TRIAZOLO[4,5-d]PYRIMIDINES. VII. THE PHOTOCHEMICAL TRANSFORMATION OF 3-PHENYL-3H-1,2,3-TRIAZOLO[4,5-d]PYRIMIDINES INTO 9H-PYRIMIDO[4,5-b]INDOLES

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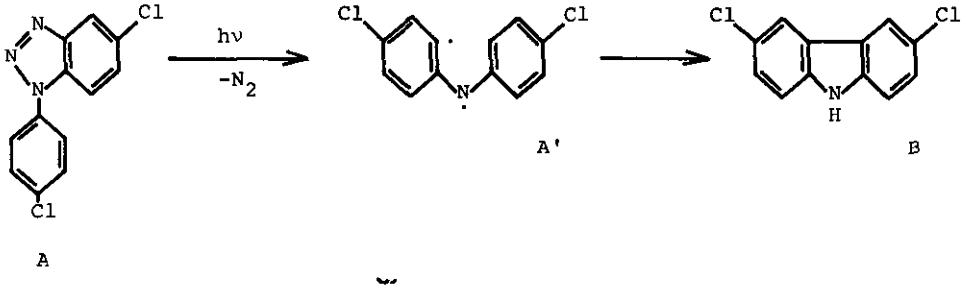
Abstract —— The photolysis of 3-phenyl-3H-1,2,3-triazolo-[4,5-d]pyrimidines in dioxane, benzene and methanol gave 9H-pyrimido[4,5-b]indoles in moderate yields. Similarly, 3-phenyl-3H-1,2,3-triazolo[4,5-b]pyridines were easily transformed by the photolysis into 9H-pyrido[2,3-b]indoles.

It was reported by Ohashi and his co-workers that on irradiation, 5-chloro-1-(4-chlorophenyl)-1H-1,2,3-benzotriazole (A) lost a nitrogen molecule to give 3,6-dichloro-9H-carbazole (B) as a sole product.[1)]

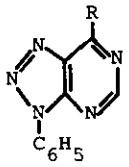


A A' B

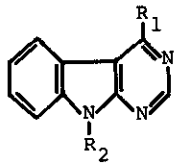
Chart 1

Anticipating that similar photochemical transformation would take place, we examined the photolysis of 3-phenyl-3H-1,2,3-triazolo[4,5-d]pyrimidines (1), and succeeded in obtaining 9H-pyrimido[4,5-b]indoles (2) in moderate yields.

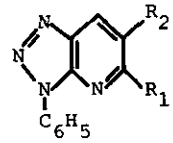
On irradiation with a high pressure mercury lamp (100 W) in a solvent such as dioxane, benzene, and methanol for 10 to 15 hr, 3-phenyl-3H-1,2,3-triazolo-[4,5-d]pyrimidine (1a)[2] and its derivatives (1b[3] and 1c[4]) having electron



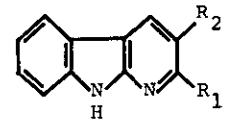
1	-R
1a	-H
1b	-Cl
1c	-CN
1d	$-NHCH_3$
1e	$-NHCH_2C_6H_5$
1f	$-N(CH_3)_2$
1g	$-OCH_3$
1h	$-OC_2H_5$
1i	$-OC_6H_5$
1j	$-CH_3$



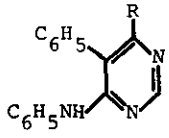
2	$-R_1$	$-R_2$
2a	-H	-H
2b	-Cl	-H
2c	-CN	-H
2d	$-NHCH_3$	-H
2e	$-NHCH_2C_6H_5$	-H
2f	$-N(CH_3)_2$	-H
2g	$-OCH_3$	-H
2h	$-OC_2H_5$	-H
2i	$-OC_6H_5$	-H
2j	$-CH_3$	-H
2k		-H
2l	$-CH_2OH$	-H
2m	-CN	$-OCH_3$



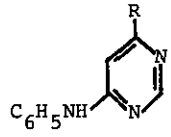
5	$-R_1$	$-R_2$
5a	-H	-H
5b	$-CH_3$	$-COOC_2H_5$
5c	$-CH_3$	$-COCH_3$
5d	$-(CH_2)_4-$	
5e	$-(CH_2)_3-$	
5f	$-C_6H_5$	-H



6	$-R_1$	$-R_2$
6a	-H	-H
6b	$-CH_3$	$-COOC_2H_5$
6c	$-CH_3$	$-COCH_3$
6d	$-(CH_2)_4-$	
6e	$-(CH_2)_3-$	
6f	$-C_6H_5$	-H



