

REACTION OF LACTIM ETHERS WITH CARBOETHOXYMETHYL PIPERIDINES

A SYNTHESIS OF 1,9-DIAZASTEROID

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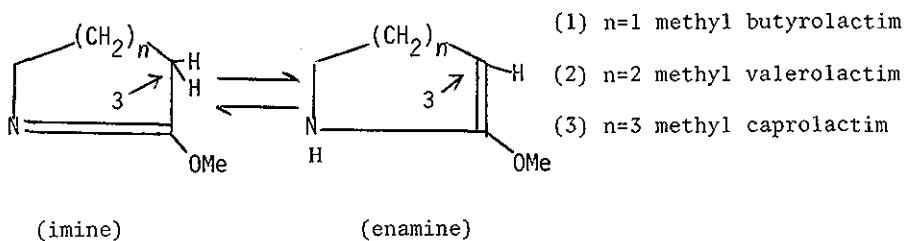
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Imine-enamine tautomerization was observed in methyl valelo-
lactim (2) and methyl caprolactim (3), whereas rarely in methyl
butyrolactim (1) on NMR. The evidence for the tautomerization
was elucidated also by the chemical behaviors of the lactim
ethers towards cyclic β -aminoesters such as, 2-carboethoxymethyl
piperidine derivatives, which often gave two kinds of products
probably resulted from both the imine and the enamine forms.
This was applied to a synthesis of the 1,9-diazasteroid.

Lactim ethers have widely been employed as activated lactims for the syn-
theses of heterocyclic systems.^{1,2} Granik et al suggested the presence of
imine-enamine tautomeric equilibrium in O-ethylvalerolactim in alcoholic
solution.³ Therefore, we examined the existence of the tautomeric equi-
librium (imine \rightleftharpoons enamine) of lactim ethers (1), (2) and (3) in CD₃OD (NMR
spectra).

As given in table I, (1) is shown to exist only in its imine form, whereas



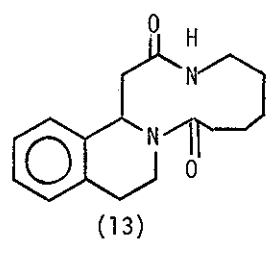
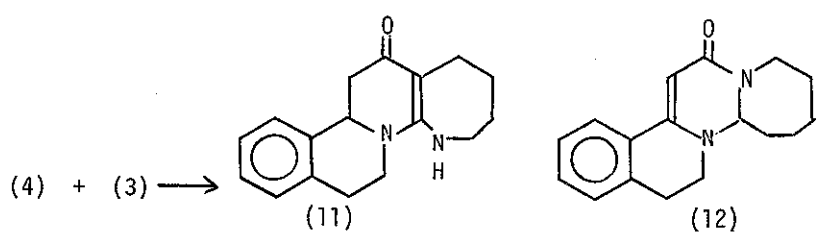
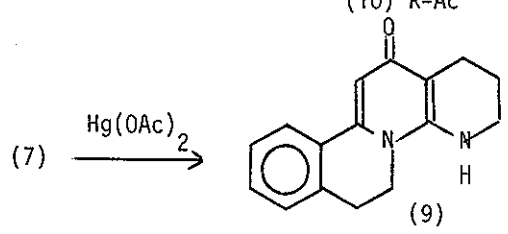
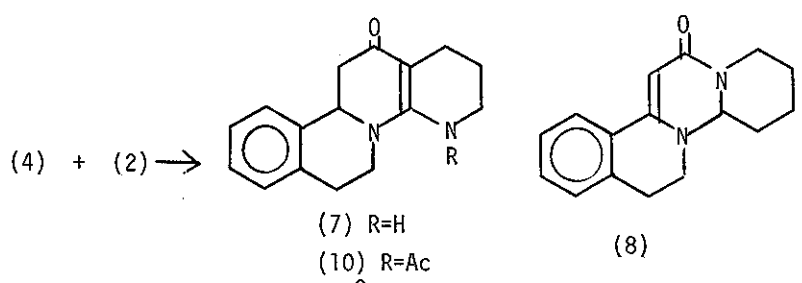
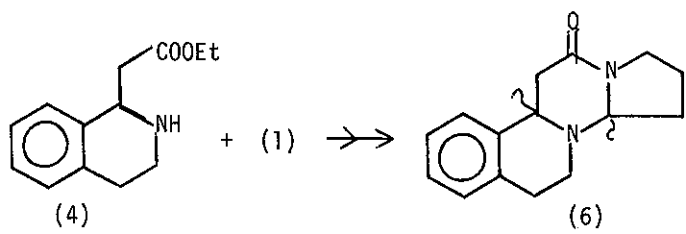
(2) and (3) in both imine and enamine forms. Actually, all examples using (1) are known to react exclusively in the imine form and the reactions employing (2) and (3) also proceeded in the imine fashion in spite of the coexistence of the enamine form.⁴

Table I*

	(1)	(2)	(3)	
a)	2.5	2.2	2.4	a) Chemical shift of 3-hydrogens (δ) ppm
b)	~0%	~65%	~10%	b) Decrease (%) in integral values of 3-hydrogens on the deuteration after 9 days on NMR

