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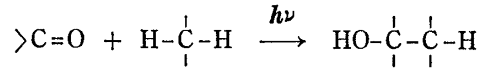
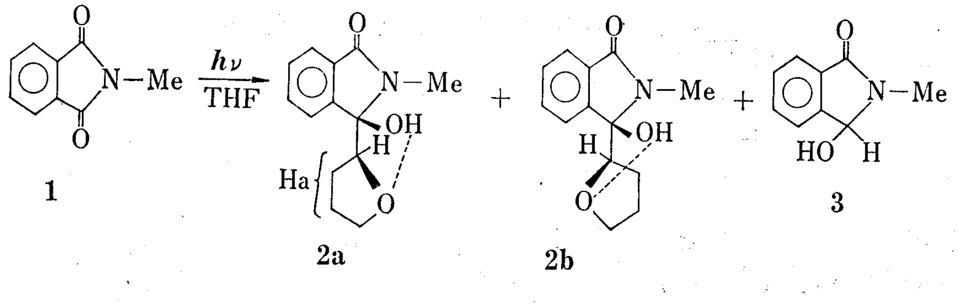
Photoaddition of Ethers and Olefins to N-Methylphthalimide[1,2]

Photoaddition reactions of carbonyl compounds bear some resemblance to aldol condensation and may be represented as in eq. (1). The methylene groups activated by an adjacent group such as double bond and oxygen atom are prone to the reactions leading to carbinols.[3] However, their synthetic value has been rather ignored perhaps because various products arise and the yields of carbinols are usually low. We have recently found that photochemical behavior of the imide carbonyl of phthalimides mainly parallels that of simple keto systems and, further, that certain N-substituted phthalimides undergo extended Norrish type II reactions.[4] As part of our systematic studies of synthetic photochemistry, the present paper reports preliminary results on such a photoaddition reaction of N-methylphthalimide (**1**), a simple model substrate.

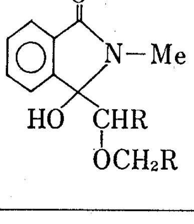


$$>C{=}O + H{-}\overset{|}{\underset{|}{C}}{-}H \xrightarrow{h\nu} HO{-}\overset{|}{\underset{|}{C}}{-}\overset{|}{\underset{|}{C}}{-}H \qquad (1)$$

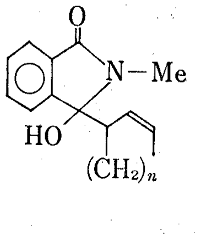
1 (10 mM solution) was irradiated with a 100 W high-pressure mercury lamp for 4—5 hr, and the reaction mixtures were purified by preparative thin-layer chromatography (TLC).[5] When tetrahydrofuran was employed as a solvent, besides the photo-reduced product (**3**, 11%) and the recovered starting material (sm) (33%), the addition products ((**2a**, mp 152—153°, 20%) and (**2b**, mp 151—152°, 19%)) were isolated as major products: Mass Spectrum *m/e*: 215 (M^+-H_2O); IR (cm^{-1}, 0.1 M $CHCl_3$), (OH) 3570—3550, free, 3300, bonded; mixed mp 122—125°. The structures of the two diastereoisomers were assigned based on the NMR of H_a (1.06 ppm, upfield due to shielding by the benzene ring) and examining their molecular models. In a similar manner, the irradiation in dioxane and diethyl ether afforded the expected addition products (**4** (16%, 69% sm) and **5** (32%, 45% sm)), respectively (approximately 1:1



1 2a 2b 3



2 : R–R=$(CH_2)_2$
4 : R–R=CH_2OCH_2
5 : R=Me



6 : $n=2$
7 : $n=3$

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[1] Photochemistry of the Phthalimide System. VIII. Part VII: Y. Sato, H. Nakai, H. Ogiwara, T. Mizoguchi, and Y. Kanaoka, in preparation.

[2] Photoinduced Reactions. XVII. For Part XVI see ref. 1).

[3] A. Schönberg, "Preparative Organic Photochemistry," Springer-Verlag, New York, 1968, p. 198.

