The Photochemistry of Acyl Azides; X: Aroylnitrenes for Heterocycle Synthesis

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Abstract: Stereoselective cycloaddition of aroylnitrenes, generated by photolysis of the corresponding azides 2a,b with the racemic mixtures of cyclic enol ethers 5b and 5c was achieved with the formation of oxazolines 8. Both the chiral auxiliary attached to the aroylnitrene and the substituent in the substrate are necessary in order to selectively allow the formation of the trans-adducts 8. The cycloaddition of aroylnitrenes bearing chiral auxiliaries with ketones did not occur stereoselectively. Benzoyl azides bearing a neighbouring amide group were found to react unexpectedly by intramolecular insertion into the N–H bond.

Key words: acyl nitrenes, photolysis, enolether, ketone, chiral auxiliaries, heterocycles

Aroylnitrenes, as a type of acyl nitrene, are highly reactive and short living intermediates which can only be generated via the excited state of the corresponding precursors. The photolysis of aromatic acyl azides matches, at best, the requirements for the effective generation of aroylnitrenes. Despite their high reactivity, aroylnitrenes generated via the excited state of the corresponding azides have been shown to react selectively with π-bonds. Depending on the character of the π-bond, three- or five-membered heterocycles are formed. One drawback of the photogeneration of aroylnitrenes is the concomitant formation of ary isocyanates via the excited singlet state. Recently we have shown that the formation of isocyanates can be avoided due to the special excitation conditions of the aroyl azides, these being the sensitisation of the azide decomposition by electron transfer from excited electron donors in the triplet state, such as Michler’s ketone.

Further problems that exist are the competitive reaction of the aroylnitrene with the solvent such as cycloaddition to acetonitrile, bond insertion with alcohols or alkanes and insertion into the C–Cl bond of dichloromethane. However, suitable conditions can be found in order to achieve the desired reaction on a preparative scale.

Recently it has been shown that the diastereoselectivity of the addition of benzylnitrene towards cyclic enol ethers is controlled by the substrate. The introduction of a chiral substituent into an alkoxycarbonyl nitrene resulted in a negligible diastereomeric excess. Therefore the question arises as to the possibility of a stereoselective cycloaddition reaction of aroyl nitrenes. Aroyl nitrenes carrying chiral auxiliaries at the phenyl group may be an alternative inducing group of stereoselective addition reactions of acyl nitrenes.

Here we present results obtained with the photolysis of newly designed aroyl azides (Scheme 1) in the absence and in the presence of cyclic enol ethers and ketones, respectively, which are known to react with acyl nitrenes by the formation of five-membered heterocycles.

In order to generate aroylnitrenes bearing chiral auxiliaries, menthyl and phenylcyclohexyl substituents were appended to the corresponding azides 2 (Table 1). The o-position of the auxiliary was chosen in order to ensure its vicinity to the reaction centre. Ester groups were used as they allow the easy removal of the auxiliary. The amide group is harder to remove but may induce better stereoselectivity due to the hindered rotation around the amide bond compared to the ester bond.

The esters 2a and 2b were synthesized by the sequence (1) shown in Scheme 1; the amide 4c was prepared in an analogous manner [sequence (2) in Scheme 1]. Achiral amido substituted benzoyl azides 4a,b,d (Table 1) were also prepared via the anhydride method.

The activation energy of the thermal Curtius rearrangement is diminished by a substituent in the o-position to the azidocarbonyl group; therefore, photoreactions of the azides have to be carried out at or below 0°C.

The most important question to be answered is whether nitrenes will be formed by photolysis of the corresponding azides. It turns out that the corresponding isocyanate identified as the urethane by the addition of methanol, was the only product that could be isolated after the photolysis of 2 in acetonitrile solution. The proportion of this undesired photo-Curtius rearrangement amounts to some 40%. Products of the nitrene reaction with the solvent acetonitrile, such as oxadiazole, were not obtained. In addition amides, which are expected to be formed from aroyl nitrenes in the triplet state, were not found.

In the case of the azide 2a, it was proven that no isocyanate was formed by sensitisation of the azide decomposition using Michler’s ketone in acetonitrile solution, however, 95% of the corresponding amide was obtained.

