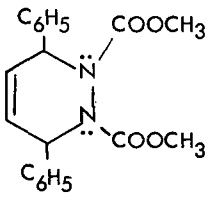
Tetrahedron Letters No. 17, pp. 1603-1609, 1967. Pergamon Press Ltd. Printed in Great Britain.

CONFORMATIONAL STUDIES ON THE AMIDO GROUP. HINDERED INTERNAL ROTATION IN N,N' - DIALKYL HYDRAZOCARBOXYLATES

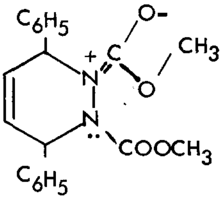
Robert M. Moriarty, Sr., M. R. Murphy,(1) S. J. Druck and Leopold May
Department of Chemistry, The Catholic University of America
Washington, D. C. 20017

(Received 4 November 1966; in revised form 22 February 1967)

Three related recent communications have appeared dealing with the n.m.r. spectra of tetrahydropyridazine derivatives such as I. (2,3,4,5) Breliere and Lehn (2) studied the temperature dependence of the line shapes for various protons in I and were able to calculate values of the barrier heights for (a) rotation about the N–CO bond, and (b) for ring inversion between two conformations. Bushweller (3) criticized the above results on the grounds that the inequality in the "heights" (6) of the methyl resonances at 35° for I observed by the French workers was inconsistent with ring inversion between two mirror image conformers. Price, Smallman and Sutherland, (4) measured independently the spectrum of I and found that the two components of the methyl resonance were in fact of equal intensity at 35° as Lehn had found and as would be expected. Agreement does prevail among the three parties, that the restricted rotation arises from the presence of the carbon-nitrogen partial double bond resulting from pπ -pπ overlap of the type indicated by structure II.



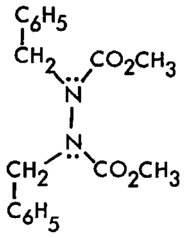
I



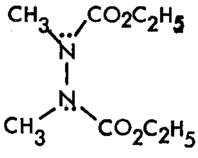
II

Similar studies have also been in progress in this Laboratory; however, our work differs from the above in both choice of compounds and also interpretation of results.

We have restricted our n.m.r. studies to several N,N'-dialkyl hydrazodicarboxylates of which III and IV are typical examples. These compounds, in relation to I, may be considered formally as acyclic analogs of the tetrahydropyridazines.



III



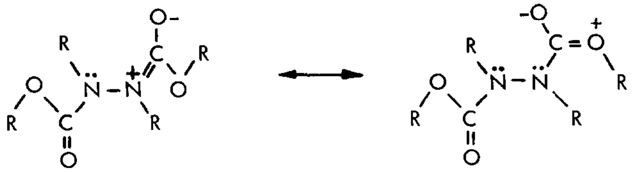
IV

In these systems ring inversion obviously is excluded, and the important rate processes amenable to study by n.m.r. are rotation about the N-N single bond, rotation involving the $-NCO_2R$ portion of the molecule, and rotation about the N-benzyl group for III.

The spectrum of III shows two fairly symmetrical singlet peaks of relative intensities 3:2 at 46°. These correspond to the OCH_3 groups at 3.36 p.p.m. and the benzylic protons at 4.58 p.p.m. relative to TMS. At 22° the $O-CH_3$ peak is split into a doublet and the benzylic methylene proton resonance becomes non-symmetrical. Further cooling to -5° results in a clear doubling of both the methyl and methylene resonances; the two OCH_3 peaks assume a relative intensity of about 2:1. Furthermore, several new peaks arise in the vicinity of the methylene proton absorption. At -22° the chemical shifts between the two components of the methyl and methylene sets are further increased and additional splitting of the methylene protons appears.

The low temperature doubling of the $O-CH_3$ resonance indicates that some rotational process is occurring that leads to interconverting isomers of different relative stabilities. While this behavior could be attributed to hindered internal rotation about the N-CO bond as occurs in amides, an alternative rotational process warrants discussion. In the first place, a structure such as V possesses the unfavorable feature of having a partially positively charged nitrogen atom adjacent to an electronegative nitrogen. Based upon this consideration, a second resonance structure should be considered for these compounds, namely, structure VI which possesses

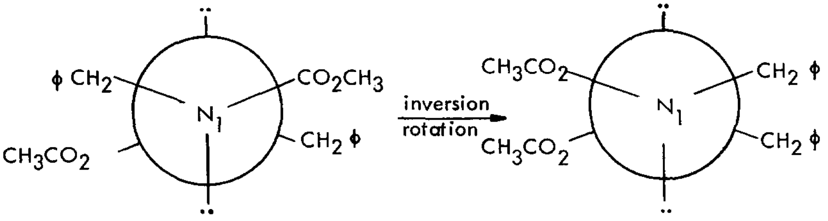
O-CO pπ-pπ of the type invoked for esters and lactones. (7) Such hindered internal rotation for esters has been detected and studied by means of n.m.r. (8)



