123-72-8; 2-methylpropanal, 78-84-2; 2-pentanone, 107-87-9; 3-pentanone, 96-22-0; cyclopentanone, 120-92-3; cyclohexanone, 108-94-1; glucose, 50-99-7; 3,3-dimethyl-2-butanone, 75-97-8; 2-methylcyclohexanone, 583-60-8; camphor, 76-22-2; benzaldehyde, 100-52-7; acetophenone, 98-86-2; 1,3-diphenyl-2-propanone, 102-04-5; 2-acetyl-5-norbornene, 5063-03-6; 2-cyclohexen-1-one, 930-68-7; 3-methylene-2-norbornanone, 5597-27-3; *l*-carvone, 99-49-0; (2-propenylthiomethyl)benzene, 6937-97-9; 6-methyl-5-hepten-2-one, 110-93-0; 3-phenyl-2-propenoic acid, 621-82-9; (propylthiomethyl)benzene, 22336-59-0; *dl*-benzyl 2,3-dideuteriopropyl sulfide, 71766-43-3; *dl*-benzyl 2-deuteriopropyl sulfide, 71766-44-4; benzyl 3-deuteriopropyl sulfide, 71766-45-5; *endo*-2-acetylnorbornane, 824-58-8; *exo*-2-acetylnorbornane, 824-59-9; 3-methyl-2-norbornanone, 643-51-6; cyclohexanone, 108-94-1; 6-methyl-2-heptanone, 928-68-7; *dl-threo*-2,3-dideuterio-3-phenylpropanoic acid, 71806-58-1; *dl*-3-deuterio-3-phenylpropanoic acid, 71806-59-2; *dl*-2-deuterio-3-phenylpropanoic acid, 71766-46-6; 3-phenylpropanoic acid, 501-52-0; cyclopentanone dinitrophenylhydrazone derivative, 2057-87-6; butyraldehyde dinitrophenylhydrazone derivative, 1527-98-6; dinitrophenylhydrazine, 119-26-6; cyclohexanone 2,4-dinitrophenylhydrazone, 1589-62-4.

Direct Synthesis of α,β-Unsaturated Nitriles from Acetonitrile and Carbonyl Compounds: Survey, Crown Effects, and Experimental Conditions

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Detailed experimental conditions are presented for the condensation of acetonitrile with a large number of carbonyl compounds. The condensation is found to be most successful with aromatic aldehydes and diaryl ketones, substrates which yield pure α,β-unsaturated nitriles. Dialkyl ketones also condense readily under the conditions described herein but yield mixtures of double bond isomers. Aliphatic aldehydes do not condense satisfactorily, and a number of base-sensitive functional groups are incompatible with this reaction. Potassium hydroxide is found to be the most efficacious base for this reaction, and a detailed study of the condensation between acetonitrile and benzaldehyde reveals that other bases and solvents may be used, but 18-crown-6 polyether is required in some of these. The condensation is also reported for certain sterically biased ketones, and a discussion of the crown effect in these cases is presented.

The introduction of a two-carbon fragment is a cornerstone of synthetic organic chemistry in the form of numerous reactions such as the malonic ester,[1] acetoacetic ester,[2] Perkin,[3] and Doebner–Knoevenagel[4] condensations. Each of these reactions can afford a substituted acetic acid derivative; the latter can yield α,β-unsaturated nitriles under the appropriate conditions.[5] In most circumstances, the formation of α,β-unsaturated nitriles poses far more problems than the preparation of either saturated or unsaturated acetic acid derivatives.

In principle, the >C=CHCN unit should be accessible by the condensation of acetonitrile (via the cyanomethide anion) with a carbonyl compound, followed by loss of water, as illustrated in eq 1. Although the metalation of

$$R_2C{=}O + MCH_2CN \rightarrow R_2C(OM)CH_2CN \xrightarrow[-H_2O]{+H^+} R_2C{=}CHCN \quad (1)$$

acetonitrile has been reported[6] and some condensations have proved successful, the reaction has not been general. The most serious problems have been: (1) acetonitrile undergoes numerous base-catalyzed side reactions,[6b,7] (2) the bases required to deprotonate acetonitrile often add to acetonitrile or induce reactions of the electrophiles, and (3) cyanomethide salts are often insoluble in low polarity media.[8] Moreover, such strong bases are usually used in nonpolar solvents like tetrahydrofuran, in which the intermediate β-hydroxynitriles (see eq 1) do not spontaneously dehydrate.[6b] We report here a detailed study of the base-induced reaction of acetonitrile with a variety of carbonyl compounds.[9]

Results and Discussion

Acetonitrile can be deprotonated by alkali metal alkoxides (NaOH, KOH), and the cyanomethide ion can then be condensed with a variety of carbonyl compounds. In excess acetonitrile (solvent), the intermediate β-hydroxynitrile apparently dehydrates spontaneously to afford either the α,β- or β,γ-unsaturated (depending on the sub-

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(1) A. C. Cope, H. C. Holmes, and H. O. House, *Org. React.*, **9**, 107 (1957); F. Freeman, *Chem. Rev.*, **69**, 591 (1969).
(2) S. O. Lawesson, M. Andersson, and C. Berglund, *Ark. Kemi.*, **17**, 429 (1961).
(3) (a) W. H. Perkin, *J. Chem. Soc.*, **21**, 53, 181 (1868); (b) J. R. Johnson, *Org. React.*, **1**, 210 (1942).
(4) (a) E. Knoevenagel, *Chem. Ber.*, **31**. 2596 (1898); (b) O. Doebner, *ibid.*, **33**, 2140 (1900).
(5) J. M. Patterson, *Org. Synth.*, **40**, 46 (1960).
(6) C. Kruger, *J. Organomet. Chem.*, **9**, 125 (1967); (b) E. M. Kaiser and C. R. Hauser, *J. Org. Chem.*, **33**, 3402 (1968); (c) D. N. Crouse and D. Seebach, *Chem. Ber.*, **101**, 3113 (1968).
(7) G. A. Reynolds, W. J. Humplett, F. W. Swamer, and C. R. Hauser, *J. Org. Chem.*, **16**, 165 (1951); (b) T. L. Cairns, A. W. Larchar, and B. C. McKusick, *J. Am. Chem. Soc.*, **74**, 5633 (1952); (c) Y. Ogata, Y. Izawa, and Y. Osumi, *Bull. Chem. Soc. Jpn.*, **37**, 74 (1964).
(8) D. Savoia, C. Trombini, and A. Umani-Ronchi, *Tetrahedron Lett.*, 653 (1977).
(9) Some portions of this work have appeared previously in preliminary form: (a) G. W. Gokel, S. A. Dibiase, and B. A. Lipisko, *Tetrahedron Lett.*, 3495 (1976); (b) S. A. DiBiase and G. W. Gokel, *Synthesis*, 629 (1977).

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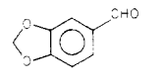
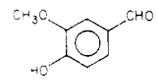
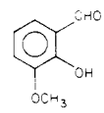
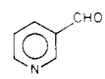
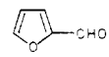
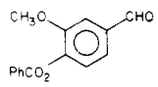
Table I.[a] Synthesis of α,β-Unsaturated Nitriles from Acetonitrile[b] According to Equation 1

carbonyl compd no.	substrate	reaction time	prod no.	isolated yield, %	E/Z[c] ratio
1	C_6H_5-CHO	3 min	42	82[f]	3.0
2	2-CH_3-C_6H_4-CHO	9 min	43	63	3.4
3	4-CH_3-C_6H_4-CHO	6 min	44	61	∞
4	4-CH_3O-C_6H_4-CHO	10 min	45	81	2.1
5	2,3-$(CH_3O)_2$-C_6H_3-CHO	3 min	46	80	5.9
6		7 min	47	86	∞
7		48 h	48	70[d,e]	5.92
8		96 h	49	50[d,e]	∞
9	3-NO_2-C_6H_4-CHO	3 h	50	trace[g]	
10	4-F-C_6H_4-CHO	7 min	51	50	3.6
11	2-Cl-C_6H_4-CHO	1 min	52	36	4.3
12	4-Cl-C_6H_4-CHO	20 s	53	57	∞
13		3 min	54	48	5.6
14		3 min	55	60	4.25
15		24 h	56	trace[h]	

[a] All reactions were conducted at reflux in the presence of powdered KOH (85%, 1 equiv), except with compound 9 which was conducted at 25 ± 3 °C. [b] Solvent. [c] Determined by GLC and/or NMR (see Experimental Section for details). [d] 18-Crown-6 added, see Experimental Section. [e] 2 equivs of KOH used. [f] Yield lower on 0.5 mol scale. [g] Cannizzaro reaction: 44% of 3-nitrobenzyl alcohol obtained when the reaction was conducted at 25 °C; at reflux, only tar was isolated. [h] 20% vanillin, 20% benzoic acid and starting material isolated.

strate) nitrile. The dehydration occurs more readily in polar (acetonitrile, ϵ = 39[10]) and in protic than in nonpolar (e.g., THF, ϵ = 7.6[11]) aprotic solution, an observation which has ample precedent in the literature. Thus, for example, 4-bromobenzaldehyde and ethyl cyanoacetate condense in aqueous ethanol under the influence of KOH to yield ethyl α-cyanocinnamate,[12] but when cinnamaldehyde and ethyl acetate react in THF under the influence of lithium hexamethyldisilazide, a 94% yield of ethyl 3-hydroxy-5-phenyl-4-pentenoate is isolated.[13]

In our case, it seems likely that the combination of solvent polarity, the presence of water (as proton source), and equilibrating conditions all favor dehydration. The direction of double bond formation, the facility of dehydration, and the influence of crown ether on the course and rate of reaction are discussed below.

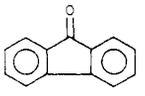
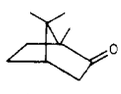
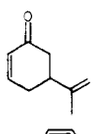
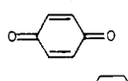
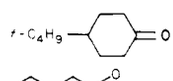
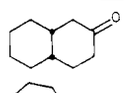
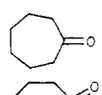
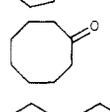
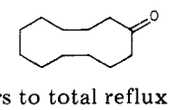
Condensation with Aromatic Aldehydes. Aromatic aldehydes have historically been excellent electrophiles for base-catalyzed condensations, in part because the carbonyl group cannot enolize. These substrates are also good reaction partners for the cyanomethide ion. In a typical reaction, benzaldehyde (1, 1 equiv) was heated for 3 min in acetonitrile (solvent, 1.0 M) in the presence of powdered 85% potassium hydroxide pellets (1 equiv). A 3:1 mixture of (*E*)- and (*Z*)-cinnamonitrile could be isolated from this reaction mixture in over 80% yield. Thirteen successful and several unsuccessful condensation reactions are recorded in Table I. In the successful cases, isolated yields of pure, distilled, or chromatographed products ranged from 36–86%, with most yields being ≥50%. In four cases (condensations of compounds **3**, **6**, **8**, and **12**), the pure *E* isomer was isolated. In all other cases, isomer mixtures were obtained, but the *E* isomer invariably predominated. Cinnamonitriles prepared by other methods often lead exclusively to the *E* isomer, probably due in part to the longer reaction times associated with these other methods. The generally lower E/Z ratios observed here stand in contrast to this.

