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NON-OXIDATIVE PHOTOCYCLIZATION OF 2-AROYL-1-METHYLENE-1,2,3,4-TETRAHYDROISOQUINOLINES

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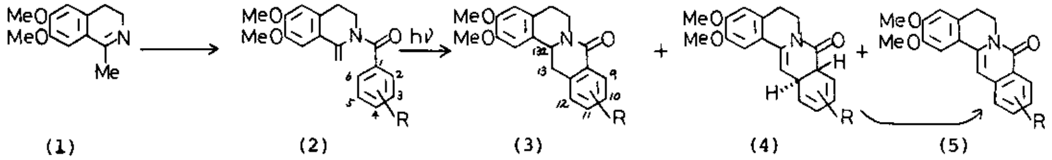
Abstract------ Non-oxidative photocyclization of the enamides (2c,d,e) in benzene at low temperature afforded a new type of the lactams (4c,d,e) and (8) which have a common dihydrobenzene moiety and were readily transformed into the corresponding dehydrolactams (5c,d,e) and (7), thus firmly established the reaction course of photocyclization of these enamides under non-oxidative condition.

Photocyclization of enamides prepared from 1-alkyl-3,4-dihydroisoquinolines has been developed as a general synthetic route toward the protoberberine alkaloids independently by two groups[1,2]. Lenz[1] reported non-oxidative photocyclization of the enamide (2e) using a Rayonet lamp (3000 Å) in a degassed t-butanol solution to give the saturated lactam (3e) as a sole product in an excellent yield. On the other hand, Ninomiya and his coworkers[2] carried out photocyclization of the same enamide (2e) using a low pressure mercury lamp (2537 Å) in methanol under nitrogen bubbling and obtained three products, one saturated lactam (3e) and two dehydrolactams (5e,f), of which the latter (5e,f) were predominantly obtained.

In continuation of our work on reductive[3] and asymmetric[4] photocyclizations of enamides with the above-mentioned subtle difference by the irradiation conditions in mind, we reinvestigated non-oxidative photocyclization of the enamides prepared from 6,7-dimethoxy-1-methyl-3,4-dihydroisoquinoline (1) and found that the primary products in the photocyclization are the hitherto unknown new type of the lactams (4c,d,e) having a dihydrobenzene moiety, which were then readily transformed into the stable dehydrolactams (5c,d,e) as the final products. When the p-methoxy-substituted enamide (2d) was irradiated with a high pressure mercury lamp (Pyrex filter) in benzene at room temperature, the dehydrolactam (5d)[5] and the saturated lactam (3d)[6] were obtained in 40 and 27 % yields respectively with the almost identical ratios as in the case of the irradiation using

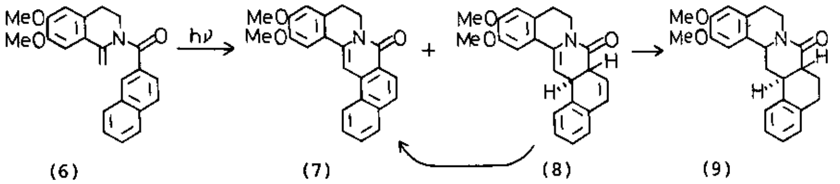
a low pressure lamp. However, irradiation at the temperature of 6°C produced a new but very unstable lactam (4d)[7] in addition to the dehydrolactam (5d) and the saturated lactam (3d), of which the newcomer (4d) was readily transformed into the dehydrolactam (5d) on prolonged irradiation or just by standing at room temperature. The stereochemistry of (4d), as shown in the figure, was deduced from its n.m.r. spectrum which showed signals for 8a-H at δ 2.90 (dt, J=21 and 2 Hz) and 12a-H at δ 3.27 (broad d, J=21 Hz).
As shown in the table, the m-methoxy-substituted (2c) and dimethoxy-substituted enamides (2e) showed similar results affording the similar new type of lactams (4c)[7] and (4e)[7] upon irradiation in benzene at 6°C. On the other hand, no new type of lactam was detected from irradiation of the o-methoxy-substituted (2b) and unsubstituted enamides (2a) presumably due to a regiospecific cyclization[8] to the root of the substituent in the former followed by elimination of the substituent and due to instability of the photo-product in the latter case.
Upon considering the fact that the saturated lactams (3a,b,c,d,e) were not oxidized to the corresponding dehydrolactams (5a,b,c,d,e) under these irradiation conditions, the predominant formation of the dehydrolactams (5c,d,e) even under non-oxidative condition using either a low or a high pressure mercury lamp at room temperature might be attributed to a considerable formation of a new type of lactams (4c,d,e) which were then readily subjected to dehydrogenation to the corresponding dehydrolactams (5c,d,e) during the course of irradiation. We next examined non-oxidative photocyclization of the enamide (6) prepared from 2-naphthoic acid. This enamide was expected to afford a more stable photocyclized product with a dihydronaphthalene moiety than the above lactams (4c,d,e). Thus, a mixture of a new type of the lactam (8) with a dihydronaphthalene moiety and the dehydrolactam (7)[7] as a byproduct was obtained. The primary photo-product (8) was so unstable that it was catalytically hydrogenated to give the tetrahydrolactam (9)[7] in 27 % yield from the enamide (6).

