RADICAL $\beta$-FRAGMENTATION OF BICYCLO[3.3.0]-CARBINOLAMIDES: SYNTHESIS OF FIVE- AND EIGHT-MEMBERED CYCLIC IMIDES

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Abstract—The influence of 4-alkyl or 4-aryl substituents in the regioselectivity of the $\beta$-fragmentation of carbinolamidyl radicals generated from the corresponding carbinolamides (7-13) by irradiation with visible light in the presence of (diace-toxyiodo)benzene and iodine is described. In the case of the less hindered carbinolamides 1-hydroxyazabicyclo[3.3.0]octan-3-one (7) and 4-(2'-phenylethyl)-1-hydroxyazabicyclo[3.3.0]octan-3-one (8) important amounts of 8-membered cyclic imides were obtained together with the expected 5-membered imides (succinimides).

In a previous paper 1 we have described the radical $\beta$-fragmentation of bicyclic carbinolamides by reaction with hypervalent organoiodine reagents and iodine as a method for the synthesis of succinimides. In the case of the 1-hydroxyazabicyclo[3.3.0]octan-3-one derivatives studied the reaction promoted by $\beta$-scission of the initially generated alkoxy radicals was completely regioselective. The fragmentation occurs exclusively between C1 and C8 to give 2,2-dialkyl-substituted succinimides in good yield (Scheme 1, path [a], $R_1 = R_2 = \text{alkyl}$). Products coming from the alternative C1-C5 bond cleavage (path [b]) could not be found, only small amounts of isocyanates being formed as by-products by amidyl radical rearrangement. 2

This observed regioselectivity is in apparent contradiction with the general rule that, in the $\beta$-fragmentation of alkoxy radicals, the relative rates of bond cleavage reflect the stabilities of the final products, and in general secondary radical intermediates are formed in preference to primary ones. 3 However, it is not unprecedented in the literature, and Beckwith et al. 4 have studied a similar case during the $\beta$-fission of the 9-decalinoxyl radical. Taking these studies into account we have proposed the mechanism outlined in Scheme 1 for the radical fragmentation of carbinolamides.

The carbinolamidyl radical may undergo a fast but reversible $\beta$-fragmentation of the C1-C5 bond to give the secondary C-radical and a slower but essentially irreversible C1-C8 bond cleavage to afford the primary C-radical. The second step rate would be dependent on the efficiency of the radical trapping. In hindered carbinolamides ($R_1 = R_2 = \text{alkyl}$) $k_2$ must be greater than $k_1$, and succinimide derivatives are formed exclusively. 1
However, with less hindered carbinolamides ($R_1 = \text{and/or } R_2 = \text{H}$) we would expect an easier trapping of the secondary radical by the iodine atom directing the equilibrium to the formation of 8-membered cyclic imides. In this paper we describe the preparation of 1-hydroxy-2-azabicyclo[3.3.0]octan-3-one (7) and its 4-monosubstituted derivatives (8-13) in order to study the influence of the C-4 tether in the trapping reaction and consequently in the regioselectivity of the carbinolamidyl radical $\beta$-fragmentation.

![Scheme 1. DIB = (diacetoxyiodo)benzene](image)

Although small ring imides, in particular succinimides and glutarimides, can be easily prepared by a variety of intramolecular reactions, the method gives low yields in the case of seven-membered rings, and e.g. adipimide is preferentially prepared by oxidation of caprolactam. To our knowledge, 8-membered cyclic imides have not been previously prepared. Nevertheless, eleven- and fourteen-membered macroimides have been synthesized using different ring expansion methodology.

RESULTS AND DISCUSSION

Synthesis of Carbinolamides (7-13). Carbinolamide (7) was synthesized by alkylation of cyclopentanone lithium enolate, generated from 1-[(trimethylsilyl)oxy]-1-cyclopentene and methyllithium, in the presence of HMPA and chlorotitanium triisopropoxide, with iodoacetonitrile following the Noyori procedure. The nitrile (1) obtained was subsequently hydrolysed with 7.5% KOH in MeOH-H$_2$O to give the required carbinolamide (7) (Scheme 2).