The reaction time reported in the table is the empirically determined (GC analysis) optimum. To the extent that any trend is apparent, reaction time is inversely proportional to carbonyl electrophilicity. Thus 2- and 4-chlorobenzaldehydes (compounds **11** and **12**) both require shorter reaction times than does benzaldehyde, and piperonal (compound **6**) requires a longer reaction period. The weakness of this generalization is apparent from the reaction times required for 2,3-dimethoxybenzaldehyde (**5**) and 4-fluorobenzaldehyde (**10**), which are respectively the same and longer than required for benzaldehyde. Since the reaction requires less than 10 min for all but the last two cases, the differences in rate are of little consequence.

Vanillin and *o*-vanillin (**7** and **8**) constitute special cases. Condensation with each aldehyde requires excess base because the first equivalent is lost in neutralization of the phenolic hydroxyl. Crown ether was added to the reaction mixture in anticipation of a solubilization effect but was found to make little difference in the ultimate yield over the length of time required for condensation. Vanillin

(10) M. Windholz, "The Merck Index", 9th ed., Merck and Co., Rahway, N.J., 1976, entry 56.
(11) "THF As a Reaction Solvent", Electrochemicals Department, E. I. duPont de Nemours and Co., Inc., Wilmington, DE, 1969.
(12) J. Zabicky, *J. Chem. Soc.*, 683 (1961).
(13) M. W. Rathke, *J. Am. Chem. Soc.*, **92**, 3222 (1970).

Table II. Synthesis of Unsaturated Nitriles from Acetonitrile[a] and Ketones

carbonyl compd no.	substrate	reaction[b] time, h	prod no.	isolated yield, %	$\alpha,\beta/\beta,\gamma$ ratio[c]
16	C_6H_5-CO-CH_3	6	**57**	15	∞
17	C_6H_5-CO-CH_2Cl	1	**58**	*e*	
18	C_6H_5-CO-$CH_2CH_2CH_3$	36	**59**	30	∞
19	C_6H_5-CO-C_6H_5	4.5	**37**	84	
20		48	**60**	68[f]	
21	CH_3CH_2-CO-CH_2CH_3	24	**62**	35	∞
22	n-C_3H_7-CO-n-C_3H_7	48	**63**	65	∞
23	n-C_4H_9-CO-n-C_4H_9	72	**64**	65	∞
24		2	**65**	*g*	
25		1.5	**38, 39**	70	4.5[h]
26		26	**66**	*i*	
27		6	**40, 41**	78	0.98
28		48		*j*	
29		4		*k*	
30		36		*l*	
31		72 (4)[d]	**68**	30 (58)[d]	∞ (0.44)[m]
32		5 (2)[d]	**69**	80 (83)[d]	3.4 (4.7)[m]
33		6	**70**	78	∞
34		33	**71**	66	5.84
35		72	**72**	45	∞

[a] Solvent. [b] Refers to total reflux time unless otherwise noted. [c] Determined by ^1H NMR spectral analysis. [d] Values in parentheses refer to experiments conducted in the presence of 18-crown-6 polyether. [e] Mixture resulted; no unsaturated nitrile was produced. [f] β-Hydroxynitrile **61** was isolated in 76% yield. Dehydration yielded **60** in overall 68% yield. [g] No cyclopentanone remained (GLC) after 2 h, nor was any volatile product detected. [h] When the reaction was run at 0.1 M concentration, 86% yield was obtained. [i] Mixture. [j] No reaction (GLC). [k] At least five products by TLC analysis. [l] Highly colored mixture yielding no organic soluble material. [m] See text.

benzoate (**15**) was more soluble in the reaction medium but suffered hydrolysis of the ester linkage.

Another competing reaction which presented problems occurred during the attempted condensation of acetonitrile with 3-nitrobenzaldehyde (**9**). In this case, the Cannizzaro reaction interferred, affording 3-nitrobenzyl alcohol in 22% yield (44% of theory for the Cannizzaro). Addition of 18-crown-6 reduced, as expected,[14] the amount of Cannizzaro byproduct but did not enhance the yield of nitrile.

The low yield of nitrile (36%) obtained from 2-chlorobenzaldehyde (**11**) might have been due to competitive formation of benzyne by base-catalyzed dehydrohalogenation. The phenolic products which should have been present under these circumstances could not be detected in the reaction mixture.

Reaction of Acetonitrile with Ketones. The attempted direct condensation of acetonitrile with aliphatic aldehydes proved unsuccessful.[15] In contrast, many aliphatic and aromatic ketones afforded unsaturated nitriles as products. The results are summarized in Table II.

The condensation was not generally useful for methyl ketones, especially for compounds like acetone which have boiling points lower than acetonitrile. One example, acetophenone (**16**), is included in the table, and it should be considered marginal at best. The condensation was clearly

(14) G. W. Gokel. H. M. Gerdes, and N. W. Rebert, *Tetrahedron Lett.*, 653 (1976).

(15) Rapid self-condensation of the aliphatic aldehydes generally was the observed result of attempted acetonitrile condensations under the conditions described here.

more successful for propyl phenyl ketones, dialkyl ketones, and cyclic ketones above five members. Especially reactive [cyclopentanone (**24**), benzoquinone (**30**)] and unreactive ketones [camphor (**28**)] yielded little useful product, as did ketones bearing reactive functional groups [e.g., phenacyl chloride (**17**)].

The condensation of acetonitrile with benzophenone (**20**) is expected to be an especially successful case. The intermediate should dehydrate readily to afford the conjugated nitrile, and a single isomer should be formed (see eq 2) since both *E* and *Z* isomers are identical and no β,γ isomerism (see below) is possible.

$$\underset{\mathbf{20}}{Ph_2C{=}O} + M^{+-}CH_2CN \rightarrow \underset{\mathbf{36}}{Ph_2C(OM)CH_2CN} \xrightarrow[\text{or MOH}]{-H_2O} \underset{\mathbf{37}}{Ph_2C{=}CHCN} \quad (2)$$

The reaction sequence described by eq 2 is reported in the literature and affords an interesting comparison. Kaiser and Hauser[6b] condensed acetonitrile and benzophenone, using sodium amide in a mixture of liquid ammonia and ether. The β-hydroxynitrile (**36**, M = H) was isolated in 93% yield and then dehydrated (H_3PO_4 catalyst) in a separate step (65%), affording **37** in 60% overall yield. By our approach, about an 85% yield of **37** could be realized in a single step from **19**.

The success of our approach is due to several factors. Acetonitrile is a polar solvent. It is a poor anion solvator so potassium hydroxide exhibits substantial basicity in this milieu. Acetonitrile is a weak acid (pK ~ 31),[16] so Hauser's use of sodamide was clearly justified. Acetonitrile as solvent for this reaction enhances hydroxide basicity, and the equilibrium conditions also favor dehydration (e.g., **36** → **37** in eq 2), eventually driving the reaction to the right. Surely, the presence of a small amount of water in the KOH assists in solvation and enhances the polarity of the medium.

Most of the ketones studied are symmetrical, so *E,Z* isomerism presented no problem. We presume that a compound such as 4-decanone (not run) would afford an *E,Z* isomer mixture such as that observed for nitriles from aromatic aldehydes (see Table I). Nevertheless, only one isomer was observed in the condensations of acetonitrile with acetophenone and butyrophenone (**16** and **17**).

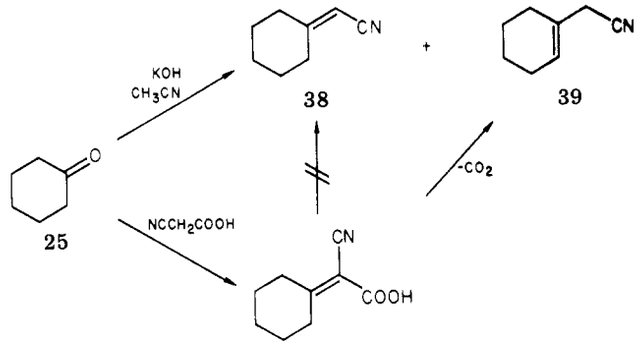
In principle, either 4-heptanone (**22**) or 5-nonanone (**23**) could have yielded mixtures of α,β vs. β,γ isomers as shown in eq 3. In either case, the product is a trisubstituted

$$\underset{\beta,\gamma \text{ isomer}}{RCH{=}\overset{CH_2CN}{\overset{|}{C}}CH_2R} \underset{-H_2O}{\overset{CH_3CN}{\rightleftharpoons}} RCH_2COCH_2R \xrightarrow[-H_2O]{CH_3CN} \underset{\alpha,\beta \text{ isomer}}{RCH_2\overset{CHCN}{\overset{\|}{C}}CH_2R} \quad (3)$$

olefin, so the more conjugated α,β isomer is favored and is formed exclusively. The conjugated isomer is also either favored or formed exclusively for all of the cyclic ketones larger than cyclohexanone which were examined.

The cyclohexane derivatives present an interesting case. Cyclohexanone (**25**) itself condenses readily with acetonitrile to give a mixture of pentamethyleneacrylonitrile (**38**) and (1-cyclohexenyl)acetonitrile (**39**) (**38**–**39** 83:17) in good yield. The yield is, in fact, proportional to the concentration at which the reaction is conducted. The isolated

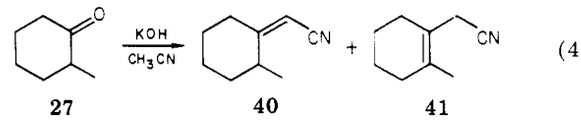
Scheme I



yields of unsaturated nitriles derived from **25** were 86, 70, 58, and 45% respectively when the reactions were run at 0.1, 0.5, 1.0, and 2.0 M, respectively. The results presented in this paper generally refer to 0.5 M concentrations.

The isomer ratio appears to represent the thermodynamic mixture resulting at least in part from equilibration. When pure **39** was treated with sodium ethoxide in ethanol (Linstead's conditions[17]), **38** was obtained as the major product (**38**–**39** 89:11). The predominance of **38** is of consequence since the Doebner–Knoevenagel reaction between cyclohexanone and cyanoacetic acid yields, after decarboxylation, exclusively **39**.[18] The above is summarized in Scheme I. Pure **38** can be obtained by titrating the mixture (**38** + **39**) with dilute bromine solution and distilling **38** from the bromine adduct of **39**.

