Tetrahedron Vol. 35, pp. 881 to 883
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# CYCLOBUTANE-BICYCLOBUTANE SYSTEM—I

## THE RELATIVE REACTIVITY OF THE CENTRAL BOND IN BICYCLOBUTANECARBONITRILE AND THE DOUBLE BOND IN CROTONONITRILE IN NUCLEOPHILIC REACTIONS

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(*Received in UK 4 October 1978*)

**Abstract**—The ease of nucleophilic cleavage of the central bond of bicyclo[1.1.0]butanecarbonitrile 1 by alkoxides was compared to that of the double bond in crotononitrile 2. With both $MeO^-$/MeOH and i-$PrO^-$/PrOH, 2 reacts faster than 1 (by a factor of ca. 8 and 3 respectively). Analysis of the activation parameter reveals that in $MeO^-$/MeOH, both substrates have about the same activation energy and the reaction rate of 1 is markedly retarded by entropy effect. In i-$PrO^-$/i-PrOH the entropy of activation is in favour of the reaction of 1 while its activation energy is higher than that of 2. Considering the steric and electronic effects of the substituents, it is concluded that the central bond of bicyclobutanecarbonitrile is more susceptible to nucleophilic attack than the analogous double bond.

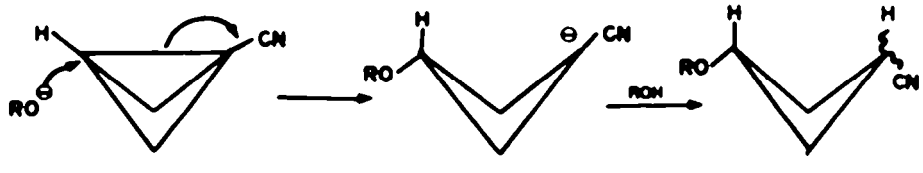
Bicyclo[1.1.0]butane is a unique molecule in terms of its chemical and physical properties. Although it is a saturated molecule, there are several indications of its having a closer similarity in chemical behaviour to a double bond rather than to a saturated molecule. For example: The ability of its central bond to add halogens, water and alcohols,[1a,b,c] trap benzyne intermediates,[1d] polymerize,[1a,b] react with radicals,[1b] etc. Bicyclobutane has the unusual feature of having all C–C bond lengths including that of the central bond equal (1.497 ± 0.004 Å).[2] According to MO–SCF calculations, the hybridization in the central bond is $sp^{2.3}$ which is equivalent to 96% p-character.[3]

Surprisingly, studies to date concentrated primarily on the theoretical and physical aspects of this molecule as well as on a qualitative description of its chemistry. A quantitative study of its reactivity in chemical reactions has been essentially neglected.

The purpose of this study was to establish the relative reactivity of the central bond in bicyclobutane, compared to that of a double bond, towards nucleophilic attack.

The simplest substrates defined by choosing the cyano group as the activating moiety would be bicyclobutanecarbonitrile (1) and acrylonitrile. However in comparing the reactivity of 1 with that of a double bond, it is desirable that both substrates possess the same degree of alkyl substitution. It is somewhat difficult to define the degree of substitution in 1. Formally, 1 can be considered as being tetrasubstituted, as each of the termini of the central bond is attached to two alkyl substituents (this degree of substitution obviously cannot be attained in the acrylonitrile series). On the other hand, the total number of alkyl substituents present in 1 is only two. Moreover, it is questionable whether the methylene groups of 1 are in fact similar in their steric and electronic effects to a Me group. The number of alkyl substituents on the double bond is a matter of crucial importance as it greatly affects the reaction rate.[4] Me substitution on acrylonitrile at the $\alpha$ and $\beta$ positions reduces the rate of iso-propoxide addition by a factor of 1500 and 350 respectively.[5] Further substitution of hydrogens by alkyl groups might lead to complete inhibition of the addition reaction.[6] As the relative reactivity within the substituted acrylonitrile series is known, we have chosen to carry out a comparative study with the member of the series whose reactivity is closest to that of 1. This will immediately determine the reactivity of 1 relative to any other member of the series.

Preliminary studies led to the selection of crotononitrile (2) as the olefinic substrate.




1

$$RO^{\ominus} + CH_3CH{=}CH{-}CN \rightarrow CH_3CH(OR)\overset{\ominus}{C}HCN \xrightarrow{ROH} CH_3CH(OR)CH_2CN$$

2

## RESULTS AND DISCUSSION

The reactions of the two substrates with $MeO^-$/MeOH and i-$PrO^-$/i-PrOH were carried out at 30.5 and 50.5° and followed by GC analysis. Substrate concentration ranged from 0.02 to 0.08 M of 1 and 0.05 to 0.1 M of 2. Alkoxide concentrations were 0.02–0.7 M. The reactions were first order in the concentrations of both the substrate and the catalytic alkoxide (correlation coefficients were better than 0.996). The reactions are essentially irreversible and go to completion. Reaction rate constants and activation parameters are given in the table. Addition of crown ether to the reaction mixture in i-PrOH, induced an increase of more than an order of magnitude in the reactions rates at 30.5°. At 50.5° in the presence of crown ether, the reactions were too fast to be measured.

