potentially involving the formation of an exocyclic bond.

This type of interaction arising from substituents on the 1 and 3 positions of an allylic system we have termed $A^{(1,3)}$ strain. The effect, however, is not confined to purely carbon systems for if we replace $C_\alpha RR''$ by oxygen, the interaction becomes that of a nonbonded pair of electrons on oxygen with R', and it reduces itself in principle to the much vaunted "2-alkyl ketone effect."[2] We must then classify the latter as a pseudo-allylic system[3] exhibiting $A^{(1,3)}$ strain.

A large number of other important examples of this type of strain will be discussed in a subsequent full paper, but a most important application of the principle is described in the succeeding communication.

The second type of steric hindrance can be demonstrated if we inspect the allylic system in conformer IIa of II. By direct measurement on a model the dihedral angle[4] $R'C_\gamma-C_\beta R$ is approximately $35°$. Thus, in the idealized case, the introduction of a $\Delta^{1,6}$-double bond into a 1e,2e-disubstituted cyclohexane causes a decrease of $25°$ in the dihedral angle between the substituents and a resulting increase in the steric or Pitzer strain between them.
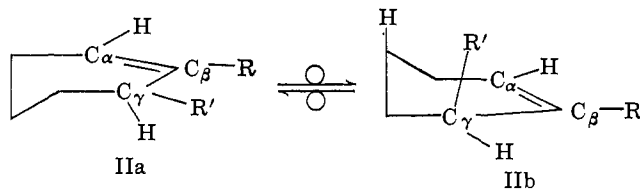
If the substituents are moderately large, relief of strain may be attained by conformational inversion to IIb in which case the dihedral angle[4] between $C_\gamma R'$ and $C_\beta R$ becomes $85°$. Strain in IIb arises only from one 1,3-diaxial interaction of R' with a hydrogen atom plus the hindrance associated with R and the C_γ-quasiequatorial hydrogen atom. Here even in the simple case where $R = R' = CH_3$ it is difficult to calculate the significant nonbonded energies associated with these conformers, and no attempt will be made to do so here. However it is fairly obvious that with substituents (R and R') of reasonable size *once again it is that conformer (IIb) with the ring substituent (quasi-) axially oriented that will constitute the greater proportion of II in the ground state.* This type of strain arising from a 1,2-disubstituted allylic system we have designated $A^{(1,2)}$ strain.

The conclusions deduced from this empirical approach are essentially the same as those reached by Garbisch[5] in his examination of a series of 1-phenyl-6-substituted cyclohexenes. Using n.m.r. spectroscopy he was able to prove that the group at the 6 position, if bulky, took up an axial orientation. This was valid

(2) B. Rickborn, *J. Am. Chem. Soc.*, 84, 2414(1962); W. D. Cotterill and M. J. T. Robinson, *Tetrahedron*, 20, 765, 777 (1964).

(3) We define a pseudo-allylic system as one in which one of the atoms of the allyl group itself has been replaced by an element other than carbon (*e.g.*, O, N, S, etc.).

(4) A vector analysis of cyclohexene has been carried out by E. J. Corey and R. A. Sneen (*J. Am. Chem. Soc.*, 77, 2505 (1955)), who calculated this angle to be $37°$ at a time when Dreiding models were not available. Thus this value, and their corresponding value for the dihedral angle $R'C_\gamma-C_\beta R$ ($83°$) in IIb, are in excellent agreement with the more empirical measurements made on the model.

(5) E. W. Garbisch, Jr., *J. Org. Chem.*, 27, 4243, 4249 (1962).

only of course provided no other substituents on the ring blocked conformational inversion.

The value of the theorem becomes apparent only from its generality, for if we replace R by an oxygen or nitrogen atom then II is reduced to an enol or an enamine, respectively. We have recently shown that both solvated enolate anions[6] and certain enamines[7] of 2-substituted cyclohexanones exist largely with the ring substituent in the quasiaxial orientation. Thus it is clear that both the systems studied by Garbisch and those examined by us fall into the same category, that of being controlled by $A^{(1,2)}$ strain.

