well with the $\Delta\nu_{1/2}{}^{exp}$ values (Fig. 3), and this confirms the fact that this band is a vibronic band. Consequently, there is no basis for the assumption that the long-wave of 2-N-pyridinia-1,3-indandione betaine is due to two electron transitions. This band is actually a band with intramolecular charge transfer from the diketo to the pyridinium part and has a vibrational structure that becomes pronounced in solvents with low polarities.

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# CONFORMATIONAL EQUILIBRIUM OF N-ACYL-1-METHYL-1,2,3,4-TETRAHYDROISOQUINOLINES

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The PMR spectra of N-acyl-1-methyl-1,2,3,4-tetrahydroisoquinolines were studied. The conformational parameters of retarded internal rotation about the partially double C—N bond were determined.

It is well known that amides, owing to the certain degree of double bond character of the C—N bond, exist in the form of two conformers, the ratio between which depends both on electronic and steric factors [1, 2].

To study the effect of steric factors on the conformational equilibrium of the amide group we synthesized N-acyl-1-methyl-1,2,3,4-tetrahydroisoquinolines (I). The choice of these substances for the investigation was due to the presence of an asymmetric center in the starting 1-methyl-1,2,3,4-tetrahydroisoquinoline (II), which makes it possible to subsequently ascertain the effect of the conformational composition on the optical activity of such amides.

The N-acyl-1-methyl-1,2,3,4-tetrahydroisoquinolines (Ia-f) were obtained by the action on amine II of the corresponding acid (for Ia), the anhydride (for Ib, c), or the acid chloride (for Id-f).

Doubling of the signals of the 1-H methylidyne proton, the protons of the 1-$CH_3$ group, and, in some cases, the protons of the acyl group, which is due to retarded internal rotation about the C—N bond, is observed in the PMR spectra of amides Ia-e at 25°C.

The character of the PMR spectrum is determined by the rate of exchange [3], which in turn depends on the temperature. Slow exchange (according to data from the PMR spectra) for Ia-e (R = H, $CH_3$, $C_2H_5$, n-$C_3H_7$, and i-$C_3H_7$) is observed at room temperature, while it was necessary to lower the temperature to −40°C for recording the PMR spectrum of both conformers of If (R = t-$C_4H_9$). Figure 1 illustrates the temperature dependence of the observed

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TABLE 1. Chemical Shifts and Spin–Spin Coupling Constants of N-Acyl-1-methyl-1,2,3,4-tetrahydroisoquinolines

| Compound | R | Temp., °C | Conformer | $\delta_{1\text{-H}}$, ppm (q) | $\delta_{1\text{-CH}_3}$, ppm (d) | I, Hz | $\delta_R$, ppm |
|---|---|---|---|---|---|---|---|
| Ia | H | 25 | E | 4,68 | 1,43 | 7,0 | 8,18 (s) |
| | | | Z | 5,37 | 1,36 | 6,9 | 8,04 |
| Ib | $CH_3$ | 25 | E | 4,93 | 1,53 | 7,0 | 2,18 (s) |
| | | | Z | 5,63 | 1,43 | 7,0 | 2,14 |
| Ic | $C_2H_5$ | 25 | E | 4,98 | 1,51 | 7,0 | 2,43 (m) ($CH_2$) |
| | | | Z | 5,66 | 1,42 | 7,0 | |
| Id | $n$-$C_3H_7$ | 25 | E | 5,00 | 1,53 | 6,9 | 2,4 (t) ($CH_2CO$) |
| | | | Z | 5,66 | 1,43 | 7,0 | |
| Ie | $i$-$C_3H_7$ | 25 | E | 5,11 | 1,56 | 7,0 | — |
| | | | Z | 5,70 | 1,43 | 6,8 | |
| If | $t$-$C_4H_9$ | −40 | E | 5,33 | 1,57 | 6,8 | 1,32 (s) |
| | | | Z | 5,64 | 1,44 | | |