The $\alpha,\beta$-unsaturated ketones (2-6) were prepared by aldol condensation of cyclopentanone with the corresponding aldehydes under basic conditions. Treatment of these enones with KCN in EtOH-H$_2$O-AcOH gave the corresponding carbinolamides (8-13).

In all cases only one carbinolamide was obtained, with the C-4 tether in the more stable exo position. We have found, using molecular mechanics calculations, that exo isomers are ca. 1 Kcal/mol more stable than the corresponding endo isomers. The observed coupling constants (2-4 Hz) between H-C$_4$ and H-C$_5$ for the exo isomers are in good agreement with the calculated ones over a minimized structure using the program PCMODEL (2-2.5 Hz). The calculated coupling constants between H-C$_4$ and H-C$_5$ for the endo isomers are
All products are racemates although only one enantiomer is shown in the range of 7-8 Hz.

The reaction of enone (4) with KCN/AcOH deserves special comment. In this case two isomeric carbinolamides (10) and (11) were obtained. After a $^1$H-nmr spectroscopic study these carbinolamides seem to be diastereoisomeric at C-1'. The relative stereochemistry of this carbon will be established by X-ray crystallographic analysis of imide(25)(vide infra).

**Fragmentation of Carbinolamides (7-13).** The β-fragmentations of carbinolamides (7-13) were performed by irradiation with visible light (two 100 W tungsten filament lamps) in the presence of (diacetoxyiodo)benzene and iodine using dichloromethane as solvent under the conditions summarized in Table 1.

The fragmentation of carbinolamides (7) gave a ca. equimolecular mixture of succinimide (14) and 8-membered cyclic imide (15) (Entry 1). Compound (15) shows in its ir spectrum a band at 1686 cm$^{-1}$ instead of the typical two-band system of the succinimides [e.g. 1786 (m) and 1709 (s) cm$^{-1}$ in the spectrum of 14]. The 8-membered cyclic structure of imide (15) can be established by $^1$H-nmr and $^{13}$C-nmr spectroscopy. The proton at C-3 appears at δ 4.64 as a one-proton multiplet, while the C-3 is at δ 21.68 (d, DEPT experiment). The carbon bearing the iodine atom in the succinimide structure should be more shielded (δ 5.24 (t) in the
Table 1. Fragmentation of Carbinolamides (7-13)\(^a\)

<table>
<thead>
<tr>
<th>Entry</th>
<th>Conditions</th>
<th>Reagents</th>
<th>Time</th>
<th>Temp.</th>
<th>Yields</th>
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<td></td>
<td></td>
<td>(mmol)</td>
<td>(min)</td>
<td>(°C)</td>
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<tr>
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<td>1.5/1.0</td>
<td>120</td>
<td>25</td>
<td>14 (24)</td>
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<td>1.5/1.0</td>
<td>30</td>
<td>20</td>
<td>16 (39)</td>
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<tr>
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<td></td>
<td>1.6/1.0</td>
<td>45</td>
<td>25</td>
<td>19 (59)</td>
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<td></td>
<td>1.5/1.0</td>
<td>40</td>
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<td>22 (56)</td>
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<tr>
<td>5</td>
<td></td>
<td>1.5/1.0</td>
<td>50</td>
<td>25</td>
<td>23 (61)</td>
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<tr>
<td>6</td>
<td></td>
<td>1.7/0.9</td>
<td>45</td>
<td>20</td>
<td>28 (52)</td>
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<tr>
<td>7</td>
<td></td>
<td>1.5/1.0</td>
<td>30</td>
<td>25</td>
<td>31 (64)</td>
</tr>
</tbody>
</table>

\(^a\) All reactions were performed by irradiation with two 100 W tungsten-filament lamps.
\(^b\) Mmol of (diacetoxyiodo)benzene/mmol of I\(_2\) per mmol of substrate in CH\(_2\)Cl\(_2\).
\(^c\) Yields are in parenthesis.
\(^d\) Only one isomeric iodine was obtained and the C-3 stereochemistry remains undetermined.
spectrum of 14]. A better yield but similar regioselectivity was obtained when the reaction was performed with carbinolamide (8) (Entry 2).

