Pergamon

Tetrahedron Letters, Vol. 36, No. 8, pp. 1295-1298, 1995
Elsevier Science Ltd
Printed in Great Britain
0040-4039/95 $9.50+0.00

0040-4039(94)02440-5

Kinetically Deduced Existence of C=O····C Close Contacts. Pericyclic Rearrangement of 1,2-Diacetyl-1,2-dihydro-3H-indazol-3-one.

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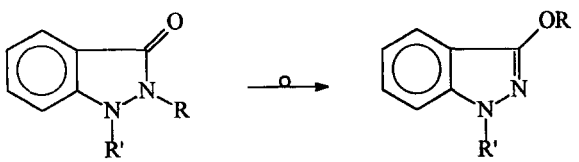
Abstract : First-order kinetics of the title rearrangement to 3-acetoxy-1-acetylindazole (2a), complete exchange of O-acyl groups in cross-experiments, insensitivity to change in reaction medium, lack of electronic substituent effects and activation parameters are considered as evidence in favour of a pericyclic mechanism through C=O····C close contacts.

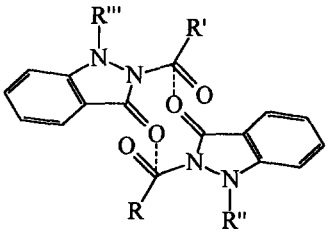
The importance of non-covalent interactions in many biological processes has led to the impressive development of supermolecular chemistry in the last decade.[1] However C=O····C close contacts have not received much attention owing to the fact that they are known only in the crystalline state and not well understood, a mathematical model having yet to be found.[2] There is no obvious effect on the valence shell charge density.[3] The best known examples are anhydrous alloxan[4] and the parabanic acid.[3] The interaction is favoured by the presence of amidic groups[5] and its existence in the nucleic acids has already been proposed on the basis of quantum mechanical calculations.[6] Closely related is the formation in the gaseous state of the Van der Waals molecule O_2C····OH_2 with an "antihydrogen-bonded" structure.[7] The existence of C=O····C close contacts in solution has now been kinetically deduced and in this letter we would like to present our results.



1 2

a: R=R'=Ac
b: R=R'=COEt
c: R=Ac; R'=COEt
d: R=COEt; R'=Ac
e: R=Ac; R'=Me

1,2-Diacetyl-3-indazolone (1a) is a particularly favourable case for this purpose possessing an imidic structure and permitting a double interaction which is an important contribution to the stability of the resulted dimer 3a. Besides the rearrangement of 1a to 3-acetoxy-1-acetyl-indazole (2a) is quantitative with no by-products and able to be easily monitored by ^{1}H-NMR .[8]



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a: R=R'=Me; R''=R'''=Ac
b: R=R'=Et; R''=R'''=COEt
c: R=Me; R'=Et; R''=Ac; R'''=COEt
d: R=R'=R''=R'''=Me

Kinetic measurements indicated a first-order reaction. The initial concentration of 1a for all determinations was a=0.4 mol/l. The rate constants were as follows : in CD_3CN $10^5k=4.50 \pm 0.25$ sec^{-1} at 126.5°; PhCN: $10^5k_{131}=6.17 \pm 0.17$ and $10^5k_{153}=40.30 \pm 0.61$ sec^{-1}. Activation parameters : $E_a=29.2 \pm 1.0$ kcal/mol and $\Delta S^{\neq}= -8.2 \pm 2.5$ e.u. Supplementary probes were carried out in benzonitrile at 121.2° and 134° (respectively $10^5k=2.53$ and 8.50 sec^{-1}; $E_a=29.1$ kcal/mol and $\Delta S^{\neq}= -8.4$ e.u.). The Arrhenius plotting of log k against 1/T yields a straight line including the four measured rate constants. Insensitivity to changes in the reaction medium was also observed. At 126.5° the rate constant in d_6-benzene showed almost no difference as compared to acetonitrile and benzonitrile ($10^5k=4.33$ sec^{-1}).

Cross-experiments between 1a and 1b displayed a complete exchange of O-acyl groups taking place quantitatively according to the pattern :

3c = 2c + 2d (50%)
3a = 2a + 2a (25%)
3b = 2b + 2b (25%)

The first equation has a double probability weight. The resulting products were formed in almost equal amounts. Their separation was carried out by GLC on capillary columns. Under the same conditions as the rearrangement, exchange of O-acyl groups was also observed between 2a and 2b but to a much lesser extent. The value of the fraction of exchange was far from a random distribution : F=0.16 as compared to F=0.98 for the rearrangement. These results remove the possibility of any significant exchange following the rearrangement.

