HETEROCYCLES, Vol 19, No 12, 1982

PHOTOCHEMICAL RING OPENING REACTIONS OF 3-ALKOXYISOCOUMARIN AND 3-HALO-1-ISOQUINOLONE

Chikara Kaneko,* Toshihiko Naito, and Chiemi Miwa
Faculty of Pharmaceutical Sciences, Kanazawa University,
Takara-machi, Kanazawa 920, Japan

Abstract — Irradiation of 3-methoxyisocoumarin (1) in an alcohol afforded two kinds of diester of homophthalic acid (3 and 4) and the mechanism including novel 1,5-sigmatropic methoxy rearrangement from initially formed ketene (5) to the isomeric ketene (6) was proposed. Similar photochemical ring opening reaction of 3-chloro- and -bromo-1-isoquinolones (8 and 9) as well as their novel photo-alkoxylation reaction is also described.

α-Pyrones upon irradiation are known to give a variety of ring-opened products via the initially formed ene-ketenes as intermediates.[1] Very recently, similar photochemical ring opening was also observed in some pyrimidones[2] and 2-pyridones.[3] While there is no example of such ring opening reaction for their higher benzenoid homologs (e.g., isocoumarins and 1-isoquinolones), all of these reactions are interpreted by the trapping of the ketene species initially formed by their photochemical ring opening.

Here, we report that irradiation of 3-methoxyisocoumarin (1) in an alcohol gave two kinds of diester of homophthalic acid (3 and 4) via the alcohol addition either to the initially formed ketene (5) or to the isomeric ketene (6) formed by an unprecedented 1,5-sigmatropic shift of the methoxy group in the former ketene (5). At the same time, we also report similar ring opening reaction of 3-halo-1-isoquinolone (8 or 9) as well as novel photo-substitution reaction of its 3-halogen atom by the alkoxy group by the irradiation in an alcohol containing triethylamine, both of them being unprecedented for 1-isoquinolone derivatives.

Irradiation[4] of 3-methoxyisocoumarin[5] (1) in methanol gave dimethyl homophthalate (2) in nearly quantitative yield. By analogy to the photochemical ring opening reaction of α-pyrones to ketenes,[1] a mechanism involving an initial formation of the ketene (5) followed by the addition of methanol to its ketene function seems to be an attractive one. However, inadequacy of this mechanism is suggested by the following experiments. Thus, if ethanol was used as a solvent, two kinds of the homophthalates (3a and 4a) were obtained as an inseparable mixture (93.5%) in *ca*. 1:2 ratio, in which only the minor product (3a) was consistent with the above mechanism (*cf*. path *a* in Chart 1). The structures of these two products were deduced from nmr spectrum (CCl_4) of the mixture in which COOMe signals differed markedly each other (δ of 3a: 3.54 and δ of 4a: 3.76). When irradiation was performed in aqueous ether, the corresponding two half esters (3b and 4b in *ca*. 1:2 ratio) were obtained, in which the major product (4b) again did not fit to the mechanism. The two half esters were separated by repeated silica gel column chromatography and each isomer was identified with authentic samples[6] [3b, mp 98-99.5 °C; δ ($CDCl_3$) of Me: 3.65 and 4b, mp 146-148°C; δ ($CDCl_3$) of Me: 3.81].

In order to account for the formation of these two isomeric homophthalates (3 and 4), we propose the mechanism shown in Chart 1. Thus, the initially formed ketene (5-Z) from 1 reacts with the solvent (ROH) to give the ester (3) (path *a*). This path competes with 1,5-sigmatropic methoxy shift in 5-Z to give the other ester (4) *via* the isomeric ketene (6) (path *b*). Such rearrangement has not been observed for ketenes derived from α-pyrones and this fact suggests that the gain of a benzenoid system is a crucial factor in the rearrangement (5→6). The same argument also suggests that the reverse process (6→5) may not occur. 3-Chloroisocoumarin[7] (7) also gave 2 (73%) by irradiation in methanol.