When the \( \beta \)-fragmentation reaction was realized with a carbinolamide possessing a bulkier substituent at C-4 9-13 (Entries 3-7) the \( \beta \)-scission occurs preferentially at the C\(_1\)-C\(_8\) bond to give the succinimide derivatives in good yield (52-64 \%). In these cases the alternative C\(_1\)-C\(_5\) bond fragmentation occurs in low yield (2-15 \%) to give a mixture of C-3 epimeric iodine derivatives.

The structure and relative stereochemistry of the 8-membered cyclic imides were determined by a single crystal X-ray analysis\(^6\) of compound (25) (Figure 1) obtained from carbinolamide (10) (Entry 4). The eight-membered ring displays a quasi-boat conformation with the C\(_2\)-C\(_3\) bond nearly parallel to the C\(_5\)-C\(_6\) linkage. The ring conformation is very similar to the boat-chair conformation of cyclooctane\(^6\) with the imide group and adjacent carbons in a plane. For a structure such as (25) the relative configuration is 2\(R^*\), 3\(S^*\), 1\(S^*\).

Consequently, the relative configuration of the macroimide (24) is 2\(R^*\), 3\(R^*\), 1\(S^*\).

![Figure 1. X-Ray structure of 25](image)

The ring conformation of 25 leads the 3\(S^*\) iodine atom into a quasi-axial position while the 2\(R^*\) substituent is in equatorial orientation. In its \(^1\)H-nmr spectrum the coupling constant between H-C\(_2\) and H-C\(_3\) is 4.1 Hz while this constant has a value of 11.4 Hz in the \(^1\)H-nmr spectrum of the C-3 epimeric compound (24). These experimental coupling constants are in good agreement with those calculated over a minimized structure (4 and 11 Hz, respectively). The assignments of the stereochemistry of the other medium cyclic C-3 epimeric pairs have been realized taking into account this difference between the H-C\(_2\) and H-C\(_3\) coupling constants.

In the fragmentation reaction of carbinolamide (13) only one 8-membered imide could be isolated in low yield (Entry 7). Due to the superimposed of the H-C\(_2\) and H-C\(_3\) signals in its \(^1\)H-nmr spectrum the stereochemistry at C-3 could not be determined.

Although the yields of macroimides are too small to be of preparative value, the formation of these compounds through some light on the mechanism of the fragmentation of carbinolamides.
EXPERIMENTAL SECTION

Melting points were determined with a Mettler FP 82 hot-stage apparatus and are uncorrected. Ir spectra were recorded on a Perkin-Elmer 1605/FTIR spectrophotometer in CHCl₃ solutions. ¹H-Nmr (200 MHz) and ¹³C-nmr (50.3 MHz) spectra were recorded on a Bruker WP 200 SY spectrometer for solutions in CDCl₃ with Me₄Si as internal standard and chemical shifts are expressed in parts per million (δ units) relative to internal reference (δ 0.00) and to the centre peak of CDCl₃ (δ 77.00), respectively. Low-resolution mass spectra were determined with Hewlett Packard 5930 A and VG Micromass ZAB-2F spectrometers and high-resolution mass spectra on a VG Micromass ZAB-2F spectrometer. Merck silica gel 0.063-0.2 mm was used for column chromatography. Circular layers of 1 mm of Merck silica gel 60 PF 254 were used on a Harrison Chromatotron for centrifugally assisted chromatography. Tlc analyses were conducted on silica gel plates and were visualized by spraying with 0.5% vanillin in H₂SO₄-EtOH (4:1) and further heating until development of color. Commercial reagents and solvents were analytical grade or were purified by standard procedures prior to use. ¹⁷(Diacetoxyiodo)benzene 98% was purchased from Aldrich.

