

ON THE TAUTOMERISM OF AMIDES

Lech Skulski<sup>1</sup>, George C. Palmer and Melvin Calvin

Department of Chemistry and Lawrence Radiation Laboratory  
University of California, Berkeley 4, California

(Received 12 July 1963; in revised form 12 August 1963)

The solvent effect on the direction of the optical rotation of certain amides has been interpreted in terms of an amide-iminol equilibrium:



whose position is solvent dependent.<sup>2</sup>

The discovery of the existence of two crystal forms of the optically active N-benzoyl- and N-(3,5-dinitro-benzoyl)- $\alpha$ -phenylethylamines was adduced as supporting evidence.

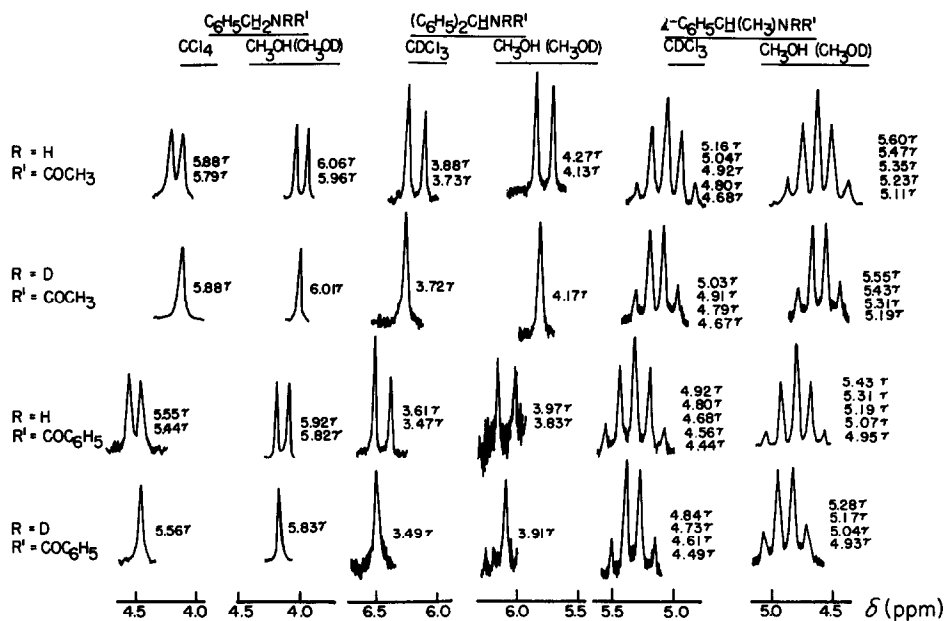
We have made spectropolarimetric measurements of the optical rotatory dispersion of N-benzoyl, N-acetyl-, N-formyl-, and N-trifluoroacetyl- $\alpha$ -phenylethylamines in benzene and methanol solutions at 25°. The experimental observations<sup>2</sup> reporting that the rotation of optically active N-benzoyl- $\alpha$ -phenylethylamines is of opposite sign in methanol from what

1. Postdoctoral Fellow, 1962-1963. On leave of absence from the Institute of Technology (Politechnika), Warsaw, Poland. Appointment supported by the Ford Foundation Polish Exchange Program administered by the Institute of International Education, New York.
2. V. M. Potapov, A. P. Terent'ev, et al., *Zhur. Obs. Khim.*, **32**, 1187 (1962), and the previous papers from this series.

it is in benzene and other non-hydroxylic solvents, have been confirmed, as well as the existence of two different solid forms of these compounds.<sup>3</sup> No difference in the sign of rotation between methanolic and benzene solutions has been found for the other optically active acyl derivatives. (cf. 4,5 where  $[\alpha]_D$  and  $[M]$  values in different solvents are given.)

Proton NMR studies carried out on the solutions of the optically active compounds and some additional amides in  $CCl_4$ ,  $CDCl_3$ ,  $CS_2$ , anhydrous dioxane,  $CH_3OH$ , and  $CH_3OD$  (predominantly at room temperature) confirm the assumption that all the amides studied exist predominantly in the amide form (A) in methanol as well as in the other solvents used. This viewpoint is supported by the fact that the same splitting of the  $CH_2$  and  $CH$  hydrogen resonances (due to spin-spin coupling) by the hydrogen of the adjacent  $NH$  group is seen in all these solvents, including methanol (Fig. 1). This splitting disappears when the hydrogen of the  $NH$  group is replaced by a deuterium or a methyl group. The benzylic methylene of *N*-methyl-*N*-benzylacetamide and the corresponding benzamide gives a single resonance with  $\gamma = 5.53$  and  $5.47$  in  $CCl_4$  and  $\gamma = 5.82$  and  $5.80$  in  $CH_3OD$ , respectively. Also, cf.<sup>7</sup> where proton NMR spectra of

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3. We could not, however, obtain two forms of the racemic compound.
  4. R. Huisgen and C. Ruchardt, Ann., 601, 21 (1956).
  5. F. Nerdel and H. Liebig, Ann., 621, 42 (1959); F. Nerdel et al., ibid., 627, 106 (1959).
  7. C. Franconi, Z. Elektrochem. 65, 654 (1961).



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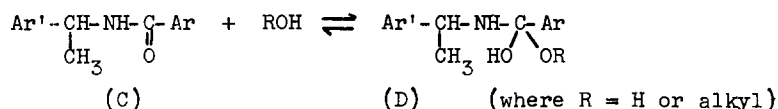
Fig. 1. Proton NMR spectra of the benzylic hydrogen atoms of substituted amides.<sup>6</sup>

6. All NMR spectra were taken with a Varian A-60 spectrometer. The abscissa is given in  $\delta$  units.

$$\delta_{\text{p.p.m.}} = \frac{\Delta(\text{Me}_4\text{Si}) \cdot 10^6}{\text{oscillator freq. (c.p.s.)}}$$

several secondary and tertiary amides have been investigated. The iminol form (B) thus cannot be present in significant amount, if it exists at all in solutions. Preliminary NMR studies at different temperatures reveal that in some of these molecules the apparent hindrance to free rotation is easily seen.<sup>7</sup> Some supporting evidence is also given by the IR studies, but a full description of these experiments will be given in a later communication.

The UV spectra of these compounds in various solvents give no indication of the equilibrium of the type (C)  $\rightleftharpoons$  (D)



with appreciable amounts of the hemiacetal or hydrate form (D) existing in alcoholic or aqueous<sup>8</sup> solutions. The formation of hemiacetal or hydrate of the type (D) in alcoholic or aqueous solutions would be expected to shift the fairly intense band at 220-230 m $\mu$  to shorter wavelengths and lower intensities. Experimentally the reverse is the case.

The solvent effect of optical rotation is therefore to be accounted for in terms other than amide-iminol tautomerism, for example, hindered rotation and intermolecular complexes in solution. The variety of crystal forms may also have its origin in the same phenomena, and, if so, would represent the first case of two crystal forms dependent upon hindered rotation in the amide.

8. L. Skulski, Bull. Acad. Polon. Sci., Ser. Sci. Chim. 10, 201 (1962); where only the locations of the K-bands were given.