In view of the lack of a reaction of a potential chiral aroyl nitrene with the solvent acetonitrile, the question arises as
Table 1 Aroyl Azides 2 and 4

<table>
<thead>
<tr>
<th>Product*</th>
<th>Yield (%)</th>
<th>Mp (°C)</th>
<th>$^1$H NMR (CDCl$_3$) δ, J (Hz)</th>
<th>$^1$C NMR (CDCl$_3$) δ</th>
<th>MS m/z (%)</th>
<th>IR (KBr) ν (CON$_2$) (cm$^{-1}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2a</td>
<td>53</td>
<td>62–64</td>
<td>0.81 (t, J = 7.0, 3 H, CH$_3$), 0.89 (t, J = 7.0, 3 H, CH$_3$), 0.93 (t, J = 6.6, 3 H, CH$_3$), 1.0–1.6 (m, 5 H, CH$_2$), 1.7 (m, 2 H, CH$<em>2$), 1.95 (m, 1 H, CH$<em>3$), 2.2 (m, 1 H, CH$<em>3$), 4.9 (m, 1 H, CH), 7.6 (m, 2 H$</em>{arom}$), 7.8 (m, 1 H$</em>{arom}$), 7.9 (m, 1 H$</em>{arom}$)</td>
<td>16.1 (CH$_3$), 20.8 (CH$_3$), 22.0 (CH$_3$), 23.3 (CH$_3$), 26.2 (CH$_3$), 31.4 (CH$_3$), 34.2 (CH$_3$), 40.4 (CH$_3$), 47.1 (CH), 76.0 (CH), 128.8 (CH), 128.9 (CH), 130.7 (CH), 131.7 (C), 132.2 (CH), 133.3 (C), 167.0 (C), 173.5 (C)</td>
<td>146 (100), 138 (97), 95 (80), 90 (84), 81 (88), 55 (84), 43 (52)</td>
<td>2185, 2140</td>
</tr>
<tr>
<td>2b</td>
<td>45</td>
<td>64–67</td>
<td>1.3–2.1 (m, 7 H, CH$<em>3$), 2.4 (m, 1 H, CH$<em>3$), 2.75 (m, 1 H, CH), 5.25 (m, 1 H, CH), 6.9 (m, 1 H$</em>{arom}$), 7.25 (m, 5 H$</em>{arom}$), 7.4 (m, 2 H$<em>{arom}$), 7.7 (m, 1 H$</em>{arom}$)</td>
<td>24.7 (CH$_3$), 25.8 (CH$_3$), 31.9 (CH$_3$), 33.9 (CH$_3$), 49.9 (CH), 77.7 (CH), 126.5 (CH), 127.6 (CH), 128.3 (CH), 129.0 (CH), 130.2 (CH), 130.5 (C), 132.4 (CH), 133.9 (C), 142.9 (C), 167.0 (C), 172.7 (C)</td>
<td>159 (17), 158 (100), 146 (50), 91 (83), 86 (77), 59 (56), 58 (38), 28 (99)</td>
<td>2188, 2143</td>
</tr>
<tr>
<td>4a</td>
<td>30</td>
<td>104</td>
<td>0.8–1.0 (m, 9 H, CH$<em>3$), 1.1–2.2 (m, 9 H, CH$<em>2$, CH), 4.5 (m, 1 H, CH), 5.8 (d, J = 10.0, 1 H, NH), 7.35 (m, 1 H$</em>{arom}$), 7.43 (m, 1 H$</em>{arom}$), 7.5 (m, 1 H$<em>{arom}$), 7.85 (m, 1 H$</em>{arom}$)</td>