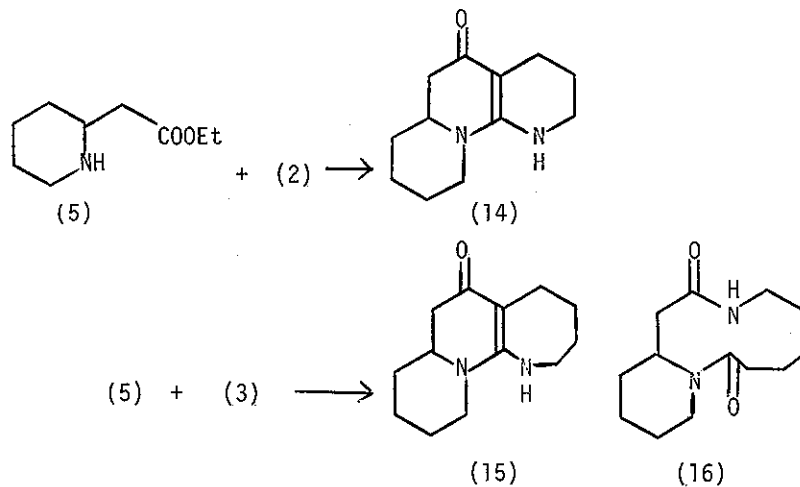
* Solutions of (1), (2) and (3) in 15% (w/v) CD₃OD were kept at room temperature for 9 days, respectively³

On the other hand, we found that lactams (2) and (3) reacted with 2-carboethoxymethyl piperidines (4) and (5) to furnish the products attributed to both enamine and imine forms. Previously one of the authors (T.Y.) reported the synthesis of 8,13-diazasteroid (6) by the reaction of 1-carboethoxymethyl-1,2,3,4-tetrahydroisoquinoline (4) with (1), which actually reacted in the imine form.⁵ The annelation reaction of (2) with (4) (at 100°C for 10 days) gave the compound (7) in the enamine fashion and compound (8) in the imine fashion in 65% yield and 7% yield, respectively. The structure of (7) is characterized as its dehydrogenation product (9) derived from mercuric acetate oxidation or its acetate (10). Similar reaction using (3) afforded (11) (1.2%), (12) (44%) and (13)⁶ (13%), which showed the



the spectral data as in Table II.

Furthermore, the same annelation of (2) with 2-carboethoxymethyl piperidine (5) proceeded smoothly to furnish only (14) in 54% yield, which that of (3) gave (15) in 26% yield and (16)⁶ in 13% yield. Imine-enamine tautomerization in (2) and (3) was thus ascertained from the products mentioned above.



Next, a synthesis of the 1,9-diazasteroid was undertaken as an application of the annelation employing (2), which reacted with the compound (17)⁷ as C-D ring segment to afford 1,9-diazagona-5(10),13-dien-6-one (18) as a sole product in 20% yield attributed to the enamine form.

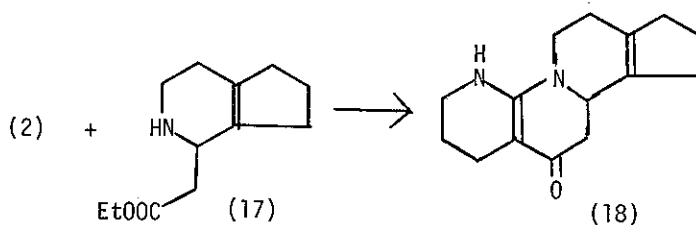


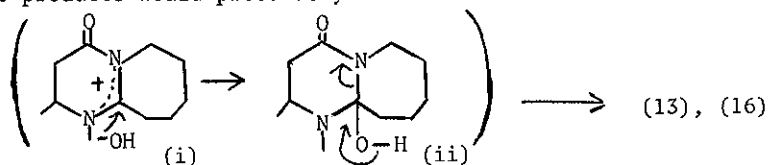
Table II⁷

Compd.	mp (°C)	IR (KBr) ν cm ⁻¹	UV (EtOH) nm (ε)	NMR (CDCl ₃) δ ppm
(7)	324	3240,1580 1560	309 (19000) 238 (10000)	
(8)	166	1620,1590 1550	366 252	5.3 (s,CH=C)
(9)	314	3160,1620 1580,1550	308 249	6.6 (s,CH=C) 6.2 (NH)
(10)	141	1660,1640 1590,1570		2.2 (s,N-Ac)
(11)	300	3280,1570 1550,1490	316 240	
(12)	162	1620,1590 1550	358 (5000) 252 (10800)	5.4 (s,CH=C)
(13)	145	3380,1640 1620,1550		8.1 (NH) ^a
(14)	292	3240,1580 1560,1500	308 (17000) 239 (7200)	
(15)	247	3280,1580 1560,1490	318 (22000) 228 (8600)	
(16)	172	3300,1660 1610,1550		6.1 (NH)
(18)	274	3240,1580 1560,1500	308 (16000) 235 (7000)	3.8 (C ₈ -H) ^b

a) (DMSO-d₆) b) (CD₃OD)

REFERENCES AND NOTES

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 b) B.M.Trost and R.A.Kunz, J. Am. Chem. Soc., 1975, 97, 7152.
- 3 V.G.Granik, B.M.Pyatin, J.V.Persianova, N.P.Kostyuchenko, R.G.Glushkov and Y.N.Shinker, Tetrahedron., 1970, 26, 4367.
- 4 A sole example in enamine fashion. T.Kato and T.Sakamoto, Chem. Pharm. Bull. (Tokyo)., 1975, 23, 2629.
- 5 T.Koizumi, Y.Yanagawa, E.Yoshii, and T.Yamazaki, Chem. Pharm. Bull. (Tokyo)., 1978, 26, 1308.
- 6 These products would presumably be formed as follows .



- 7 A.I.Meyers and W.N.Beverung, Chem. Commun., 1968, 877.
- 8 Mass spectra of all compounds showed molecular ion peaks.

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