The literature value for the reaction of 2 with i-$PrO^-$/i-PrOH is 0.05 $M^{-1}\,min^{-1}$ at 24°.[5] Extrapolation of data from the table to this temperature yields a value of 0.04 $M^{-1}\,min^{-1}$ which is in good agreement with the literature value.

As expected from its higher ground state energy,[7] the *trans* isomer is more reactive in $MeO^-$/MeOH than the *cis*. In i-$PrO^-$/i-PrOH isomerization is much faster than addition, therefore the rate constant in the table represents the rate of disappearance of an equilibrium mixture of the two isomers (*ca.* 2:3). Taking into account a statistical correction factor of 2 as the double bond can undergo nucleophilic attack on both faces while nucleophile approach to 1 is limited to one direction only, one finds that the relative reactivity of 1 and 2 ranges from 1:1 to 1:5 depending upon the nucleophile and the reaction conditions. The lower reactivity of 1 with $MeO^-$/MeOH as compared to that of 2 results from a lower entropy of activation, since its enthalpy of activation is equal to that of the *trans* and even lower than that of the *cis* isomer of 2. In contrast to reactions in MeOH, the difference in reactivity in i-PrOH stems from a lower enthalpy of activation for 2 while the activation entropy is greatly in favour of 1. These results show that bicyclobutane has about the same reactivity toward nucleophiles as that of the double bond.

The retarding effect of alkyl substituents on the rate of nucleophilic reactions results from both their steric and electronic effects.[4] An examination of models shows that a nucleophile's approach to 1 is more sterically hindered than its approach to 2, which means that the net reactivity (after deduction of steric factors) of the central bond in 1 is *greater* than that of the double bond in 2.

Experimental support for the relative steric effects present in 1 and 2, was obtained from reactions with i-$PrO^-$/i-PrOH in the presence of 18-crown-6-ether. This probe is generally used to characterize the more sterically hindered protons participating in HX elimination reactions.[8] The removal of the sodium cation from the ion pair nucleophile-metal reduces its size, leading, in general, to an increase in the reaction rate. Clearly, the more sterically hindered substrate will benefit more from this reduction in the size of the reagent. An examination of the data in the table reveals that the relative rate of i-$PrO^-$ addition to 2 and 1 at 30.5° changes from 3.4 to 2.7 as crown ether is added to the reaction mixture supporting the previous conclusion based on the models that nucleophilic approach to 1 is more hindered than in 2. On the reasonable assumption that the electronic rate retardation caused by the two methylenes in 1 is at least equal to that of the single Me group in 2, one concludes that the *intrinsic reactivity* of the central bond in 1 is greater than that of the analogous double bond.

C–C single bonds do not usually cleave as a result of a nucleophilic attack on one of the C atoms. The nucleophilic cleavage of a cyclopropyl ring usually necessitates the presence of two activating groups such as nitrile.[9a] Mono-activated cyclopropanes can be cleaved only if subjected to powerful nucleophiles under drastic conditions.[9b,c] A single cyano group is sufficient to make such a process feasible in an unsaturated system. Thus, the general reactivity scale for this type of reaction including the bicyclobutanic bond is: C–C (normal <C–C (cyclopropane) <C=C <C–C (central bond of bicyclobutane).

Low energy LUMO's in cyano, carbomethoxy and pyridinium substituted bicyclobutanes are said to be responsible for the various spectral and chemical behavior, characteristic of these systems.[10,11] Wiberg[11] reported that the lowest energy transition in bicyclobutane which is from the $\pi$-like central bond orbital to the corresponding $\pi^*$-like orbital is lower in energy than the $\pi \rightarrow \pi^*$ transition in ethylene. In light of the above observation it is not unreasonable to expect that the $\pi^*$-like orbital in bicyclobutane lies at a lower energy than the $\pi^*$ in ethylene. The observed higher reactivity of 1 is explicable in terms of frontier orbital theory which treats nucleophilic reactions as being initiated by the interaction between the HOMO of the nucleophile and the LUMO of the electrophile.[12] As the electrophile's LUMO becomes closer in energy to the nucleophile's HOMO, the stabilization energy of the orbital interaction (S.E. = $\beta^2/\Delta E$) is increased leading to a lower transition state energy and a larger reaction rate constant.