<td>20.7 (CH$_3$), 21.1 (CH$_3$), 22.3 (CH$_3$), 25.5 (CH$_3$), 27.0 (CH), 29.7 (CH), 34.7 (CH$_3$), 39.5 (CH$_3$), 46.2 (CH), 46.8 (CH), 127.8 (CH), 129.5 (CH), 130.1 (CH), 133.0 (CH), 139.1 (C), 168.1 (C), 172.3 (C)</td>
<td>300 (2), 163 (34), 146 (100), 138 (4), 95 (12), 81 (10), 55 (16), 43 (19)</td>
<td>2150, 2134</td>
</tr>
<tr>
<td>4b</td>
<td>33</td>
<td>89–91</td>
<td>0.9–1.9 (m, 16 H, CH$<em>3$, CH$<em>2$), 2.7 (m, 1 H, CH), 3.05 (m, 1 H, CH), 7.2 (m, 1 H$</em>{arom}$), 7.4 (m, 1 H$</em>{arom}$), 7.6 (m, 1 H$<em>{arom}$), 8.0 (m, 1 H$</em>{arom}$)</td>
<td>19.8/20.1 (CH$_3$), 20.4 (CH$_3$), 25.1/25.3 (CH$_3$), 25.6 (CH$_3$), 26.6 (CH$_3$), 9.2/29.8 (CH$_3$), 30.4/30.7 (CH$_3$), 46.9/51.2 (CH), 4.7/60.0 (CH), 6.2/126.3 (CH), 127.0/127.1 (C), 128.0/128.14 (CH), 30.6 (CH), 133.7/133.85 (CH), 140.8/140.9 (C), 169.3/169.4 (C), 71.48/171.53 (C)</td>
<td>286 (1), 243 (6), 203 (3), 146 (100), 130 (62), 102 (24), 90 (45), 76 (10), 70 (10), 55 (22), 43 (25), 41 (34)</td>
<td>2171, 2137</td>
</tr>
<tr>
<td>4c</td>
<td>45</td>
<td>93–96</td>
<td>0.8–2.0 (m, 26 H, CH$<em>3$, CH$<em>2$), 3.0–3.2 (m, 3 H, CH$<em>2$, CH), 3.5 (m, 2 H, CH$<em>2$), 4.4 (m, 1H, CH), 7.2 (m, 1 H$</em>{arom}$), 7.3 (m, 1 H$</em>{arom}$), 7.4 (m, 2 H$</em>{arom}$), 7.6 (m, 2 H$</em>{arom}$), 8.0 (m, 2 H$_{arom}$)</td>
<td>14.2/16.0 (CH$_3$), 25.1 (CH$_3$), 25.6 (CH$_3$), 25.9 (CH$_3$), 30.4 (CH$_3$), 31.3 (CH$_3$), 36.4/39.7 (CH$_3$), 54.2/59.1 (CH), 126.7/127.5 (CH), 27.1/127.4 (C), 28.36/128.40 (CH), 130.5/130.6 (CH), 133.7 (CH), 139.9/140.1 (C), 169.3 (C), 170.2/171.5 (C)</td>
<td>286 (2), 243 (7), 174 (13), 146 (100), 90 (41), 55 (17), 43 (16), 41 (20)</td>
<td>2168, 2131</td>
</tr>
<tr>
<td>4d</td>
<td>39</td>
<td>oil</td>
<td>1.8–2.0 (m, 4 H, CH$<em>3$), 3.1 (t, J = 6.7, 2 H, CH$<em>3$), 3.7 (t, J = 6.7, 2 H, CH$<em>3$), 7.3 (m, 1 H$</em>{arom}$), 7.4 (m, 1 H$</em>{arom}$), 7.6 (m, 1 H$</em>{arom}$), 8.0 (m, 1 H$_{arom}$)</td>
<td>24.2 (CH$_3$), 25.5 (CH$_3$), 45.3 (CH$_3$), 48.0 (CH$_3$), 126.7 (C), 126.9 (CH), 128.6 (CH), 130.1 (CH), 134.0 (CH), 139.5 (C), 168.5 (C), 171.4 (C)</td>
<td>2170, 2136</td>
<td></td>
</tr>
</tbody>
</table>

