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N → O ACYL MIGRATION IN CIS AND TRANS-2-AMINOMETHYLCYCLOHEXANOL AND CIS- AND TRANS-2-HYDROXYMETHYLCYCLOHEXYLAMINE DERIVATIVES

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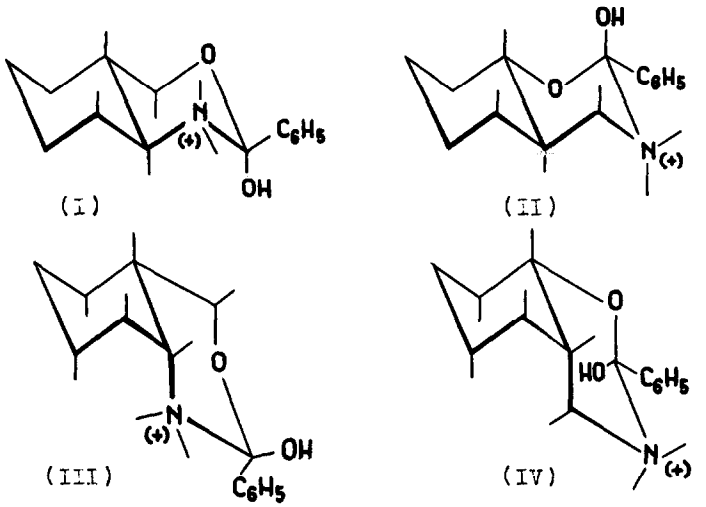
Many papers, including kinetical studies, have been published concerning N → O acyl migrations in 1,2-aminoalcohols /e.g. 1, 2/ and in alicyclic systems /e.g. 3/; details of the mechanism are still under investigation /4/. The similar reactions of 1,3-aminoalcohols /5-7/ and 1,4-aminoalcohols /8,9/, especially when the functional groups are attached to an alicyclic ring, have been studied in a few cases only.

We compared the N → O acyl migration and some other stereospecific reactions of alicyclic 1,2-, 1,3- and 1,4-aminoalcohols. Our aim was to obtain information concerning the conformational and energetical conditions of the starting alicyclic skeletons and the bicyclic intermediates of the reactions. This paper deals with the N → O acyl migration reactions of N-benzoyl and p-substituted N-benzoyl derivatives of the compounds given in the title.

Cis- and trans-2-aminomethylcyclohexanol and cis- and trans--2-hydroxymethylcyclohexylamine were prepared by stereospecific synthesis, the last step being the reduction with $LiAlH_4$ of cis- and trans-2-hydroxycyclohexanecarboxylic amide and cis- and trans-ethyl 2-aminocyclohexanecarboxylate, respectively. A kinetic study of the N → O acyl migration reactions in the N-benzoyl and p-substituted N-benzoyl derivatives of these compounds was made in anhydrous dioxan, in presence of a 0,5 mole excess of HCl, between 80° and 112°, at 3-5 different temperatures for each compound. The reaction rate constants, calculated by second-order equation, the activation energies and activation entropies are given in Table I.

It is seen that N → O acyl migration takes place at a higher rate in the case of the trans isomers, when the transitory formation of a mono-aza-mono-oxa-trans-decalin structure /I,II/ is more favoured than the cis-decalin-like intermediate /III,IV/ arising from the corresponding cis-isomers. Since the reverse order of relative stabilities is expected for the intermediates, it is the formation of the cyclic intermediates which decides the reaction rates.



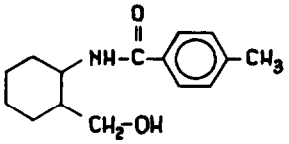
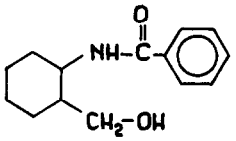
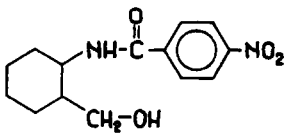
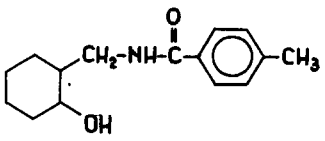
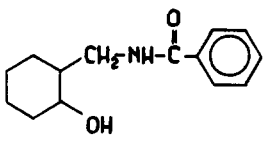
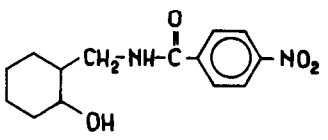
The reaction rate is decreased by the presence of a p-NO_2 group and increased by a p-CH_3 group. The benzoyl derivatives have low activation energy and high negative entropy values as compared to the p-substituted benzoyl derivatives. This fact shows that in N → O acyl migrations occuring with retention, the effects of the p-substituents of the benzoyl group on the various part-processes /4/ are different.

