Table I

Nmr Parameters for Simulated Spectrum of **2a**[a]

ω_a	ω_b	ω_c	ω_d	J_{ab}	J_{ac}	J_{ad}	J_{bc}	J_{bd}	J_{cd}
281.57	281.57	307.90	134.79	0.0	6.57	3.19	6.57	3.19	6.06

[a] Frequencies in hertz downfield from TMS; coupling constants (absolute values) in hertz.

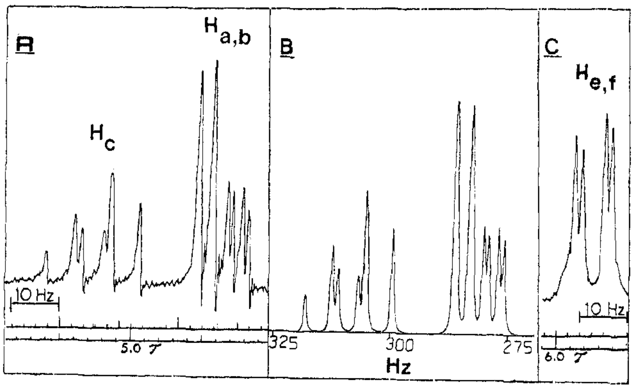

Figure 1.—A, 60-MHz pmr spectrum of the allenic protons in **2a**; B, computer-simulated spectrum of protons in A; C, 60-MHz pmr spectrum of the methylene protons in **2c**.

particularly interesting with respect to long-range proton–proton coupling and the effects of a remote asymmetric center. See Figure 1.

Owing to the asymmetric atom (C_2) in **2**, the methylene protons (H_e and H_f) are diastereotopic, giving rise to two doublets instead of one. The close similarity in chemical shift precludes observation of coupling between H_e and H_f. The two doublets are best resolved in the spectrum of **2c** ($\Delta\delta$ = 1.6 Hz; $|J_{de}| = |J_{df}|$ = 6.5 Hz) shown in Figure 1C.

More interesting, however, were the absorptions due to the allenic protons. All three compounds gave spectra in which the allenic regions were virtually superimposable, except for small differences in chemical shift. A typical spectrum is shown in Figure 1A.[5] The patterns, however, were considerably more complex than would have been anticipated from consideration of the spectra of 2,2-dimethyl-3,4-pentadienol[6] and 3,4-pentadienol,[2] which display typical A_2B and A_2BX_2 patterns, respectively.

The rigid geometry of the allenic system and the presence of the asymmetric atom render H_a and H_b diastereotopic.[5] One possible explanation for the added spectral complexity, then, could be that H_a and H_b were observably magnetically distinct. Such a long-range effect of an asymmetric center is not without precedent. It has been shown[7] that compounds of generic structure **3** give rise to diastereomers where the H* proton resonances are distinguishable.

$$R{-}O{-}CH^*{=}C{=}CHCH(R')OR''$$

3

An alternative explanation for the added complexity is the importance of second-order effects in what can be regarded as an A_2BX system (H_a *not* distinguishable from H_b), where X (H_d) is coupled to both terminal allenic protons with a coupling constant of ~3 Hz.[8] In either of these cases coupling between H_a and H_b should *not* be observable owing to the identity (or close similarity) in chemical shift, although the magnitude of such geminal coupling ranges from 13–15 Hz.[9] Also, it should be realized that the symmetry of the system places H_c on a plane which bisects the asymmetric atom; thus the resonance for H_c must be independent of the configuration about C_2.

That the second explanation in fact accounts for the added complexity was first suggested by decoupling experiments. Both field-swept and frequency-swept decoupling of the complex pattern attributed to H_d caused the collapse of the resonances due to H_a and H_b to a slanting doublet, indicating that coupling between the terminal protons and H_d *was* important. Similarly the multiplet due to H_c collapsed to a slanting triplet, and the methyl and methylene absorptions (not shown in the figures) collapsed to broad singlets.

Final confirmation that the second explanation accounts fully for the observed spectrum was obtained from a computer-simulated spectrum[10] (Figure 1B) using values shown in Table I.

Thus we see no reason to invoke magnetic distinguishability between diastereotopic protons H_a and H_b to explain our observations. The chemical shifts of H_a and H_b can differ no more than 1 Hz. It is interesting to note that H_d has the distinction of being coupled to all eight other protons shown in **2**!

Registry No.—**2a**, 26674-94-2; **2c**, 26674-95-3.

Acknowledgments.—This work was supported by a grant from the Petroleum Research Fund of the American Chemical Society. The author also wishes to thank Professor Fred Kaplan (University of Cincinnati) and Professor Sanford Smith (University of Kentucky, Lexington) for their help in obtaining the computer-simulated spectra.

