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SELECTIVE PHOTOSUBSTITUTION AT THE 2-POSITION OF INDOLE[1)]

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It is generally recognized that thermal, electrophilic substitution reaction on indole takes place at the 3-position;[3,4)] while either 1- or 3-position is reactive in radical reactions.[5)] In the case of photo-excited indoles, the reactions proceed less selectively; the main product is either one of 1-, 3- or 4-substituted indole as observed in reactions with acrylonitrile[6)] and methyl chloroacetate.[7)] Photo-Fries rearrangements of 1-substitutied indoles also yield the correspondingly 3-substituted indoles as the main products.[8)]

In the present experiment, indole at the ground state was allowed to react with photo-excited dibromomaleimide and the homologues. Photoinduced elimination of hydrogen bromide took place, and 2-substituted indoles were almost exclusively obtained (the product distribution > 90%)

Photo-induced reactions between N-methyl-2,3-dibromomaleimide and indole: Dioxane solutions containing N-methyl-2,3-dibromomaleimide (1) (1.0×10^{-2}M) and indole (2) (1.4×10^{-2}M) was internally irradiated with 313 and 334 nm light. The solvent was evaporated under reduced pressure, and the residue was treated with column chromatography to obtain N-methyl-2-bromo-3-(2-indolyl)maleimide (3), which was identified by the procedure described bellow. The overall yield of 3 was 21% for 1.7 hrs irradiation. The same type of product (4) was also obtained when 3-methylindole was used instead of indole (yield, 19%). The corresponding reaction, however, was not observed with 2-methylindole.

The products were identified with substituted indoles on the basis of both elemental analysis and mass spectra. In the case of 3-methylindole, the substituted position was at first examined by the aid of ^{1}H nmr. The complicated multiplet structure of the ring protons of the product clearly indicated that the substituent is not at the benzene ring but at the 2-position. Lanthanide shifts (Eu(DPM)$_3$) were also helpful in elucidating the substituted position. High-field shifts were observed of the protons at the 5-, 6- and 7-positions. The proton signal assigned to the 4-position was hardly affected. These lanthanide shifts for 4, as summarized in Fig. 1, could be reasonably explained by assuming coordination of Eu(DPM)$_3$ to the carbonyl groups of the imide substituted at the 2-position. The Proton signals of 3 were affected by Eu(DPM)$_3$ in exactly the same manner as observed of 4. Then, 3 was also suggested to be 2-substituted indole. This suggestion was finally confirmed by X-ray diffraction study of 3. The results of the X-ray analysis will be reported in an other paper.

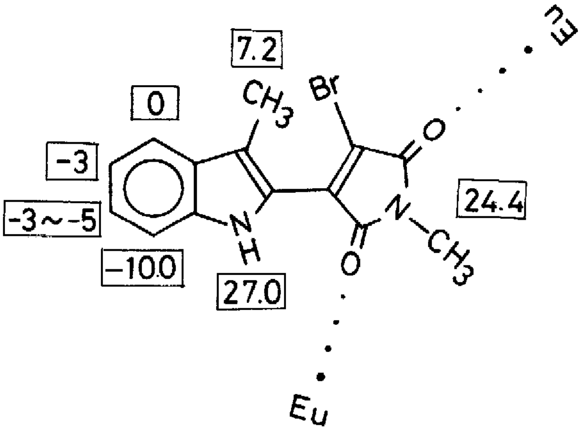


Fig. 1. Lanthanide shifts of 4 as induced by Eu(DPM)$_3$ in CDCl$_3$ (90 MHz). Molar ratio of Eu(DPM)$_3$ to 4 was 0.4. The positive values indicate lowfield shifts in Hz.

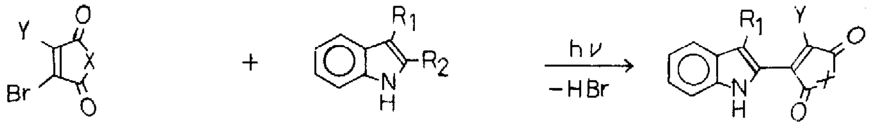
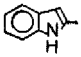
The yield of 3 is fairly dependent on the choice of solvents. The quantum yield increases on going from nonpolar to moderately polar solvents, but decreases in highly polar solvents. This solvent effect is in accordance with a mechanism where the reaction proceeds via exciplex formation.[9] Chemical modifications of the reactants also strongly affect the photoreactivity (Table 2). No reaction occured when dibromomaleic anhydride (5) was used instead of 1.

Table 1. Solvent effects on the quantum yield of the photosubstitution of 3a) under irradiation with 334 nm-light

Solvent	E_T (kcal/mol)b)	ε c)	Φ
Cyclohexane	-	2.02	0.14
Carbon tetrachloride	32.5	2.23	0.13
Diethyl ether	34.6	4.22	0.49
Dioxane	36.0	2.21	0.25
Dichloromethane	41.1	8.9	0.17
Acetonitrile	46.0	37.5	0.02

a) 10^{-2}M solutions. b) Dimroth's E_T-value.
c) Dielectric constant.

Table 2. Photosubstitution reactions between 2-bromomaleic anhydride homologues and indole derivatives

<table>
<tr><th colspan="3">2-bromomaleic anhydride homologues</th><th colspan="2">Indole derivatives</th><th colspan="2">Products</th></tr>
<tr><td colspan="7"> </td></tr>
<tr><th>Compound number</th><th>X</th><th>Y</th><th>R_1</th><th>R_2</th><th>Irradiation time (hr)</th><th>Yield (%)</th></tr>
<tr><td>1</td><td>$N-CH_3$</td><td>Br</td><td>H</td><td>H</td><td>1.7</td><td>21</td></tr>
<tr><td>1</td><td>$N-CH_3$</td><td>Br</td><td>CH_3</td><td>H</td><td>1.5</td><td>19</td></tr>
<tr><td>1</td><td>$N-CH_3$</td><td>Br</td><td>H</td><td>CH_3</td><td>6.0</td><td>0</td></tr>
<tr><td>5</td><td>O</td><td>Br</td><td>H</td><td>H</td><td>1.0</td><td>0</td></tr>
<tr><td>6</td><td>O</td><td> </td><td>H</td><td>H</td><td>1.7</td><td>17</td></tr>
<tr><td>7</td><td>$N-CH_3$</td><td> </td><td>H</td><td>H</td><td>1.0</td><td>0</td></tr>
</table>

Photosubstituted products were obtained, however, if one of the bromine atoms in **5** was replaced with an electrondonating thienyl group (compound **6**). The reactivity was also completely suppressed by the substitution of a bromine atom of 1 with a strongly electrondonating indolyl group (compound **7**). The electron affinities of the investigated maleimide homologues are expected to be in the following order: $\mathbf{5} \gg \mathbf{6} \simeq \mathbf{1} \gg \mathbf{7}$

Then it is suggested that moderately strong donor-acceptor type interaction in the exciplex is required for the photosubstitution. In other words, donor-acceptor interactions are likely to enhance the photosubstitution. If the interaction is too strong, however, radiationless transitions in the exciplex is considered to overcome the photosubstitution. The above described solvent effect is also in good agreement with this suggestion. The reason for the specific substitution at the 2-position is not clear at the present stage. Some stereochemical requirements for the exciplex might be a rate determining factor in the photosubstitution.

References and Notes

1) Contribution No. 424 from the Department of Organic Synthesis, Faculty of Engineering, Kyushu University.

2) Location: a) Hakozaki, Higashi-ku, Fukuoka 812, Japan; b) Ropponmatsu, Chuo-ku, Fukuoka 810, Japan.

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