In the reactions investigated by us, we found lower $E^{\ddagger}$ values than usual in 1,2-acyl migration reactions, together with high $-\Delta S^{\ddagger}$ values, this can be accounted for by hindered rotation in the cyclic intermediate. The decrease of the $-\Delta S^{\ddagger}$ values according to the order III, I, II, IV may be explained by steric compression which is especially high for III.

The reaction rate of derivatives containing a primary hydroxyl group is considerably higher than that of the corresponding isomers carrying secondary hydroxyl. While the ratio k_{trans}/k_{cis} equals about 4 for primary hydroxyl derivatives, for compounds with secondary hydroxyl this ratio is about 2. The ratio of the rate constants of identically substituted primary and secondary hydroxyl derivatives is about 2 in the cis series, and 5-6 in the trans series. The latter value may be explained by a deformation of the cyclohexane skeleton /10/ required to allow the formation of the intermediate. This deformation should be particularly considerable in the trans secondary hydroxyl derivatives, where relatively high $\Delta E^{\ddagger}$ values are accompanied by high $-\Delta S^{\ddagger}$ values.

Satisfactory analyses, together with IR and NMR spectra consistent with the given structures, have been obtained for the model compounds used. A description of the stereospecific synthesis of the aminoalcohols, our

TABLE I

Compound		$k_2.10^3.sec^{-1}$ t=100±0.3°C	$\Delta E^{\ddagger}$ Kcal/mole	$\Delta S^{\ddagger}$ e.u.
	cis	7.50	14.70	-31.19
	trans	24.04	12.58	-32.42
	cis	5.15	11.66	-40.00
	trans	20.28	11.10	-38.70
	cis	3.67	14.67	-32.75
	trans	13.17	11.83	-25.94
	cis	2.93	18.30	-23.60
	trans	4.83	15.42	-30.28
	cis	2.20	15.84	-30.66
	trans	4.80	14.70	-32.16
	cis	1.17	18.17	-25.72
	trans	2.14	14.76	-33.65

method of preparation resulting in some differences in the physical properties of the products as compared to those reported /11,12/ and a detailed discussion of the acyl rearrangement reaction will soon be published in Acta Chim. Acad. Sci. Hung.

REFERENCES

/1/. K. Koczka and G. Fodor, Acta Chim. Acad. Sci. Hung. 13, 83 /1958/.

/2/. T. Ishimaru, Nippon Kogaku Zasshi 81, 1592 /1960/.

/3/. G. Fodor and É. Fodor-Varga, Á. Furka, Croat. Chem. Acta 29, 303 /1957/.

/4/. L. H. Welsh, J. Org. Chem. 32, 119 /1967/.

/5/. G. Drefahl and H. Hörhold, Chem. Ber. 94, 1641 /1961/.

/6/. I. Weisz and A. Dudás, Monatshefte, 91, 840 /1960/.

/7/. B. I. Kurtev, N. M. Mollov and A. S. Orahovats, Monatshefte, 95, 64 /1964/.

/8/. G. Adam and K. Schreiber, Chem. Ber. 99, 3173 /1966/.

/9/. D. V. Ioffe and S. G. Kuznetsov, Z. Obsch. Khim. 33, 991 /1963/.

/10/. S. J. Angyal and C. G. McDonald, J. Chem. Soc. 686 /1952/.

/11/. M. Mousseron, F. Winternitz and M. Mousseron-Canet, Bull. soc. chim. France 737 /1953/.

/12/. E. J. Moriconi and P. H. Mazzocchi, J. Org. Chem. 31, 1372 /1966/.