[5] No absolute selection between H_a and H_b is intended.

[6] R. S. Bly, A. R. Ballentine, and S. U. Knock, *J. Amer. Chem. Soc.*, **89**, 6993 (1967). We wish to thank Professor Bly for copies of the spectra of 2,2-dimethyl-3,4-pentadienol and derivatives.

[7] M. L. Martin, R. Mantione, and G. J. Martin, *Tetrahedron Lett.*, 4809 (1967).

[8] Typical coupling constants are for $H_3CC\mathbf{H}{=}C\mathbf{H}Cl$ J = −5.8 Hz; $\mathbf{H}_3CCH{=}C{=}C\mathbf{H}_2$ J = 3.0 Hz: J. W. Emsley, J. Feeney, and L. H. Sutcliffe, "High Resolution Nuclear Magnetic Resonance Spectroscopy," Vol. I., Pergamon Press, London, 1967.

[9] M. L. Martin and G. J. Martin, *J. Mol. Spectrosc.*, **34**, 53 (1970).

[10] The program was LAOCOON III (used in the iterative mode) and NMRPLT, a plotting routine.

Reactions of Enamines. XI. The Reaction of Enamines with Cyanoacetic Acid[1]

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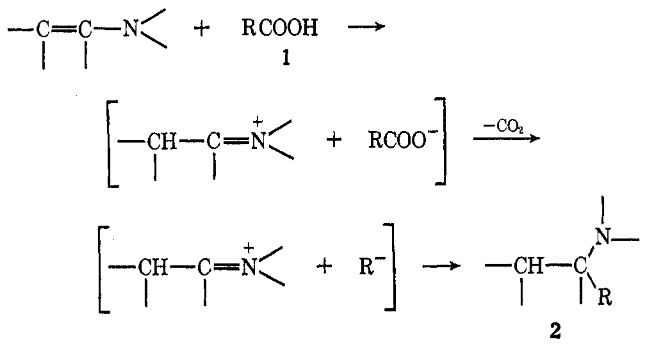
In previous papers in this series,[1,2] it was shown that enamines react with trichloroacetic acid (**1**, R = $-CCl_3$)

[1] Part X: G. H. Alt, *J. Org. Chem.*, **33**, 2858 (1968).

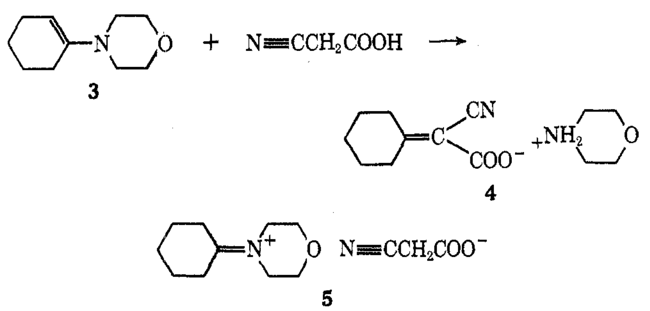
[2] G. H. Alt and A. J. Speziale, *ibid.*, **31**, 1340 (1966).

SCHEME I



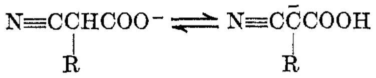
according to Scheme I. It seemed to us that other carboxylic acids capable of facile decarboxylation such as nitroacetic acid (**1**, R = $-CH_2NO_2$) and cyanoacetic acid (**1**, R = $-CH_2CN$) should undergo similar reaction sequences. Partial confirmation for this postulate has appeared in a recent publication[3] which demonstrates that enamines react with nitroacetic acid to give the α-amino compound **2** (R = $-CH_2NO_2$) or the nitro olefin by loss of amine from **2** and prompts us to report on the somewhat different course of the reaction of cyanoacetic acid with enamines.

Treatment of 1-morpholino-1-cyclohexene (**3**) with 1 equiv of cyanoacetic acid in ethyl acetate solution gave an immediate exothermic reaction and a crystalline salt separated in almost quantitative yield. This proved to be the morpholine salt of α-cyanocyclohexylideneacetic acid (**4**) and not the iminium cyanoacetate (**5**) which had been anticipated. The constitution of **4** was established by its nmr spectrum, and by its conversion to the free acid which was identical with an authentic sample.[4] Treatment of α-cyanocyclohexylideneacetic acid with 1 mol of morpholine in ethyl acetate gave a crystalline salt identical with **4**.

