PHOTOCHEMICAL SYNTHESIS OF INDOL[2,1-a]ISOINDOLE DERIVATIVES
BY THE CYCLIZATION OF N-(o-TOLYL)PHTHALIMIDES1,2

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On irradiation, N-(o-tolyl)phthalimides 1 possessing a variety of substituents on the benzene rings afforded indol[2,1-a]isoindole derivatives 2 (or 3) in most cases. Phthalimides with electron-donating groups on the A ring resisted to the cyclization. The photochemical behavior of 1 qualitatively parallels that of phenyl ketones.

In our exploration of the photochemistry of carbonyl derivatives, participation of an imide carbonyl in the Norrish type II reaction has been first found by observing that N-o-tolylphthalimide 1a on irradiation cyclizes to form the cyclopentanol 2a3. This finding led us to investigate a variety of synthetic possibilities of the photochemical reactions of the phthalimide system1. In the present work, we intended to examine the photocyclization of the N-o-tolylphthalimides 1 possessing various substituents on the A or B ring in the hope to provide the scope and limitation of the reaction, and to gain an insight into the fundamental photochemical behavior of the imide carbonyl group.

A series of phthalimide derivatives 1, in which either the A or B ring has a substituent, were synthesized from the corresponding phthalic anhydrides and the
In a typical experiment, a solution of $\text{Lb}$ in $t$-butanol (8 mL) was irradiated with a 1 kW high pressure (hp) mercury lamp for 2.5 hr under a nitrogen atmosphere. The expected cyclized product $2_{\text{a}}$ was obtained in 62% isolation yield accompanied by recovered $1_{\text{b}}$(13%). Likewise, those phthalimides $1_{\text{c}}$-$g$ which have a methyl, methoxyl, or chloro group on the B ring gave rise to the cyclized products $2_{\text{c}}$-$g$, respectively. Nitro derivatives $1_{\text{h},i}$, however, failed to give $2$ although the substrates were consumed on irradiation. Probably photo-lability of a nitro group led to side reactions.

In a similar fashion substituted phthalimides $1_{\text{j}-n}$ with a chloro, cyano, methoxycarbonyl or amide group on the A ring underwent the photocyclization to afford $2_{\text{j}}$ and/or $2_{\text{k}}$. The products were obtained usually as an approximately 1:1 mixture of the positional isomers which were separable after repeated TLC. In the case of $2_{\text{m}}$, for example, two isomers (mp 182-3$^\circ$; mp 214-5$^\circ$) were separated by TLC, which were converted by dehydration with acid into the indolo[2,1-a]isoindoles $3_{\text{m}}$ (mp 176-7$^\circ$; mp 222-3$^\circ$), respectively. Notably those which have an electron-donating substituent such as amino, dimethylamino and methoxyl group on the A ring resisted to the reaction to recover the starting material after the irradiation. These results are summarized in Table I$^6$.

The currently accepted mechanism for the type II reactions of phenyl ketone triplets involves hydrogen abstraction from a suitable (usually $\text{Y}$) carbon atom with a biradical as a common intermediate$^5$. From the analogy to this, intermediacy of such a biradical $4$ has been assumed also for photoreactions of the imide carbonyl.$^3,6$ The results in Table I(X=H) seem in no conflict with this assumption because the substituent $\text{Y}$ influences only the stability of the benzyl radical $4$.

On the other hand, the substituent $\text{X}$ must have a direct effect on the excited states of the imide carbonyl. It is well known that the $\pi, \pi^*$ triplets of phenyl alkyl ketones ($5$; $X=H$) lie closely above the $\pi, \pi^*$ triplets, and that the electron-donating
Table I  Photolytic Products from 1: Yields of 2 (and/or 3), %

<table>
<thead>
<tr>
<th>X=H; Y=H: g a)</th>
<th>3-Cl f a)</th>
<th>5-Cl g a)</th>
<th>4-NO₂ h a)</th>
<th>5-NO₂ i a)</th>
</tr>
</thead>
<tbody>
<tr>
<td>65(B,3,10)</td>
<td>62(B,2,5,13)</td>
<td>20(B,3,33)</td>
<td>74(B,2,5,11)</td>
<td>29(B,6,5,18)</td>
</tr>
<tr>
<td>36m) (B,3,20)</td>
<td>66m) (B,2,8)</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>X=H; Y=3-Cl: a)</th>
<th>4-Cl k c)</th>
<th>4-CN l b)</th>
<th>4-CO₂Me m b)</th>
<th>4-CONH₂ n b)</th>
</tr>
</thead>
<tbody>
<tr>
<td>35* d) (B,2,11)</td>
<td>31* (B,3,54)</td>
<td>17* (A,1,19)</td>
<td>21* (A,1,5,29)</td>
<td>17* (A,2,8)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>21* (B,1,46)</td>
<td>20* (B,2,19)</td>
<td>18* (B,1,28)</td>
</tr>
</tbody>
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<tr>
<th>3,4,5,6-Cl₄ o a)</th>
<th>4-NMe₂ p c)</th>
<th>4-NH₂ q c)</th>
<th>4-MeO r c)</th>
</tr>
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<td>22 d) (B-N,25,8)</td>
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</table>

In parenthesis are shown: solvent, time(hr), 1 recovered %. Solvent: A, acetone; B, 2-butanol; N, acetonitrile. Light sources: a) 1Kw (hp) mercury lamp; b) 400w (hp); c) 200w (hp) lamp. Yields: * a mixture of the positional isomers; d) a dehydrated product 3; m) a mixture of 2 and 3.
substituents X invert the order of the states\(^5\). All these ketones with \( \pi, \pi^* \) lowest triplets show substantially reduced reactivity in intramolecular hydrogen abstraction. The similar reasoning would explain, at least qualitatively, the behavior of \( 1p-t \) shown in Table I.

The photocyclization of \( 1a \) may be a useful synthetic reaction which proceeds under mild conditions and utilizes relatively accessible phthalimides as the substrates. In an extensive application, the methyl group in \( 1a \) can be replaced by other alkyl and alicyclic methylene groups\(^7\).

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REFERENCES

2 Photoinduced Reactions. XXII. Part XXI, see ref. 1.
4 Structural assignment of the products were supported by elemental analyses and their spectral (uv, ir, nmr, mass) data, although for \( 3t \) and \( 2k-t \) positions of the substituent on the A ring were unknown yet.
7 Y. Kanaoka, unpublished results.

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