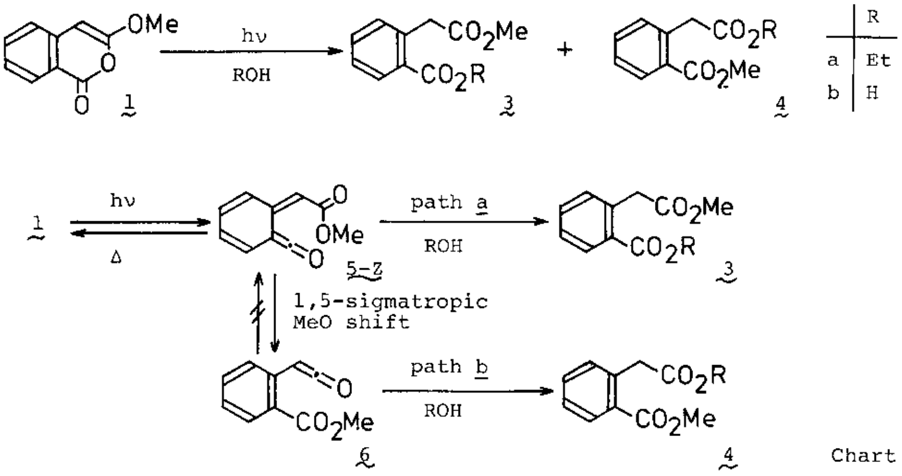

Chart 1

Similar photochemical ring opening reaction has also been found to occur, if 3-halo-1-isoquinolone (8 or 9) is irradiated in an alcohol containing triethylamine (TEA). Thus, irradiation of 3-chloro-1-isoquinolone[8] (8) in methanol containing 5% volume of TEA afforded three products (10a, 11a, and 12) in the respective yields of 74, 8, and 2.5%. The structure of the former two products were determined as 3-methoxy-1-isoquinolone (10a: mp 206-207°C) and methyl 1-(cyanomethyl)-benzoate (11a: mp 46.5-47.5°C) by direct comparison with authentic samples.[9] Though no direct evidence is available, the mechanism shown in Chart 2 involving similar ring opening of 8 seems to be reasonable to account for the formation of these two products. The structure of 12 (mp 211-213°C) was determined as 1-isoquinolone by mixed melting point determination with an authentic sample.[10] Irradiation of 8 in 5% TEA-ethanol also gave 10b, 11b, and 12 in the respective yields of 71, 11, and 6%, whose ratio was almost the same with that obtained in the TEA-methanol. 3-Bromo-1-isoquinolone[8] (9) also gave the same products (10a,b, 11a,b, and 12) by irradiation in methanol or ethanol containing 5% volume of TEA, though in these cases the relative amounts of 12 increased appreciably as compared with those obtained from 8 (22% of 12 in the TEA-methanol and 28% in the TEA-ethanol). By irradiation in these alcohols in the absence of TEA, only very slow decomposition of 8 or 9 to give tarry materials is observed. This fact indicates that an ene-ketene (13) suffers decomposition as such but may revert mostly to the original isoquinolone, in the absence of efficient ketene trappers (*e.g.*, an