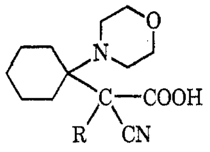


Iminium salts have been proposed as intermediates in the Knoevenagel condensation of cyanoacetic acid with aldehydes and ketones in the presence of primary and secondary amines,[5] and it seems reasonable that the initial reaction between **3** and cyanoacetic acid would be the iminium cyanoacetate (**5**). The cyanoacetate anion, instead of undergoing decarboxylation and addition to the cation, is able to set up a tautomeric equilibrium with the carbanion[6] (Scheme II), and it is the latter[7] which adds to the cation to give **6** (R = H). The zwitterion of **6** (R = H) is ideally set up to lose morpholine and give the observed product **4**.

SCHEME II



$$N{\equiv}C\underset{R}{CH}COO^- \rightleftharpoons N{\equiv}C\underset{R}{\bar{C}}COOH$$



6

An attempt was made to isolate the intermediate **6** (R = cyclohexyl) by reacting cyclohexylcyanoacetic acid with the enamine **3**. Only the iminium salt was formed as shown by the isolation of its hydrolysis products with no evidence for any addition taking place.[8] An explanation for this behavior may be the greater bulk of the cyclohexyl group which prevents addition for steric reasons. Alternatively, it might be expected that the electron-releasing properties of an alkyl group would displace the equilibrium in Scheme II toward the left and suppress formation of the carbanion. Both of these effects complement each other and probably account for the lack of addition.

Cyanoacetic acid reacted readily with the enamines of aldehydes and ketones; in each case the salt of the corresponding α-cyanoalkylideneacetic acid was isolated. The enamines of hindered ketones, however, failed to react. A similar reaction between cyanoacetic acid and the Schiff bases of aldehydes and ketones to give the corresponding primary amine salts of the α-cyanoalkylideneacetic acids has already been described.[9]

These reactions provide positive evidence for the intermediacy of iminium salts[10] in the Knoevenagel and related reactions and account for the fact that tertiary amines do not catalyze these reactions.

Experimental Section[11]

The required enamines were purchased or prepared by the standard method.[12]

α-Cyanocyclohexylideneacetic Acid Morpholinium Salt (4).—A.—To a solution of 1-morpholino-1-cyclohexene (8.35 g, 0.05 mol) in ethyl acetate (25 ml) was added with vigorous agitation a solution of cyanoacetic acid (4.25 g, 0.05 mol) in ethyl acetate (15 ml). An exothermic reaction took place and on cooling the

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[3] W. L. F. Armarego, *J. Chem. Soc. C*, 986 (1969).

[4] A. C. Cope, A. A. D'Addieco, D. E. Whyte, and S. A. Glickman, "Organic Syntheses," Collect. Vol. IV, Wiley, New York, N. Y., 1963, p 234.

[5] H. O. House, "Modern Synthetic Reactions," W. A. Benjamin, New York, N. Y., 1965, p 227, and references there cited.

[6] D. J. G. Ives and K. Sames, *J. Chem. Soc.*, 513 (1943).

[7] The possibility that a dianion (formed by reaction of cyanoacetate with some external base, *e.g.*, enamine) is the reactive species is not ruled out.

[8] A β-amino acid intermediate of this type has been obtained by the reaction of *N*-benzylidenemethylamine with phenylacetic acid: see T. I. Bieber, R. Sites and Y. Chiang, *J. Org. Chem.*, **23**, 300 (1958).

[9] G. Charles, *Bull. Soc. Chim. Fr.*, 1566 (1963).

[10] N. J. Leonard and J. V. Paukstelis, *J. Org. Chem.*, **28**, 3021 (1963), have shown that iminium salts may be formed directly from aldehydes or ketones and secondary amine salts.

[11] Melting points were taken on a Mel-Temp capillary melting point apparatus and are uncorrected. Infrared spectra were taken on a Perkin-Elmer Infracord Model 137. Nmr spectra were taken with a Varian A-60 instrument in deuteriochloroform using tetramethylsilane as internal standard.

[12] S. Hünig, E. Lücke, and W. Brenniger, *Org. Syn.*, **41**, 65 (1961).

product crystallized. Two recrystallizations from ethyl acetate afforded the pure salt, 9.8 g (78%), as prisms: mp 89–91°; ir ($CHCl_3$) 2720, 2470 (NH_2^+), 2205 (C≡N), 1610 cm^{-1} (CO_2); nmr τ 8.33 (m, 6, CH_2), 7.4 and 7.00 (m, 4, CH_2), 6.80 (q, 4, CH_2N), 6.04 (q, 4, CH_2O), −0.3 (s, 2).