Further refinement and elaboration of these ideas will be presented later in a subsequent article but, without citing specific examples, it can be stated that many anomalous stereochemical observations recorded in the literature can be explained easily by application of the above principles.

(6) S. K. Malhotra and F. Johnson, *J. Am. Chem. Soc.*, 87, 5513 (1965).

(7) F. Johnson and A. Whitehead, *Tetrahedron Letters*, 3825 (1964); S. K. Malhotra and F. Johnson, *Tetrahedron Letters*, 4027 (1965).

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Steric Interference in Allylic and Pseudo-Allylic Systems. II. Stereochemistry of Exocyclic Enolate Anion Protonation

Sir:

In the preceding communication[1] we have discussed strain which arises in substituted allylic systems that constitute part of a six-membered ring. Empirically it was deduced that molecules containing either an exocyclic or an endocyclic double bond would, with the appropriate substitution, have internal nonbonded interactions. These were classified as $A^{(1,3)}$ and $A^{(1,2)}$ strain, respectively.

In the exocyclic double bond case shown below, if R and R' are small, the equilibrium should lie to the left. If R and R' are medium or large in size it should lie to the right. Axiomatically, the extent of
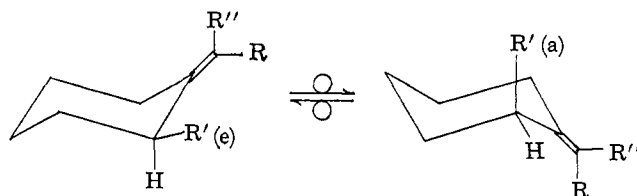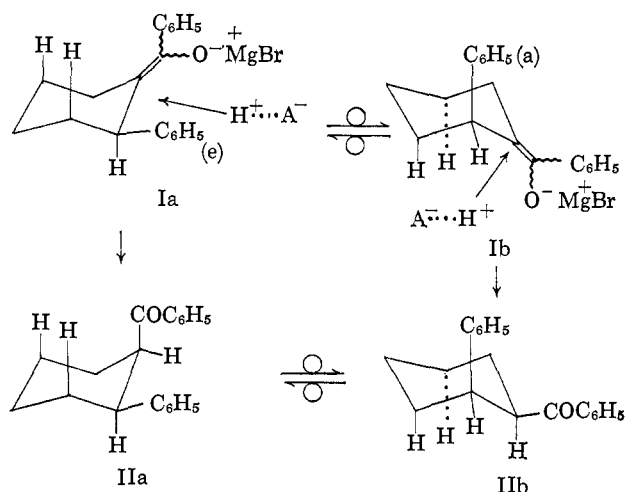

conformation inversion from left to right in the ground state will depend on the free-energy difference between the conformers.

A logical vehicle on which to test these ideas appeared to be the systems discussed at length by Zimmerman and co-workers.[2] In 1955 it was reported that

(1) Part I: F. Johnson and S. K. Malhotra, *J. Am. Chem. Soc.*, 87, 5492 (1965).

(2) (a) H. E. Zimmerman, *J. Org. Chem.*, 20, 549 (1955); (b) H. E. Zimmerman, *J. Am. Chem. Soc.*, 78, 1168 (1956); (c) H. E. Zimmerman, *ibid.*, 79, 5554 (1957); (d) H. E. Zimmerman and T. E. Nevins, *ibid.*, 79, 6559 (1957); (e) H. E. Zimmerman and T. W. Cutshall, *ibid.*, 80, 2893 (1958); (f) H. E. Zimmerman and T. W. Cutshall, *ibid.*, 81, 4305 (1959).