## EXPERIMENTAL

*General.* For analytical purposes, a Packard Model 878 (Flame ionization detector) gas-chromatograph was used, whereas for preparative purifications of starting materials and products a Varian 920 gas-chromatograph (Thermal conductivity detector)

Table 1. Second order rate constant for the reaction of 1 and 2 with $MeO^-$/MeOH and i-$PrO^-$/i-PrOH.

| | Solvent/ Nucleophile | $k^{30.5°}/M^{-1}\,min^{-1}$ | $k^{50.5°}/M^{-1}\,min^{-1}$ | $\Delta H^{\ddagger}$ kcal/mol | $\Delta S^{\ddagger}$ e.u. |
|---|---|---|---|---|---|
| 1 | MeOH/$MeO^-$ | 0.00356 | 0.0269 | 18.8 | −15.9 |
| 2 *trans* | MeOH/$MeO^-$ | 0.0332 | 0.248 | 18.8 | −11.5 |
| 2 *cis* | MeOH/$MeO^-$ | 0.0256 | 0.203 | 19.3 | −10.1 |
| 1 | i-PrOH/i-$PrO^-$ | 0.0186 | 0.108 | 15.3 | −24.3 |
| 2 | i-PrOH/i-$PrO^-$ | 0.063 | 0.243 | 12.4 | −31.2 |
| 1† | i-PrOH/i-$PrO^-$ | 0.32 | | | |
| 2† | i-PrOH/i-$PrO^-$ | 0.86 | | | |

†Equivalent amount of 18-crown-6-ether was added to reaction mixture.

was used. In both cases the columns were of 20% XE 60 on chromosorb W acid washed, 60–80 mesh. NMR spectra were recorded on a Varian HA100 spectrometer. Mass spectra were taken with a Hitachi Perkin Elmer RMU6 mass spectrometer.

*Reactants, preparation and purification.* Bicyclo[1.1.0]butanecarbonitrile was prepared from allene and acrylonitrile by a published procedure.[1b] Commercially available mixture of *cis* and *trans* crotononitrile was distilled at 112°/760 mm Hg and then separated on a preparative GC to give the pure isomers. Alkoxide solutions were prepared by dissolving Na metal in the pure alcohol. Alkoxide concentration was determined by titration with aqueous HCl soln. Biphenyl (BDH) was sublimed, anisol (Merck) was used without further purification. 18-Crown-6-ether was purified by the acetonitrile method.[13]

*3-Alkoxybutyronitrile and 3-alkoxycyclobutanecarbonitrile.* The general procedure for alkoxide addition to 1 and 2 is as follows: About 1 g (0.013 mol) of the substrate was dissolved in 25 ml of the appropriate alkoxide/alcohol soln (ca. 0.2 M) and was left overnight at 50°. The alcohol was evaporated and the residue was extracted by ether and water. The ethereal phase was washed with dil HCl aq and water. The ether was evaporated and the crude product was separated on a preparative gas-chromatograph. The yield of the pure alkoxide adducts was about 50% for the 3-alkoxybutyronitrile and 35% for the two isomers of 3-alkoxycyclobutanecarbonitrile. 3-Alkoxybutyronitriles are well known compounds.[5] The preparation of 3-methoxycyclobutanecarbonitrile has been reported in literature,[1b] its separation into *cis* and *trans* isomers and their identification is also known.[15] The *cis* and *trans* isomers of 3-isopropoxycyclobutanecarbonitrile were identified by their NMR spectra and GC retention times analogously to the OMe derivatives. For *trans* 3-isopropoxycyclobutanecarbonitrile NMR ($CDCl_3$) is: $\delta$ 1.15 (d, 6H), 2.45 (m, 4H), 2.95 (m, 1H), 3.5 (m, 1H) and 4.3 (q, 1H). (Found: C, 68.99; H, 9.47; N, 10.20. Calc. C, 69.06; H, 9.35; N, 10.07%). For the *cis* isomer: NMR ($CDCl_3$) $\delta$ 1.15 (d, 6H), 2.1–2.6 (m, 5H), 3.5 (m, 1H) and 3.9 (m, 1H). (Found: C, 68.92; H, 9.53; N, 10.24. Calc. C, 69.06; H. 9.35; N, 10.07%).

*Kinetic procedure.* Stock solns of the substrates containing internal standard (biphenyl for reactions with 1 and anisol with 2) were prepared and mixed at the reaction temps with the appropriate aliquots of the alcohol-alkoxide solns. Samples of *ca.* 50 $\mu$l were periodically removed by means of syringe and quenched by 50 $\mu$l of cold acidic soln (HOAc for 1 and HCl for 2) of the corresponding alcohol. The quenched solns were analyzed by GC. Their composition remained unchanged for at least 10 days.

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