TABLE 2. Parameters of the Conformational Equilibrium for N-Acyl-1-methyl-1,2,3,4-tetrahydroisoquinoline Molecules

| Compound | R | Temp., °C | Fraction of the conformer, % (± 1%) | | $K$* (±0,07) | −ΔG, kcal/mole (± 0.03) |
|---|---|---|---|---|---|---|
| | | | Z | E | | |
| Ia | H | 25 | 62 | 38 | 1,63 | 0,29 |
| Ib | $CH_3$ | 25 | 61 | 39 | 1,56 | 0,27 |
| Ic | $C_2H_5$ | 25 | 63 | 37 | 1,70 | 0,32 |
| Id | $n$-$C_3H_7$ | 25 | 61 | 39 | 1,56 | 0,27 |
| Ie | $i$-$C_3H_7$ | 25 | 67 | 33 | 2,03 | 0,52 |
| If | $t$-$C_4H_9$ | 25 | 72 | 28 | 2,57 | 0,56 |
| If | $t$-$C_4H_9$ | −40 | 78 | 22 | 3,55 | 0,75 |

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*For the Z ⇄ E process in $CDCl_3$.

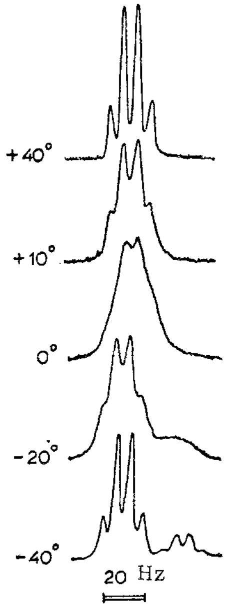

Fig. 1. Temperature dependence of the form of the lines of the signal of the methylidyne proton for N-pivaloyl-1-methyl-1,2,3,4-tetrahydroisoquinoline.

TABLE 3. Physicochemical and Spectral Characteristics of N-Acyl-tetrahydroisoquinolines Ia-f

| Compound | $R^*_f$ | $\nu$, cm$^{-1}$ |  | Found, % |  | Empirical formula | Calc., % |  | Yield, % |
|---|---|---|---|---|---|---|---|---|---|
|  |  | CO | amide II | C | H |  | C | H |  |
| Ia | 0,49 | 1690 | 1510 | 75,5 | 7,3 | $C_{11}H_{13}NO$ | 75,4 | 7,4 | 85 |
| Ib | 0,36 | 1690 | 1500 | 76,3 | 7,8 | $C_{12}H_{15}NO$ | 76,2 | 7,9 | 94 |
| Ic | 0,61 | 1660 | 1500 | 76,9 | 8,3 | $C_{13}H_{17}NO$ | 76,8 | 8,3 | 90 |
| Id | 0,76 | 1660 | 1510 | 77,2 | 9,1 | $C_{14}H_{19}NO$ | 77,4 | 8,7 | 90 |
| Ie | 0,70 | 1660 | 1530 | 77,1 | 8,3 | $C_{14}H_{19}NO$ | 77,4 | 8,7 | 87 |
| If | — | 1630 | 1530 | 78,0 | 9,1 | $C_{15}H_{21}NO$ | 77,9 | 9,1 | 80 |

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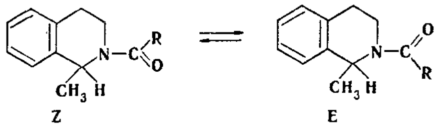
*Silufol with a benzene—acetone system (3:1).

form of the line of the signal of the 1-H methylidyne proton in If. Data from the PMR spectra of Ia-f are presented in Table 1.



Ia R=H; b $R=CH_3$; c $R=C_2H_5$; d $R=n\text{-}C_3H_7$; e $R=i\text{-}C_3H_7$; f $R=t\text{-}C_4H_9$

The signal of the methylidyne 1-H proton is the most informative signal for obtaining information regarding the conformational composition of Ia-f. In the case of the Z conformer this signal lies at weaker field than in the case of the E conformer. This assignment of the signals was made starting from an examination of the stereochemistry of the tetrahydroisoquinoline system. In a number of papers [4, 5] the preferableness of a pseudoaxial orientation of the methyl group in the 1 position in tetralins and tetrahydroisoquinolines has been pointed out. It might be assumed that the introduction of an acyl group at the nitrogen atom would not have a substantial effect on the conformation of the piperidine ring. The latter in Ia-f will preferably assume a distorted chair conformation with a pseudoaxial orientation of the methyl group. An examination of molecular models showed that in this conformation the pseudoequatorial methylidyne proton of the Z conformer is located in the plane of the carbonyl group, i.e., it is found in the deshielding region [1, 6], in contrast to the methylidyne proton of the E conformer. The latter evidently is found in the shielding region, and its signal lies at stronger field.