the C-protonation of the bromomagnesium enolate anion I (generated by the addition of phenylmagnesium bromide to benzoylcyclohexene) led to the formation of the less stable isomer of 1-benzoyl-2-phenylcyclohexane (II).[2a] The rationale suggested for this result

C₆H₅
H H   C-O⁻MgBr⁺
                ↑
          ─H⁺···A⁻
        —C₆H₅
       H
      (e)
      Ia

        C₆H₅ (a)
      H H H
            —C₆H₅
      A⁻···H⁺ O⁻ MgBr⁺
      Ib

↓   ↓

H H   COC₆H₅
        —H
      —C₆H₅
     H
     IIa

        C₆H₅
      H H H
            —COC₆H₅
      H H   H
      IIb

was that C-protonation operates on conformer Ia and with a nonbulky acid occurs from an equatorial direction. The further explanation of this deduction was that steric interference arising from the axial hydrogens on the alicyclic ring at positions C-3 and C-5 seriously hindered axial protonation.

According to $A^{(1,3)}$ *strain,[1] however, I should exist largely as the conformer Ib in the ground state,* and we now present evidence that very strongly suggests that this is the case.

The enolate anion I was prepared according to the published procedure and trapped as the enol acetate by inverse quenching with acetic anhydride.[3] That the enolate anion is a mixture of two geometric isomers (~1:1) was evident from the n.m.r. spectrum of the acetylated product. It showed two bands of almost equal intensity, at 1.97 and 1.8 p.p.m. for COCH_3 hydrogen. The isomeric acetates were readily separated as the pure substances by fractional crystallization, then chromatography, the first being obtained as prisms, m.p. 99–100° (Found: C, 82.26; H, 7.36) and the second as rosettes, m.p. 51–53° (Found: C, 82.14; H, 7.07).

The n.m.r. spectra of these isomers each showed poorly resolved triplets for benzylic hydrogen, at 3.96 p.p.m. (W_H = 7 c.p.s.; $J \sim 3.5$ c.p.s.) and at 4.01 p.p.m. (W_H = 7 c.p.s.; $J \sim 3.5$ c.p.s.), respectively. The splitting patterns and the coupling values are highly characteristic of *an equatorial hydrogen atom* split by adjacent axial and equatorial protons (*i.e.*, both are ABX systems where ideally $\psi_{AX} = \psi_{BX} = 60°$).[4] With no stretch of the imagination it can therefore be concluded that *the two isomeric enolate anions of I do exist overwhelmingly in conformation* Ib, since the OMgBr moiety and the acetate group undoubtedly
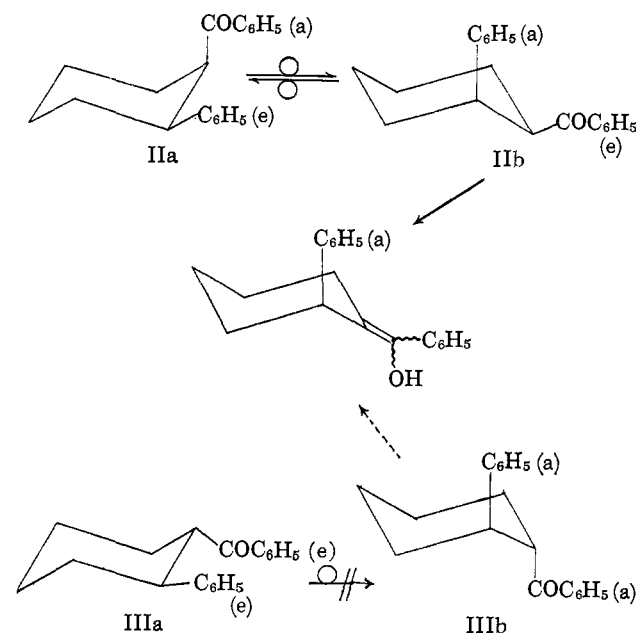
are comparable in steric size, the latter being only slightly bigger than a hydroxyl group.[5,6]

The formation of the less stable *cis* isomer II, on ketonization of I, can readily be rationalized if protonation of conformer Ib occurs axially, as depicted. Protonation can still be considered as occurring on the less hindered side.[7] This would then give conformer IIb, with the phenyl group axial, which would enter into the mobile equilibrium with its conformational isomer IIa.