*a Satisfactory microanalyses obtained.

b Two rotamers.

c HRMS: m/z Calcd 216.0898, found 216.0899.

to whether trapping the nitrene by electron rich alkenes such as dihydropyrans 5 will be possible. Indeed, it is only by using a large excess of the enol ether (5 M) that the reaction of the nitrene generated by the photolysis of 2a with the achiral enol ether 5a (see Scheme 2) yields the oxazoline that was characterised by the ring-opened product 7 at a low yield (Scheme 2). The asymmetric induction in the product 7 provided by the chiral auxiliary amounts to only 2%, according to $^{13}$C NMR spectra.

The trans-axial position of the substituents of 7 is concluded by the coupling constant of $J = 2.4$ Hz between the protons at C-2 and C-3 which are typical for the equatorial position of both hydrogen atoms.
The addition of aroylnitrenes to cyclic enol ethers 5b,c results in two diastereomers; in the cis-diastereomer the newly formed bonds and the substituent are situated at the same site; in the trans-diastereomer they are on opposite sites of the ring plane (Scheme 3). These two diastereomers can be differentiated by their $^{13}$C NMR spectra. C-5 and C-3a, of the trans-3a,6,7,7a-tetrahydro-5$H$-pyran[3,2-d]oxazoles resonate at about 98 ppm whilst those of the cis-diastereomer resonate at about 100 ppm.³

Scheme 3

The cycloadduct 8a was also obtained by the sensitised decomposition of 2a by Michler’s ketone using the excitation wavelength of 365 nm. In this case, the formation of the isocyanate can be avoided, but the yield of the cycloadduct amounts to only 8% because the main product is the corresponding amide.

The addition of the aroylnitrenes generated from 2 towards the carbonyl group of 9 and 11, is not hampered by the presence of the bulky auxiliary (Scheme 4). However, neither the chiral auxiliary of the azide 2a nor that of 2b induced a degree of selectivity regarding the addition of the corresponding nitrenes towards the diastereotopic faces of the ketones 9 and 11 (see Scheme 4 and Table 2).

The aroylnitrene generated from 4a was designed to provide better stereoselectivity due to the more rigid amide function, however, it turned out that only the intramolecular insertion into the neighboured N–H bond is able to occur, as displayed in Scheme 5.
## Table 2  Aroyl Nitrene Aducts