(2-Oxocyclopentyl)acetonitrile (1). To a solution of 1-[(trimethylsilyl)oxy]-1-cyclopentene (1.95 g, 12.5 mmol), in ether (30 ml), was added dropwise a 1.6 M ethereal solution of methyllithium (8.6 ml, 1.1 equiv.) for 30 min under an argon atmosphere at room temperature. The solvent was evaporated under vacuum and dry tetrahydrofuran (100 ml) was added and the mixture was cooled to -50 °C and then hexamethylphosphoramid (22 ml, 125 mmol), chlorotitanium triisopropoxide (3 ml, 12.5 mmol), and iodoacetonitrile (4.5 ml, 62.5 mmol) were added, and the resulting solution was stirred at this temperature for 10 h. The reaction mixture was allowed to reach room temperature and then poured into water and extracted with CH₂Cl₂. The organic phase was washed with 5% HCl and H₂O, dried over Na₂SO₄, and evaporated. The residue was purified by column chromatography (hexane-EtOAc, 85:15) to give cyanide derivative (1) (600 mg, 39%): amorphous; ir νmax 2252, 1745 cm⁻¹; ¹H-nmr (200 MHz) δ 1.6-2.6 (8H, m), 2.75 (IH, m); ¹³C-nmr (50.3 MHz) δ 17.15 (t), 20.08 (t), 28.81 (t), 36.98 (t), 45.32 (d), 117.88 (s), 216.05 (s); ms m/z (rel intensity) 123 (M⁺, 49), 94 (9), 80 (10), 68 (61), 55 (100), 41 (94); hrrms Calcd for C₇H₉N0 123.06841. Found 123.06805.

Analytical data: C, 67.98; H, 7.60; N, 11.06.

General Procedure for the Synthesis of Enones (2-6). To a solution of cyclopentanone (8.4 g, 100 mmol) and aldehyde (0.5-1 equiv.) in methanol (50 ml), at 0 °C and with stirring, was added dropwise for 30 min, 0.5 M NaOH in methanol-H₂O (14:1) (60 ml). The mixture was allowed to warm up to room temperature and the stirring continued for the time stated in each case, then it was poured into water and the resulting aqueous solution acidulated with 5% HCl and extracted with dichloromethane. The organic phase was washed with saturated aqueous NaHCO₃, H₂O, dried (anhydrous Na₂SO₄), and concentrated. The crude product was purified by chromatography.

2-(3'-Phenylpropylidene)cyclopentanone (2). Cyclopentanone (18.25 g, 217 mmol) and 3-phenylpropionaldehyde (15.29 g, 114 mmol) in MeOH (50 ml) were treated with 2.7% NaOH methanolic solution (75 ml) for 1 h, and the residue in C₆H₆ (65 ml) with p-tsa (10.2 g, 54.3 mmol) according to the general method. Column chromatography of the residue (hexane-EtOAc, 9:1) gave 2 (8.4 g, 37%): amorphous; ir νmax 3075,
chromatography which was purified by column chromatography (hexane-ethyl acetate, 20:7.06) for 24 h. The residue in C6H6 (50 ml) was treated with p-tsa (10.5 g, 55.9 mmol) according to the general method. Column chromatography of the residue (hexane-ethyl acetate, 97:3) gave 4 (13.98 g, 58 %): amorphous; ir νmax 1712, 1635 cm⁻¹; 1H-nmr (200 MHz) δ 1.42 (3H, d, J = 7.0 Hz, 1'-Me), 1.93 (2H, qui, J = 7.4 Hz, 4-H2), 2.33 (2H, t, J = 8.4 Hz, 5-H2), 2.63 (2H, dt, J = 7.2, 2.6 Hz, 3-H2), 3.63 (1H, m, 2'-H), 6.67 (1H, dt, J = 9.6, 2.7 Hz, 1'-H), 7.27 (5H, m, Ar-H3); 13C-nmr (50.3 MHz) δ 19.69 (t), 21.37 (q), 26.71 (t), 38.39 (t), 40.03 (d), 126.51 (d), 126.99 (2xd), 128.64 (2xd), 135.93 (s), 139.34 (d), 144.30 (s), 207.06 (s). Anal. Calcd for C9H14O: C, 83.96; H, 10.21. Found: C, 83.47; H, 9.98.