V VI

Several conformations for III are conceivable. One set may be drawn for the s-cis arrangement of the carboalkoxy groups about the N-N bond; a second set derives from the s-trans conformation. Within each set, s-cis and s-trans arrangements for the O-CH_3 and carbonyl oxygen of the carboalkoxy group may also exist. Furthermore, torsional isomerism about the nitrogen carbonyl bond is also possible, but in structure i-v the barrier height for such rotation should be small (for the reason cited above). Structures i and ii correspond to conformers resulting from rotation N-CO bond. Structures iii and iv result from rotation about the CO -OCH_3 bond. In all, eighteen conformers may be drawn for III. The complexity of the low temperature n.m.r. spectra of III indicates the presence of at least four conformers.

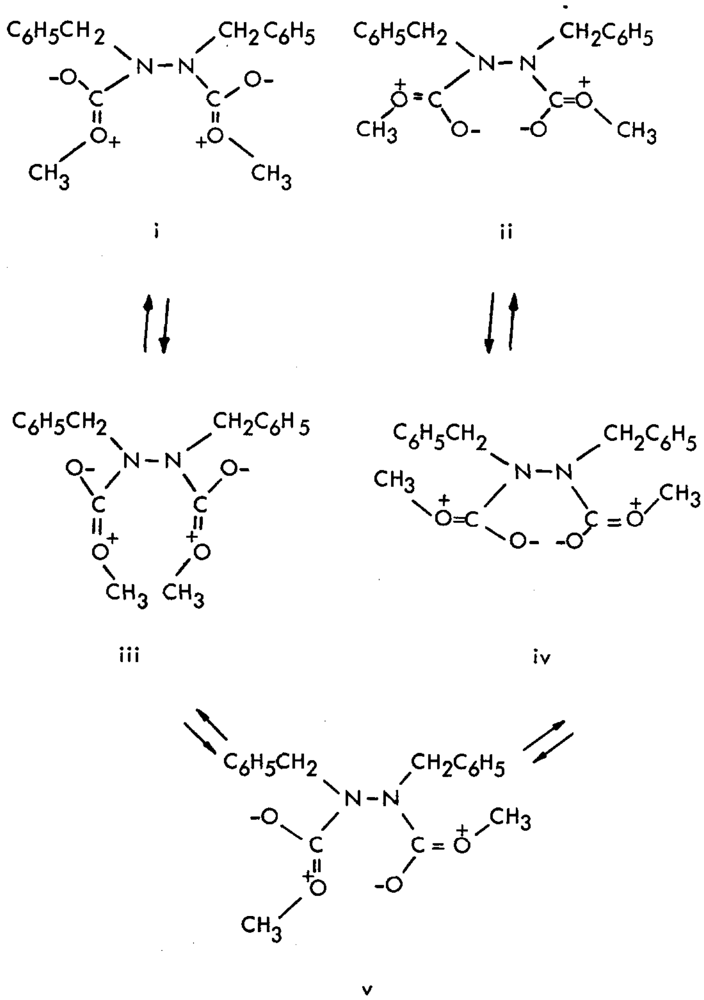
A further point of conformation relates to rotation and inversion about the N-N single bond. Thus, the following rotamers should be considered:



A B

Inversion at nitrogen rapidly interconverts the above diasteriomers; however, one would expect at thermal equilibrium both A and B should exist. The chemical shifts of related protons in these conformation could be non-equal.

Similar behavior was also observed for N,N'-dimethyl diethylhydrazodicarboxylate (IV). The room temperature spectrum of IV is that expected for averaged chemical shifts due to rapid intramolecular rotation. At 4° the $\underline{CH_3}$ CH_2 methyl is clearly a doublet of triplets, and the CH_3 $\underline{CH_2}$ quartet is broadened; also, the CH_3


i
ii
iii
iv
v

N resonance begins to broaden into an asymmetric doublet at this temperature. At -26° all the proton resonances are doubled. The observed changes may be due to hindered internal rotation about the CO-Obond due to partial double bond character.

Another spectral phenomenon which may also be associated with the existence of conformational isomers of the type discussed above is the presence of a doublet carbonyl stretching frequency bond in some of these compounds in the infrared spectrum.