<table>
<thead>
<tr>
<th>Azide</th>
<th>Trap</th>
<th>Conc./Irrad.</th>
<th>Adduct$^a$</th>
<th>Yield (%)/de (%)</th>
<th>$^1$H NMR (CDCl$_3$), $^3$J (Hz)</th>
<th>$^1$H NMR (CDCl$_3$), $^3$J (Hz)</th>
<th>$^{13}$C NMR (CDCl$_3$)</th>
<th>HRMS (M$^+$) or MS m/z (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2a</td>
<td>5a</td>
<td>5 M/27</td>
<td>7$^a$</td>
<td>12/2</td>
<td>0.7 (d, $J$ = 6.9, 3 H, CH$_3$), 0.8 (m, 6 H, CH$_3$), 1.0–2.2 (m, 13 H, CH$_3$), 3.3 (s, 3 H, CH$_2$), 3.5 (m, 1 H, CH$_2$), 3.8 (dt, $J$ = 2.4, 11.4, 1 H, CH), 4.1 (m, 1 H, CH)$<em>2$, 4.5 (m, 1 H, CH)$<em>2$, 4.8 (dt, $J$ = 3.9, 10.6, 1 H, CH), 6.3 (m, 1 H, CH), 6.3 (m, 1 H, NH), 7.3–7.5 (m, 3 H$</em>{arom}$), 7.8 (m, 1 H$</em>{arom}$)</td>
<td>16.2 (CH$_3$), 20.7 (CH$_3$), 20.8 (CH$_3$), 22.0 (CH$_3$), 22.4/22.5 (CH$_3$), 23.3 (CH$_3$), 26.1/26.19 (CH$_3$), 31.4 (CH$_3$), 34.2 (CH$_3$), 40.6 (CH$_3$), 46.94/46.98 (CH$_3$), 47.1 (CH$_3$), 54.8 (CH$_3$)$_2$, 59.6 (CH$_3$)$_2$, 75.4/75.5 (CH$_3$)$_2$, 99.5 (CH$_3$), 127.8 (CH), 129.4 (CH), 129.6/129.7 (C), 129.9 (CH), 131.7 (CH), 138.3/138.4 (C), 165.8/165.9 (C), 168.6/168.7 (C)</td>
<td>Calcd for C$_2$H$_7$NO$_4$ + H$_2$O 418.2593 Found 418.2591</td>
<td></td>
</tr>
<tr>
<td>2a</td>
<td>5b</td>
<td>1 M/25</td>
<td>8a$^b$</td>
<td>10/11</td>
<td>0.71 (d, $J$ = 6.9, 3 H, CH$_3$), 0.72 (d, $J$ = 6.9, 3 H, CH$_3$), 0.9 (m, 12 H, CH$_3$), 1.0–2.4 (m, 26 H, CH$_2$, CH), 3.4 (s, 3 H, CH$_3$), 3.46 (s, 3 H, CH$_3$), 3.9 (m, 2 H, CH)$_2$, 4.5 (m, 2 H, CH)$<em>2$, 4.8 (dt, $J$ = 4.3, 10.9, 2 H, CH), 6.07 (d, $J$ = 7.2, 1 H, CH), 6.14 (d, $J$ = 7.2, 1 H, CH)$<em>2$, 7.3–7.5 (m, 6 H$</em>{arom}$), 7.8 (m, 2 H$</em>{arom}$)</td>
<td>16.17/16.22 (CH$_3$), 20.9 (CH$_3$)$_2$, 22.0 (CH$_3$)$_2$, 22.3 (CH$_3$)$_2$, 26.1/26.2 (CH), 27.6 (CH)$_2$, 31.4 (CH)$_2$, 34.2 (CH)$_2$, 40.6 (CH)$_2$, 47.1 (CH)$_2$, 49.3 (CH)$_2$, 55.9 (CH)$_2$, 56.2 (CH)$_2$, 75.5/75.6 (CH)$_2$, 100.2 (CH)$_2$, 101.0 (CH)$_2$, 127.9/128.0 (CH)$_2$, 129.5 (CH)$_2$, 129.6/129.7 (C), 129.8/129.88 (CH)$_2$, 131.7 (CH)$_2$, 138.1/138.2 (C)$_2$, 166.0/166.1 (C)$_2$, 168.9/168.05 (C)$_2$</td>
<td>Calcd for C$_2$H$_7$NO$_4$ 415.2359 Found 415.2347</td>
<td></td>
</tr>
<tr>
<td>2a</td>
<td>9</td>
<td>1 M/34</td>
<td>10a</td>
<td>41/-</td>
<td>0.8 (d, $J$ = 7.0, 3 H, CH$_3$), 0.9 (m, 6 H, CH$<em>3$), 1.0–2.2 (m, 9 H, CH$<em>2$, CH), 4.9 (8 (dt, $J$ = 4.4, 10.9, 1 H, CH), 7.5 (m, 2 H$</em>{arom}$), 7.7 (m, 2 H$</em>{arom}$)</td>
<td>16.2 (CH$_3$), 20.8 (CH$_3$), 22.0 (CH$_3$)$_2$, 23.4 (CH$_3$)$_2$, 24.6 (CH)$_2$, 26.2 (CH)$_2$, 31.4 (CH)$_2$, 34.2 (CH)$_2$, 34.3 (CH)$_2$, 40.7 (CH)$_2$, 47.1 (CH)$_2$, 47.6 (CH)$_2$, 117.0 (C)$_2$, 123.2 (C)$_2$, 129.2 (CH)$_2$, 130.1 (CH)$_2$, 130.8 (CH)$_2$, 131.0 (CH)$_2$, 132.7 (C)$_2$, 158.1 (C)$_2$, 166.0 (C)$_2$</td>
<td>Calcd for C$_2$H$_7$NO$_4$ 399.2410 Found 399.2410</td>
<td></td>
</tr>
<tr>
<td>2a</td>
<td>11</td>
<td>neat/41</td>
<td>12a$^b$</td>
<td>21/2</td>
<td>0.79 (d, $J$ = 6.9 Hz, 3 H, CH$_3$), 0.80 (d, $J$ = 6.9 Hz, 3 H, CH$_3$), 0.8–2.2 (m, 46 H, CH$_3$, CH$<em>2$, CH), 4.9 (m, 2 H, CH)$<em>2$, 7.5 (m, 4 H$</em>{arom}$), 7.7 (m, 4 H$</em>{arom}$)</td>
<td>7.46/7.53 (CH$_3$), 16.22/16.25 (CH$_3$), 20.8 (CH$_3$), 22.0 (CH)$_2$, 23.0 (CH)$_2$, 23.4 (CH)$_2$, 26.2 (CH)$_2$, 31.13/31.15 (CH)$_2$, 31.4 (CH)$_2$, 34.2 (CH)$_2$, 40.57/40.63 (CH)$_2$, 47.0 (CH)$_2$, 75.5/75.63 (CH)$_2$, 118.3 (C)$_2$, 122.8 (C)$_2$, 128.9/129.0 (CH)$_2$, 129.80/129.85 (CH)$_2$, 130.8 (CH)$_2$, 132.9 (C)$_2$, 157.9 (C)$_2$, 166.3 (C)$_2$</td>
<td>Calcd for C$_2$H$_7$NO$_4$ 373.2253 Found 373.2254</td>
<td></td>
</tr>
</tbody>
</table>
Even in solvents such as methanol or in neat ketones, no intermolecular reaction could be observed. This finding is surprising in so far as the intermolecular insertion of a nitrene into the N–H bond of an amide has never been observed.\(^8\) The isocyanate formed in parallel with the nitrene reacts with the tautomeric isomer of 13.