In connection with this Zimmerman has also reported[2a] that the bromination of II in acetic acid is quite rapid; he found it to be complete in 10 min. at 80°. The more stable *trans* isomer (III) was observed to be quite resistant to bromination under the same conditions. These facts are now much better explained in the light of the $A^{(1,3)}$ strain involved in the formation of the intermediate enols. As could

COC₆H₅ (a)   C₆H₅ (a)
                  ⇌
        C₆H₅ (e)   —COC₆H₅
   IIa   IIb   (e)

                    ↓

          C₆H₅ (a)
                —C₆H₅
              OH

                    ↓

    C₆H₅ (a)
        COC₆H₅ (e)   C₆H₅ (a)
      —C₆H₅   ─//→   COC₆H₅ (a)
      (e)
   IIIa   IIIb

be deduced from above, II offers no resistance to enol formation since a pathway is available *via* conformer IIb. However, enolization of IIIa would be resisted by $A^{(1,3)}$ strain, and its conformational isomer IIIb is undoubtedly too energetic a species to invoke its use for a ready pathway to an enolic form. Interestingly, we have found that bromination of benzoylcyclohexane (where no axial substituent or $A^{(1,3)}$ strain is involved) is complete in 1 min. at 80°. Further studies are in progress here.

(3) H. J. Ringold and S. K. Malhotra, *J. Am. Chem. Soc.*, 84, 3402 (1962); H. O. House and V. Kramar, *J. Org. Chem.*, 28, 3362 (1963).

(4) *Cf.* R. V. Lemieux, R. K. Kullnig, H. J. Bernstein, and W. G. Schneider, *J. Am. Chem. Soc.*, 80, 6098 (1958); F. V. Lichtenthaler and H. O. L. Fisher, *ibid.*, 83, 2005 (1961); also note N. S. Bhacca and D. H. Williams, "Applications of NMR Spectroscopy in Organic Chemistry," Holden Day, Inc., San Francisco, Calif., 1964, p. 51, and E. W. Garbisch, *J. Org. Chem.*, 27, 4243, 4249 (1962); W. R. Vaughan and R. Caple, *J. Am. Chem. Soc.*, 86, 4928 (1964).

(5) E. L. Eliel, N. L. Allinger, S. J. Angyal, and G. A. Morrison, "Conformational Analysis," John Wiley and Sons, Inc., New York, N. Y., 1965, p. 44.

(6) Probably protonation of I occurs on oxygen first followed by rearrangement to the ketonic form. However this is only incidental to the argument since the size of hydroxyl in the enolic form undoubtedly is large enough to ensure that conformation Ib is essentially the preferred state of I.

(7) An alternate and plausible explanation is that the transition state for equatorial protonation is of considerably higher energy than that for axial protonation. Justification for this assumption lies in the fact that in the former transition state two new 1,3-diaxial interactions (H–COC₆H₅ or H–NO₂) are being produced whereas in the latter the only new interaction arising is a *gauche* interaction(C₆H₅–COC₆H₅ or C₆H₅–NO₂), and this is generally considered to be the less energetic of the two possibilities. Nevertheless, a survey of the literature on the protonation of other exocyclic enolates yields compelling evidence for the steric approach theory, and the latter is preferred by the authors.

Another case discussed by Zimmerman, and of great similarity to the protonation of I above, is the C-protonation of 1-*aci*-nitro-2-phenylcyclohexane (IV).[2d] Here it was thought that C-protonation occurred equatorially (*i.e.*, from the less hindered side)[7] on conformation IVa. However, by $A^{(1,3)}$ strain theory the more stable ground state of IV should be conformer IVb. Protonation of this conformer axially (*i.e.*, from the less hindered side) would also give the known product *cis*-1-phenyl-2-nitrocyclohexane (Vb) *via* the less stable conformer Va.

