HETEROCYCLES, Vol 16, No 7, 1981

REDUCTIVE PHOTOCYCLIZATION OF ENAMIDES

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Abstract----- Irradiation of the enamides (1a and b) and (7a and b), prepared from N-cyclohexylidenebenzylamine and 3,4-dihydro-1-methylisoquinoline, in the presence of a hydride agent led to the reductive photocyclization to afford the hydrogenated lactams (3a and b), (4a and b), and (9a and b), respectively.

Enamides have been shown to undergo smooth photocyclization under both non-oxidative and oxidative conditions, thus regarded as a useful synthetic reaction for the construction of nitrogeneous heterocycles.[1] With the intention of developing a predictive model of its reactivity and further synthetic utility, we have undertaken basic study on the reductive photocyclization of enamides in the presence of a hydride agent.

Contrary to the stereospecific photocyclization of enamides that has been well known[1,2] as particularly useful for the construction of six-membered lactams, irradiation of the enamide (1a) in ether-methanol (20:1) at 5-10° with high pressure mercury lamp in the presence of sodium borohydride led to the formation of two hydrogenated lactams (3a) and (4a) in 11 and 43 % yields respectively in addition to small amount of another unidentified lactam. Since these two hydrogenated lactams (3a) and (4a) were readily dehydrogenated to give the corresponding B/C-trans-lactam (2)[2] simply by refluxing in benzene respectively, the stereochemistry of the lactams (3a) and (4a) was firmly established. The diene structures of the lactams (3a) and (4a) were also assigned from their u.v. spectra [(3a), λ_{max} 254; (4a), λ_{max} 234 nm]. their p.m.r. spectra collected in the table and the fact that the Diels-Alder reaction of the lactam (3a) with maleic anhydride afforded the exo-endo-adduct (5) [m/z 391 (M^+), 390, 241, and 91; ν_{max} 1850, 1780, and 1625 cm^{-1};

Table

Compds.	4a-	6a-	7-	8-	9-,10-	10a-	10b-
	Protons δ(CDCl$_3$) (200 MHz)						
(3a)	2.92(td, J=11, 3)	2.93(d, J=21)	6.57(br.d, J=9)	6.20-5.98 (m)		2.18(ddd, J=21, 11, 2)	1.56(qd, J=11, 3)
(3b)	----	2.93(d, J=21)	6.57(br.d, J=9)	6.19-5.97 (m)		2.16(ddd, J=21, 11, 2)	1.55(td, J=11, 3)
(4a)	3.04(td, J=10, 3)	----	7.00 (br.s)	2.89(2H, m)	5.82(s-like)	2.73(m)	1.54(qd, J=11, 3)
(4b)	----	----	7.00 (br.s)	2.88(2H, m)	5.82(s-like)	2.73(m)	1.53(td, J=11, 3)

Compds.	9-	10-	11-	12-	13ax-	13a-
	Protons δ(CDCl$_3$) (200 MHz)					
(8a)	6.40(br.d, J=9)	6.05 (m)		5.77(br.d, J=9)	1.67(ddd, J=12, 11.5, 11)	4.64(dd, J=11.5, 5.5)
(8b)	6.42(br.d, J=9)	6.02 (m)		5.77(br.d, J=9)	1.67(dd, J=12, 11)	----
(9a)	6.97(br.s)	2.90(2H, m)	5.90-5.59 (m)		1.61(q, J=13)	4.57(dd, J=11.5, 4.5)
(9b)	6.96(br.s)	2.88(2H, m)	5.84-5.56 (m)		1.59(t, J=13)	----

δ6.50 (1H, dd, J=8 and 6Hz, 13-H), 6.30 (1H, dd, J=8 and 6Hz, 12-H), 4.21 (1H, ddd, J=6, 3, and 2Hz, 7-H), 3.45 (1H, ddd, J=6, 3, and 2Hz, 11-H), 3.26 (1H, dd, J=9 and 3Hz, 7a-H), 3.20 (1H, dd, J=9 and 3Hz, 10a-H), 3.08 (1H, br., 4a-H), 2.75 (1H, dd, J=11 and 2Hz, 6a-H), and 1.96 (1H, td, J=11 and 2Hz, 11a-H)]. The assignment of the exo-endo-structure to this Diels-Alder adduct (5) is also supported by the report[3] of Jacobson and coworkers that the Diels-Alder reactions of the hexahydronaphthalene with some dienophiles occur to afford the exclusive formation of the exo-endo adduct.

Compared with p.m.r. spectra of the lactams (3a) and (4a), the p.m.r. analysis, particularly their decoupling, of the photocyclized lactams (3b) and (4b), which were prepared from the enamide (1a) upon irradiation in the presence of sodium borodeuteride and deuterated [m/z 294 (M^+)], also supported the stereostructures of the lactams (3a, b) and (4a, b) as shown in the figure.