(±)-2-(2'-Phenylpropyldiene)cyclopentanone (4). Cyclopentanone (9.94 g, 118.3 mmol) and (±)-2-phenylpropionaldehyde (16.18 g, 120.6 mmol) in methanol (50 ml) were treated with NaOH (4.2 g, 105 mmol) in methanol-H2O (15:1) (160 ml) for 2 h at 0 °C. The residue in C6H6 (50 ml) was treated with p-tsa (10.5 g, 55.9 mmol) according to the general method. Column chromatography of the residue (hexane-ethyl acetate, 97:3) gave 4 (13.98 g, 58 %): amorphous; ir νmax 3080, 3060, 1713, 1642, 1605, 1490, 1450, 1400, 1375, 1290, 1270, 1190, 1050, 1030, 830, 700 cm⁻¹; 1H-nmr (200 MHz) δ 1.42 (3H, d, J = 7.0 Hz, 1'-Me), 1.93 (2H, qui, J = 7.4 Hz, 4-H2), 2.33 (2H, t, J = 8.4 Hz, 5-H2), 2.63 (2H, dt, J = 7.2, 2.6 Hz, 3-H2), 3.63 (1H, m, 2'-H), 6.67 (1H, dt, J = 9.6, 2.7 Hz, 1'-H), 7.27 (5H, m, Ar-H3); 13C-nmr (50.3 MHz) δ 19.69 (t), 21.37 (q), 26.71 (t), 38.39 (t), 40.03 (d), 126.51 (d), 126.99 (2xd), 128.64 (2xd), 135.93 (s), 139.34 (d), 144.30 (s), 207.06 (s). Anal. Calcd for C9H14O: C, 83.96; H, 10.21. Found: C, 83.47; H, 9.98.

2-(2',2'-Diphenyldiene)cyclopentanone (5). Cyclopentanone (8.53 g, 101.4 mmol) and diphenylacetaldehyde (9.95 g, 50.7 mmol) in methanol (80 ml) were treated with NaOH (2.1 g, 52.5 mmol) in methanol-H2O (9:1) (53 ml) for 24 h. The residue in C6H6 (45 ml) was treated with p-tsa (9.5 g) and led to a crude which was purified by column chromatography (hexane-ethyl acetate, 95:5) to give 5 (7.57 g, 57 %): mp 80-81 °C (EtOAc-hexane); ir νmax 1715, 1650, 1605, 1495, 1455, 1410, 1362, 1180, 1040, 990, 910, 700 cm⁻¹; 1H-nmr (200 MHz) δ 1.95 (2H, qui, J = 7.4 Hz, 4-H2), 2.36 (2H, t, J = 7.7 Hz, 5-H2), 2.66 (2H, dt, J = 7.2, 2.6 Hz, 3-H2), 4.83 (1H, d, J = 9.9 Hz, 1'-H), 7.03 (1H, dt, J = 9.9, 2.7 Hz, 1'-H), 7.17 (10H, m, Ar-H10); 13C-nmr (50.3 MHz) δ 19.43 (t), 26.63 (t), 38.33 (t), 50.75 (d), 126.56 (2xd), 127.97 (4xd), 128.48 (4xd), 136.02 (d), 137.20 (s), 142.33 (2xs), 206.85 (s); ms m/z (rel intensity) 262 (M⁺, 100), 247 (10), 244 (7), 232 (6), 217 (6), 206 (81), 205 (51), 191 (28), 178 (13), 167 (19), 165 (43), 152 (18), 143 (21), 129 (21), 115 (24), 91 (63), 77 (13); hrmrs Calcd for C19H18O2 262.1358. Found 262.1367. Anal. Calcd for C19H18O: C, 86.99; H, 6.92. Found: C, 86.88; H, 7.15.

