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PHOTO-INDUCED FORMATION OF META-BRIDGED AROMATIC LACTAMS HAVING ELEVEN MEMBERED RING

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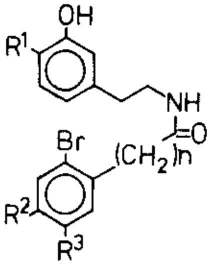
Abstract——Irradiation of N-[2-(2- or 4-hydroxyphenyl)ethyl]-3-(2-bromophenyl)propionamides (10) under basic conditions gave eleven membered ring lactams (12a,b,e and 13), which were formed by aryl-aryl coupling at the ortho and para positions to a hydroxyl group in 10, in moderate yields.

It is well known that photochemical reaction of phenolic bromophenylacetamides (1) or (±)-bromotetrahydroisoquinolin-7-ols (2) under basic conditions gave dibenz[d,f]azonin-8-ones (3 and 4)[1] or (±)-aporphines (5)[2a] and (±)-homoaporphine (6)[2b]. Recently, photolysis of a phenolic bromophenylpropionamide (7) was reported to give ortho-bridged aromatic lactams (8 and 9)[3] bearing ten membered ring. However, no photo-induced formation of meta-bridged aromatic lactams such as 13, which would be a useful compound for synthesis of (±)-homoaporphine, has appeared in the literature so far. We now wish to report formation of the title lactams (12a,b,e and 13) by photolytic reaction.

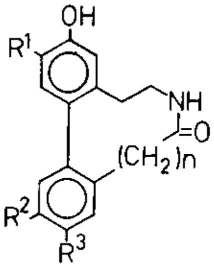
In a typical example, an ice-cooled, stirred solution of 10a[4,5] (500 mg) and KOH (1.12 g) in MeOH (220 ml) was irradiated in a stream of N_2 by a 200W-high pressure mercury lamp (quartz), until the starting material was not detected on t.l.c. After irradiation for 2.5 h, a residue obtained on removal of the solvent in vacuo was dissolved in H_2O and the alkaline solution was treated with NH_4Cl (solid). The product was taken up in $CHCl_3$-i-PrOH (4:1). Usual work-up of the organic layer gave an oil (487.1 mg), which was separated by silica gel column chromatography (C_6H_6-AcOEt=2:1) into a debrominated amide (11a)[4](149.9 mg, 36.7%), 12a[4,6] (18.1 mg, 4.9%)[after further purification of the eluate on preparative t.l.c. (SiO_2;C_6H_6-AcOEt=1:5)], and 13a[4,6](189 mg, 46.3%), respectively. Structures of 11a,



1 (n=1)

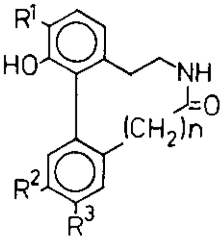
7 (n=2)

n	R^1	R^2	R^3
1	OMe	OMe	OMe
	OPr^i	OMe	H
	H	OPr^i	OMe
2	OMe	OCH_2O	



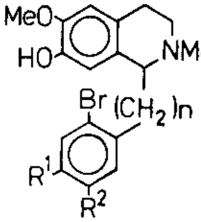
3 (n=1)

8 (n=2)



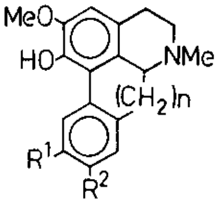
4 (n=1)

9 (n=2)



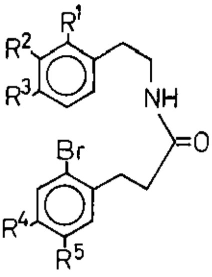
2

n	R^1	R^2
1	OMe	OMe
	OCH_2O	
	H	OH
2	OMe	OMe

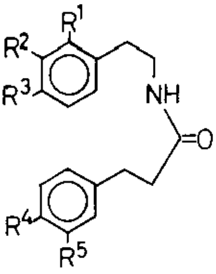


5 (n=1)

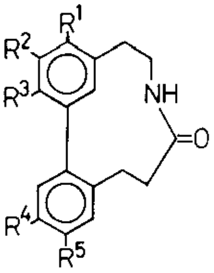
6 (n=2)



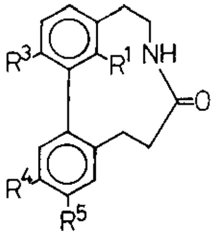
10



11



13



12

	R^1	R^2	R^3	R^4	R^5
a	OH	OMe	H	OMe	OMe
b	OH	OMe	H	OCH_2O	
c	OH	OMe	H	H	H
d	OH	H	H	OMe	OMe
e	H	OMe	OH	OMe	OMe

	R^1	R^3	R^4	R^5
a(=d)	OH	H	OMe	OMe
b	OH	H	OCH_2O	
c	OH	H	H	H
e	H	OH	OMe	OMe

12a , and 13a were confirmed on the basis of spectroscopic data.