Replacement of the 1-acetyl group in 1a by a methyl group would allow to observe an electronic substituent effect. Owing to a lower steric hindrance at N-1 and a much stronger nucleophilicity at N-2, 2-acetyl-1-methyl-3-indazolone (1e), over 100°, reversibly rearranges to an

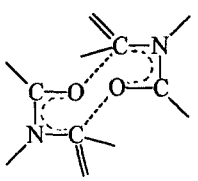
equilibrium mixture with 2e, the degree of transformation being 0.79.[8] Starting from 1e kinetic measurements were in accordance with a first- and second-order equilibrium :

$$3d \underset{k'}{\overset{k}{\rightleftharpoons}} 2e + 2e$$

The first-order rate constant at 133° harmonised with the Arrhenius plot of 1a: $10^5k=7.41 \pm 0.15$ sec^{-1} (solvent benzonitrile).

A strong electronic substituent effect should be observed in the case of a heterocyclic cleavage of the 2-Ac group. This could be done by using pyridine as a solvent which acts by nucleophilic catalysis and strongly differentiates the reactivities of 1a and 1e. The migration of the 2-Ac group of 1a took place rapidly at room temperature ($t_{1/2}$=12 min). Compound 1e showed no change after one hour at 80°. The explanation lies in the alpha effect which strongly enhances the nucleophilicity at the position 2-N of 1e.

Discussion. First-order kinetics and complete exchange of O-acyl groups can be accommodated only if we take into consideration association of compounds 1 into dimers 3. In this way the rearrangement can be considered as intramolecular with respect to the dimer 3a. Further evidence is brought by the fact that 1a did not rearrange on a nonpolar chromatographic column at 200° while in boiling benzonitrile the transformation occurred in a few minutes. In the first place the existence of double interactions of the type EDA were envisaged, the corresponding complex of 1a representing at the same time a resonance structure of a polarised transition state. The insensitivity toward solvents and electronic substituent effects indicated however a pericyclic mechanism and consequently a transition state and a molecular association without charge transfer. These requirements are consistent with C=O····C close contacts.



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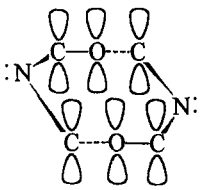

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In this way nonpolarised association leads to a corresponding nonpolarised transition state 4 of the Hückel type involving ten p electrons (5). The reaction should be thermally allowed and photochemically forbidden which is just the case. The rearrangement does not take place under the action of UV radiation. This rules out the formation of intermediate acyl free radicals which are known to decompose rapidly over 100°. They could be stabilised by a cage effect but the internal

return would be much favoured and complete exchange made impossible. The same is true for the acylium ions stabilised in intimate pairs.

Activation parameters are in accordance with the above conclusions. The activation energy is much lower than expected for a bond dissociation while the negative value of $\Delta S^{\neq}$ suggests a constrained transition state. The very close values of the rate constant in different solvents allowed us to assume complete association to the cyclic dimers 3. As expected on strong dilution the reaction rate decreased and this could be attributed to the nonassociated 1a as well as to open-chain oligomers.[9] Examination of ^{1}H-NMR spectra revealed no significant changes on dilution so that the latter possibility was considered as more plausible. If we regard the equilibrium rates as very fast, the ^{1}H-NMR spectra being averaged, the initial rate of rearrangement will furnish the proportion of cyclic dimer 3a. The obtained values were 93% in acetonitrile at a/8, 84% in benzonitrile at a/4 and in benzene 49% for a/4 and 14% for a/8.

Steric hindrance between the two acetyl groups of 1a does not interfere with association since the imido moiety is coplanar with the benzene ring (the two carbonyl groups being syn) while the N-1 is slightly deviated as peak of an envelope, the 1-acetyl group being twisted by 38° (MOPAC AM 1 6.0 program) and a NOE effect being displayed between the corresponding methyl group and the H-7 proton.

Related transformations which deserve mention are the Mumm isoimide-imide rearrangement[10] which is intramolecular and the equilibrium 4-acetoxypyridine/N-acetyl-4-pyridone of unknown mechanism.[11]

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(*Received in UK* 5 *August* 1994; *revised* 15 *December* 1994; *accepted* 16 *December* 1994)