The isomer problem is more severe for the case of 2-methylcyclohexanone (see eq 4). The position of the



(4)

double bond is influenced by conjugation (**40**) vs. tetrasubstitution of the double bond (**41**). As a result, a nearly 1:1 mixture of **40** and **41** is formed. The mixture of **40** and **41** could be separated by the bromination technique described above for a mixture of **38** and **39**; hydrogenation of the **40**–**41** mixture afforded pure 1-(cyanomethyl)-2-methylcyclohexane in essentially quantitative yield.

Special problems were encountered with the sterically biased 4-*tert*-butylcyclohexanone (**31**) and *cis*-octalone (**32**) systems. The condensation of **31** with acetonitrile was extremely slow and afforded a poor overall yield of product. In the presence of catalytic 18-crown-6 polyether, however, the reaction required 4 h rather than 72 h, and an ultimate yield of 58% rather than 30% was realized. Furthermore, only the α,β-unsaturated nitrile was isolated in the absence of 18-crown-6, whereas a preponderance of the other isomer was obtained in its presence. The reaction rate for **32** more than doubled (5 to 2 h) in the presence of crown, but neither the ultimate yield of nitrile nor the isomer ratio was appreciably affected (see Table II). The influence of crown on the cyclohexanone condensation was assessed and, outside of some small variations in isomer distribution, was found to be marginal.

A possible explanation for the crown effect is that crown complexed potassium hydroxide assists in the dehydration

(16) (a) F. G. Bordwell and W. S. Matthews, *J. Am. Chem. Soc.*, **96**, 1216 (1974); (b) F. G. Bordwell, J. E. Bartmess, G. E. Drucker, Z. Margolin, and W. S. Matthews, *ibid.*, **97**, 3226 (1975); (c) D. Algrim, J. E. Bares, J. C. Branca, and F. G. Bordwell, *J. Org. Chem.*, **43**, 5024 (1978).

(17) (a) R. P. Linstead and C. J. May, *J. Chem. Soc.*, 2565 (1927); (b) R. P. Linstead, *ibid.*, 2579 (1927); (c) R. P. Linstead and G. A. R. Kow, *ibid.*, 1269 (1929); (d) R. P. Linstead and A. Kandiah, *ibid.*, 2139 (1929).

(18) A. C. Cope, A. A. D'Addieco, D. E. Wayte, and S. A. Glickman, "Organic Synthesis", Collect. Vol. IV, Wiley, New York, 1963, p 234.

step. We therefore prepared 1-hydroxy-1-(cyanomethyl)-4-*tert*-butylcyclohexane (by condensation of lithium cyanomethide with **31**) and subjected it to the reaction conditions. The hydroxynitrile dehydrated smoothly to a mixture of α,β and β,γ isomers in 5 h in essentially the same yield (79 ± 6%), although the isomer ratios (with crown 2.4; without, 6.5) differed slightly.

Another possible explanation for the crown effect is that such ketones as **31** or **32**, each of which contains 10 carbon atoms, are quite insoluble in acetonitrile, especially in the presence of salt. Because of this lack of solubility, molecular association between ketone and crown with its multiple functional groups (polyether) might help solubilize the former and therefore enhance the reaction. If this explanation is valid, it is difficult to understand why the condensation of benzophenone (**19**) is so successful and why the condensation of cyclododecanone (**35**) is unaffected by crown. At present, we do not have a satisfactory explanation for these results.

Some Factors Influencing the KOH-Catalyzed Condensation of Acetonitrile with Benzaldehyde. We have already noted that the yields of cyclohexanone-derived nitriles are influenced by concentration and that the effect of 18-crown-6 on the reaction with 4-*tert*-butylcyclohexanone is significant. The condensation of benzaldehyde with acetonitrile was examined in somewhat greater depth than the other processes to learn if crown played an important role as a phase-transfer catalyst.[19]

A perusal of Table III indicates that, as expected, reaction occurred much more rapidly at elevated than at ambient temperature (entries 1 and 3). The addition of 5 mol % of 18-crown-6 was without influence on the reaction at either temperature (entries 2 and 4). If a solvent of substantially lower polarity was used (i.e., benzene instead of acetonitrile), crown clearly enhanced the reaction rate. In this case, crown seems to play a role similar to that played by acetonitrile since a 1:1 mixture of acetonitrile and benzene without crown is more efficacious than 1 equiv of acetonitrile in benzene with crown, although there is clearly a kinetic influence here as well. Again crown has an auspicious influence on the reaction when the amount of base is reduced.

A change of base from potassium to sodium hydroxide is actually an alteration of two variables. The change in size, electronegativity, hardness, etc., associated with the difference in metal is obvious. The presence of water is a more subtle difference. Reagent grade KOH contains 15% by weight of water, or about 0.5 equiv. Reagent grade NaOH is clearly not anhydrous but is much more nearly so than KOH. Sodium hydroxide was, in general, a poorer catalyst than KOH for the condensation, but addition of either 5 mol % 18-crown-6 or 0.5 equiv of water to the NaOH-containing reactions had a similar influence. It is also worth noting that the reactions reported here were conducted in the presence of 1 equiv of HO^-, even though only a catalytic amount of base is theoretically required. This was done for purely pragmatic reasons.

Attempted Condensations with Miscellaneous Electrophiles. As noted above, aliphatic aldehydes could not be induced to condense with acetonitriles under the conditions described here, although the reaction was much more successful for aromatic aldehydes and ketones. A variety of other potential electrophiles was surveyed, but none afforded useful yields of condensation products. In most of these cases, either mixtures or intractable tars resulted. Included in this group were benzonitrile (although no benzoic acid was formed), 4-bromobenzenediazonium tetrafluoroborate, crotonaldehyde, maleic anhydride, and styrene oxide. 4-Chloronitrobenzene and cyclohexene oxide proved inert, and benzyl chloride hydrolyzed and condensed to yield dibenzyl ether in 30% yield.

(19) W. P. Weber and G. W. Gokel, "Phase Transfer Catalysis in Organic Synthesis", Springer-Verlag, New York, 1977.

Summary

The direct, KOH-catalyzed condensation of acetonitrile with aromatic aldehydes and aliphatic or aromatic ketones constitutes an efficient, economical, and convenient preparative method for unsaturated nitriles. The yields obtained are competitive with those realized from Doebner–Knoevenagel condensation, and the lack of a separate dehydration or decarboxylation step makes our approach more convenient. The predominance of α,β isomers which result by our method, especially for the aliphatic cases, stands in contrast to the usual results of the cyanoacetic acid condensation with aliphatic ketones. Addition of 18-crown-6 ether exhibited a yield-enhancing effect under certain conditions, but its influence in acetonitrile medium, using KOH as base, is hard to predict. The compatibility of this condensation with reactive, especially base-sensitive, functional groups is generally poor. Nevertheless, the acetonitrile condensation is clearly a general reaction for a variety of carbonyl compounds.

Experimental Section

Melting points were determined on a Thomas-Hoover capillary device and are uncorrected. Infrared spectra were recorded on a Perkin-Elmer Model 257 as Nujol mulls unless otherwise specified and are calibrated agaist the 1601-cm^{-1} band of polystyrene. NMR spectra were recorded on a Varian Associates A-60A as ca. 15 wt % solutions in $CDCl_3$ unless otherwise specified. Chemical shifts are reported in ppm (δ) downfield from internal Me_4Si. Mass spectra were determined on an AEI-MS 902 instrument at an ionizing voltage of 79 eV. Gas chromatographic analyses were conducted using either a Varian Associates Model 2720 or 920 analytical gas chromatograph equipped with a thermal-conductivity detector and a 5 ft. × 0.25 in. 10% SE-30 column on NAW Chromosorb P. Helium was used as a carrier gas, and the flow rate was ca. 60 mL/min.

NaOH and KOH were ACS reagent grade and were powdered under an N_2 atmosphere immediately prior to use. MeCN was distilled from P_2O_5 and stored under an N_2 atmosphere. Tetrahydrofuran (THF) was distilled from $LiAlH_4$ immediately prior to use. All gases were passed through a column of Drierite (90 × 2.5 cm in diameter) before use.

Preparative chromatography columns were packed with either activated alumina (80–300 mesh, MC&B) or silica gel 60 (70–230 mesh, E. Merck). Unless otherwise indicated, ether–hexane, 1/9 (v/v), was used as the developing solvent.

General Procedure for the Reaction of Nonenolizable Carbonyl Compounds with MeCN in the Presence of KOH. A 100-mL, three-necked, round-bottomed flask, equipped with a pressure equalizing addition funnel, reflux condenser, N_2 purge, and magnetic stirring bar, was charged with powdered KOH (0.01–0.05 mol) and dry MeCN (10–40 mL). The mixture was heated to reflux (internal temperature 83 ± 3 °C), and a solution of the carbonyl compound (0.01–0.05 mol) in MeCN (10–20 mL) was added in a stream. Preparative scale reactions were normally conducted at concentrations of 0.5–1.0 M in carbonyl electrophile. After the addition was complete, stirring was continued for the specified time and then the hot solution was poured onto cracked ice (100 g). This mixture was extracted with three 75-mL portions of CH_2Cl_2, dried over Na_2SO_4, and evaporated in vacuo. During evaporation, the bath temperature was maintained at ca 30 °C in order to minimize decomposition. The crude product thus obtained was purified by column chromatography (alumina, 80-325 mesh) as specified.

Preparation of (*E*)- and (*Z*)-Cinnamonitrile (42). Benzaldehyde (**1**, 5.32 g, 0.05 mol) was heated with MeCN (50 mL) in the presence of KOH (3.30 g, 0.05 mol) for 3 min as described

in the general procedure. After chromatography [1:4, (v/v) ether–hexane] **42** (5.28 g, 82%) was obtained as a light yellow oil [*E*/*Z* ca. 3.0 (GLC)]: bp 60 °C (0.1 torr) [lit[20] bp 139 °C (30 torr)]; NMR (CCl_4) *E* isomer, δ 5.71 (d, 1 H, *J* = 17 Hz), 7.3 (s, 5 H); NMR (CCl_4) *Z* isomer, δ 5.31 (d, 1 H, *J* = 12 Hz), 7.3 (s, 5 H); IR (neat) 2223 cm^{-1}.