O
↑
N—OH
C₆H₅ (e)
H
IVa
C₆H₅(a)
H N→O
A⁻···H⁺ OH
IVb

C₆H₅(a)
H NO₂
H
(e)
Va
NO₂(a)
H
C₆H₅(e)
H
Vb
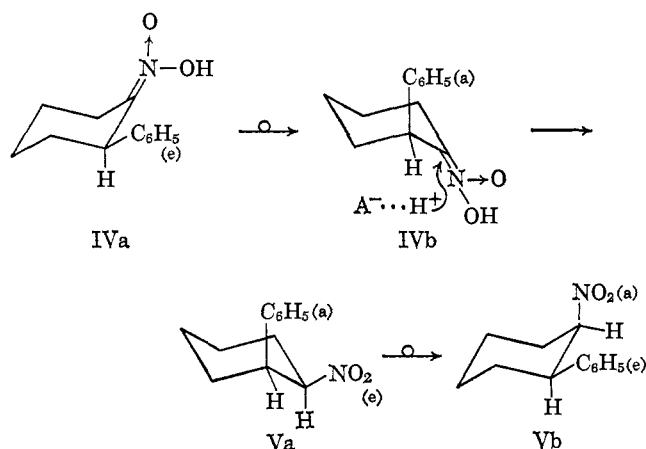
We find that in the n.m.r. spectrum of IV the benzylic proton appears as a narrow triplet ($J = 4.0$ c.p.s.; $W_H = 9.0$ c.p.s.) at 4.6 p.p.m. Again *this is highly characteristic of a benzylic equatorial proton* on a cyclohexyl ring split by adjacent CH_2 hydrogen atoms.[4]

The cases discussed above demonstrate unequivocally that $A^{(1,3)}$ strain in these exocyclic double bond systems is real and that the much ignored conformers with axial substituents at the 2 position are in fact the stable ground states. In addition we arrive at the conclusion that Zimmerman's views of the ketonization of the exocyclic enolates under discussion must be abandoned in favor of the alternate interpretation presented above.

This general principle of $A^{(1,3)}$ strain surely opens up new vistas in conformational analysis, for now it becomes possible, as will be shown in future articles, to relate quite simply the reactivity of nonrigid molecules to that of their rigid homologs, a relationship lacking in the past.

Acknowledgment. We wish to thank Mr. D. F. Moakley for technical assistance with this work.

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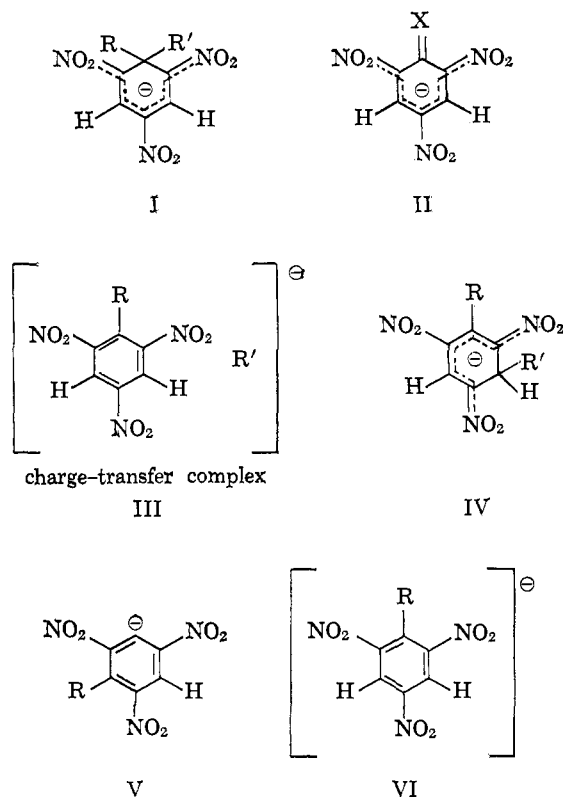Wayland, Massachusetts