In order to block the insertion position, the tertiary amides 4b and 4c were synthesised and studied with respect to their photoproducts. However, despite the lack of N–H bonds, these nitrenes also react by intramolecular reaction at the amide group, by either substituting the alkyl group, or by rearrangement (see Scheme 5).

As usual, about 50% isocyanate was obtained by direct azide excitation (254 nm).

The single crystal structure of compound 13 (Figure, see Experimental Section) reveals the loss of the isopropyl group and the dipolar structure shown in Scheme 5 is likely to be the intermediate in the reaction sequence. Depending on the stability of the carbenium ion to be formed, elimination or rearrangement dominates, yielding either 13 or 14. To test this assumption, the azide 4d (Scheme 1) was irradiated. Indeed, the intramolecular nitrene reaction yields the hydrazide 15 (Scheme 5).
Commercially available chemicals were used as received, unless otherwise stated. Solvents were dried according to standard procedures. Column chromatography (CC) was carried out on 200 mesh silica gel (Merck). Analytical high-pressure liquid chromatography and preparative HPLC were carried out with the help of equipment provided by Fa. Knauer, Berlin; both UV- and Chiralizer-detectors were used. Columns containing Eurospher Si 100 (NP), Eurospher 100 (RP 18), Chiralcel OD, Chiralcel ODH and Chiral AGP served as stationary phases. All NMR spectra were recorded in CDCl 3 solution, unless otherwise indicated, using a Bruker DPX 300 spectrometer ( 1 H NMR, 300 MHz; 13 C NMR, 75 MHz). Mass spectra were obtained using a Concept 1H spectrometer (MSI) and a GCMS-5995-A (Hewlett-Packard).

Photolyses were carried out using homemade merry-go-round equipment fitted with low-pressure mercury lamps HNU 6 (6 W) (NARVA, Berlin) and a rayonet reactor fitted with RPR-3500 lamps (Southern N. E. Ultraviolet Co). The solutions were cooled by the use of a thermostat (Haake K20) and a cryostat (NARVA, Berlin) and a rayonet reactor fitted with RPR-3500 equipment fitted with low-pressure mercury lamps HNU 6 (6 W). Photolyses were carried out using homemade merry-go-round GCMS-5995-A (Hewlett-Packard).

1 H NMR: δ = 0.9–1.9 (m, 32 H, CH 2, CH 3), 2.7 (m, 2 H, CH), 3.05 (m, 2 H, CH), 3.7 (s, 6 H, CH 3), 7.1 (m, 1 H arom), 7.2 (m, 1 H arom), 7.35 (m, 2 H arom), 7.5 (m, 2 H arom), 8.0 (m, 2 H arom).

13 C NMR: δ = 19.1/19.2 (CH 3), 19.6/19.8 (CH 2), 24.3/24.6 (CH 2), 24.8 (CH 2), 25.8 (CH 2), 28.6/29.0 (CH 2), 29.5/30.0 (CH 2), 45.9/50.3 (CH), 51.1 (CH 3), 53.6/59.0 (CH), 125.07/125.17 (CH), 127.18/127.23 (CH), 129.87 (CH), 131.75/131.87 (CH), 125.86/125.98 (C), 139.74/139.90 (C), 165.35/165.42 (C), 168.97/169.03 (C)

The ester was hydrolyzed with KOH (1.4 g in EtOH–H 2 O) by refluxing for 2 h. After evaporation of the solvent the residue was treated with HCl to separate 3b, which was dissolved in Et 2 O and dried (MgSO 4 ). After removing the solvent under reduced pressure the oily residue (6.5 g) was dissolved in acetone (40 mL) and consecutively treated with Et 3 N (2.7 g, 22.5 mmol) in acetone (10 mL), ethyl chlorocarbonate (3.2 g, 29 mmol) in acetone (10 mL) and NaN 3 (2.3 g, 35 mmol) in NaOH (8 mL, 0.5 M) according to the general procedure.