2-Benzylidene cyclopentanone (6). To a mixture of cyclopentanone (10.9 g, 130 mmol) and benzaldehyde (6.58 g, 62 mmol) was added a solution of NaOH (7.17 g, 179.3 mmol) in water (864 ml) for 10 h. Column chromatography of the residue gave 6 (7.46 g, 70 %): mp 69-70 °C (pentane) (lit., 69-71 °C); ir νmax 1712, 1624, 1576, 1493, 1451, 1410, 1308, 1290, 1275, 1180, 692 cm⁻¹; 1H-nmr (200 MHz) δ 2.03 (2H, qui, J = 7.4 Hz, 4-H2), 2.41 (2H, t, J = 7.7 Hz, 5-H2) 2.99 (2H, dt, J = 7.2, 2.8 Hz, 3-H2), 7.41 (6H, m, 1'-H and
Ar-H$_5$; $^{13}$C-nmr (50.3 MHz) $\delta$ 20.01 (t), 29.17 (t), 37.48 (t), 128.54 (2xd), 129.14 (d), 130.34 (2xd), 131.95 (d), 135.37 (s), 135.96 (s), 207.68 (s); ms m/z (rel intensity) 172 (M$^+$, 83), 171 (100), 157 (1), 143 (6), 129 (32), 115 (32), 102 (4), 91 (4), 89 (5), 77 (3), 71 (6); hrmr Caled for C$_{12}$H$_2$O 172.0888. Found 172.0886. 

**Anal.** Caled for C$_{12}$H$_1$NO$_2$: C, 83.69; H, 7.02. Found: C, 83.54; H, 7.06.

(±)-(1R*,SS*)-1-Hydroxy-2-azabicyclo[3.3.0]octan-3-one (7). To a solution of cyanide (1) (50 mg, 4.07 mmol) in EtOH (14 ml) was added 7.5% KOH in MeOH-H$_2$O (9:1) (40 ml, 50.8 mmol) and the resulting mixture was stirred at room temperature for 48 h. Chromatotron chromatography of the residue (EtOAc-acetone, 75:25) gave the carbinolamide (7) (320 mg, 56%): mp 138-140 °C (acetone); ir $\nu_{\text{max}}$ 3601, 3423, 1702 cm$^{-1}$; $^1$H-nmr (200 MHz) $\delta$ 1.46 (1H, m, 6-H), 1.74 (2H, m, 7-H$_2$), 1.94 (2H, dd, $J$ = 5.3, 7.8 Hz, 8-H$_2$), 2.06 (1H, dd, $J$ = 3.8, 17.8 Hz, 4-H), 2.14 (1H, m, 6-H), 2.55 (1H, m, 5-H), 2.83 (1H, dd, $J$ = 9.6, 17.8 Hz, 4-H), 5.20 (1H, m, O-H), 7.43 (1H, m, N-H); $^{13}$C-nmr (50.3 MHz) $\delta$ 24.45 (t), 33.97 (t), 37.69 (t), 39.77 (t), 45.69 (d), 98.27 (s), 177.70 (s); ms m/z (rel intensity) 141 (M$^+$, 14), 126 (4), 112 (100), 98 (36), 84 (22), 69 (16), 55 (36); hrmr Caled for C$_7$H$_{11}$NO$_2$ 141.07898. Found 141.07993. 


**General Procedure for the Synthesis of 4-Alkyl-1-hydroxy-2-azabicyclo[3.3.0]octan-3-ones (8-13).** To a solution of enone (10 mmol) in ethanol (25 ml) was added a solution of KCN (1.3 g, 20 mmol) in EtOH-water (20:1) (25 ml). To the resulting mixture was added dropwise acetic acid (0.3 ml, 5 mmol) in EtOH (15 ml) and the mixture stirred for the time and temperature stated in each case, then poured over water and extracted with CH$_2$Cl$_2$. The organic phase was washed with saturated aqueous NaHCO$_3$ and water, dried, evaporated, and the residue purified by chromatography.