[4] *a*) Y. Kanaoka and K. Koyama, *Tetrahedron Letters*, **1972**, 4517; *b*) Y. Kanaoka, Y. Migita, Y. Sato, and H. Nakai, *ibid.*, **1973**, 51; *c*) Y. Kanaoka, Y. Migita, K. Koyama, Y. Sato, H. Nakai, and T. Mizoguchi, *ibid.*, **1973**, 1193; *d*) Y. Sato, H. Nakai, H. Ogiwara, T. Mizoguchi, Y. Migita, and Y. Kanaoka, *ibid.*, **1973**, 4565.

[5] New compounds gave satisfactory analyses and their structures were supported by spectral (ultraviolet, infrared (IR), nuclear magnetic resonance (NMR), mass) data.

mixture of the isomers). Together with our previous finding that addition of alcohol occurs on irradiation,[4a)] it has now been established that the imide carbonyl of **1** is capable of photochemically adding the methylene (or methine) adjacent to oxygen. In contrast to the well-known corresponding reactions of ketones, none of pinacol formation has been observed.

On irradiation with a 100 W high-pressure mercury lamp (pyrex filter) for 8 hr in acetonitrile solution containing olefin such as cyclopentene and cyclohexene (2.0M), **1** (30 mM) underwent similar addition to afford carbinols (**6** (3%, 74% sm) and **7** (10%, 70% sm)). It is again worthy to note that no corresponding oxetanes have so far been isolated. In conclusion, the major photoreactions of the phthalimide system in the presence of ether, alcohol, and olefin are the carbinol formation (eq. 1). Synthetic scope and mechanism of the reactions are under investigation.

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Beta Unsubstituted Cyclopentenone, a Structural Requirement for Antimicrobial and Cytotoxic Activities[1)]

The recent report[2)] of two new antibiotics, pentenomycins I and II (I and II), which possess a beta unsubstituted cyclopentenone ring system by Umino and his co-workers[3)] prompts this communication of our work.

During the course of an investigation for the relationship between the sesquiterpene lactone structure and the antitumor/cytotoxic activity,[4)] we had also screened a series of helenalin (III) related derivatives[5)] for the antimicrobial activity according to Mitscher's method.[6)] A comparison of the values for the minimum inhibitory concentration of these compounds suggests that a beta unsubstituted cyclopentenone ring moiety such as in helenalin (III) and plenolin (IV)[7)] (Table I) contributes to the antimicrobial activity. The corresponding saturated compounds (V and VI) gave a more than 10-fold decrease in activity. The significant antimicrobial activity appears to be independent of the presence or absence of an α-methylene-γ-lactone moiety (compare compounds III with IV and V with VI). A more than 10-fold diminution in antimicrobial activity was also observed when the beta position of the cyclopentenone ring was substituted such as in deacetoxymatricarin (VII)[8)] and compound IX

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1) Previous paper in this series: Antitumor Agents VIII, K.H. Lee, S.H. Kim, C. Piantadosi, E.S. Huang and T.A. Geissman, *J. Pharm. Sci.*, in press.
2) This report came to the authors' attention after the completion of their work.
3) K. Umino, T. Furumai, N. Matsuzawa, Y. Awataguchi, Y. Ito and T. Okuda, *J. Antibiotics (Tokyo), Ser. A.*, **26**, 506 (1973).
4) K.H. Lee, *J. Pharm. Sci.*, **62**, 1028 (1973); and references cited therein.
5) Over 30 derivatives had been screened and their biological data will be discussed in detail elsewhere.
6) L.A. Mitscher, R.P. Leu, M.S. Bathala, W.N. Wu and J.L. Beal, *Lloydia*, **35**, 157 (1972).
7) K.H. Lee, T. Ibuka, A.T. McPhail, K.D. Onan, T.A. Geissman and T.G. Waddell, *Tetrahedron Letters*, **1974**, 1149.
8) T.A. Geissman, T. Stewart and M.A. Irwin, *Phytochemistry*, **6**, 901 (1967).