3	-R
3a	-H
3b	-Cl
3c	-CN



4	-R
4b	-Cl
4c	-CN
4d	$-OCH_3$

Chart 2

attracting substituents such as chloro and cyano groups at the 7-position gave the corresponding ring transformation products, 9H-pyrimido[4,5-b]indoles (2a[7] to 2c) as main products together with by-products (2k to 2m, 3a[5] to 3c, and 4b[6] to 4d). Thus, in the case of 1a in dioxane 2k as a by-product was formed by the photoreaction of the resulting 2a with dioxane used, introducing a substituent

Table I. The Photolysis of 1 and 5

Starting material	Solvent	Product No.	Mp (°C)	Yield (%)	No.	Mp (°C)	Yield (%)
1a	Dioxane	2a	237-240	33	2k	248-249	9
1a	Benzene	2a		50	3a	113-114	11
1a	Methanol	2a		54	2l	250-252	15
1b	Dioxane	2b	274-277	14	4b	158-159	2
1b	Benzene	2b		32	3b	167-169	8
1b	Methanol	2b		7	4d	149-151	2
1c	Dioxane	2c	284-286	25	4c	150-152	12
1c	Benzene	2c		54	3c	218-220	19
1c	Methanol	2c		85	2m	260-261	4
1d	Dioxane	2d	249-250	69			
1e	Dioxane	2e	256-257	62			
1f	Dioxane	2f	238-239	91			
1g	Dioxane	2g	208-210	85			
1h	Dioxane	2h	190-191	55			
1i	Dioxane	2i	199-200	48			
1j	Dioxane	2j	260-262	23			
5a	Dioxane	6a	115-116	61			
5b	Dioxane	6b	227-228	38			
5c	Dioxane	6c	255-257	34			
5d	Dioxane	6d	254-255	48			
5e	Dioxane	6e	294-295	69			
5f	Dioxane	6f	245-246	52			

into the 4-position. Similarly, the reaction of 1a in methanol gave 4-hydroxymethyl derivative of 2a (2l) as a by-product. The reaction of 1b and 1c in dioxane gave the corresponding ring fission products (4b and 4c) as by-products. In the case of 1b in methanol, 4d as a by-product was formed by the nucleophilic substitution of the resulting 4b with methanol. In the case of 1c in methanol, 2m as a by-product was formed by the photoreaction of the resulting 2c with methanol used, introducing a methoxy group into the 9-position. In the cases of 1a to 1c in benzene, 3a to 3c as by-products were formed by the photoreaction of the ring fission intermediates, like A', with benzene, introducing a phenyl group into the 5-position. How to depend on a solvent used for formation of by-products is not clear as yet.

The photolysis of triazolopyrimidines (1d to 1j)[4] having electron donating substitutents such as amino, alkoxyl, and alkyl groups at the 7-position resulted in the formation of the corresponding 4-substituted pyrimidoindoles (2d to 2j) as sole products.

Similarly, 3-phenyl-3H-1,2,3-triazolo[4,5-b]pyridines (5a to 5f)[8, 9] were subjected to the photolysis in dioxane, the corresponding 9H-pyrido[2,3-b]indoles (6a[10] to 6f) were obtained in moderate yields.

The structures of the products, 2, 3, 4, and 6 were assigned on the basis of the spectral data as shown in Table II.