(±)-(1R*,4S*,5S*)-4-(2-Phenylethyl)-1-hydroxy-2-azabicyclo[3.3.0]octan-3-one (8). Enone (2) (6 g, 30 mmol) in EtOH (150 ml) and water (7.5 ml) was allowed to react for 20 h at 45 °C with KCN (3.9 g, 60 mmol) and acetic acid (0.9 ml, 15 mmol) according to the general method. Column chromatography of the residue (hexane-EtOAc, 1:1) gave the carbinolamide (8) (3.89 g, 53%): mp 162-163 °C (EtOAc); ir $\nu_{\text{max}}$ 3585, 3400, 3080, 3060, 1680, 1585, 1490, 1450, 1300, 1290, 1180, 1080, 698 cm$^{-1}$; $^1$H-nmr (200 MHz) $\delta$ 1.4-1.9 (6H, m), 2.0-2.3 (3H, m), 2.5-2.8 (3H, m), 6.41 (1H, br s, O-H), 6.52 (1H, br s, N-H), 7.23 (5H, m, Ar-H$_5$); $^{13}$C-nmr (50.3 MHz) $\delta$ 24.73 (t), 33.52 (2xt), 33.83 (t), 40.28 (t), 49.52 (d), 52.29 (d), 96.71 (s), 125.92 (d), 128.34 (2xd), 128.45 (2xd), 141.34 (s), 179.43 (s); ms m/z (rel intensity) 245 (M$^+$, 2), 227 (4), 182 (4), 168 (5), 155 (15), 141 (100), 124 (38), 113 (19), 91 (79), 77 (16); hrmr Caled for C$_{13}$H$_{19}$NO$_2$ 245.1416. Found 245.1438. 

**Anal.** Caled for C$_{13}$H$_{19}$NO$_2$: C, 73.44; H, 7.81; N, 5.71. Found: C, 73.53; H, 7.68; N, 5.85.

(±)-(1R*,4S*,5S*)-4-Isopropyl -1-hydroxy-2-azabicyclo[3.3.0]octan-3-one (9). Enone (3) (4.83 g, 35 mmol) in EtOH (200 ml) and H$_2$O (9 ml) was treated with KCN (4.55 g, 70 mmol) and AcOH (1.05 ml, 17.5 mmol) for 30 h at 50 °C. Column chromatography of the residue (benzene-EtOAc, 65:35) gave the carbinolamide (9) (3.66 g, 57%): mp 123-124 °C (acetone-pentane); ir $\nu_{\text{max}}$ 3590, 3405, 1685 cm$^{-1}$; $^1$H-nmr (200 MHz) $\delta$ 0.90 (3H, d, $J$ = 6.8 Hz, 1'-Me), 0.98 (3H, d, $J$ = 6.8 Hz, 1'-Me), 1.4-1.95 (6H, m), 2.0-2.3 (3H, m), 2.54 (1H, m, O-H), 6.33 (1H, m, N-H); $^{13}$C-nmr 18.02 (q), 20.47 (q), 24.76 (t), 28.27 (d), 34.32 (t), 40.69 (t), 47.32 (d), 56.41 (d), 96.31 (s), 178.86 (s); ms m/s (rel intensity) 183 (M$^+$, 19), 168 (20), 165 (1), 154 (7), 140 (100), 124 (16), 122 (13), 112 (20), 99 (27), 85 (41); hrmr Caled for C$_{10}$H$_{17}$NO$_2$: 183.1259. Found 183.1255. 

**Anal.** Caled for C$_{10}$H$_{17}$NO$_2$: C, 65.54; H, 9.35; N, 7.64. Found: C, 65.39; H, 9.38; N, 7.78.
(±)-(1R*,4S*,5S*,1'S*)- and (±)-(1R*,4S*,5S*,1'R*)-4-(1-Phenylethyl)-1-hydroxy-2-azabicyclo[3.3.0]octan-3-ones (10) and (11). Enone (4) (10 g, 50 mmol) was treated as described previously at 50 °C for 12 h. Column chromatography of the residue (hexane-EtOAc, 60:40) gave the carbinolamides (10) (6.49 g, 53 %) and (11) (1.2 g, 10 %).