2-[[Cyclohexyl(isopropyl)amino]carbonyl]benzoic Acid (3b, two rotamers)

A mixture of phthalic anhydride (7.2 g, 56.7 mmol) and N-cyclohexyl-N-isopropylamine (10 g, 67.6 mmol) was heated to 130–145°C for 3 h. After cooling to r.t., the mixture was dissolved in acetone (10 mL). The substituted benzoic acid crystallised from the solution; yield: 4.6 g (30%); mp 149–152°C.

1 H NMR: δ = 0.8–2.0 (m, 26 H, CH 3, CH 2), 3.0–3.2 (m, 3 H, CH 3, CH 2), 3.3–4.1 (m, 2 H, CH 3), 4.4 (m, 1 H, CH), 7.2 (m, 1 H arom), 7.3 (m, 1 H arom), 7.4 (m, 2 H arom), 7.6 (m, 2 H arom), 8.0 (m, 2 H arom), 10.7 (s, 2 H, OH)

13 C NMR: δ = 14.0/15.9 (CH 3), 25.1 (CH 2), 25.6 (CH 2), 25.7/25.9 (CH 2), 30.3 (CH 3), 30.9/31.4 (CH 2), 36.5/39.8 (CH 3), 54.3/59.1 (CH 2), 126.2/127.2 (CH), 127.1/127.3 (C), 128.3/128.4 (CH), 131.0/131.2 (CH), 132.6/132.7 (CH), 139.3/139.6 (C), 169.5/169.6 (C), 170.6/171.4 (C).

Figure X-ray crystal analysis of the compound 20
2-Substituted Benzyol Azides 2a,b and 4a–d; General Procedure
A suspension of the corresponding phthalate 1 or 3 (16.4 mmol) in acetone (20 mL) was cooled to −5 °C. A clear solution was formed by the addition of Et3N (2 g, 19.8 mmol) in acetone (8 mL). Ethyl chlorocarbonate (2.6 g, 24.1 mmol) in acetone (8 mL) was added slowly to form the insoluble mixed acid anhydride. After stirring for 30 min at −5 °C, NaNO2 (1.7 g, 26.2 mmol) in NaOH (20 mL, 0.5 M) was added dropwise and the suspension stirred for 1 h at −5 °C yielding a clear solution. The mixture was then poured onto ice and the water phase extracted with Et3O (5 × 50 mL). The combined organic layers were then dried (MgSO4) and the solvent evaporated.

Photolysis of 2a and 2b in Acetonitrile; General Procedure
Photolysis of 2a and 2b in Acetonitrile; General Procedure

**Photolysis of Azides 2a and 2b in the Presence of Nitrene Quenchers; General Procedure**

A solution of 2a or 2b, respectively, in MeCN (50 mL, 50 mmol) was irradiated at 0 °C and −10 °C, respectively, at 254 nm for 9 h until at least 95% of the azide was consumed (see Table 2).

**X-Ray Crystal Structure Analysis of 13b**

Crystal Data: C21H21NO6, O4 × 1/3 C, H2O, M = 226.32, monoclinic, C2/c no. 15, a = 28.030(3) Å, b = 16.743(3) Å, c = 18.026(4) Å, α = 90.°, β = 92.17(3)°, γ = 90.°. T = 298(2) K, λ(Mo Kα) = 0.71073 Å, V = 8543(4) Å³, Z = 24. D calc (calculated): 1.235 Mg/m³, ρ (calculated): 0.85 mm³. F(000): 3376.

