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SYNTHESIS OF 2,4-DIMETHYL-1,2,3,4,4a,5,6,10b-OCTAHYDROBENZO(f)QUINOLINES AND THEIR DERIVATIVES BY REDUCTIVE PHOTOCYCLIZATION OF ENAMIDES

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Abstract ------- Reductive photocyclization of the enamides (1 and 7) afforded the hydrogenated lactams (4a, 5a, and 6a) and (8, 9, and 10) respectively, which were readily converted into the corresponding octahydrobenzo(f)quinolines (4b, 5b, and 6b) and hexahydrobenzo(f)quinoline (12) as the despyrrole analogues of ergot alkaloids.

Hydrobenzo(f)quinolines have attracted much interests of synthetic chemists from many years since they can be regarded as the despyrrole analogues of ergot alkaloids[1] which are known to possess both dopamine agonist and antagonist activities.[2] We now report a simple and convenient synthesis of two types of hydrobenzo(f)quinolines by applying reductive photocyclization of enamides which were readily prepared from 2-tetralone and two acid chlorides.

Acylation of the 2-tetraloneimine with methacryloyl chloride in the presence of triethylamine afforded a mixture of the enamide (1) and the already cyclized lactam (2) in a ratio of ca. 5 : 1, the latter of which was assumed to be formed directly from the above treatment.[3,4]

Although irradiation of the enamide (1) with a high pressure mercury lamp using Pyrex filter in benzene or methanol at room temperature afforded the lactams (2 and 3) in 45 and 10 % yields respectively,[5] its reductive photocyclization[6] in the presence of sodium borohydride at 4 - 5°C led to the formation of three hydrogenated lactams (4a, 5a, and 6a) with the different ratios depending on the solvent used as shown in the Table I.

Reduction of these lactams (4a, 5a, and 6a) with lithium aluminum hydride gave the corresponding octahydrobenzo(f)quinolines (4b, 5b, and 6b) which were identical with their authentic samples upon comparisons with the melting points of their methiodides.[7,8,9]

A similar reductive photocyclization of the enamide (1) in the presence of sodium borodeuteride in benzene-methanol (10 : 1) afforded a mixture of two hydrogenated lactams (4c and 5c) in 4 and 29 % yields, both of which were found to contain deuterium at the 4a-position quantitatively on the basis of their mass and n.m.r. spectra. This results firmly show that reductive photocyclization of this type of enamide (1) proceeds by the same mechanism as described previously.[6] Thus, we succeeded in a four-step synthesis of three types of octahydrobenzo(f)quinolines from 2-tetralone and established a useful synthetic route to the alkaloids such as festuclavine and costaclavine.

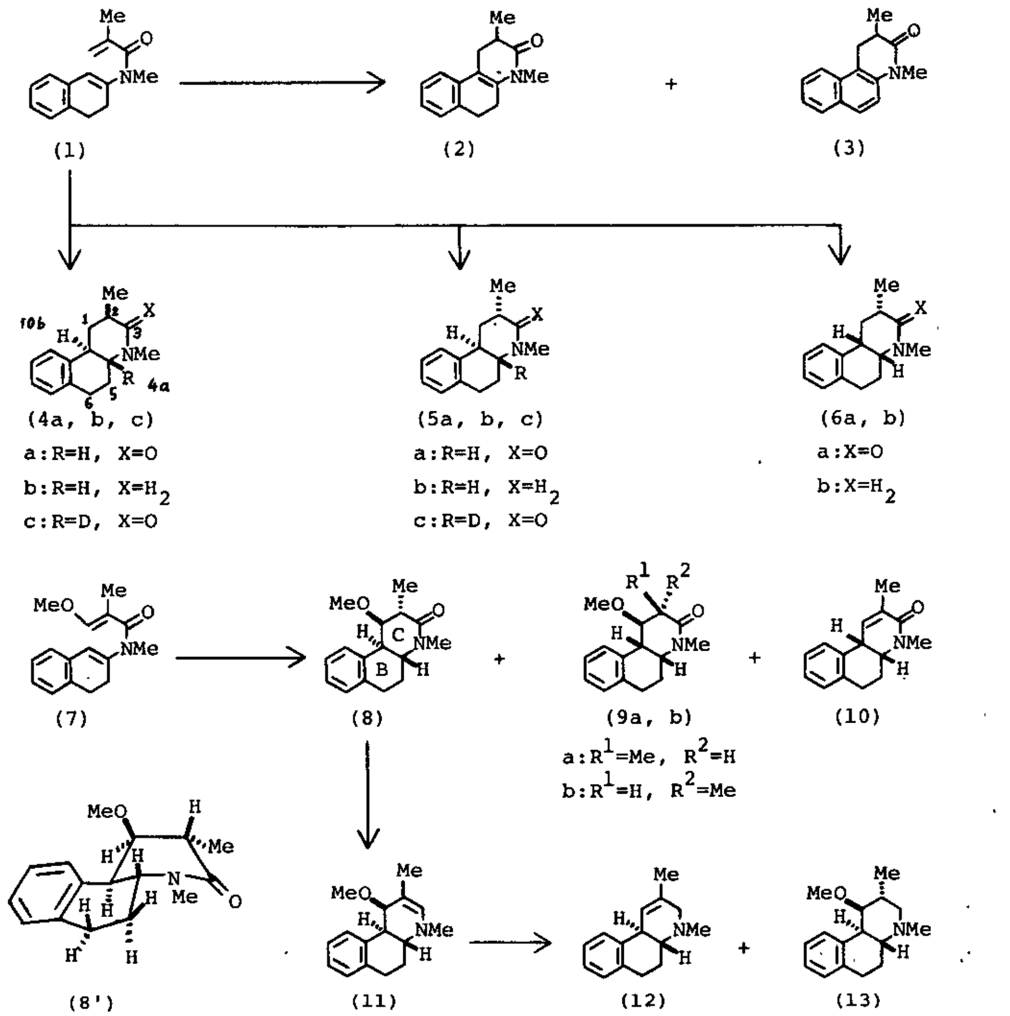
Since there has been reported no synthetic approach to the compounds of 3,4,4a-5,6,10b-hexahydrobenzo(f)quinoline structure which can be regarded as the despyrrole analogue of agroclavine, we next examined reductive photocyclization of the methoxy-substituted enamide (7) which would be expected to provide a key and common intermediate for the synthesis of either agroclavine or lysergine analogue.

