SYNTHESIS AND SPECTROSCOPIC STUDY OF SOME NEW N-NAPHTHYL SUBSTITUTED 2-PHENYLACETAMIDES

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ABSTRACT

In a continuation of our previous works the conformations of new N-(1,2,3,4-tetrahydro-1-naphtyl and 1,2,3,4-tetrahydro-2--naphtyl)substituted 2-phenylacetamides, PhCH₂CONHR, were investigated by vibrational, ¹H n.m.r. and mass spectra. N-monosubstituted 2-phenylacetamides were obtained by using the known Schotten-Baumann reaction of acylation of synthetized amides with phenylacetic chloride.

On the basis of IR-data for diluted solutions(concentration below 10^{-3} mol.dm⁻³) of N-monosubstituted 2-phenylacetamides in carbontetrachloride the exact position of N-H stretching band were established. The informations concerning the fragmentation routes, the effect of overall and partial structures as well as the influence of the amide group substituents on the fragmentation pattern, were obtained by the study of the metastable ions. The investigation of the mass spectra of the deuterium labelled and the comparison with the corresponding unlabelled compound, gave the fragmentation pattern of the various conformers. From IR, NMR and mass data it can be concluded that our synthetized N-naphthyl substituted 2-phenylacetamides exist in cis and trans form.

INTRODUCTION

This paper is part of a series whose purpose is to obtain some more informations about conformations of some new N-substituted 2-phenylacetamides. The conformations of N-substituted 2-phenylacetamides has been extensively studied in our previous works (ref.1-3) because of importance in understanding the structure of amide derivatives of phenylacetic acid. N-substituted 2-phenylacetamides are particularly useful as model compounds due to their structural similarity to the lateral chain of natural benzylpenicillin (ref.4). Studies employing infrared (ref.5,6) and ¹H n.m.r. spectroscopy (ref.7) have provided valuable information on the cis- and trans-conformational isomers in N-monosubstituted amides. Some theoretical studies (ref.8) have also been employing to examine structural factors affecting the conformations in amides.

Transition between the two conformational isomers about the CO(N) bond presumably occurs very rapidly on the NMR time scale in typical N-monosubstituted amide. As Stewart and Sidall point out (ref.7) exist a wide variations in relative abudndance of iso mers which may be considerable solvent and temperature dependence.

In order to examine the structural effects on barrier heights to rotation, we wish to report the results of a spectroscopic and spectrometric study of some new N-naphtyl substituted 2-phenylacetamides. In general, we expect that N-substituted 2-phenylacetamides may exist as the cis- (to carbonyl oxygen) or trans--isomers. These two possible conformational isomers may be presented at the following Scheme 1.



Scheme 1. Two possible conformational isomers in some new N-naphtyl substituted 2-phenylacetamides

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EXPERIMENTAL

The synthesis of two new rigid N-bicyclo substituted 2-phenylacetamides of general formula PhCH₂CONHR, wherein, R is 1,2,3,4tetrahydronaphtyl-1 and 1,2,3,4-tetrahydronaphtyl-2 residue were performed. These N-monosubstituted 2-phenylacetamides were obtained by using the known Schotten-Baumann reaction of acylation of amines with phenylacetyl chloride. The reaction were carried out in presence of potassium hydroxide which were added to take up the hydrochloric acid.

Both necessary amines we synthetized in advance. 1,2,3,4-tetrahydronaphtyl-1-amine (sign.I on Scheme 1), and 1,2,3,4-tetrahydronaphtyl-2-amine (sign.II) were obtained by the hydrogenation of 1-aminonaphtaline and 2-aminonaphtaline, respectively (ref.9). 1,2,3,4-tetrahydronaphtyl-1-amine (I) was obtained by the hydrogenation of 1-aminonaphtaline in autoclave at pressure of 17,75 MPa and temperature at 150°C with Raney-nickel as a catalyst (activity W-7)(ref.10,11). 1,2,3,4-tetrahydronaphtyl-2--amine (II) was obtained by the same way, by the first procedure, except that as the starting material was used 2-aminonaphtaline (ref.12).By the second procedure reduction of 2-aminonaphtaline was performed by sodium in boiling aps. isoamyl alcohol (ref.13).

^LH n.m.r. spectra were determined in solution in deuterochloroform (CDCl₃) with Varian EM 390 instrument, using tetramethylsilane as internal standard.

Infrared spectra were recorded on a Perkin-Elmer infrared spectrophotometer, model 580, in the form of KBr pellets or in the diluted solutions (concentration below $10^{-3} \text{ mol.dm}^{-3}$) of N-monosubstituted 2-phenylacetamides in carbontetrachloride.

Mass spectra were obtained on a Varian Mat 311A Mass spectrometer, using a direct probe and 70 eV ionizing energy, for the both deuterium labelled and unlabelled compounds.

All the synthetized compounds have very high purity (GC) and satisfactory elemental C, H, N analyses.

RESULTS AND DISCUSSION

The structures were examined by infrared, ¹H n.m.r. and mass data. The cis/trans isomer ratios for N-naphtyl 2-phenylacetamides were studied on the basis of $\nu^{\rm NH}$ frequency in the infrared spectra, particularly N-H stretching vibrations for the amide monomers in carbontetrachloride (concentration 10^{-3} mol.dm⁻³) at ambient temperature.

On the basis of IR-data for diluted solutions of N-naphtyl substituted 2-phenylacetamides in carbontetrachloride the exact positions N-H streching bond were established. It can be seen that these amides show characteristics for trans and cis forms (Table I).

R	trans		cis	
	$\nu^{\rm NH}$, cm ⁻¹	%	$v^{\rm NH}$, cm ⁻¹	%
l,2,3,4-tetrahydro-l- -naphtyl	3448	20	3427	80
1,2,3,4-tetrahydro-2- -naphtyl	344 3	25	3420	75

Table I. Isomer ratios in N-naphtyl substituted 2-phenylacetamides, PhCH₂CONHR

The presented IR data indicate that the investigated phenylacetamides exist predominantely in the cis- conformation, although our previous investigation (ref.4), have shown that the trans- conformation of N-monosubstituted amides often predominates over the cis- conformation. To check the validity of our experimental data, ¹H n.m.r. spectra were determined in solution in deuterochloroform. At ambient temperature only one set of resonance peaks was observed. It is possible that only one isomer is present in an appreciable amount or that the rate of rotation about the amide C(O)-N bond is so fast that we observe only an averaging of rotational isomers.

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The mass spectra of these amides have been also investigated. Representative deuterated analogs of 2-phenylacetamides have been synthetized and their mass spectra compared with those of the non-labeled parent substances. The principal fragmentation and rearrangement ions characterizing each of the groups are noted.

The first characteristic of fragmentation for these amides results from cleavage of a bond on the carbon α to the oxygen function.



The informations concerning the fragmentation routhes as well as the influence of the amide bond group substituents on the fragmentation pattern, were obtained by the study of the metastable ions. McLafferty rearrangement is confirmed by the presence of corresponding very intensive peaks (m/z 136 and m/z 118) but it is possible only in the trans forms of the molecules.



On the basis of the obtained spectroscopic and spectrometric data, it can be concluded that our synthetized N-naphtyl substituted 2-phenylacetamides exist in trans and cis form.

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