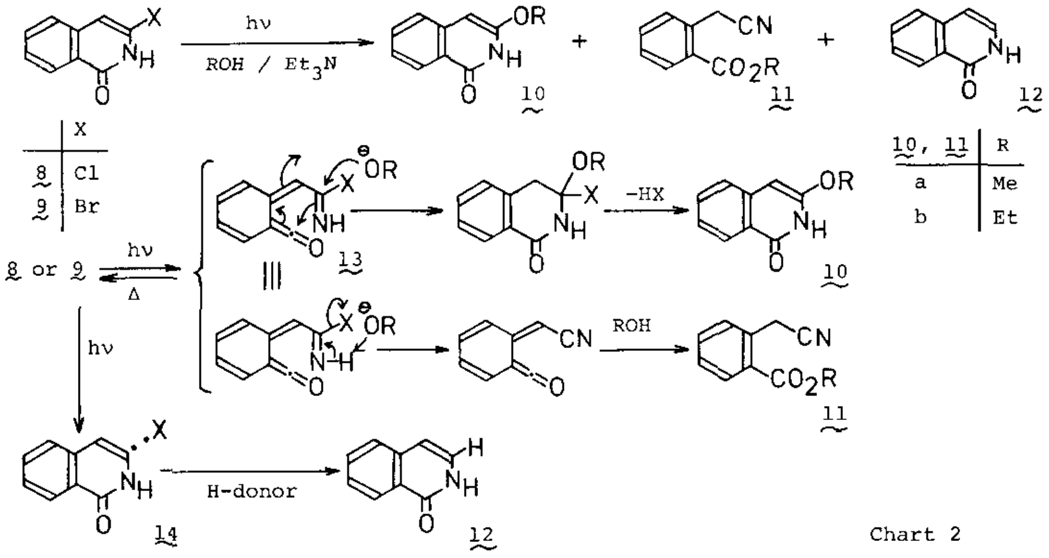

Chart 2

alkoxide ion). 1-Isoquinolone (**12**) may be derived from an abstraction of hydrogen atom from triethylamine, *via* a solvent-caged radical pair (**14**) formed by homolytic fission of the C-X bond in these 3-halo-1-isoquinolones. Increased amounts of **12** in the products obtained from **8** than from **9** fit well to the above explananation, because C-Br bond is much weaker than C-Cl bond.

The present results showed not only novel aspects of photochemical ring opening in 3-alkoxyisocoumarin, but also the same photochemical opening is also possible for 3-halocoumarin and -1-isoquinolone. Furthermore, the present finding strongly suggests that the photoarylation of 3-chloro-1-isoquinolone derivatives recently found by us[11] may proceed more readily if these are replaced by 3-bromo-1-isoquinolones. The study along this line as well as complete elucidation of complex photochemical reactions of 3-halo-1-isoquinolones is in progress.

REFERENCES AND NOTES

1. a) W.H. Pirkle and L.H. Mckendry, *J. Amer. Chem. Soc.*, 1969, **91**, 1179; b) J.P. Gunthrie, C.L. McIntosh, and P. de Mayo, *Can. J. Chem.*, 1970, **48**, 237; c) C. T. Bedford, J.M. Forrester, and T. Money, *Can. J. Chem.*, 1970, **48**, 2645; d) O.L. Chapman, C.L. McIntosh, and J. Pacansky, *J. Amer. Chem. Soc.*, 1973, **95**, 244; e) C.L. McIntosh and O.L. Chapman, *J. Amer. Chem. Soc.*, 1973, **95**, 247; f) R.G. S Pong and J.S. Shirk, *J. Amer. Chem. Soc.*, 1973, **95**, 248.
2. T. Nishio, K. Katahira, and Y. Omote, *J. Chem. Soc. Perkin I*, 1981, 943.
3. C. Kaneko, H. Fujii, and K. Kato, *Heterocycles*, 1982, **17**, 395.
4. Irradiation was carried out under argon with a Toshiba 400P high-pressure mercury lamp using a Pyrex filter.
5. J. Schnekenburger, *Arch. Pharm.*, 1965, **298**, 4.
6. The ester (**3b**) was obtained from dimethyl homophthalate (**2**) by partial hydrolysis and the ester (**4b**) from homophthalic anhydride by methanolysis.
7. W. Davies and H.G. Poole, *J. Chem. Soc.*, 1928, 1616.
8. G. Simchen and W. Krämer, *Chem. Ber.*, 1969, **102**, 3656. See also, G. Simchen, *Angew. Chem.*, 1966, **78**, 674.
9. S. Kimoto, M. Okamoto, K. Nogimori, and H. Usami, *Yakugaku Zasshi*, 1976, **96**, 154.
10. M. Ishikawa, S. Yamada, H. Hotta, and C. Kaneko, *Chem. Pharm. Bull.*, 1966, **14**, 1102.
11. C. Kaneko, T. Naito, and C. Miwa, *Chem. Pharm. Bull.*, 1982, **30**, 752.

Received, 12th August, 1982