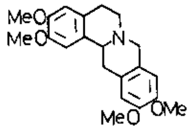
Based on the above results, we now can depict the detailed reaction course of non-oxidative photocyclization of enamides prepared from the Bischler-Napieralski products as follows; from a common cyclic intermediate (A)[8], formed photochemically from the enamide, either one of two possible thermal [1,5]-sigmatropic shifts of hydrogens, Ha or Hb, would occur to bring about the formation of either one or two lactams (B) and (C), of which the saturated lactam (B) would be formed as a result of Ha-shift and a new type of the lactam (C) as a

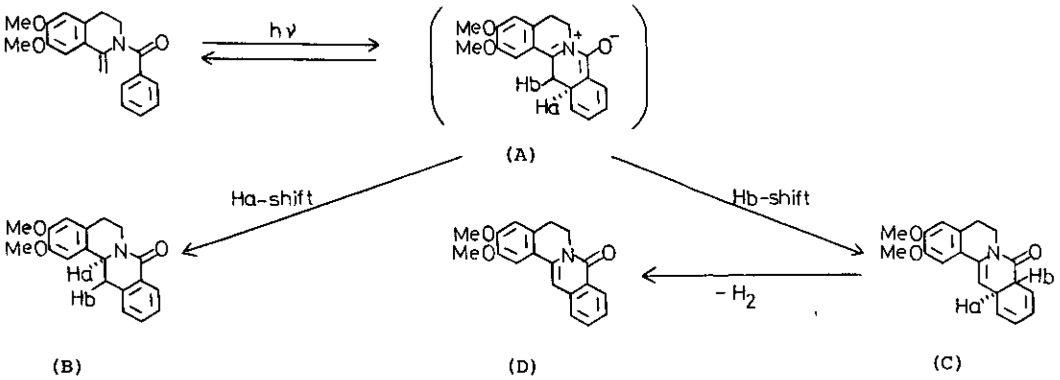


Table

	R	Temp.	(3a,b,c,d,e)	(4c,d,e)	(5a,b,c,d,e,f)
			(Product) R (Yield (%))		
a	H	r.t.	(3a) H (25)	-----	(5a) H (15)
		6°C	(3a) H (25)	-----	(5a) H (15)
b	o-OMe	r.t.	-----	-----	(5b) H (60)
		6°C	(3b) H (13a-OMe) (31)	-----	(5b) H (30)
c	m-OMe	r.t.	(3c) 10-OMe (13)	-----	(5c) 10- + 12-OMe (45)
		6°C	(3c) 10-OMe (15)	(4c) 12-OMe (30)	(5c) 10- + 12-OMe (20)
d	p-OMe	r.t.	(3d) 11-OMe (27)	-----	(5d) 11-OMe (40)
		6°C	(3d) 11-OMe (29)	(4d) 11-OMe (22)	(5d) 11-OMe (23)
e	3,4-$(OMe)_2$	r.t.	(3e) 10,11-$(OMe)_2$ (5)	-----	(5e) 10,11-$(OMe)_2$ (40) (5f) 11,12-$(OMe)_2$ (5)
		6°C	(3e) 10,11-$(OMe)_2$ (25)	(4e) 10,11-$(OMe)_2$ (4)	(5e) 10,11-$(OMe)_2$ (35)




(10)



result of Hb-shift, of which the latter (C) would be then readily dehydrogenated to the dehydrolactam (D) as a final product. In the photocyclization of the enamide (6) of N-naphthoylenamine-type, Hb-shift occurred selectively while both Ha- and Hb- shifts occurred concomitantly or competingly in the photocyclization of the enamides (2a,c,d,e) of N-benzoylenamine-type.

Finally we also found that irradiation of the enamides (2c,d,e) in the presence of sodium borohydride (1.5 moles) in a benzene solution containing small amount of methanol enough to dissolve the hydride reagent suppressed the formation of a new type of the lactams (4c,d,e) and afforded the saturated lactams (3c,d,e) with the yields of about 80 %, of which the lactam (3e) was further converted into (±)-xylopinine (10) in overall yield of 52 % from the Bischler-Napieralski product (1).

Thus, with the establishment of the detailed reaction course of non-oxidative photocyclization of enamides coupled with their reductive photocyclization[3], the enamide photocyclization in the presence of small amount of sodium borohydride (1.5 moles) might make a great promise of mass production of saturated lactams.

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