Anal. Calcd for $C_{13}H_{20}N_2O_3$: C, 61.88; H, 7.99; N, 11.10. Found: C, 61.60; H, 7.86; N, 11.28.

B.—To a solution of α-cyanohexylideneacetic acid[4] (1.65 g, 0.01 mol) in a minimum amount of hot ethyl acetate was added morpholine (0.9 g, 0.01 mol). On cooling the salt crystallized and had mp 88–91° not depressed in admixture with the material above.

α-Cyanocyclohexylideneacetic Acid.—To the salt **4** (2.5 g, 0.01 mol) in 50% aqueous ethanol (7 ml) was added excess concentrated hydrochloric acid. The free acid which precipitated was filtered and recrystallized from water to give 1.4 g (87%) of α-cyanocyclohexylideneacetic acid, mp 108–110°, not depressed in admixture with authentic material[4] of the same melting point.

The following compounds were prepared by similar procedures.

α-Cyanocyclopentylideneacetic acid morpholinium salt was obtained in 75% yield after recrystallization from ethyl acetate: mp 106–109° dec; ir ($CHCl_3$) 2740, 2475 (NH_2^+), 2220 (C≡N), 1625 cm^{-1} (CO_2); nmr τ 8.22 (m, 4, CH_2), 7.13 (m, 4, CH_2), 6.78 (q, 4, CH_2N), 6.07 (q, 4, CH_2O), −0.40 (s, 2).

Anal. Calcd for $C_{12}H_{18}N_2O_3$: C, 60.49; H, 7.61; N, 11.76. Found: C, 60.30; H, 7.85; N, 11.75.

α-Cyanocyclopentylideneacetic Acid.—The free acid had mp 131–134° (H_2O) (lit.[13] mp 130–131°).

α-Cyanocyclododecylideneacetic acid morpholinium salt was obtained in 73% yield after recrystallization from ethyl acetate: mp 115–118° dec; ir ($CHCl_3$) 2717, 2470 (NH_2^+), 2215 (C≡N), 1615 cm^{-1} (CO_2); nmr τ 8.58 (m, 18, CH_2), 7.50 and 7.12 (m, 4, CH_2), 6.78 (m, 4, CH_2N), 6.06 (m, 4, CH_2O), −0.21 (s, 2).

Anal. Calcd for $C_{19}H_{32}N_2O_3$: C, 67.82; H, 9.59; N, 8.33. Found: C, 67.80; H, 9.28; N, 8.26.

α-Cyanocyclododecylideneacetic Acid.—The free acid had mp 164–167° (H_2O containing a little ethanol); ir (Nujol) 2640 (bonded OH), 2215 (C≡N), 1690 cm^{-1} (C=O); nmr τ 8.60 (m, 18, CH_2), 7.25 (m, 4, CH_2), 0.38 (m, 1, acidic H).

Anal. Calcd for $C_{15}H_{23}NO_2$: C, 72.25; H, 9.30; N, 5.62. Found: C, 72.21; H, 9.28; N, 5.61.

α-Cyanoisobutylideneacetic acid dimethylammonium salt was obtained in 63% yield after recrystallization from ethyl acetate: mp 114–116° dec; ir (CHCl) 2740, 2440 (NH_2^+), 2205 (C≡N), 1630 cm^{-1} (CO_2); nmr τ 8.89 [d, 6, J = 7 Hz, $CH(CH_3)_2$], 7.28 [s, 6, $N(CH_3)_2$], 6.98 [m, 1, $CH(CH_3)_2$], 2.68 (d, 1, J = 10 Hz, vinyl H), 0.22 (m, 2).

Anal. Calcd for $C_9H_{16}N_2O_2$: C, 58.67; H, 8.75; N, 15.21. Found: C, 58.81; H, 8.66; N, 15.02.

α-Cyanoisobutylideneacetic acid.—The free acid had mp 87–89° (chloroform–methylcyclohexane) (lit.[14] mp 89°).

Attempted Preparation of 6 (R = Cyclohexyl).—1-Morpholino-1-cyclohexene (1.7 g, 0.01 mol) in benzene or ethyl acetate was treated with cyclohexylcyanoacetic acid[6] (1.7 g, 0.01 mol) at the reflux temperature for 2 hr. Evaporation of the solvent afforded an oil (*ca.* 3.4 g) which partially solidified on standing. Trituration with petroleum ether afforded a solid which on recrystallization from chloroform–petroleum ether gave 1.5 g of a solid, mp 96–98°, which from its nmr spectrum appeared to be the morpholine salt of cyclohexylcyanoacetic acid.