Large-Scale Preparation of (*E*)- and (*Z*)-Cinnamonitrile (42). A 1-L, three-necked, round-bottom flask equipped with a mechanical stirrer, reflux condenser, and addition funnel was charged with KOH pellets (33 g, 0.5 mol) and MeCN (400 mL). The mixture was brought to reflux under static N_2, and a solution of **1** (53 g, 0.5 mol) in MeCN (100 mL) was added in a stream. After addition, stirring was continued for 10 min, and then the hot solution was poured onto cracked ice (500 g). Steam distillation (bp 95–99 °C) of the resultant mixture gave **42** (22–29 g, 35–45%) as a pale yellow oil [*E*/*Z* ca. 5.5 (GLC)] which was pure by TLC and GLC.

Preparation of (*E*) and (*Z*)-2-Methylcinnamonitrile (43). 2-Methylbenzaldehyde (**2**, 1.20 g, 0.01 mol) was heated with MeCN (10 mL) in the presence of KOH (0.66 g, 0.01 mol) for 9 min as described in the general procedure. After chromatography [1:4 (v/v), ether–hexane], **43** (0.90 g, 63%) was obtained as a pale yellow oil [*E*/*Z* ca. 3.43 (GLC)]: bp 84–85 °C (0.5 torr) [lit.[21] bp 147–150 °C (24 torr)]; NMR (CCl_4) *E* isomer, δ 2.3 (s, 3 H), 5.66 (d, 1 H, *J* = 16.5 Hz), 7.55 (d, 1 H, *J* = 16.5 Hz), 7.0–7.4 (m, 4 H); NMR (CCl_4) *Z* isomer, δ 2.3 (s, 3 H), 5.42 (d, 1 H, *J* = 12.5 Hz), 7.0–7.4 (m, 5 H); IR (neat) 2223 cm^{-1}.

Preparation of (*E*)-4-Methylcinnamonitrile (44). 4-Methylbenzaldehyde (**3**, 6.0 g, 0.05 mol) was heated with MeCN (50 mL) in the presence of KOH (3.30 g, 0.05 mol) for 6 min as described in the general procedure. After chromatography [1:4 (v/v), ether–hexane], **44** (4.39 g, 60%) was obtained as a white solid [pure *E* isomer (NMR)]: mp 71–72 °C (lit.[20] mp 60–70 °C (mixture)); NMR (CCl_4) δ 2.38 (s, 3 H), 5.67 (d, 1 H, *J* = 16.5 Hz), 6.18 (d, 1 H, *J* = 16.5 Hz), 7.18 (s, 5 H); IR 2210 cm^{-1}.

Preparation of (*E*)-and (*Z*)-4-Methoxycinnamonitrile (45). 4-Methoxybenzaldehyde (**4**, 6.8 g, 0.05 mol) was heated with MeCN (50 mL) in the presence of KOH (3.30 g, 0.05 mol) for 10 min as described in the general procedure. After chromatography [3:7 (v/v), ether–hexane], **45** (2.33 g, 29%) was obtained as a yellow oil [*E*/*Z* mixture, *E*/*Z* = 2.0 (NMR)] and an off-white solid [4.15 g, 52% pure *E* isomer (NMR)]. Total yield of **45** was 81%: mp of *E* isomer 62–63 °C (lit.[22] mp 61–64 °C) (isomer distribution unknown, presumed to be pure *E*); NMR (CCl_4) *E* isomer, δ 3.75 (s, 3 h), 5.62 (d, 1 H, *J* = 16.5 Hz), 7.21 (d, 1 H, *J* = 16.5 Hz), 6.85 (d, 2 H, *J* = 9 Hz), 7.38 (1/2 of AB, 2 H, *J* = 9 Hz); NMR (CCl_4) *Z* isomer, δ 3.75 (s, 3 H), 5.21 (d, 1 H, *J* = 12 Hz), 7.2 (1/2 of AB, 2 H, *J* = 9 Hz); IR 2209 (s) cm^{-1}.

Preparation of (*E*)- and (*Z*)-2,3-Dimethoxycinnamonitrile (46). 2,3-Dimethoxybenzaldehyde (**5**, 1.71 g, 0.01 mol) was heated with MeCN (10 mL) in the presence of KOH (0.66 g, 0.01 mol) for 3 min as described in the general procedure. After chromatography [3:7 (v/v), ether–hexane], **46** (1.51 g, 80%) was obtained as an off-white solid [*E*/*Z* ca. 5.9 (NMR)]: mp 770–71 °C (lit[23] mp 77 °C) (isomer distribution unknown, presumed to be pure *E*); NMR (CCl_4) *E* isomer, δ 3.82 (s, 6 H), 5.85 (d, 1 H, *J* = 17 Hz), 7.55 (d, 1 H, *J* = 17 Hz), 6.95 (s, 3 H); NMR (CCl_4) δ 3.82 (s, 6 H), 5.39 (d, 1 H, *J* = 12 Hz), 7.45 (d, 1 H, *J* = 12 Hz), 6.95 (s, 3 H); IR 2220 (s) cm^{-1}.

Preparation of (*E*)-3,4-Methylenedioxycinnamonitrile (47). 3,4-Methylenedioxybenzaldehyde (**6**, 7.5 g, 0.05 mol) was heated with MeCN (50 mL) in the presence of KOH (3.30 g, 0.05 mol) for 7 min as described in the general procedure. After chromatography [2:3, (v/v), ether–hexane], **47** (7.44 g, 86%) was obtained as a yellow solid [pure *E* isomer (NMR)]: mp 91–92 °C (lit.[22] mp 94 °C); NMR δ 5.61 (d, 1 H, *J* = 16 Hz), 6.0 (s, 2 H), 6.85 (m, 3 H), 7.28 (d, 1 H, *J* = 16 Hz); IR 2210 (s) cm^{-1}.

Reaction of Vanillin with MeCN for 48 h at Reflux in the Presence of KOH and 5.0 Mol % 18-Crown-6. Vanillin (**7**, 1.52 g, 0.01 mol) was heated with MeCN (20 mL) in the presence of KOH (1.32 g, 0.02 mol) and 18-crown-6 (0.264 g, 0.001 mol, 5.0 mol %) for 48 h as described in the general procedure. After workup and chromatography (as above), (*E*)- and (*Z*)-4-hydroxy-3-methoxycinnamonitrile (**48**) (1.21 g, 70%) were obtained as a yellow solid [*E*–*Z* *ca* 5.9 (NMR)]: mp 93–96 °C (lit.[22] mp 106–107 °C) (isomer distribution unknown, presumed to be pure *E*): NMR *E* isomer, δ 3.90 (s, 3 H), 5.7 (d, 1 H, *J* = 16.5 Hz), 6.0–6.3 (m, 1 H, OH), 6.95 (s, 3 H), 7.3 (d, 1 H, *J* = 16.5 Hz); NMR *Z* isomer, δ 3.90 (s, 3 H), 5.25 (d, 1 H, *J* = 12 Hz), 6.0–6.3 (m, 1 H, OH), 6.95 (s, 3 H), 7.1 (d, 1 H, *J* = 12 Hz): IR 3365 (s), 2210 (s) cm^{-1}.

Preparation of 2-Hydroxy-3-methoxycinnamonitrile (49). *o*-Vanillin (**8**, 1.52 g, 0.01 mol) was heated with MeCN (20 mL) in the presence of KOH (1.32 g, 0.02 mol) and 18-crown-6 (0.264 g, 0.01 mol, 5.0 mol %) for 96 h at reflux as described in the general procedure. After workup and chromatography (as above), (*E*)-**49** (0.88 g, 50%) was isolated as a yellow solid: mp 84–86 °C; NMR δ 3.96 (s, 3 H), 6.0 (m, 1 H), 6.15 (d, 1 H, *J* = 16.5 Hz), 7.59 (d, 1 H, *J* = 16.5 Hz), 6.92 (s, 3 H); IR 3381 (s), 2221 (s) cm^{-1}; high-resolution mass spectrum; calcd for $C_{10}H_9NO_2$ 175.0633, found 175.0635.

Attempted Preparation of 3-Nitrocinnamaldehyde (50). *m*-Nitrobenzaldehyde (**9**, 1.51 g, 0.01 mol) was stirred for 3 h at ambient temperature with MeCN (20 mL) in the presence of KOH (0.66 g, 0.01 mol) as described in the general procedure. Chromatography [3:7 (v/v), ether–hexane] afforded an off-white solid (ca. 100 mg) which appeared by NMR analysis (CCl_4) to be a mixture of 3-nitrobenzyl alcohol and **50** [6.08 (d, *J* = 16.5 Hz)]. Continued elution gave *m*-nitrobenzyl alcohol (0.32 g, 22 or 44% based on theory for the Cannizzaro reaction) as a yellow oil, identified by IR and NMR spectra.

Preparation of (*E*)- and (*Z*)-4-Fluorocinnamonitrile (51). 4-Fluorobenzaldehyde (**10**, 1.24 g, 0.001 mol) was heated with MeCN (10 mL) in the presence of KOH (0.66 g, 0.01 mol) for 7 min as described in the general procedure. After chromatography [1:4 (v/v), ether–hexane], **51** (0.74 g, 50%) was obtained as a wet yellow solid [*E*/*Z* ca. 3.6 (NMR)]: bp 65–75 °C (0.2–0.3 torr); *E* isomer mp 64–66 °C (lit[24] mp 64–65 °C); NMR (CCl_4) *E* isomer, δ 5.80 (d, 1 H, *J* = 16.5 Hz), 6.85–7.95 (m, 5 H); NMR (CCl_4) *Z* isomer, 5.41 (d, 1 H, *J* = 12.5 Hz), 6.85–7.95 (m, 5 H); IR (neat) 2219 (s) cm^{-1}.

Preparation of (*E*)- and (*Z*)-2-Chlorocinnamonitrile (52). 2-Chlorobenzaldehyde (**11**, 1.40 g, 0.01 mol) was heated with MeCN (10 mL) in the presence of KOH (0.66 g, 0.01 mol) for 1 min as described in the general procedure. After chromatography [1:4 (v/v), ether–hexane], **52** (0.59 g, 36%) was obtained as a pale yellow oil [*E*/*Z* ca. 4.3 (GLC)]: bp 97–99 °C (0.75 torr) [lit.[21] bp 143–146 °C (13 torr)]; NMR (CCl_4) *E* isomer, δ 5.85 (d, 1 H, *J* = 16.5 Hz), 7.68 (d, 1 H, *J* = 16.5 Hz), 7.1–7.5 (m, 4 H); NMR (CCl_4) *Z* isomer, δ 5.55 (d, 1 H, *J* = 12.5 Hz), 7.1–7.5 (m, 5 H); IR (neat) 222 (s) cm^{-1}.