Nuclear Magnetic Resonance Studies of Meisenheimer Complexes

Sir:

In 1902 Meisenheimer[1] succeeded in the isolation and structure determination of a compound, I (R = OCH₃, R′ = OCH₂CH₃), which is today commonly taken as the prototype of the activated complex in nucleophilic aromatic substitution.[2] Since that time,

(1) J. Meisenheimer, *Ann.*, 323, 205 (1902).

the structure of the anions formed from other trinitro-aromatic compounds has been the subject of numerous investigations and much speculation.[3] Proposed structures include the anions I–VI.[3a–d,4] We wish to report on the nuclear magnetic resonance spectra of the anions obtained on treating a series of 1-substituted 2,4,6-trinitrobenzenes with sodium methoxide in dimethyl sulfoxide (DMSO). These results clearly establish the structures of the resultant anions. Crampton and Gold[5] have recently reported their conclusions from a similar study. Our conclusions differ from theirs in several important aspects; since they report no data it is difficult to learn the origin of the differences. Their apparent failure to observe some of the species may be due to the rapid equilibration of these anions at the higher methanol concentrations used in their study.

R R′
NO₂ NO₂
⊖
H H
NO₂
I

X
NO₂ NO₂
⊖
H H
NO₂
II

R
NO₂ NO₂
⊖ R′
H H
NO₂
charge-transfer complex
III

R
NO₂ NO₂
⊖ R′
H H
NO₂
IV

NO₂ ⊖ NO₂
R H
NO₂
V

R
NO₂ NO₂
⊖
H H
NO₂
VI

A solution of sodium methoxide in methanol (7 *M*) was added to a 1 *M* solution of the aromatic compound in DMSO; the n.m.r. spectra were recorded immediately after mixing using a Varian A-60 n.m.r. spectrometer. The results are summarized in Table I. Due to overlap with the solvent peaks areas for the NH₃ and OCH₃ resonances could not be measured but were visually estimated and were consistent with the assignments in Table I. In all cases, the ring

(2) For recent reviews see: (a) R. Huisgen and J. Sauer, *Angew. Chem.*, 72, 91, 294 (1960); (b) S. D. Ross, *Progr. Phys. Org. Chem.*, 1, 3 (1963).
(3) (a) J. B. Ainscough and E. F. Caldin, *J. Chem. Soc.*, 2528, 2540, 2546 (1956); (b) L. K. Dyall, *ibid.*, 5160 (1960); (c) R. C. Farmer, *ibid.*, 3425, 3430, 3433 (1959); (d) V. Gold and C. H. Rochester, *ibid.*, 1687, 1692, 1697 (1964); (e) R. Foster, *ibid.*, 3508 (1959); (f) R. Destro, C. M. Gramaccioli, A. Mugnoli, and M. Simonetta, *Tetrahedron Letters*, 2611 (1965); (g) W. P. Norris and J. Osmudsen, *J. Org. Chem.*, 30, 2407 (1965).
(4) (a) R. Foster and R. K. Mackie, *J. Chem. Soc.*, 3843 (1962); (b) R. Foster and R. K. Mackie, *Tetrahedron*, 18, 161 (1962); (c) R. E. Miller and W. F. K. Wynne-Jones, *J. Chem. Soc.*, 2375 (1959); (d) R. J. Pollitt and B. C. Saunders, *Proc. Chem. Soc.*, 176 (1962); (e) E. F. Caldin and G. Long, *Proc. Roy. Soc.* (London), 228A, 263 (1955).
(5) M. R. Crampton and V. Gold, *Chem. Commun.*, 256 (1965).