**Data Collection and Reduction**: Crystal Size: 0.19 × 0.77 × 0.77 mm, 2.7–2.50°. Index ranges: 33 ≤ h ≤ 33, −19 ≤ k ≤ 19, −21 ≤ l ≤ 21. Reflections collected: 41042. Independent reflections: 7105 [R(int) = 0.056]. Absorption correction: None. Refinement method: Full-matrix least-squares on F², Data/restraints/parameters: 7105/0/ 705, Goodness-of-fit on F²: 0.924, Final R indices [I>2σ(I)]: R1 = 0.0523, wR2 = 0.1373, R indices (all data): R1 = 0.0828, wR2 = 0.1340. Largest diff. Peak and hole: 0.32 and −0.25 eÅ³. IPDS-2.75 (Stoe, 1997), Computing cell refinement: IPDS-2.75 (Stoe, 1997), Computing data reduction: IPDS-2.75 (Stoe, 1997), Computing structure solution: SHEXL-86 (Sheldrick, 1990), Computing structure refinement: SHEXL-97 (Sheldrick, 1997), Computing molecular Graphics: Diamond-2.1c (Brandenburg, 1999), Computing publication material: Platon-99 (Farrugia, 1999), Full details have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC 155600. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge, CB2 1EZ, UK.

**Photolysis of Azides 2a and 2b in the Presence of Nitrene Quenchers; General Procedure**

A solution of nitrene 2 (1.9 mmol), the appropriate cyclic enol ether (250 mmol) or ketone, 9 (250 mmol) in MeCN (50 mL) were irradiated (254 nm) at 0 °C; in the case of 2a at −10 °C and in the case of 2b until at least 95% of the azide was consumed (see Table 2). The solution was concentrated, treated with MeOH and worked up by preparative HPLC (RP18-column, CH₃CN–H₂O, 10%). Beside the urethane formed from the rearrangement product isocyanate, the adducts were separated (Table 2).

**4-Hydroxy-2-(15S,2S,5R)-2-isopropyl-5-methylcyclohexyl-1,2-dihydro-1-phthalazinone/o-(1S,2S,5R)-2-Isopropyl-5-methylcyclohexyl-1,2,3,4-tetrahydro-1,4-phthalazidine (13a)**

A solution of 4a (165 mg, 0.53 mmol) in MeCN (25 mL) was irradiated (254 nm) at −10 °C for 94 h. The precipitate consisting of the isocyanate adduct was filtered. The filtrate was treated with MeOH and concentrated. By CC (ligroin–EtOAc, 4:1) 13a (50 mg, 31%) was obtained as white solid; mp 244 °C.

**4-Hydroxy-2-(15S,2S,5R)-2-isopropyl-5-methylcyclohexyl-1,2-dihydro-1-phthalazinone/o-(1S,2S,5R)-2-Isopropyl-5-methylcyclohexyl-1,2,3,4-tetrahydro-1,4-phthalazidine (13a)**

A solution of 4a (165 mg, 0.53 mmol) in MeCN (25 mL) was irradiated (254 nm) at −10 °C for 94 h. The precipitate consisting of the isocyanate adduct was filtered. The filtrate was treated with MeOH and concentrated. By CC (ligroin–EtOAc, 4:1) 13a (50 mg, 31%) was obtained as white solid; mp 244 °C.

HC NMR: δ = 0.8–2.2 (m, 18 H, CH₃, CH₂, CH), 5.4 (m, 1 H, CH), 7.1–7.4 (br s, 1 H, OH), 7.8 (m, 2 H arom), 8.0 (m, 1 H arom), 8.5 (m, 1 H arom).

1H NMR: δ = 1.0–1.8 (m, 10 H, CH₂), 1.1 (t, J = 7.2 Hz, 3 H, CH₃), 1.1–1.3 (m, 5 H, CH₂), 1.6 (d, J = 10.9 Hz, 1 H, CH₂), 1.8 (m, 2 H, CH₂), 1.9 (m, 2 H, CH₂), 3.4 (m, 3 H, CH₂, CH), 7.8 (m, 2 H arom), 7.85 (m, 2 H arom).
Photolysis of 4d
A solution of 4d (187 mg, 0.865 mmol) in MeOH (50 mL) was irradiated (254 nm) at −10°C for 70 h. The reaction mixture containing unreacted 4d (16%) and 15 besides uncharacterised byproducts was concentrated and separated by CC (ligroin–propan-2-ol, 20%).

2-Tetrahydro-1H-1-pyrrolylisodolin-1,3-dione (15)
White solid (28 mg, 18%); mp 140–145°C.

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References
(8) Experiments carried out with benzoylnitrene and N-cyclohexyl, N-i-propylbenzamide in MeCN revealed that the amide was not attacked by the nitrene.