Attempted Isolation of Phenolic Products Formed during the Preparation of 52. 2-Chlorobenzaldehyde (**11**, 1.40 g, 0.01 mol) was heated with MeCN (20 mL) in the presence of KOH (0.66 g, 0.01 mol) for 1.5 min at reflux as described in the general procedure. After workup, **52** was detected by TLC (R_f ca. 0.5) in the organic phase. The aqueous phase was acidified with concentrated hydrochloric acid and extracted in vacuo to give a tan paste (0.03 g). NMR analysis indicated the presence of aromatic protons; however, no resonance attributable to a phenol or acid could be detected. Infrared analysis indicated the possible presence of nitrile and carbonyl functions, but an unequivocal absorption due to a hydroxyl group could not be detected: NMR δ 7.12–7.42 (m, 100 mm integral); 7.8–8.0 (m, 15 mm integral); IR 2915 (s), 2845 (s), 2213 (s), 1685 (s), 1588 (w), 1265 (w), 1040 (s), 943 (s), 692 (s) cm^{-1}.

Preparation of (*E*)-4-Chlorocinnamonitrile (53). 4-Chlorobenzaldehyde (**12**, 7.04 g, 0.05 mol) was heated with MeCN (50 mL) in the presence of KOH (3.30 g, 0.05 mol) for 20 s, as described in the general procedure. After chromatography [3:7 (v/v), ether–hexane], **53** (4.67 g, 57%) was obtained as a white solid [pure *E* isomer (NMR)]: mp 84–86 °C, (lit.[22] mp 84–87 °C);

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(21) C. F. Koelsch, *J. Am. Chem. Soc.*, **65**, 57 (1943).
(22) M. Harfenist and A. P. Phillips, *J. Am. Chem. Soc.*, **80**, 6261 (1958).
(23) H. Richtzenhain and P. Nippus, *Chem. Ber.*, **82**, 408 (1949).
(24) G. P. Schiemenz and H. Engelhard, *Chem. Ber.*, **95**, 195 (1962).

NMR (CCl_4) δ 5.83 (d, 1 H, J = 16.5 Hz), 7.3 (d, 1 H, J = 16.5 Hz), 7.38 (s, 4 h); IR 2210 (s) cm^{-1}.

Preparation of (*E*)- and (*Z*)-2-(3-Pyridyl)acrylonitrile (54). 3-Pyridinecarboxaldehyde (**13**, 1.07 g, 0.01 mol) was heated with MeCN (20 mL) in the presence of KOH (0.66 g, 0.01 mol) for 3 min as described in the general procedure. After chromatography [1:1 (v/v), ether–hexane], **54** (0.63 g, 48%) was obtained as a white solid [*E*/*Z* ca. 5.6 (NMR)]: mp 93–96 °C (lit.[25] mp 106–107 °C) (isomer distribution unknown, presumed to be pure *E*); NMR *E* isomer, δ 6.0 (d, 1 *H*, J = 16.5 Hz), 7.3 (d, 1 H, J = 16.5 Hz), 6.9–7.85 (m, 2 H), 8.4–8.7 (m, 2 H); NMR *Z* isomer, δ 5.4 (d, 1 H, J = 13 Hz), 6.9–7.85 (m, 3 H), 8.4–8.7 (m, 2 H); IR 2219 (s) cm^{-1}.

Preparation of (*E*)- and (*Z*)-2-(2-Furyl)acrylonitrile (55). Furfural (**14**, 4.7 g, 0.05 mol) was heated with MeCN (50 mL) in the presence of KOH (3.3 g, 0.05 mol) for 3 min as described in the general procedure. After chromatography [1:1 (v/v), ether–hexane], **55** (3.53 g, 59%) was obtained as a light yellow oil [*E*/*Z* ca. 4.25 (NMR)]; bp 42–59 °C (0.1–0.15 torr) [lit.[23] bp 95–97 °C (11 torr)]; NMR (CCl_4) *E* isomer, δ 5.75 (d, 1 H, J = 16.5 Hz), 7.18 (d, 1 H, J = 16.5 Hz), 6.48–7.6 (m, 3 H); NMR (CCl_4) *Z* isomer, δ 5.28 (d, 1 H, J = 12 Hz), 6.8 (d, 1 H, J = 12 Hz), 6.48–7.6 (m, 3 H); IR (neat) 2219 (s) cm^{-1}.

Attempted Preparation of 3-Methoxy-4-(benzoyloxy)-cinnamonitrile (56). Vanillin benzoate (**15**, 0.92 g, 0.005 mol) was heated at reflux with MeCN (10 mL) in the presence of KOH (0.33 g, 0.005 mol) for 24 h as described in the general procedure. After chromatography [alumina, 3:7 (v/v), ether–hexane], a yellow oil (0.14 g) was obtained. This material appeared to be largely unreacted vanillin benzoate contaminated by a small amount of the anticipated α,β-unsaturated nitrile (as judged by NMR analysis): NMR (CCl_4) δ 5.82 (d, J = 16.5 Hz), 9.96 (s). The aqueous phase was acidified with concentrated hydrochloric acid, extracted with ether (2 × 50 mL), dried over Na_2SO_4, and evaporated in vacuo. After chromatography [silica, 1:4 (v/v), ether–hexane], benzoic acid (0.24 g, 20%) was obtained as a white solid: mp 121–122 °C, mmp 122.5–123.5° C (lit.[26] mp 122 °C). Further elution gave **7** (0.30 g, 20%) as a white solid, mp 82–83 °C (lit.[26] mp 82–83 °C).

General Procedure for the Condensation of MeCN with Enolizable Carbonyl Compounds in the Presence of KOH. A 100-mL, three-necked, round-bottomed flask, equipped with a pressure equalizing addition funnel, reflux condenser, nitrogen purge, and magnetic stirring bar, was charged with freshly powdered KOH (85%, 0.66 g, 0.01 mol) and dry MeCN (15 mL). The mixture was brought to reflux, and a solution of the carbonyl compound (0.01 mol) in MeCN (5 mL) was added dropwise over a period of 0.5–1.0 h. These reactions were normally conducted at concentrations of 0.5–1.0 M of carbonyl compound in MeCN. After addition, the reaction mixture was stirred at reflux for the specified time, and then the hot solution was poured onto cracked ice (100 g). This mixture was extracted with CH_2Cl_2 (3 × 75 mL), dried over Na_2SO_4, and evaporated in vacuo. The crude product thus obtained was purified by chromatography, using the specified eluents unless otherwise indicated.

Preparation of (*E*)- and (*Z*)-2-Methyl-2-phenylacrylonitrile (57). Acetophenone (**16**, 6.0 g, 0.05 mol) was condensed with MeCN (50 mL) in the presence of KOH (85%, 3.30 g, 0.05 mol) for 6 h as described in the general procedure. After chromatography [1:4 (v/v), ether–hexane], **57** (1.1 g, 15%) was obtained as a pale yellow oil [*E*/*Z* ca. 4.0 (NMR)]: bp 78 °C (0.2 torr) [lit[27] bp 120–129 °C (2 torr)]; NMR (CCl_4) *E* isomer, δ 2.5 (d, 3 H, J = 2 Hz), 5.7 (m, 1 H), 7.55 (s, 5 H); NMR (CCl_4) *Z* isomer, δ 2.3 (d, 3 H, J = 2 Hz), 5.45 (m, 1 H), 7.55 (s, 5 H); IR (neat) 2221 (s) cm^{-1}.

Attempted Preparation of 2-(Chloromethyl)cinnamonitrile (58). Phenacyl chloride (**17**, 1.54 g, 0.01 mol) was heated with MeCN (20 mL) in the presence of KOH (85%, 0.66 g, 0.01 mol) for 1 h as described in the general procedure. Thin-layer chromatographic analysis (alumina) of the resulting mixture indicated that all of the starting material was consumed and at least five products had been formed, none in dominant yield.

Preparation of (*E*)- and (*Z*)-2-Propyl-2-phenylacrylonitrile (59). Butyrophenone (**18**, 1.48 g, 0.01 mol) was heated with acetonitrile (20 mL) in the presence of KOH (85%, 0.66 g, 0.01 mol) for 36 h as described in the general procedure. After chromatography [1:9 (v/v), ether–hexane], **59** (0.51 g, 30%) was obtained as a colorless oil [*E*/*Z* ca. 3.6 (NMR)]: bp 73–83 °C (0.35 torr) [lit.[28] bp 87–88 °C (0.4 torr)]; NMR (CCl_4) *E* isomer, δ 0.7–1.7 (m, 5 H), 2.82 (t, 2 H), 5.42 (s, 1 H), 7.35 (s, 5 H); NMR (CCl_4) *Z* isomer, δ 0.7–1.7 (m, 1 H), 7.35 (s, 5 H); IR (neat) 2219 (s) cm^{-1}.

Preparation of 2,2-Diphenylacrylonitrile (37). Benzophenone (**19**, 9.1 g, 0.05 mol) was heated with MeCN (50 mL) in the presence of KOH (3.30 g, 0.05 mol) for 4.5 h as described in the general procedure. After chromatography [1:4 (v/v), ether–hexane], **37** (8.58 g, 84%) was obtained as a colorless oil: bp 128–131 °C (0.2 torr) [lit.[29] mp 47–48 °C; bp 160–200 °C (1.5 torr)]; NMR (CCl_4) δ 5.69 (s, 1 H), 7.4 (d, 10 H); IR (neat) 2218 (s) cm^{-1}.

Attempted Preparation of 2,2-(9-Fluorenylidene)acrylonitrile (60). Fluorenone (**20**, 0.90 g, 0.005 mol) was stirred with MeCN (10 mL) in the presence of KOH (0.33 g, 0.005 mol) for 48 h at ambient temperature as described in the general procedure. After chromatography [1:1 (v/v), ether–hexane], **61** (0.85 g, 76%) was obtained as a tan-colored, glassy solid: mp 107–109 °C, mmp 108–109 °C (lit.[15] mp 97.5–98.5 °C). The sample used in the mixture melting point was prepared according to the literature (see above). A small amount of **20** (0.06 g, 7%) was recovered: mp 80–81 °C, mmp 82–83 °C (lit.[26] mp 84–86 °C).

When the same reaction was conducted for 48 h at reflux temperature, some **20** (39%) was recovered, and no other product could be characterized.