Thus, the establishment of the trans-configuration between 10a- and 10b-hydrogens in the lactams (3a) and (4a) provided a strong support to the structure of a presumed intermediate (6), therefore the proposed mechanism for the photocyclization of enamide; first, the photochemical electrocyclic ring closure of 6 π-electron system would occur to give a 10a/10b-trans cyclic intermediate (6), which would then in the presence of a hydride agent undergo reduction to yield the hydrogenated lactams (3a and b) by a concomitant incorporation of a solvent into the 6a-position and of a hydride or a deuteride ion into the 4a-position respectively.

A similar reductive photocyclization of the enamide (7a)[4], which was prepared from the 3,4-dihydroisoquinoline and benzoyl chloride, afforded two hydrogenated lactams (8a) and (9a) in 12 and 23 % yields respectively in addition to small amount of another unidentified lactams. Comparison between their p.m.r. spectra of the lactams (8a) and (9a) and the 13a-deuterated congeners (8b) and (9b), the latters of which were obtained from the enamide (7a) upon irradiation in the presence of sodium borodeuteride, supported their structures as shown in the figure.

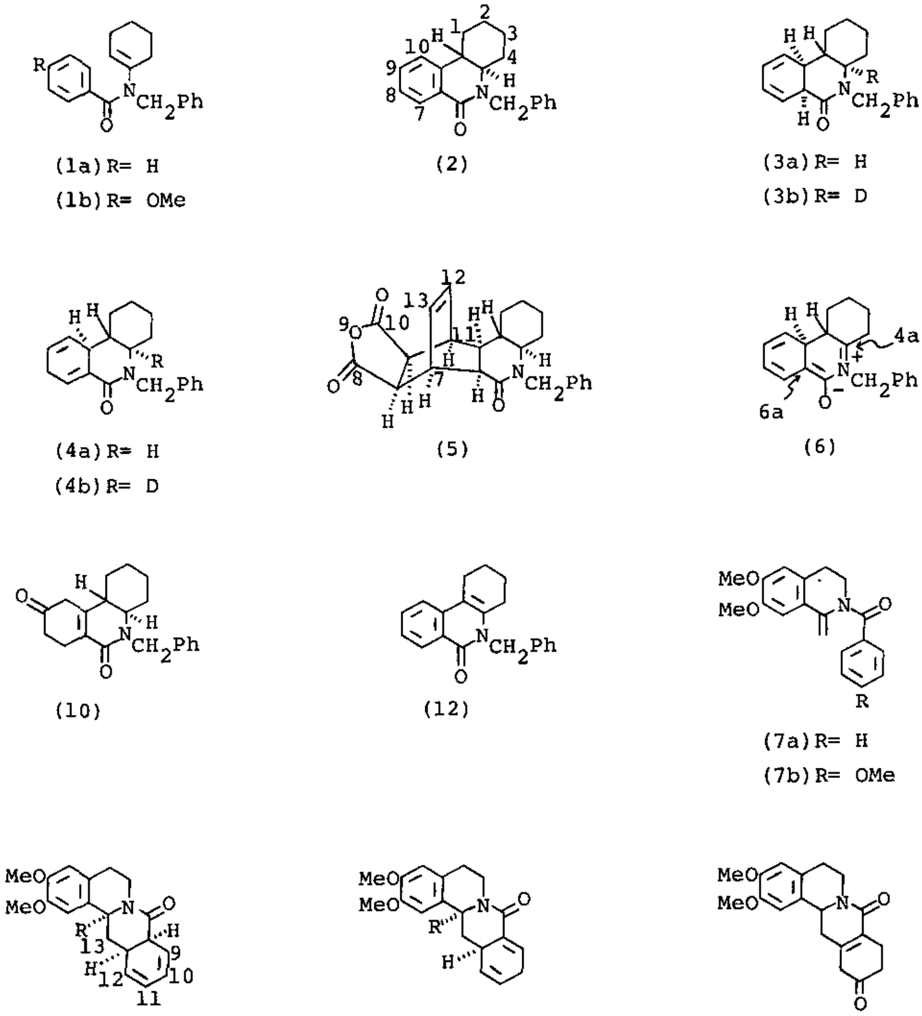
Similarly, the para-methoxy substituted enamides (1b)[5] and (7b)[4] were also irradiated in the presence of sodium borohydride to give the corresponding hydrogenated lactams as an inseparable mixture presumably as to the diene structure, which were so unstable that they were without further purification hydrolyzed under acidic condition (HCl-MeOH) to give the corresponding ketones (10) [ν_{max} 1720, 1660, and 1603 cm^{-1}] and (11) [ν_{max} 1715 and 1630 cm^{-1}] respectively.

In addition to the previous results,[1,2,4,5] the above mentioned reductive photocyclization of enamides thus established that enamide (1a) for instance can undergo cyclization under either non-oxidative, oxidative, or reductive conditions to yield the corresponding trans-lactam (2), the dehydro-lactam (12), or the hydrogenated lactams (3a) and (4a), respectively. Thus, the enamide photocyclization becomes a very potential synthetic strategy for the synthesis of various types of heterocyclic compounds.

ACKNOWLEDGEMENT

We thank the Ministry of Education, Science, and Culture (Japan) for a research grant.

Figure



(8a) R= H
(8b) R= D

(9a) R= H
(9b) R= D

(11)

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Received, 26th March, 1981