Reductive photocyclization of the enamide (7), prepared from 2-tetralone and 3-methoxy-2-methylacryloyl chloride[10], afforded four hydrogenated lactams (8, 9a, 9b, and 10) in different yields depending on the solvent used as shown in the Table I. Among these lactams, the dehydrogenated lactam (10) was also obtained from the lactam (9a) upon heating with $KHSO_4$ and was converted into the saturated lactam (6a) upon catalytic hydrogenation over 10 % palladium on charcoal.

The stereochemistry of these lactams (8, 9a, 9b, and 10) was deduced from their n.m.r. spectra as summarized in the Table II, particularly from their decoupling evidences, which firmly established the B/C-ring junction of the lactam (8) as trans and those of other lactams (9a, 9b, and 10) as cis.

Unexpectedly, reduction of the trans-lactam (8) with lithium aluminum hydride gave the unstable enamine (11) in a quantitative yield, which was then treated with sodium borohydride to give two amines (12 and 13) in 47 and 23 % yields respectively. The structure of the amine (12) was firmly established from the signal of $\delta(CDCl_3)$: 6.06 due to an olefinic proton in the n.m.r. spectrum and also from the fact that the amine (12) was catalytically hydrogenated into the saturated amine (4b).

Thus, we also succeeded in a simple synthesis of the despyrrole analogue (12) of agroclavine from 2-tetralone. Synthesis of the analogues of lysergine from the



remaining hydrogenated lactams (9a, 9b, and 10) is now under progress.

The formation of the enamine (11) by reduction of the trans-lactam (8) with lithium aluminum hydride can be explained by assuming that the preferred conformation of the ring C in the trans-lactam (8) would be a boat form (8') due to the trans-configuration of 1-methoxy and 2-methyl groups. This also can explain an unsuccessful reduction of the trans-lactam (8) into the corresponding amine (13).

(Table I)

Solvent	Yield(%)			Yield(%)			
	(4a)	(5a)	(6a)	(8)	(9a)	(9b)	(10)
C_6H_6-MeOH (10:1)	23	41	10	10	16	38	13
MeCN-MeOH (10:1)	14	32	5	22	--	15	27
Et_2O-MeOH (10:1)	13	8	19	--	--	--	--

(Table II) Protons ($CDCl_3$) (200MHz)

Compds.	1-H	1-OMe	2-H	2-Me	4a-H	10b-H	N-Me
(8)	3.96(dd, J=8, 5)	3.50 (s)	2.91(m)	1.32(d, J=7)	3.23(ddd,J= 11, 10, 4.5)	3.00(m)	2.98 (s)
(9a)	3.76(dd, J=6, 4)	3.42 (s)	2.34(qd, J=7, 4)	1.20(d, J=7)	3.85(td, J= 6, 2.5)	3.54(t, J=6)	2.98 (s)
(9b)	3.10 (d-like)	2.98 (s)	2.43(m)	1.33(d, J=7)	3.56(ddd,J= 12.5, 5, 2.5)	3.10 (d-like)	3.02 (s)
(10)	6.06(dt, J=3.5, 2)	----	----	1.84(dd, J=3, 2)	3.60(dddd,J= 10, 7, 5.5, 2)	4.07(ddd,J= 7, 3.5, 3)	3.09 (s)

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9 Melting points of methiodides of two amines (4b and 6b) were different from those reported[7,8]. However, the authentic samples, which were prepared by the procedure according to the literature, showed identical melting points with our samples in this paper.

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