Preparation of 61 by *n*-Butyllithium-Catalyzed Addition of MeCN to 20. A 250-mL, three-necked, round-bottomed flask equipped with a mechanical stirrer, addition funnel, N_2 inlet, and serum cap was charged with MeCN (2.05 g, 0.05 mol) and dry THF (50 mL). The solution was cooled to ca. −50 °C, *n*-butyllithium (18 mL, 0.05 mol) was then introduced (syringe), and the MeCN was allowed to stir for 15 min. Fluorenone (**20**, 9.0 g, 0.05 mol) in THF (25 mL) was then added dropwise and the solution stirred. After 25 h, it was poured into saturated aqueous NH_4Cl (100 mL) and then diluted with ether (50 mL). The phases were separated, the organic phase was washed with H_2O, and the ether phase was dried over $MgSO_4$. After evaporation in vacuo, the crude reaction mixture was purified by column chromatography (alumina). Elution with 10% ether in hexane gave unreacted **20** (2.10 g, 23%) as a yellow solid. Further elution with 50% ether in hexane gave **61** (5.39 g, 49%) as a light yellow glass, mp 107–108 °C. Recrystallization of a portion of the sample from heptane–acetone gave a colorless crystalline solid, mp 108–109 °C (lit.[31] mp 97.5–98.5 °C). The IR spectrum of the material compared well with the spectrum reported in the literature; NMR (CCl_4) δ 2.73 (s, 2 H), 2.95 (m, 1 H), 7.25–7.75 (m, 9 H). Anal. Calcd for $C_{15}H_{11}NO$: N, 6.33. Found, N, 6.55.

Acid-Catalyzed Dehydration of 61. 9-Hydroxy-9-(cyanomethyl)fluorene (1.5 g, 0.0068 mol) was dehydrated with 85% phosphoric acid (40 mL) as described by Hauser et al.[6b] with the following modification. After being quenched, the reaction mixture was extracted with CH_2Cl_2 (3 × 125 mL), dried over $MgSO_4$, and evaporated in vacuo. After chromatography, [3:7 (v/v), ether–hexane], **60** (1.24 g, 89%) was obtained as a yellow solid, mp 109–110 °C (lit.[30] mp 109–111 °C). The method is reported in the literature to give a 55% yield after recrystallization: NMR δ 5.98 (s, 1 H), 7.2–7.7, 8.2–8.35 (m, 8 H); IR (CCl_4) 2205 (s) cm^{-1}.

Preparation of 2,2-Diethylacrylonitrile (62). 3-Pentanone (**21**, 1.72 g, 0.02 mol) was heated with MeCN (50 mL) in the presence of KOH (85%, 1.32 g, 0.02 mol) for 24 h as described in the general procedure. After chromatography [1:19 (v/v), ether–hexane], **62** (0.79 g, 36%) was obtained as a colorless oil: bp 69–70 °C (ca. 20 torr); NMR (CCl_4) δ 1.15 (m, 6 H), 2.1–2.72 (m, 4 H), 5.18 (m, 1 H); IR (neat) 2222 (s) cm^{-1}; high-resolution

(25) J. M. Patterson, "Organic Synthesis", Collect. Vol. V, Wiley, New York, 1973, p 585.
(26) R. S. DeSimone, U.S. Patent 3910923 (1976); *Chem. Abstr.*, **85**, 123387 (1976).
(27) See ref 20, p C-137.
(28) A. Uchida, S. Saito, and S. Matsuda, *Bull. Chem. Soc. Jpn.*, **42**, 2991 (1969).
(29) M. Strell and E. Kopp, *Chem. Ber.*, **91**, 1621 (1958).
(30) T. A. Geissman, *Org. React.*, **2**, 94 (1944).
(31) See ref 20, p C-302.

mass spectrum; calcd for $C_7H_{11}N$ 109.0891, found 109.0886.

Preparation of 2,2-Di-*n*-propylacrylonitrile (63). 4-Heptanone (**22**, 5.70 g, 0.05 mol) was heated with MeCN (50 mL) in the presence of KOH (85%, 3.30 g, 0.05 mol) for 48 h as described in the general procedure. After chromatography [1:19 (v/v), ether–hexane], **63** (4.71 g, 65%) was obtained as a colorless oil: bp 44–47 °C (0.35 torr); NMR (CCl_4) δ 0.8–1.2 (m, 6 H), 1.2–1.9 (m, 4 H), 2.1–2.6 (m, 4 H), 5.2 (m, 1 H); IR (neat) 2221 (s) cm^{-1}; high-resolution mass spectrum, calcd for $C_9H_{15}N$ 137.1204, found 137.1195.

Preparation of 2,2-Di-*n*-butylacrylonitrile (64). 4-Nonanone (**23**, 1.42 g, 0.01 mol) was heated with MeCN (20 mL) in the presence of KOH (85%, 0.66 g, 0.01 mol) for 72 h as described in the general procedure. After chromatography [1:9 (v/v), ether–hexane], **64** (1.00 g, 67%) was obtained as a pale yellow oil: bp 48–50 °C (0.1 torr); NMR (CCl_4) 0.8–1.8 (m, 14 H), 2.05–2.60 (m, 4 H), 5.09 (m, 1 H); IR (neat) 2220 (s) cm^{-1}; high-resolution mass spectrum, calcd for $C_{11}H_9N$ 165.1517, found 165.1519.

Attempted Preparation of Tetramethyleneacrylonitrile (65) from 24. Cyclopentanone (**24**, 4.2 g, 0.05 mol) was heated with MeCN (50 mL) and KOH (3.3 g, 0.05 mol) for 2 h as described in the general procedure for enolizable carbonyl compounds. After chromatography [1:9 (v/v), ether–hexane], a yellow oil (1.64 g) was obtained. IR analysis indicated the presence of C≡N, C=O, and C=C. No volatile product in the boiling point range anticipated for **65** could be detected by gas chromatographic analysis.

Preparation of Pentamethyleneacrylonitrile (38) and Cyclohexenylacetonitrile (39). Cyclohexanone (**25**, 4.9 g, 0.05 mol) was condensed with MeCN (100 mL) in the presence of KOH (3.30 g, 0.05 mol) for 1.5 h as described in the general procedure. After chromatography [1:9 (v/v), ether–hexane], a mixture of **38** and **39** (4.38 g, 72%) was obtained as a colorless oil [$\alpha,\beta/\beta,\gamma$ = ca. 4.5 (NMR)]: bp 50 °C (0.5 torr) [lit.[31] bp 82–84 °C (3–4 torr)]; NMR (CCl_4) for **39**, δ 1.25–2.0 (m, 6 H), 1.25–2.0 (m, 4 H), 2.0–2.8 (m, 4 H), 3.05 (s, 2 H); NMR (CCl_4) for $-CH_2CN$, δ 5.75 (m, 1 H); IR (neat) 2252 (w), 2221 (s) cm^{-1}.

Large-Scale Preparation of 38 and 39. A 1-L, three-necked, round-bottomed flask equipped with a reflux condenser, mechanical stirrer, and addition funnel was charged with KOH pellets (85%, 33.0 g, 0.5 mol) and MeCN (250 mL). The mixture was brought to reflux, and a solution of **25** (49 g, 0.5 mol) in MeCN (100 mL) was added dropwise over a period of 0.5–1 h. Heating was continued for 2 h after addition, and the hot solution was poured onto cracked ice (600 g). The resulting binary mixture was separated and the aqueous phase extracted with ether (3 × 200 mL). The combined organic phase was reduced in volume on a steam bath (internal temperature ca. 50 °C), and there was obtained after steam distillation (bp 81–99 °C) a pale yellow oil (35 g, 58%) consisting of a mixture of isomers (α,β ~83%; β,γ ~17%).

Isolation of Pure 38. A 250-mL Erlenmeyer flask equipped with a magnetic stirring bar was charged with the isomeric nitriles **38** + **39** (20 g, 0.165 mole) and CCl_4 (20 mL), and a solution of Br_2 in CCl_4 (1:9 v/v) was added dropwise until the Br_2 color persisted (ca. 25–30 mL). The reaction mixture was cooled in an ice bath (30 min) and filtered and the solvent evaporated in vacuo. There was obtained after distillation (45–55 °C (0.4–0.5 torr)) pure (by NMR) **38** (15 g, 0.124 mol, 75%), IR (neat) 2219 (s) cm^{-1}.

Preparation of 38 and 39 in Dilute MeCN Solution. Cyclohexanone (**25**, 0.49 g, 0.005 mol) was heated with MeCN (50 mL) in the presence of KOH (85%, 0.33 g, 0.005 mol) for 1.25 h as described in the general procedure. After chromatography [1:9 (v/v), ether–hexane], a mixture of **38** and **39** (0.52 g, 86%) was obtained as a colorless oil [$\alpha,\beta/\beta,\gamma$ = **38**/**39** = 4.57 (NMR)].

Decarboxylation of α-Cyano-$\Delta^{1,\alpha}$-cyclohexaneacetic Acid (67) by Pyridium Nitrate in Refluxing Pyridine. A 100-mL, single-necked, round-bottomed flask equipped with a magnetic stirring bar and reflux condenser was charged with **67** (prepared by the method of Cope,[18] 8.0 g, 0.48 mol) and pyridine (50 mL). Nitric acid (70%, 4.5 g, 0.05 mol) was added, and the solution was stirred at reflux overnight (ca. 15 h). The reaction was allowed to cool to ambient temperature, was then poured into 6 N hydrochloric acid (200 mL), and was extracted with CH_2Cl_2 (3 × 100 mL); the combined CH_2Cl_2 phase was backwashed with 10% aqueous HCl (150 mL). The organic phase was then dried over $MgSO_4$ and evaporated in vacuo. After distillation (100–113 °C (ca. 20 torr)), **39** (4.24 g, 73%) was obtained as a colorless oil,[32] which was identified by NMR.

Sodium Ethoxide Catalyzed Equilibration of 29. (1-Cyclohexenyl)acetonitrile (**39**) was equilibrated in NaOEt according to the method of Linstead et al.[17] to a mixture which consisted of 89% **38** and 11% **29** (NMR). A similar mixture was reported by Linstead (85:15), who determined the isomer ratio by titration of the mixture with I_2 in $CHCl_3$.

Attempted Preparation of (2-Chlorocyclohexylidene)acrylonitrile (66). 2-Chlorocyclohexanone (**26**, 6.6 g, 0.05 mol) was condensed with MeCN (50 mL) in the presence of KOH (3.30 g, 0.05 mol) for 26 h as described in the general procedure for enolizable compounds. The only apparent product was an intractable oil which did not appear by IR and NMR analysis to be the desired nitrile. Base-promoted elimination and/or polymerization is the presumed mode of reaction.

Preparation of (2-Methylcyclohexylidene)acetonitrile (40) and (2-Methyl-1-cyclohexyl)acetonitrile (41). 2-Methylcyclohexanone (**27**, 5.70 g, 0.05 mol) was heated with MeCN (50 mL) and KOH (85%, 3.30 g, 0.05 mol) for 4 h as described in the general procedure. After chromatography [1:9 (v/v), ether–hexane], a mixture of **40** and **41** (5.31 g, 78%) was obtained as a colorless oil: bp 44–46 °C (0.15 mm) [$\alpha,\beta/\beta,\gamma$ = 1.1 (NMR)] [lit.[17] bp 101 °C (14 torr)]; NMR (CCl_4) for **40**, δ 1.1 (d, 3 H), 1.25–2.5 (m, 9 H), 5.04 (m, 1 H); NMR for **41**, δ 1.6–2.4 (m, 1 H), 3.05 (s, 2 H); IR (neat) 2258 (s), 2220 (s) cm^{-1}.

