

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

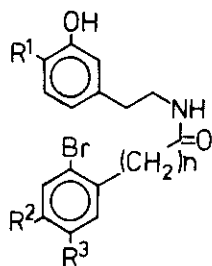
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Abstract—Irradiation of N-[2-(2- or 4-hydroxyphenyl)ethyl]-3-(2-bromophenyl)propionamides (10) under basic conditions gave eleven membered ring lactams (12a,b,e and 13), which were formed by aryl-aryl coupling at the ortho and para positions to a hydroxyl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

It is well known that photochemical reaction of phenolic bromophenylacetamides (1) or (\pm)-bromotetrahydroisoquinolin-7-ols (2) under basic conditions gave dibenz[d,f]azonin-8-ones (3 and 4)¹ or (\pm)-aporphines (5)^{2a} and (\pm)-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 (\pm)-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.

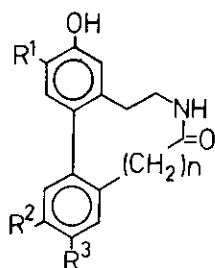
In a typical example, an ice-cooled, stirred solution of 10a^{4,5} (500 mg) and KOH (1.12 g) in MeOH (220 ml) was irradiated in a stream of N₂ by a 200W-high pressure mercury lamp (quartz), until the starting material was not detected on t.l.c. After irradiation for 2.5 h, a residue obtained on removal of the solvent in vacuo was dissolved in H₂O and the alkaline solution was treated with NH₄Cl (solid). The product was taken up in CHCl₃-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 (C₆H₆-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. (SiO₂; C₆H₆-AcOEt=1:5)], and 13a^{4,6} (189 mg, 46.3%), respectively. Structures of 11a,



1 (n=1)

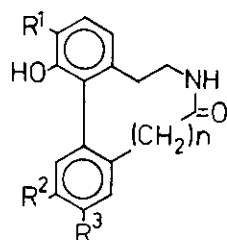
2 (n=2)

n	R ¹	R ²	R ³
1	OMe	OMe	OMe
	OPr ⁱ	OMe	H
	H	OPr ⁱ	OMe
2	OMe	OCH ₂ O	



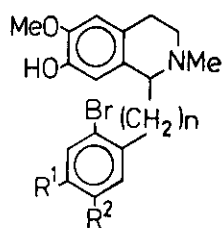
3 (n=1)

8 (n=2)



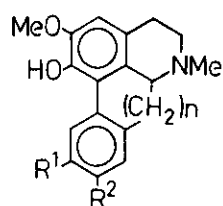
4 (n=1)

9 (n=2)



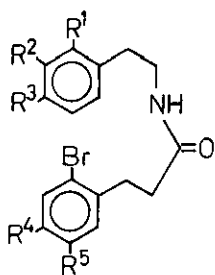
2

n	R ¹	R ²
1	OMe	OMe
	OCH ₂ O	H
	H	OH
2	OMe	OMe

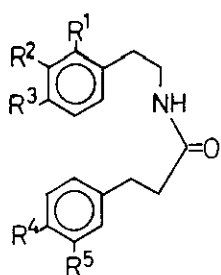


5 (n=1)

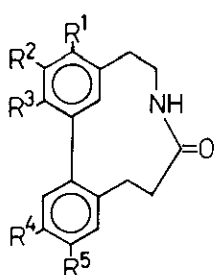
6 (n=2)



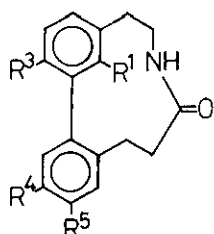
10



11



13



12

	R ¹	R ²	R ³	R ⁴	R ⁵
a	OH	OMe	H	OMe	OMe
b	OH	OMe	H	OCH ₂ O	
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 ₂ O	
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-d⁴ 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
<u>a</u>	120-121(MeOH)	MeOH	KOH	2.5	36.7	4.9	46.3
		EtOH	NaOH	2.0	27.7	4.7	35.8
<u>b</u>	145-145.5(EtOH)	MeOH	KOH	2.0	12.8	1.7	22.2
<u>c</u>	oil	MeOH	KOH	2.0	20.1	-- ^{b)}	30.1
<u>d</u>	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,b⁷, 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(C₆H₆-n-hexane)]⁴ was performed to afford 12e^{4,6,7} (13.1%) and 13e^{4,6} (17.6%) together with 11e⁴ (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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REFERENCES AND FOOTNOTES

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- 2) a) T. Kametani, S. Shibuya, H. Sugi, O. Kusama, and K. Fukumoto, J. Chem. Soc. (C), 1971, 2446; R.J. Spangler and D.C. Boop, Tetrahedron Lett., 1971, 4851; B. R. Pai, H. Suguna, S. Rajeowani, and G. Manikumar, Ind. J. Chem., 1978, 16B, 421; b) T. Kametani, Y. Satoh, H. Koizumi, and K. Fukumoto, J. Org. Chem., 1971, 36, 3733.
- 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 (CHCl₃), IR ν (KBr): 3460, 3325, 1640. ¹H-NMR δ (CDCl₃): 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. ¹H-NMR δ (CDCl₃): 7.26-6.98 (3H, m, ArH), 6.91, 6.87 (each 1H, d, J=1Hz, OCH₂O). 12e:mp 280-283°C (dec.), IR ν (KBr): 3480, 3270, 1630. ¹H-NMR δ (DMSO-d₆): 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. ¹H-NMR δ (CDCl₃): 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. ¹H-NMR δ (CDCl₃): 6.76, 6.68 (each 1H, s, ArH), 6.58, 6.28 (each 1H, d, J=2.5Hz, ArH), 5.92 (2H, s, OCH₂O), 3.87 (3H, s, OMe). 13c:mp 257-259°C (dec.) (MeOH), IR ν (KBr): 3410, 3290, 1640. ¹H-NMR δ (CDCl₃): 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. ¹H-NMR δ (DMSO-d₆): 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. ¹H-NMR δ (CDCl₃): 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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