Anal. Calcd for $C_{13}H_{22}N_2O_3$: C, 61.39; H, 8.72; N, 11.02. Found: C, 61.84; H, 8.95; N, 10.60.

The compound dissolved in water and acidified with concentrated hydrochloric acid gave cyclohexylcyanoacetic acid, mp and mmp 79–81°. Evaporation of the petroleum ether extracts (above) gave an oil which was shown to be cyclohexanone by its ir spectrum.

Registry No.—1 (R = CH_2CN), 372-09-8; **4**, 27521-93-3; α-cyanocyclopentylideneacetic acid, 21369-42-6; α-cyanocyclododecylideneacetic acid morpholinium salt, 27521-90-0; α-cyanocyclododecylideneacetic acid, 27521-91-1; α-cyanoisobutylideneacetic acid dimethylammonium salt, 27521-92-2; cyclohexylcyanoacetic acid morpholinium salt, 27521-88-6.

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[13] G. A. R. Kon and J. F. Thorpe, *J. Chem. Soc.*, **115**, 686 (1919).

[14] R. A. Letch and R. P. Linstead, *ibid.*, 443 (1932).

The Bromination of *tert*-Butylbenzene in Trifluoroacetic Acid. The Meta Partial Rate Factor

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The tritium exchange, noncatalytic bromination, and chlorination reactions of toluene, *tert*-butylbenzene, and other alkylbenzenes in trifluoroacetic acid and other mixed solvents rich in trifluoroacetic acid were examined to clarify the role of the solvent, in particular a nonnucleophilic solvent, in the determination of the substituent effects of alkyl groups.[2–6] The order of reactivity for the *p*-alkyl groups depends on the solvent. For the extreme case of the bromination reaction, $k_{p\text{-Me}}/k_{p\text{-}t\text{-Bu}}$ is 3.0 for acetic acid and 0.67 for trifluoroacetic acid.[3,4] The reversal in reactivity may be attributed, largely, to the selective increase in the free energy of solution (activity coefficient) of *tert*-butylbenzene in trifluoroacetic acid.[5] This interpretation is supported by the fact that $o_f^{t\text{-Bu}}$ and $m_f^{t\text{-Bu}}$ are unusually large for tritium exchange ($m_f^{t\text{-Bu}} = 32$)[2] and chlorination ($m_f^{t\text{-Bu}} = 39$)[5] in trifluoroacetic acid rich media. The interpretation is also supported by the finding that the partial molal enthalpy of solution of toluene and *tert*-butylbenzene in acetic acid and trifluoroacetic acid differ significantly and suggest that the activity coefficient of *tert*-butylbenzene is selectively enhanced.[5]

Unfortunately, $m_f^{t\text{-Bu}}$ values for the bromination reaction were not determined in the earlier work.[3,4] Study of the available data for the bromination reaction suggested that, if ground-state solvation effects were important, then *m*-bromo-*tert*-butylbenzene would be produced in a measurable amount. Accordingly, we carried out the bromination of *tert*-butylbenzene under the same conditions used in the prior investigations and analyzed the reaction product by capillary vpc. The bromo-*tert*-butylbenzenes were completely resolved on capillary columns with Apiezon L and Carbowax 20M. To test the procedure, we redetermined the isomer distribution for the bromination of *tert*-butylbenzene in 85% acetic acid.[7] The results obtained by vpc were in good agreement with the results obtained earlier by infrared spectroscopy.[7] The products of the bromination of *tert*-butylbenzene in three solvents rich in trifluoroacetic acid were examined. We were unable to detect *o*-bromo-*tert*-butylbenzene in these product mixtures.[8] The meta isomer, on the other hand, was evident in the chromatograms. In addition, the absorption bands for the meta isomer were apparent in the infrared spectrum of a concentrated

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[1] National Science Foundation Undergraduate Research Program Participant.

[2] (a) C. Eaborn and R. Taylor, *Chem. Ind.* (*London*), 949 (1959); (b) C. Eaborn and R. Taylor, *J. Chem. Soc.*, 247 (1961).

[3] H. C. Brown and R. A. Wirkkala, *J. Amer. Chem. Soc.*, **88**, 1447 (1966).

[4] W. M. Schubert and D. F. Gurka, *ibid.*, **91**, 1443 (1969).

[5] A. Himoe and L. M. Stock, *ibid.*, **91**, 1452 (1969).

[6] The problems involved in the definition of the substituent effects of alkyl groups are reviewed in ref 4 and 5.

[7] H. C. Brown and L. M. Stock, *ibid.*, **81**, 5615 (1959).

[8] The detection limit is estimated to be 0.05%.