Attempted Preparation of Camphorylideneacetonitrile. Camphor (**28**, 7.65 g, 0.05 mol) was heated with MeCN (50 mL) and KOH (3.3 g, 0.05 mol) for 48 h as described in the general procedure for enolizable compounds. After workup, TLC analysis (alumina) and GC analysis revealed the presence only of unreacted **28**.

Attempted Preparation of the Carvone–MeCN Adduct. Carvone (**29**, 7.51 g, 0.05 mol) was heated with MeCN (50 mL) and KOH (3.3 g, 0.05 mol) for 4 h as described in the general procedure for enolizable carbonyl compounds. After workup, TLC analysis [alumina, 2:3 (v/v), ether–hexane] revealed four mobile compounds (R_f's ca. 0.01, 0.21, 0.37, and 0.81) with the major component remaining at the origin.

Attempted Preparation of the *p*-Benzoquinone–MeCN Adduct. *p*-Benzoquinone (**30**, 5.4 g, 0.05 mol) was heated with MeCN (50 mL) and KOH (3.3 g, 0.05 mol) for 36 h as described in the general procedure for enolizable compounds. After reaction, the mixture was highly colored, but no organic soluble material could be obtained on workup. Identical results were obtained when the reaction was conducted at ambient temperature for 48 h.

KOH-Catalyzed Synthesis of (4-*tert*-Butylcyclohexylidene)acetonitrile (68) from 4-*tert*-Butylcyclohexanone and MeCN. 4-*tert*-Butylcyclohexanone[33] (**31**, 3.86 g, 0.025 mol) was heated with MeCN (60 mL) and KOH (85%, 1.65 g, 0.025 mol) for 80 h as described in the general procedure. After chromatography [5:95 (v/v), ether–hexane], **68** (1.39 g, 31%) was obtained as a white solid [ca. 98% of the α,β isomer (NMR)], mp 53–55 °C. Continued elution gave unreacted **31** (1.2 g, 31%), which was identified by IR.

KOH-Catalyzed Reaction of 31 with MeCN in the Presence of 5.0 Mol % 18-Crown-6. 4-*tert*-Butylcyclohexanone[33] (**31**, 1.54 g, 0.01 mol) was heated with MeCN (20 mL), KOH (85%, 0.66 g, 0.01 mol), and 18-crown-6 (0.132 g, 0.0005 mol, 5.0 mol %) for 4 h as described in the general procedure. After chromatography (as above), **68** (0.75 g, 42%) was obtained as a white solid [ca. 95% of the α,β isomer (NMR)], mp 50–51 °C. Further elution gave a colorless oil (0.33 g, 18%), which consisted of a mixture of positional isomers [$\alpha,\beta/\beta,\gamma$ ca. 0.61 (NMR)]: bp 83–85 °C (0.6 torr). **68**: NMR (CCl_4) (α,β-isomer) δ 0.9 (s, 9 H), 1.0–2.4 (m, 9 H), 5.02 (m, 1 H). 4-*tert*-Butyl-(1-cyclohexenyl)acetonitrile (β,γ isomer): NMR δ 0.9 (s, 9 H), 1.0–2.4 (m, 7 H), 3.0 (m, 2 H),

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(33) R. S. Monson, "Advanced Organic Synthesis", Academic Press, New York, 1971, p 1.

Table III. Factors Affecting the Direct Preparation of Cinnamonitrile from Acetonitrile

expt no.	solvent system[a]	equiv of base[b]	time, h	temp,[c] °C	mol % of crown[d] added	yield,[e] %	E/Z[e]
1	CH_3CN	1.0 KOH	48	25 ± 3		88	4.0
2	CH_3CN	1.0 KOH	48	25 ± 3	5	91	3.1
3	CH_3CN	1.0 KOH	0.25	83 ± 3		88	4.1
4	CH_3CN	1.0 KOH	0.25	83 ± 3	5	91	2.6
5	1 equiv CH_3CN in C_6H_6	1.0 KOH	0.25	83 ± 3		12	3.0
6	1 equiv CH_3CN in C_6H_6	1.0 KOH	0.25	83 ± 3	5	29	2.5
7	1:1 CH_3CN:C_6H_6	1.0 KOH	0.25	83 ± 3		60	4.7
8	1:1 CH_3CN-C_6H_4	1.0 KOH	0.25	83 ± 3	5	80	4.4
9	CH_3CN	0.05 KOH	48	25 ± 3		9	4.8
10	CH_3CN	0.05 KOH	94	25 ± 3		8	4.8
11	CH_3CN	0.05 KOH	48	25 ± 3	5	20	
12	CH_3CN	0.5 KOH	48	25 ± 3		65	
13	CH_3CN	0.5 KOH	48	25 ± 3	5	91	5.8
14	CH_3CN	1.0 NaOH	48	25 ± 3		27	4.6
15	CH_3CN	1.0 NaOH	48	25 ± 3	5	43	4.5
16	CH_3CN	1.0 NaOH	0.25	83 ± 3		26	5.2
17	CH_3CN	1.0 NaOH	0.25	83 ± 3	5	62	5.7
18	CH_3CN	1.0 NaOH[f]	48	25 ± 3		29	4.3
19	CH_3CN	1.0 NaOH[f]	48	25 ± 3	5	44	4.0
20	CH_3CN	1.0 NaOH[f]	0.25	83 ± 3		53	6.9
21	CH_3CN	1.0 NaOH[f]	0.25	83 ± 3	5	65	5.5

[a] All solvents were dried, redistilled, and stored under nitrogen over 4A sieves. [b] 85% KOH (ACS reagent grade) and 100% NaOH (ACS reagent grade) powdered under nitrogen. [c] Internal. [d] 18-Crown-6.[31] [e] Determined by GLC, using a 5 ft × 0.25 in. 10% SE 30 on NAW Chromosorb P 60/80 mesh column. [f] 15 wt % water added.

5.65 (m, 1 H). **68**: IR 22.9 (s) cm^{-1}. (5-*tert*-Butyl-1-cyclohexenyl)acetonitrile (β,γ isomer): IR 2250 (s) cm^{-1}. Anal. Calcd for $C_{12}H_{19}N$: C, 81.3; H, 10.8; N, 7.9. Found: C, 81.5; H, 10.8; N, 7.9.

***n*-Butyllithium-Induced Reaction of 31 with MeCN.** A 250-mL, three-necked, round-bottomed flask equipped with a mechanical stirrer, addition funnel, nitrogen inlet, and serum cap was charged with MeCN (1.61 g, 0.04 mole) and dry THF (55 mL). The solution was cooled to ca. −50 °C, *n*-butyllithium (18.3 mL, 0.042 mol) was introduced (syringe), and the MeCN was metalated for 0.5 h. **31** (6.16 g, 0.04 mol) in THF (25 mL) was then added dropwise over a period of 5 min. After the addition was complete, stirring was continued for 0.5 h, and the reaction was then poured onto a slurry of ice and HCl (5 mL) and brine (50 mL). The mixture was extracted with ether (2 × 50 mL), and the combined ethereal extracts were washed with saturated aqueous $NaHCO_3$ (50 mL) and brine (50 mL) and dried over Na_2SO_4. After evaporation of the solvent in vacuo, the crude 1-(cyanomethyl)-1-hydroxy-4-*tert*-butylcyclohexane was recrystallized from ether–petroleum ether to give a white solid (3.2 g, 40%): mp 110–112 °C; NMR 0.85 (s, 9 H), 0.9–2.15 (m, 9 H), 2.58 (s, 2 H), 2.60 (s, 1 H); IR 3560–3100 (s), 2248 (s) cm^{-1}.

KOH-Catalyzed Dehydration of 1-(Cyanomethyl)-1-hydroxy-4-*tert*-butylcyclohexane. 1-(Cyanomethyl)-1-hydroxy-4-*tert*-butylcyclohexane (0.50 g, 0.0025 mol) was heated in MeCN (15 mL) in the presence of KOH (0.17 g, 0.0025 mol) for 5 h as described in the general procedure. After chromatography [1:4, (v/v), ether–hexane], **68** was obtained in two portions. The first fraction (0.187 g, 40%) was isolated as a white solid [$\alpha,\beta/\beta,\gamma$ ca. 15.7 (NMR)], mp 50–53 °C. Further elution gave a light yellow oil (0.193 g, 43%) which consisted of a mixture of positional isomers [$\alpha,\beta/\beta,\gamma$ ca. 1.18 (NMR)]. The overall isomer ratio was ca. 6.5.

KOH-Catalyzed Dehydration of 1-(Cyanomethyl)-1-hydroxy-4-*tert*-butylcyclohexane in MeCN in the Presence of 5.0 Mol % 18-Crown-6. 1-(Cyanomethyl)-1-hydroxy-4-*tert*-butylcyclohexanone (0.50 g, 0.0025 mol) was heated in MeCN (15 mL) in the presence of KOH (0.17 g, 0.0025 mol) and 18-crown-6 (0.033 g, 0.000 125 mol, 5.0 mol %) for 5 h as described in the general procedure. After chromatography (as above), **68** (0.32 g, 73%) was obtained as a wet solid [$\alpha,\beta/\beta,\gamma$ = 2.4 (NMR)].

Preparation of 3-(Cyanomethylidene)bicyclo[4.4.0]decane (69). *cis*-Octalone[34] (**32**, 1.52 g, 0.01 mol) was heated with MeCN (20 mL) and KOH (0.66 g, 0.01 mol) for 5 h as described in the general procedure. After chromatography [1:4, (v/v), ether–hexane], **69** (1.45 g, 83%) was obtained as a colorless oil [$\alpha,\beta/\beta,\gamma$ ca. 3.44 (NMR)]: bp 77–82 °C (0.1 torr). **69** (α,β isomer): NMR (CCl_4) δ 1.0–2.1 (m, 12 H), 2.1–2.8 (m, 4 H), 5.0 (d, 1 H). **69** and 3-(cyanomethyl)bicyclo[4.4.0]dec-2-ene (β,γ isomer): NMR (CCl_4) δ 2.95 (m, 2 H), 5.62 (m, 1 H); IR (neat) 2221 (s) cm^{-1}; high resolution mass spectrum, calcd for $C_{12}H_{17}N$ 175.1360, found 175.1361.

Large-Scale Preparation of 69. *cis*-Octalone[34] (**32**, 4.56 g, 0.03 mol) was condensed with MeCN (50 mL) in the presence of KOH (1.98 g, 0.03 mol) as above. Chromatography gave **69** (4.0 g, 76%) as a colorless oil (see above).