It follows from a comparison of the intensities of the weak-field and strong-field signals of the protons of the $1\text{-}CH_3$ group with the corresponding intensities of the signals of the methylidyne proton that the signals of the protons of the $CH_3$ group lie at stronger field in the case of the Z conformer than in the case of the E isomer.

The conformational parameters of retarded internal rotation about the partially double C—N bond were determined from data from integration of the 1-H signals in the two conformers of Ia-e in the slow-exchange spectra. In the case of If the data obtained at —40°C were converted to their values at room temperature by the average-shift method (Table 2).

It is apparent from Table 2 that the ratio of the conformers for Ia-d remains virtually unchanged as a function of the size of substituent R. An appreciable change in the ratio of the conformers in favor of an increase in the fraction of the Z conformer is observed only for Ie ($R = iso\text{-}C_3H_7$) and If ($R = tert\text{-}C_4H_9$); the change is greater for If than for Ie. This can be explained by an increase in the energy of the ground state of the E conformer as a consequence of steric interaction of the bulky substituents with the $1\text{-}CH_3$ group, which makes the Z conformer preferable. An examination of molecular models confirmed the existence of such interactions, particularly when $R = tert\text{-}C_4H_9$.

A similar pattern has been described in the literature for N-acyl-L-prolines [8]. It was shown that N-pivaloyl-L-proline exists only in the S-trans conformation, which corresponds to the Z conformer of the N-acyl-1-methyl-1,2,3,4-tetrahydroisoquinolines investigated in our research.

Thus, in contrast to N-acyltetrahydroquinolines [6, 9], the size of the substituent in the acyl part of N-acyl-1-methyl-1,2,3,4-tetrahydroisoquinolines has little effect on the conformational composition, and an appreciable increase in the fraction of the Z conformer is observed only in the case of the N-pivaloyl derivative.

## EXPERIMENTAL

The PMR spectra of solutions in $CDCl_3$ were measured with a Varian HA-100 NMR spectrometer with tetramethylsilane as the internal standard.

N-Formyl-1-methyl-1,2,3,4-tetrahydroisoquinoline (Ia, Table 3). A 0.82-ml sample of 99% formic acid was added to 2 g (0.014 mole) of amine II [10], and the mixture was heated at ∿100°C for 1 h. The excess acid was then removed by distillation, and the residue was distilled to give a product with bp 170-172°C (7 mm).

N-Acetyl-1-methyl-1,2,3,4-tetrahydroisoquinoline (Ib, Table 3). A 1.03-g (0.007 mole) sample of amine II was added with cooling to ∿0°C to 2 ml of acetic anhydride, and the mixture was heated at ∿100°C for 30 min. The excess anhydride and acid were removed by distillation, and the residue was distilled to give a product with bp 188-189°C (15 min).

N-Propionyl-1-methyl-1,2,3,4-tetrahydroisoquinoline (Ic, Table 3). This compound was obtained as in the preceding experiment.

N-Butyryl- and N-Isobutyryl-1-methyl-1,2,3,4-tetrahydroisoquinolines (Id, e, Table 3). A mixture of 0.005 mole of amine II, 0.005 mole of butyryl chloride, 0.3 g of sodium carbonate, and 25 ml of benzene was refluxed for 3 h, after which the reaction mixture was washed with water, and the solvent was removed by distillation.

N-Pivaloyl-1-methyl-1,2,3,4-tetrahydroisoquinoline (If, Table 3). A 0.034-mole sample of triethylamine was added to 0.017 mole of amine II in 25 ml of absolute ether, after which 0.017 mole of pivaloyl chloride was added dropwise with stirring. The precipitated triethylamine hydrochloride was removed by filtration and washed with absolute ether, and the ether extracts were evaporated. The residue was recrystallized from benzene—petroleum ether to give a product with mp 98°C.

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