Reference to Table I reveals that a number of acyclic and cyclic hydrazocarboxylate derivatives display this behavior. Furthermore, the appearance of the doublet absorption bond is solvent dependent; for example, the doublet carbonyl absorption found in the solid state appears as a singlet in $CHCl_3$ and CCl_4 solutions.

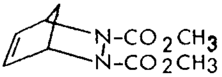
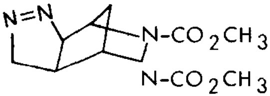
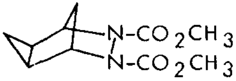
In the compounds with hydrogens on the nitrogens, the doubling can clearly be ascribed to hydrogen bonding. This is also supported by the appearance of the N-H stretching frequencies near 3300 cm^{-1} (VII and VIII). In solution only a singlet carbonyl bond is present, and the N-H band appears in the region assigned to non-bonded N-H stretching frequency. When methyl or phenyl is substituted for hydrogen, only a single absorption bond is found in the carbonyl region (X, XI). The spectra of some cyclic compounds (XII-XV) display a doublet absorption in the carbonyl region.

In the non-cyclic dicarboxylates (VII-IX), the carbonyl absorption appears near 1738 cm^{-1}. This is at a frequency slightly higher than that observed for secondary carbamates (1705-1722 cm^{-1}). (9) This is expected based on the hypothesis outlined above, since the adjacent nitrogen atom decreases the double-bond character of the carbonyl group. The introduction of the nitrogen into a ring broadens the range in which the carbonyl absorptions are observed to 1678 to 1731 cm^{-1}. Generally the bands observed in the cyclic compounds (XII-XV) fall into this extended range. In the cyclic compounds (XII-XV) where two bands appear, one band is observed near the region where tertiary carbamates and linear carbamates with cyclic nitrogens exhibit absorption. (9) This band is near 1700 cm^{-1}. The second band is generally twenty to thirty cm^{-1} higher. These bands can be attributed to the non-equivalence of the two carbonyl groups such as would be present in structure VI.

1. Taken in part from the Master's dissertation of Sr. M. R. Murphy, The Catholic University of America, 1964.
2. J. C. Breliere and J. M. Lehn, Chem. Comm., 426 (1966).

Table I

CARBONYL AND N-H STRETCHING FREQUENCIES FOR SOME N, N' HYDRAZOCARBOXYLATES (cm^{-1})[a]

Compound	KBr	Nujol	CHCl$_3$	CCl$_4$
$CH_3O_2CNHNHCO_2CH_3$(VII)	1715	1715	173?	insol
	1746	1740		
	3325	3300	3455	insol
			3350	
$C_2H_5O_2CNHNHCO_2C_2H_5$(VIII)	1703	1700	1737	insol
	1763	1755		
	3345	3350	3480	insol
$C_2H_5O_2CNDNDCO_2C_2H_5$(IX)	1692	1688	1738	
	1745	'37		insol
	2423	113	2436	
$CH_3CONCH_3NCH_3COCH_3$(X)	1674	1676	1675	1693
$C_6H_5CONCH_3NCH_3COCH_3$(XI)	1668	1661	1670	----
 N-CO$_2$CH$_3$ (XII) N-CO$_2$CH$_3$	1678	1682		1754
	1704			
				1713
 N-CO$_2$CH$_3$ (XIII) N-CO$_2$CH$_3$	1739			1754[b]
	1704			
				1713
 N-CO$_2$CH$_3$ (XIV) N-CO$_2$CH$_3$				
				1748[b]
				1704
 (XV)	1737	1744	1706	1740
CHO_2C-N-N-CO_2CH_3	1718	1724		1699

a.) Spectra determined using a Perkin Elmer Model 13 infrared spectrophotometer.

b.) Compounds synthesized and spectra determined by Dr. T. Van Auken, The University of Texas, Austin, Texas. Spectra were determined using a Beckman IR 7 instrument.

3. C. M. Bushweller, Chem. Comm., 80 (1966).

4. B. J. Price, R. V. Smallman, and I. O. Sutherland, Chem. Comm., 319 (1966)

5. R. Daniels and K. A. Roseman, Tetrahedron Letters, 13, 1335 (1966).

6. In a private communication from Dr. Lehn, University of Strasbourg, the point of equal intensities and unequal heights was discussed. At 35° the heights of the two methyl peaks are indeed unequal but the integrated intensities of the two peaks are equal within experimental error.

7. R. Huisgen, Angew, Chem., 69, 341 (1957).

8. G. J. Karabatsos, N. Hsi and C. E. Orzech, Jr. Tet. Let. 38, 4639 (1966).

9. S. Pinchas and D. Ben-Ishai, J. Am. Chem. Soc. 79, 4099 (1957).