Preparation of Cycloheptylideneacetonitrile (70). Cycloheptanone (**33**, 5.60 g, 0.05 mol) was heated with MeCN (50 mL) and KOH (3.3 g, 0.05 mol) for 6 h as described in the general procedure. After chromatography [1/19, (v/v), ether–hexane], **70** (5.27 g, 78%) was obtained as a colorless oil (only the α,β isomer could be detected by NMR): bp 123–214 °C (ca. 20 torr) [lit.[35] bp 105–112 °C (15 torr)]; NMR (CCl_4) δ 1.68 (s, 8 H), 2.3–2.88 (m, 4 H), 5.2 (m, 1 H); IR (neat) 2215 (s) cm^{-1}.

Preparation of Cyclooctylideneacetonitrile (71). Cyclooctanone (**34**, 1.26 g, 0.01 mol) was heated with MeCN (20 mL) and KOH (0.66 g, 0.01 mol) for 33 h as described in the general procedure. After chromatography [1:9, (v/v), ether–hexane], **71** (0.99 g, 66%) was obtained as a colorless oil [$\alpha,\beta/\beta,\gamma$ ca. 5.84 (NMR)]: bp 55 °C (0.25 torr); **71** (α,β isomer) NMR (CCl_4) δ 1.3–2.0 (m, 10 H), 2.08–2.65 (m, 4 H), 5.15 (m, 1 H). (1-Cyclooctenyl)acetonitrile (β,γ isomer): NMR (CCl_4) δ 1.3–2.65 (m, 12 H), 2.98 (s, 2 H), 5.7 (m, 1 H); IR (neat) 2220 (s) cm^{-1}; high resolution mass spectrum calcd for $C_{10}H_{15}N$ 149.1204, found 149.1195.

Preparation of Cyclododecylideneacetonitrile (72). Cyclododecanone (**35**, 4.65 g, 0.025 mol) was condensed with MeCN (55 mL) in the presence of KOH (1.65 g, 0.025 mol) for 72 h as described in the general procedure. After chromatography [1:9, (v/v), ether–hexane], **72** (2.34 g, 45%) was obtained as a white solid (only the α,β isomer could be detected by NMR): mp 50–52 °C; NMR (CCl_4) 1.0–1.9 (m, 18 H), 2.2–2.7 (m, 4 H), 5.3 (m, 1 H); IR 2221 (s) cm^{-1}. Anal. Calcd for $C_{14}H_{23}N$: C, 81.9; H, 11.3; N, 6.8. Found: C, 81.8; H, 11.4; N, 6.6.

General Procedure for the Reaction of Benzaldehyde with MeCN in the Presence of KOH or NaOH (GLC Scale Reaction). Specific Results Found in Table III. The procedure described below was followed unless otherwise specified. A 25-mL, single-necked, round-bottomed flask equipped with a magnetic

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(35) F. Sorm and J. Beranek, *Chem. Listy*, *47*, 708 (1953); *Chem. Abstr.*, **49**, 194 (1955).

stirring bar and reflux condenser, if required, was charged with the hydroxide base (0.01 mol), which has been powdered, MeCN (10 mL), benzaldehyde (0.01 mol), 18-crown-6 (if used), and cumene (ca. 0.00375 mol), which was used as the internal standard. The suspension was stirred at the indicated temperature under an atmosphere of dry N_2. After the given period of time, an aliquot was removed and analyzed (GLC, comparison with a standard solution). For experiments conducted at reflux (83 ± 3 °C), the reaction vessel was immersed in an oil bath maintained at ca. 100 °C, and the aliquot was immediately frozen in liquid nitrogen until GLC analysis could be performed.

General Procedure for the Hydrogenation of α,β- and β,γ-Unsaturated Nitriles. A thick-walled hydrogenation bottle (473 mL) was charged with 95% ethanol (10 mL), Pd catalyst (5–10% on carbon, 1 g %) and the unsaturated nitrile (0.01 mol). The mixture was then shaken under 2–3 atm of H_2 in a Parr apparatus at ambient temperature until H_2 consumption ceased. The crude reaction mixture was filtered through alumina (ca. 20 g) and then evaporated in vacuo to give the corresponding saturated nitrile. This procedure was followed for all substrates unless otherwise specified.

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Registry No. **1**, 100-52-7; **2**, 529-20-4; **3**, 104-87-0; **4**, 123-11-5; **5**, 86-51-1; **6**, 120-57-0; **7**, 121-33-5; **8**, 148-53-8; **9**, 99-61-6; **10**, 459-57-4; **11**, 89-98-5; **12**, 104-88-1; **13**, 500-22-1; **14**, 98-01-1; **15**, 790-16-9; **16**, 98-86-2; **17**, 532-27-4; **18**, 495-40-9; **19**, 119-61-9; **20**, 486-25-9; **21**, 96-22-0; **22**, 123-19-3; **23**, 502-56-7; **24**, 120-92-3; **25**, 108-94-1; **27**, 583-60-8; **28**, 464-49-3; **29**, 99-49-0; **30**, 106-51-4; **31**, 98-53-3; **32**, 1579-21-1; **33**, 502-42-1; **34**, 502-49-8; **35**, 830-13-7; **37**, 3531-24-6; **38**, 4435-18-1; **39**, 6975-71-9; **40**, 53153-81-4; **41**, 49673-58-7; (*E*)-**42**, 1885-38-7; (*Z*)-**42**, 24840-05-9; (*E*)-**43**, 26155-19-1; (*Z*)-**43**, 57103-23-8; (*E*)-**44**, 35121-93-8; (*E*)-**45**, 14482-11-2; (*Z*)-**45**, 30115-95-8; (*E*)-**46**, 71750-07-7; (*Z*)-**46**, 71750-08-8; (*E*)-**47**, 49711-07-1; (*E*)-**48**, 71750-09-9; (*Z*)-**48**, 71750-10-2; (*E*)-**49**, 71750-11-3; **50**, 1504-76-3; (*E*)-**51**, 27530-50-3; (*Z*)-**51**, 71750-12-4; (*E*)-**52**, 51220-00-9; (*Z*)-**52**, 51219-99-9; (*E*)-**53**, 14378-04-2; (*E*)-**54**, 54356-27-3; (*Z*)-**54**, 54356-28-4; (*E*)-**55**, 6125-63-9; (*Z*)-**55**, 6137-73-1; **56**, 71750-13-5; (*E*)-**57**, 14799-78-1; (*Z*)-**57**, 14799-79-2; **58**, 71750-14-6; (*E*)-**59**, 64723-70-2; (*Z*)-**59**, 64723-71-3; **60**, 4425-74-5; **61**, 17190-25-9; **62**, 5631-82-3; **63**, 54353-88-7; **64**, 54353-88-7; **65**, 5732-88-7; **67**, 37107-50-9; **68**, 71750-15-7; **69**, 64723-67-7; **70**, 22734-05-0; **71**, 63909-22-8; **72**, 64723-66-6; MeCN, 75-05-8; *m*-nitrobenzyl alcohol, 619-25-0; (4-*tert*-butyl-1-cyclohexenyl)acetonitrile, 67674-39-9; 1-(cyanomethyl)-1-hydroxy-4-*tert*-butylcyclohexane, 71750-16-8; 3-(cyanomethyl)bicyclo[4.4.0]dec-2-ene, 64723-68-8; (1-cyclooctenyl)acetonitrile, 71750-17-9.

Ring Opening of 1,2-Bis(trimethylsiloxy)-1,2-dimethylcyclopropane with Hydrogen Bromide and Bromine

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The reaction of HBr and Br_2 with 1:1 mixtures of *cis*- and *trans*-1,2-bis(trimethylsiloxy)-1,2-dimethylcyclopropane (**1** and **2**) in CCl_4 under anhydrous conditions at 0 °C was examined. In both cases cyclopropane cleavage occurred exclusively at the 1,3-bond. With HBr, 3-methyl-3-hydroxy-2-butanone (**6**), 3-bromo-3-methyl-2-butanone (**7**), and 1,3,3,4,6,6-hexamethyl-2,5,7-trioxabicyclo[2.2.1]heptane (**8**) were formed in yields of 38, 26, and 36%, respectively. With Br_2 (dark), a 63% yield of 4-bromo-3-hydroxy-3-methyl-2-butanone (**12**) was obtained along with di-, tri-, and tetrabromo-substituted 1,3,3,4,6,6-hexamethyl-2,5,7-trioxabicyclo[2.2.1]heptanes. Both reactions produced bromotrimethylsilane (**4**) and hexamethyldisiloxane (**5**).

With the recent interest in the mechanism of attack of electrophiles on cyclopropane rings,[1a,b] and especially cyclopropanols and their derivatives,[2] we wish to report the results of the anhydrous HBr and Br_2 ring opening of a bis(trimethylsiloxy)cyclopropane.

Results and Discussion

A mixture of *cis*- and *trans*-1,2-bis(trimethylsiloxy)-1,2-dimethylcyclopropanes (**1** and **2**) was synthesized by carbene insertion on 2,3-bis(trimethylsiloxy)-2-butene.[3]

The 2,3-bis(trimethylsiloxy)-2-butene *E*, *Z* mixture was prepared in 58% yield by using the procedure of Ruhlmann and Poredda.[4] Methylene insertion in the 3*Z*, 3*E* mixture was carried out by using the modified Simmons–Smith reagent of Rawson and Harrison,[5] and an approximate 1:1 mixture of **1** and **2** was obtained in 42% yield. Neither the butene nor the cyclopropane mixtures could be separated by spinning-band distillation. The IR and NMR spectra of the **1** and **2** mixture agrees with that reported by Audibrand and co-workers,[3] but there is a discrepancy in the NMR spectrum proton assignments. The partial NMR spectrum of the mixture of **1** and **2** in Figure 1 shows our proton assignments. Spin–spin decoupling experiments indicate that the broadening of H_a and H_c is due to long-range coupling to the methyl groups. We suggest that this indicates a W arrangement[6] of H_a and H_c with the methyl groups. The only proton which does not show such broadening or W relationship then must be H_b.

Ring openings were carried out on 20% solutions of an approximate 1:1 mixture of **1** and **2** in anhydrous CCl_4 at 0 °C by using 1 equiv of HBr in one experiment and 1 equiv of Br_2 in another.

For the reaction with HBr, distillation of the reaction mixture gave three distinct fractions: a CCl_4 fraction containing trimethylsilyl bromide (**4**) and hexamethyldisiloxane (**5**), a fraction containing 3-hydroxy-3-methyl-2-butanone (**6**) and 3-bromo-3-methyl-2-butanone (**7**), and a third fraction containing 1,3,3,4,6,6-hexamethyl-2,5,7-

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