Analogously, photolysis of 10a and NaOH in EtOH gave 11a, 12a and 13a, respectively (*Table 1*).

In order to explore the scope of the reaction, similar photolytic reaction of 10b-d[4] was carried out. The results are shown in Table 1.

Table 1. *Reaction Conditions and Yields* a)

Starting Material		Reaction Conditions			Yields(%)		
(10)	mp(°C)	Solvent	Base	Reaction Time(h)	11	12	13
a	120-121(MeOH)	MeOH	KOH	2.5	36.7	4.9	46.3
		EtOH	NaOH	2.0	27.7	4.7	35.8
b	145-145.5(EtOH)	MeOH	KOH	2.0	12.8	1.7	22.2
c	oil	MeOH	KOH	2.0	20.1	-- b)	30.1
d	125-126(EtOH)	MeOH	KOH	1.0	15.2	-- b)	38.1

a) Reaction conditions have not been optimized.
b) 12c and 12d(=12a) were not isolated.

As shown in Table 1, photolysis of 10a,b afforded 12a,b[7], which were cyclized at the ortho position to a hydroxyl group though in low yield, suggesting that the similar photolytic reaction of 10e would give rise to a cyclized product.

With this expectation in mind, the similar photolysis of 10e [mp 101-102°C(C_6H_6-n-hexane)][4] was performed to afford 12e[4,6,7](13.1%) and 13e[4,6] (17.6%) together with 11e[4] (23.9%).

Thus, photolytic reaction of propionamides (10) was proved to provide meta-bridged aromatic lactams having eleven membered ring. Further transformation of 13 to (±)-homoaporphines is in progress.

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3) H. Tanaka, Y. Takamura, K. Ito, K. Ohira, and M. Shibata, *Chem. Pharm. Bull.*, 1984, **32**, 2063.

4) New compounds described in this text gave satisfactory analytical data.

5) Similar photolysis of 10a (106 mg) through a quartz (2 h) or pyrex filter (4 h) gave 13a (43.1% or 30.7%) and 11a (32.7% or 3.2%), respectively. 12a was not isolated.

6) 12a:mp 247-248°C($CHCl_3$),IR ν(KBr):3460,3325,1640.^{1}H-NMR δ($CDCl_3$):7.20-6.96(3H,m,ArH),6.84,6.78(each 1H,s,ArH),3.93,3.88(each 3H,s,2xOMe). 12b:mp 235°C(MeOH), IR ν(KBr):3420,3325,1660.^{1}H-NMR δ($CDCl_3$):7.26-6.98(3H,m,ArH),6.91,6.87(each 1H, d,J=1Hz,OCH_2O). 12e:mp 280-283°C(dec.),IR ν(KBr):3480,3270,1630.^{1}H-NMRδ(DMSO-d_6): 7.30-6.30(5H,m,ArH),3.70,3.62(each 3H,s,2xOMe). 13a:mp 245°, 260-262°C(dec.) (MeOH),IR ν(KBr):3470,3360,1630.^{1}H-NMR δ($CDCl_3$):6.80,6.69(each 1H,s,ArH),6.61, 6.29(each 1H,d,J=2.5Hz,ArH),3.90,3.88,3.86(each 3H,s,3xOMe). 13b:mp>300°C(MeOH), IR ν(KBr):3380,3280,1630.^{1}H-NMR δ($CDCl_3$):6.76,6.68(each 1H,s,ArH),6.58,6.28(each 1H,d,J=2.5Hz,ArH),5.92(2H,s,OCH_2O),3.87(3H,s,OMe). 13c:mp 257-259°C(dec.)(MeOH), IR ν(KBr):3410,3290,1640.^{1}H-NMR δ($CDCl_3$):7.20-7.08(4H,m,ArH),6.62,6.29(each 1H, d,J=2.5Hz,ArH),3.86(3H,s,OMe). 13d:mp>300°C(MeOH),IR ν(KBr):3370,3280,1605.^{1}H-NMR δ(DMSO-d_6):6.92-6.64(5H,m,ArH),3.80,3.75(each 3H,s,2xOMe). 13e:mp 227-227.5°C (MeOH),IR ν(KBr):3550,3370,1670.^{1}H-NMR δ($CDCl_3$):6.82,6.72(each 1H,s,ArH),6.64, 6.23(each 1H,d,J=2.5Hz,ArH),3.89,3.87,3.84(each 3H,s,3xOMe).

7) A photocyclization by elimination of a methoxyl group has been known; I. Ninomiya and T. Naito, *J. Chem. Soc. Perkin I*, 1975, 1720.

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