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IMINOETHER-ENAMIN TAUTOMERISM

L.Tőke, G.Blaskó, L.Szabó and Cs.Szántay
Institute of Organic Chemistry, Technical University, Budapest

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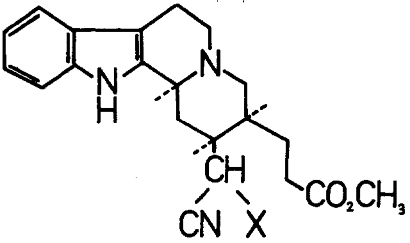
During investigations aiming at the synthesis of indole-alkaloids having the alloyohimbane skeleton, the appropriate ketone[1] was reacted with malonic acid dinitrile. On reducing the received product with $NaBH_4$, the derivative 1a was obtained [mp. 184° /from dioxan/, IR ν_{max}^{KBr} 1740 cm^{-1} /C=O/; 2260 cm^{-1} /C≡N/; 3390 cm^{-1} /N-H/; NMR /DMSO-d_6/: δ 3,58 /methoxy-protons/; δ 10,58 /indole-NH/].



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	X
a	-CN
b	$-C\genfrac{}{}{0pt}{}{\nearrow NH}{\searrow OCH_3}$
c	$-C\genfrac{}{}{0pt}{}{\nearrow NH}{\searrow OCH_2-CH_3}$
d	$-COOCH_3$
e	$-CONH_2$

On treating 1a in abs. methanol with base /$NaOCH_3$, NaOAc etc./, 1b precipitated from the solution after 10-15 min. as colourless crystals [mp. 214-217°, IR ν_{max}^{KBr} 1717 cm^{-1} /C=O/; 1670 cm^{-1} /C=N/; 2250 cm^{-1} /C≡N/; 3290 cm^{-1} /imino-NH/; 3350 cm^{-1} /indole-NH/]. Iminoether 1c was obtained from ethanolic solution in a similar manner [mp. 203-205°, IR ν_{max}^{KBr} 1735 cm^{-1} /C=O/; 1660 cm^{-1} /C=N/; 2250 cm^{-1} /C≡N/; 3200 cm^{-1} and 3350 cm^{-1} /N-H/].

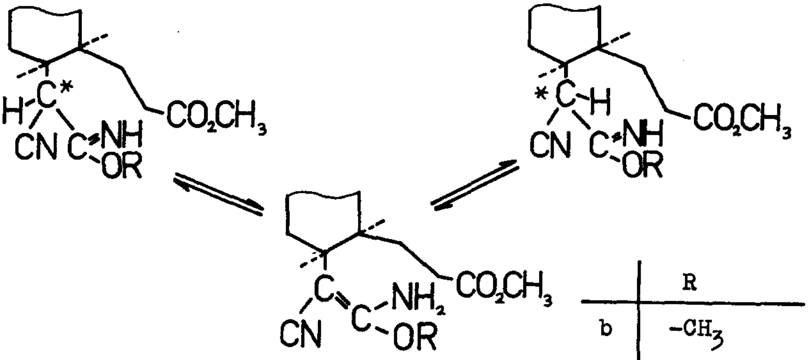
Iminoether bases 1b and 1c are surprisingly stable materials, very likely owing to the neighbouring ester group. They are poorly soluble in organic solvents and can be stored for a long time under vacuum.

In solution, the tautomeric enamine forms of 1b and 1c are detectable, this being the first case of an iminoether-enamine tautomerism to be described in the literature according to our best knowledge.

In the IR spectrum of the solution of 1b in DMSO intensive conjugated C≡N streching frequency is observed at 2190 cm^{-1} beside of the C=N /1670 cm^{-1}/, NH$_{def.}$/1630-1660 cm^{-1}/ and C=C /1600 cm^{-1}/ absorptions. The IR spectrum of 1c in DMSO has nearly the same character as 1b [2190 cm^{-1} /C≡N/; 1735 cm^{-1} /C=O/; 1660 cm^{-1} /C=N/; 1610-1660 cm^{-1} /NH$_{def.}$ and C=C/].

In the UV difference spectra[2] of solution of 1b in methanol the characteristic enamine chromophore[2] /253 nm ε = 6630/ is observed. In the presence of acid the latter absorption disappears while the one at 226 nm /originally ε = 7200/ enhances.

On the bases of the NMR spectra it is possible to estimate the relative amount of the tautomeric forms. The iminoether itself represents two diastereoisomers. A similar phenomenon was observed with analogous cyanoesters[3] and with 1d.



	R
b	$-CH_3$
c	$-CH_2-CH_3$

According to the NMR data in Table 1 and Table 2, there are about 15% enamine and 85% iminoether in the equilibria in DMSO solutions of 1b and 1c, the ratio between the diastereomers is 1:3. In DMF solution of 1b 36% enamine and 64% iminoether are to be found and the ratio of the diastereomers is about 1:1,3.

Treatment of **1b** with water affords the ester **1d** [mp. 171-173° /from methanol/, IR ν_{max}^{KBr} 1730 cm^{-1} and 1740 cm^{-1} /C=O/; 2250 cm^{-1} /C≡N/; 3410 cm^{-1} /N-H/, NMR /DMSO-d_6/: δ 3,69 /methoxy-protons/, δ 3,88 and 3,92 /methoxy-protons of cyanoester group/, δ 10,88 and 10,99 /indole-NH/], whilst with methanolic-HCl the acid-amide **1e** [mp. 214-215° /from methanol/, IR ν_{max}^{KBr} 1690 cm^{-1} /amid C=O/; 1730 cm^{-1} /ester C=O/; 2260 cm^{-1} /C≡N/; 3220 cm^{-1} and 3410 cm^{-1} /amid- and indole-NH/, NMR /DMSO-d_6/: δ 3,67 /methoxy-protons/, δ 8,25 /NH_2-protons/, δ 11,5 /indole-NH/] was obtained. All the new materials /**1a**-**e**/ had satisfactory elemental analyses and mass-spectra.

The iminoether **1b** alkylates carboxylic acids easily in DMF, by acid catalysis, even in room temperature, converting itself into **1e**. The alkylating power of iminoethers is also known in the literature[4].

Table 1: NMR spectra of **1b** /δ/[a]

Solv.	indole-NH	C=N-H	-O-CH_3	-NH_2
DMF-d_7	10,73 /0,36/	6,65 /0,36/	3,90 and 3,95	8,8 /0,72/
-"-	10,89 /0,28/	6,48 /0,28/	3,80 and 3,85	
-"-	11,06 /0,36/		3,63 and 3,65	
DMF-d_6	11,01	6,63 /0,61/	3,84 and 3,87	8,85 /0,30/
-"-	11,16	6,54 /0,24/	3,78	
-"-	11,21		3,65	

Table 2: NMR spectra of 1c /δ/^{a}

Solv.	indole-NH	C=N-H	$-O-CH_3$	$-O-CH_2-/CH_3/$	$-NH_2$
DMSO-d_6	10,60	6,41	3,48	3,99 /q, J=6 cps/	8,6 /0,30/
-"-	10,65	6,30		4,05 /q, J=6 cps/	
-"-	10,80				

a./ The sign intensities in brackets are given in proton units. UV spectra was made by Unicam-SP-700, IR spectra by UR-10, NMR spectra by Perkin-Elmer R-12 J.N.M.C 60, mass-spectra by MS-902 at 70eV and 180° with accuracy of 2 ppm.

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