Table II. The Spectral Data for 2, 3, 4, and 6

Compd.	MS: M^+ m/e	IR ν_{max}^{KBr} cm^{-1}	NMR (in $CDCl_3$): ppm C^2-H^s	NH^{bs}	C_6H_5^{m}	Other
2a	169	3132(NH)	9.00	12.3	-	$9.50^s(C^4\text{-H})$, $7.2\text{-}8.4^m(C^{5\text{-}8}\text{-H})$ a)
2b	203	3120(NH)	8.70	12.6	-	$7.2\text{-}8.4^m(C^{5\text{-}8}\text{-H})$
2c	194	3120(NH) 2230(CN)	8.79		-	$7.2\text{-}8.4^m(C^{5\text{-}8}\text{-H})$ b)
2d	198	3450, 3110(NH)	8.45	11.9 7.1	-	$3.20^d(N\text{-}CH_3)$, $7.2\text{-}8.5^m(C^{5\text{-}8}\text{-H})$ a)
2e	274	3455, 3120(NH)	8.45	12.0	7.1-8.6	$5.00^d(NHCH_2)$, $7.1\text{-}8.6^m(C^{5\text{-}8}\text{-H})$ a)
2f	212	3180(NH)	8.35		-	$3.42^s(N(CH_3)_2)$, $7.2\text{-}8.2^m(C^{5\text{-}8}\text{-H})$ b)
2g	199	3120(NH)	8.20	11.7	-	$4.30^s(OCH_3)$, $7.3\text{-}8.3^m(C^{5\text{-}8}\text{-H})$
2h	213	3120(NH)	8.73	11.5	-	4.79^q, $1.62^t(OC_2H_5)$, $7.3\text{-}8.3^m(C^{5\text{-}8}\text{-H})$
2i	261	3120(NH)	8.53	12.2	7.69^s	$7.2\text{-}8.4^m(C^{5\text{-}8}\text{-H})$ a)
2j	183	3100(NH)	8.80		-	$3.05^s(CH_3)$, $7.2\text{-}8.3^m(C^{5\text{-}8}\text{-H})$ b)
2k	255	3110(NH)	8.82	12.3	-	$3.1\text{-}5.5^m$(7H, CH), $7.2\text{-}8.4^m(C^{5\text{-}8}\text{-H})$
2l	199	3130(NH or OH)	8.92	12.2	-	$5.20^s(CH_2O)$, 5.2^{bs}(OH), $7.2\text{-}8.4^m$
2m	224	2225(CN)	8.50	-	-	$4.20^s(OCH_3)$, $7.2\text{-}7.9^m(C^{5\text{-}8}\text{-H})$ a)
3a	247	3230(NH)	8.26	6.9	7.1-7.8	$8.76^s(C^6\text{-H})$
3b	281	3220(NH)	8.50	6.5	6.9-7.8	
3c	272	3275(NH) 2230(CN)	8.70	6.7	7.1-7.7	
4b	205	3230(NH)	8.41	8.2	7.35^s	$6.71^s(C^5\text{-H})$
4c	196	3230(NH) 2240(CN)	8.61	9.7	7.0-7.8	$7.12^s(C^5\text{-H})$
4d	201	3210(NH)	8.50	8.7	7.2-7.8	$6.24^s(C^5\text{-H})$, $4.00^s(OCH_3)$
6a	168	3130(NH)		12.0	-	$7.1\text{-}8.7^m$(7H, $C^{2\text{-}8}$-H)
6b	254	3130(NH) 1710(CO)	-	11.5	-	$8.90^s(C^4\text{-H})$, $7.2\text{-}8.2^m(C^{5\text{-}8}\text{-H})$, 4.50^q, $1.45^t(OC_2H_5)$, $3.05^s(CH_3)$
6c	224	3120(NH) 1670(CO)	-		-	$8.72^s(C^4\text{-H})$, $7.2\text{-}8.2^m(C^{5\text{-}8}\text{-H})$, $2.89^s(CH_3)$, $2.73^s(COCH_3)$ b)
6d c)	222	3130(NH)	-		-	$8.00^s(C^4\text{-H})$, $7.0\text{-}8.1^m(C^{5\text{-}8}\text{-H})$,

6e[c]	208	3130(NH)	-	11.4	-	1.6-3.2^{m}($(CH_2)_4$) [b] 8.17^{s}(C^4-H), 7.0-8.3^{m}(C^{5-8}-H),
6f	244	3130(NH)	-	11.7	-	2.0-3.4^{m}($(CH_2)_3$) [a] 7.0-8.5^{m}(11H, C^{3-8}-H, C_6H_5)

a) In $CDCl_3$-$(CD_3)_2SO$.

b) IN $CDCl_3$-CD_3OD.

c) The numbering used is that of 9H-pyrido[2,3-b]indole ring system.

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REFERENCES

1) M. Ohashi, K. Tsujimoto, and T. Yonezawa, Chem. Commun., 1970, 1089.

2) T. Higashino, T. Katori, and E. Hayashi, Chem. Pharm. Bull. (Tokyo), 27, 2431 (1979).

3) D. J. Brown and M. N. Paddon-Row, J. Chem. Soc. (C), 1967, 1856.

4) T. Higashino, T. Katori, H. Kawaraya, and E. Hayashi, Chem. Pharm. Bull. (Tokyo), 28, 337 (1980)

5) G. Tsatsaronis and F. Effenberger, Chem. Ber., 94, 2876(1961).

6) H. C. Carrington, F. H. S. Curd, and D. N. Richardson, J. Chem. Soc., 1955, 1858.

7) R. G. Glushkov, V. A. Volokova, and O. Yu. Magidson, Khim. Farm. Zh., 1, 25 (1967)(Russ). [Chem. Abstr., 68, 105143f (1968)].

8) R. L. Clark, A. A. Pessolano, and T.Y. Shen, U.S. Patent 4,000,286 (1976). [Chem. Abstr., 86, P189951^{a} (1977)].

9) T. Higashino, T. Katori, and E. Hayashi, Chem. Pharm. Bull. (Tokyo), 27, 2861 (1979).

10) V. M. Clark, A. Cox, and E. J. Herbert, J. Chem. Soc. (C), 1968, 831.

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