$: C, 58.5; H, 5.4; N, 6.2; Cl, 15.7.

Found: C, 58.9; H, 5.5; N, 6.3; Cl, 15.7.

α-[3,4-(Methylenedioxy)phenyl]-4-morpholineacetonitrile 4-Oxide (27). To a solution of 12.3 g (0.05 mol) of α-[3,4-(methylenedioxy)phenyl]-4-morpholineacetonitrile in 50 mL of dichloromethane was added 11.2 g (0.055 mol) of *m*-chloroperbenzoic acid in 200 mL of dichloromethane. The exotherm was moderated with a cold water bath. After 18 h of stirring at room temperature, the mixture was filtered and the filtrate washed with 10% sodium sulfite and with saturated $NaHCO_3$ solution. The organic layer was dried ($MgSO_4$) and concentrated to a gum (12.1 g). Trituration with hexane gave 11.4 g (87%) of white crystals, mp 99–101 °C. A 0.50-g sample was recrystallized from acetone-hexane to give 0.40 g of white crystals, mp 104–105 °C.

Anal. Calcd for $C_{13}H_{14}N_2O_4$: C, 59.5; H, 5.4; N, 10.7. Found: C, 59.2; H, 5.7; N, 10.5.

3,4-(Methylenedioxy)benzoic Acid (30). A solution of 2.62 g (0.01 mol) of α-[3,4-(methylenedioxy)phenyl]-4-morpholineacetonitrile 4-oxide in 40 mL of 90% acetic acid was refluxed for 2 h. Cooling and filtering gave 0.52 g (31%) of tan crystals, mp 218–226 °C. The filtrate was diluted with water until turbid. Filtration gave 1.04 g of solid. The solid was heated with acetic acid and filtered from insoluble solid, and the filtrate was diluted with water until turbid. Cooling and filtering gave 0.70 g (42%) of tan crystals, mp 214–217 °C (lit.[12c] mp 229–231 °C). The IR and ^1H NMR spectra were identical with those of authentic piperonylic acid.

4-[3,4-(Methylenedioxy)benzoyl]morpholine (29). A 0.44-g (0.011 mol) sample of sodium hydride (60% in oil) was washed with hexane under argon. To the hydride were added 15 mL of *N,N*-dimethylformamide and a solution of 2.62 g of α-[3,4-(methylenedioxy)phenyl]-4-morpholineacetonitrile 4-oxide in 15 mL of DMF. The solution turned purple and a brown solid precipitated. After 4 h of stirring at room temperature, the solvent was removed under vacuum and the residue was partitioned between dichloromethane and water.

The CH_2Cl_2 layer was washed with saline solution and dried ($MgSO_4$), and the solvent was removed under vacuum. Toluene was added several times and the solvent removed to give 1.91 g (82%) of an amber gum. Bulb-to-bulb distillation of the gum gave 1.75 g (75%) of a pale yellow gum, bp 170–175 °C (0.1 mm) (lit.[15] bp 180–186 °C (0.4 mm)).

Anal. Calcd for $C_{12}H_{13}NO_4$: C, 61.3; H, 5.6; N, 6.0. Found: C, 61.4; H, 5.6; N, 6.0.

