HETEROCYCLES, Vol. 6, No. 1, 1977

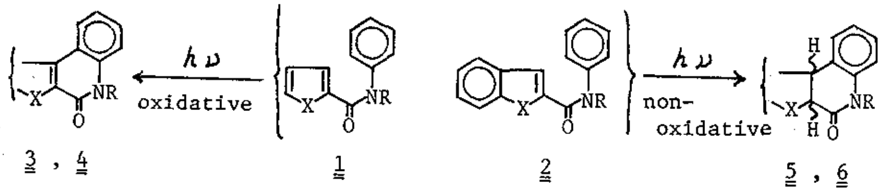
SYNTHESES OF THIENO[2,3-c]-, PYRROLO[2,3-c]-, AND INDOLO[2,3-c]DIAZANAPHTHALENES BY PHOTOCYCLIZATION OF ACYLAMINOPYRIDINES

Yuichi Kanaoka*, Kunio San-nohe, Yasumaru Hatanaka, Kazuhiko Itoh,
Minoru Machida[2] and Masanao Terashima[2]
Faculty of Pharmaceutical Sciences, Hokkaido University, Sapporo 060, Japan

By the photocyclization of the amides derived from thiophene-2-, N-methylpyrrole-2-, and N-methylindole-2-carboxylic acids and aminopyridines, novel polycyclic heteroaromatic systems such as thieno[2,3-c]-, pyrrolo[2,3-c]-, and indolo[2,3-c]diazanaphthalenes were synthesized.

The photocyclization reactions of anilides have been found earlier[3], studied over the last few years and have shown to be potentially valuable in building polycyclic heteroaromatics from easily accessible precursors.[1a,4] Closely related photoreactions[5a] of various types of enamides have also been vigorously studied by Ninomiya et al.[5] and several other groups.[6] Our recent studies of the photochemical behavior of thiophene-2-, pyrrole-2-, and indole-2-carboxanilides (1 and 2) have shown that these anilides exhibit a varied and interesting reactions, undergoing cyclization in ei-

Scheme 1



a:X=NR′ b:X=S c:X=O

ther oxidative or nonoxidative fashion depending on the reaction conditions[1a,4] (Scheme 1). As part of broadly based research on photochemical syntheses of heterocycles, our attention was directed to the application of this photocyclization for syntheses of polycyclic systems containing multiple heteroatoms. Previous work on benzoylaminopyridines has uncovered that substitution of a ring carbon of the substrate anilides with a nitrogen may significantly influence the reaction courses,[4c] suggestive of complicated factors operating in the mechanism. In an attempt to elucidate the synthetic scope and limitation of the reactions the present work deals with photolysis of anilides derived from the five-membered heterocyclic carboxylic acids and aminopyridines as a first logical variation of the method.

Solutions (200 mg in 200 ml) of the acyl derivatives of aminopyridines in benzene containing 10% ethanol were irradiated with a 100w high-pressure

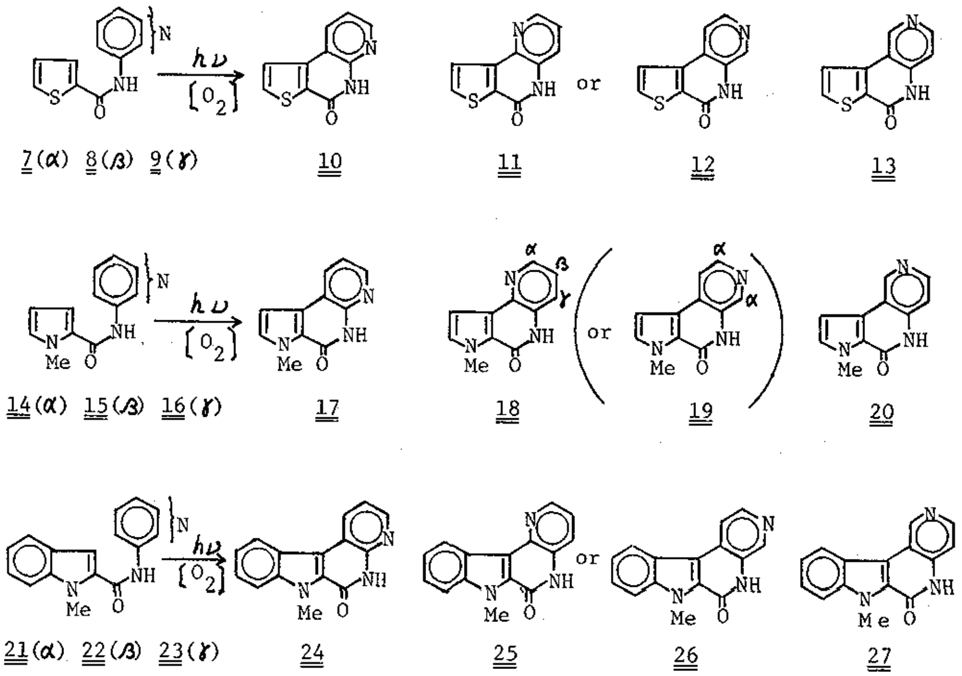
Table I. Photocyclization Products a)