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Registry No. **3**, 71818-91-2; **4**, 71818-92-3; **5**, 15190-10-0; **7**, 1144-74-7; **8**, 1503-49-7; **9**, 41938-65-2; **10**, 71818-93-4; **11**, 3457-46-3; **12**, 33599-26-7; **13**, 71818-94-5; **15**, 71818-95-6; **16**, 71818-96-7; **17**, 71818-97-8; **18**, 71818-98-9; **19**, 17221-37-3; **20**, 19867-89-1; **21**, 71818-99-0; **22**, 71819-00-6; **23**, 71819-01-7; **25**, 21724-87-8; **26**, 71819-02-8; **27**, 71819-03-9; **28**, 19202-04-1; **29**, 63916-59-6; **30**, 94-53-1; 9-ethyl-α-morpholino-3-carbazoleacetonitrile, 71819-04-0; *N*-ethylcarbazole-3-carboxaldehyde, 7570-45-8; morpholine, 110-91-8; potassium cyanide, 151-50-8; 4-methyl-2-morpholino-2-phenylglutaronitrile, 71819-05-1; methacrylonitrile, 126-98-7; 3-benzoyl-2-methylpropionic acid, 1771-65-9; 3-(*p*-chlorobenzoyl)propionitrile, 40394-87-4; 3-(*m*-chlorobenzoyl)propionitrile, 34555-37-8; *p*-fluorobenzonitrile, 1194-02-1; α-phenyl-α-(α,α,α-trifluoro-2-nitro-*p*-tolyl)-4-morpholineacetonitrile, 71818-72-9; 4-chloro-3-nitro-1-(trifluoromethyl)benzene, 121-17-5; *p*-fluoronitrobenzene, 350-46-9; ethyl chloroformate, 541-41-3; *p*-chlorobenzoyl chloride, 122-01-0; ethyl bromoacetate, 105-36-2; 3-phenyl-2-pyrazolin-5-one, 4860-93-9; epibromohydrin, 3132-64-7; epichlorohydrin, 106-89-8; α-[3,4-(methylenedioxy)phenyl]-α-(2,3-epoxypropyl)-4-morpholineacetonitrile, 71818-73-0; α-[3,4-(methylenedioxy)phenyl]-4-morpholineacetonitrile, 37673-10-2; allyl chloride, 107-05-1; α-(4-methoxyphenyl)-4-morpholineacetonitrile, 15190-13-3; α-(4-acetamidophenyl)-4-morpholineacetonitrile, 71818-74-1; α-(1-benzyl-3-indolyl)-4-morpholineacetonitrile, 71818-75-2; α-(2-pyridyl)-4-morpholineacetonitrile, 53813-00-6; α-(4-pyridyl)-4-morpholineacetonitrile, 71818-76-3; α-(3-pyridyl)-4-morpholineacetonitrile, 36740-09-7; acrylonitrile, 107-13-1; ethyl acrylate, 140-88-5; γ-(2-pyridyl)-γ-cyano-4-morpholinebutyronitrile, 71818-77-4; ethyl γ-(2-pyridyl)-γ-cyano-4-morpholinebutanoate, 71818-78-5; ethyl γ-(4-pyridyl)-γ-cyano-4-morpholinebutanoate, 71818-79-6; γ-cyano-γ-(4-methoxyphenyl)-4-morpholinebutyronitrile, 71818-80-9; γ-(4-acetamidophenyl)-γ-cyano-4-morpholinebutyronitrile, 71818-81-0; ethyl γ-cyano-γ-(4-methoxyphenyl)-4-morpholinebutanoate, 71818-82-1; γ-cyano-γ-(4-pyridyl)-4-morpholinebutyronitrile, 71818-83-2; ethyl γ-cyano-γ-(3-pyridyl)-4-morpholinebutanoate hydrochloride, 71818-84-3; ethyl γ-cyano-γ-(2-pyridyl)-4-morpholinebutanoate hydrochloride, 71818-85-4; ethyl γ-cyano-γ-(4-pyridyl)-4-morpholinebutanoate hydrochloride, 71818-86-5; 4-methoxy-γ-oxobenzenebutyronitrile, 55234-56-5; 4-acetamido-γ-oxobenzenebutyronitrile, 71000-25-4; ethyl 4-methoxy-γ-oxobenzenebutanoate, 15118-67-9; γ-oxo-2-pyridinebutyronitrile, 71818-87-6; γ-oxo-4-pyridinebutyronitrile, 49835-53-2; ethyl γ-oxo-3-pyridinebutanoate hydrochloride, 71818-88-7; ethyl γ-oxo-2-pyridinebutanoate hydrochloride, 71818-89-8; ethyl γ-oxo-4-pyridinebutanoate hydrochloride, 71818-90-1.

Construction and Base-Promoted Cyclization of a C_{2v}-Symmetric Diepoxy Tetraquinane Disulfone

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A scheme is presented for elaborating dimethyl 2a,3,3a,5a,6,6a,6b,6c-octahydrodicyclopenta[*ch,gh*]pentalene-*endo,endo*-3,6-dicarboxylate (**5**) into a bis-homologated C_{2v}-symmetric diepoxy disulfone (**4**). Although the twofold cyclization of the bis carbanion of **4** could in principle give rise to a functionalized hexaquinane of C_2 symmetry (i.e., **3**), the reaction of **4** with dimsyl anion does not follow this course. Rather, a single α-sulfonyl carbon attacks both epoxides under the basic conditions to deliver a product which contains a newly constructed norbornane ring (i.e., **20**). However, the cyclized material is no longer serviceable for the construction of the dodecahedrane framework.

In connection with investigations aimed at the synthesis of dodecahedrane (**1**), we have considered the possibility that twofold intramolecular cyclization within a centrosymmetric molecule might serve as an efficient means of rapidly enhancing the polyquinane level[1,2] of the structure. Of particular interest to us are those molecules where the nucleophilic and electrophilic centers remain incorporated within the framework to serve later as activated sites conducive to further structural elaboration. The concept is exemplified by the retrosynthetic sequence shown, where

(1) Jacobson, T. Ph.D. Thesis, University of Lund, 1973.

(2) Paquette, L. A. *Fortschr. Chem. Forsch.* **1979**, *79*, 43.

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