amide	Time(hr)	Products(yield, mp)	amide recovered
7	5	10 (27% ; > 320°C)	33%
8	4	11 or 12 (62 ; ")	-
9	4	13 (45 ; ")	29
14	5	17 (10 ; 303-5)	35
15	4	18 (or 19)(38 ; 290-2)	-
16	5	20 (35 ; 277-9)	45
21	7	24 (8 ; > 320)	53
22	3	25 or 26 (60 ; ")	-
23	2	27 (58 ; ")	6

a) Thieno[2,3-c][1,x]diazanaphthalene : 10,x=8 ; 11,x=5 ; 12,x=7 ; 13,x=6.
3-Methylpyrrolo[2,3-c][1,x]diazanaphthalene : 17,x=8 ; 18,x=5 ; 19,x=7; 20,x=6.
Indolo[2,3-c][1,x]diazanaphthalene : 24,x=8 ; 25,x=5 ; 26,x=7 ; 27,x=6.

mercury lamp. Products were purified by preparative TLC and the results are listed in Table I.[7]

Scheme 2



These results reveal that the aza derivatives of the heterocyclic carboxanilides generally undergo smooth oxidative photocyclization to afford the corresponding condensed diazanaphthalene systems. It was observed that yields are relatively low with the α-pyridyl amides. The causes of these substitution effects of a nitrogen atom on the reactivity are not yet understood.[4c,d] Cyclization of the β-pyridyl amides (8, 15 and 22) would lead to either the α-(11, 18 and 25) or the γ-(12, 19 and 26), or both of the possible positional isomers, respectively. Structures of these products were yet undetermined except that the structure of the photo-product from 15 is assigned to be 18, since the nmr data are consistent with those of 18 which show only one C_α-H(8.43 ppm, d, J=4Hz; DMSO-d_6) of the pyridine ring, and not with those of **19** which must have two C_α-protons.

In summary, oxidative photocyclization of the anilides derived from the five-membered heterocyclic carboxylic acids and aminopyridines provides a simple synthetic route to novel polycyclic systems such as thieno[2,3-c]-, pyrrolo[2,3-c]- and indolo[2,3-c]diazanaphthalenes. Studies of the application of this reaction to syntheses of a variety of heterocycles and of their mechanistic features are currently under way.

ACKNOWLEDGEMENT We wish to thank the Ministry of Education, Science and Culture, and the Foundation of the Promotion of Reasearch on Medicinal Resources for financial support.

REFERENCES

1 a) Photochemistry of the Amide System. VII. Part VI: Y. Kanaoka, S.Nakao and Y. Hatanaka, *Heterocycles*, 1976, in press ; b) Photoinduced Reactions. XXIX. Part XXVIII: M. Terashima, K. Koyama and Y. Kanaoka, submitted.

2 Present address: Faculty of Pharmaceutical Sciences, Higashi Nippon Gakuen University, Ishikari-Tobetsu, Hokkaido 061-02.

3 a) B.S. Thyagarajan, N. Kharasch, N.B. Lewis and W. Wolf, *Chem.Comm.*, 1967, 614 ; b) E. Winterfeldt and H.J. Altman, *Angew.Chem.*, 1968, **80**, 486.

4 a) Y. Kanaoka and K. Itoh, *Synthesis*, 1972, 36 ; b) *Idem.*, *Chem.Comm.*, 1973, 647 ; c)*Idem.*, *Chem.Pharm.Bull.*, 1974, **22**, 1431 ; d) K. Itoh, Thesis, Hokkaido University, 1974 ; e) Y. Kanaoka, K. Itoh, Y. Hatanaka, J.L. Flippen, I.L. Karle and B. Witkop, *J.Org.Chem.*, 1975, **450** 3001 ; f) Y. Kanaoka, K. San-nohe, K. Itoh and Y. Hatanaka, the 96th Annual Meeting of the Pharmaceutical Society of Japan, Abstracts of Papers, II p.89, April, 1976, Nagoya.

5 a) For a review see: I. Ninomiya, *Heterocycles*, 1974, **2**, 105 ; b) I. Ninomiya, T. Naito and H. Takasugi, *J.C.S. Perkin I*, 1975, 1791 and earlier papers cited therein.

6 a) O.L. Chapman and W.R. Adams, *J.Am.Chem.Soc.*, 1968, **90**, 2333 ; b) M. Ogata and H. Matsumoto, *Chem.Pharm.Bull.*, 1972, **20**, 2264 ; c) Y. Ogata, K. Takagi and I. Ishino, *J.Org.Chem.*, 1971, **36**, 3975 ; d) G.R. Lenz, *ibid.*, 1976, **41**, 2201, and earlier papers cited therein.

7 Structures of all the new compounds were supported by elemental analyses and their spectral (uv, ir, nmr, and mass)data.

Received, 25th October, 1976