Compound (10): mp 122-123 °C (hexane); ir νmax 3530, 3515, 3418, 3090, 3060, 1680, 1600, 1495, 1450, 1405, 1370, 1290, 1080, 1045, 1002, 700 cm⁻¹; ¹H-nmr (200 MHz) δ 1.42 (3H, d, J = 8.0 Hz, 1'-Me), 1.35-1.75 (6H, m), 2.15 (1H, m, 5-H), 2.19 (1H, m, O-H), 2.37 (1H, dd, J = 3.2, 2.4 Hz, 4-H), 3.64 (1H, dq, J = 3.4, 7.2 Hz, 1'-H), 5.83 (1H, m, N-H), 7.32 (5H, m, Ar-H₅); ¹³C-nmr (50.3 MHz) δ 18.66 (q), 24.45 (t), 34.52 (t), 39.18 (t), 39.46 (d), 47.24 (d), 57.13 (d), 96.14 (s), 126.93 (d), 128.00 (2xd), 128.38 (2xd), 142.54 (s), 178.10 (s); ms m/z (rel intensity) 245 (M⁺, 42), 230 (3), 227 (5), 202 (10), 162 (58), 145 (17), 141 (73), 124 (23), 122 (13), 115 (17), 105 (100), 91 (27), 85 (59), 77 (34); hrms Calcd for C₁₅H₁₉N₀₂ 245.1415. Found 245.1410. Anal. Calcd for C₁₅H₁₉N₀₂: C, 73.44; H, 7.81; N, 5.71. Found: C, 73.35; H, 8.01; N, 5.66.

Compound (11): mp 142-144 °C (acetone-hexane); ir νmax 3610, 3515, 3418, 3085, 3060, 1690, 1600, 1492, 1451, 1408, 1385, 1130, 1080, 1050, 1000, 705 cm⁻¹; ¹H-nmr (200 MHz) δ 1.50 (3H, d, J = 7.0 Hz, 1'-Me), 1.2-1.9 (6H, m), 2.00 (1H, m), 2.24 (1H, dt, J = 9.3, 3.7 Hz, 5-H), 2.45 (1H, t, J = 3.8 Hz, 4-H), 3.27 (1H, dq, J = 4.0, 6.9 Hz, 1'-H), 6.25 (1H, m, O-H), 6.31 (1H, m, N-H), 7.30 (5H, m, Ar-H₅); ¹³C-nmr (50.3 MHz) δ 16.41 (q), 24.59 (t), 34.19 (t), 40.21 (d), 40.23 (t), 49.78 (d), 56.71 (d), 96.00 (s), 126.61 (d), 127.60 (2xd), 129.51 (2xd), 143.62 (s), 177.43 (s); ms m/z (rel intensity) 245 (M⁺, 56), 230 (4), 227 (6), 202 (11), 162 (100), 145 (29), 141 (47), 129 (10), 124 (17), 115 (13), 105 (85), 91 (22), 85 (37), 77 (26); hrms Calcd for C₁₅H₁₉N₀₂ 245.1415. Found 245.1409. Anal. Calcd for C₁₅H₁₉N₀₂: C, 73.44; H, 7.81; N, 5.71. Found: C, 73.48; H, 7.70; N, 5.83.

(±)-(1R*,4S*,5S*)-4-Diphenylmethyl-1-hydroxy-2-azabicyclo[3.3.0]octan-3-one (12). Compound (5) (2 g, 7.63 mmol) was treated as described above, for 24 h at 50 °C. To the residue in EtOH (50 ml) was added NaOH (0.5 g, 12.5 mmol) and the resulting solution stirred at room temperature for 24 h. Column chromatography of the residue (hexane-EtOAc, 1:1) gave the carbinolamide (12) (1.478 g, 63 %): mp 174-175.5 °C (acetone-hexane); ir νmax 3550, 3420, 1695, 1600, 1490, 1450, 1400, 1340, 1085, 1000, 975, 695 cm⁻¹;
¹H-nmr (200 MHz) δ 1.7-1.9 (5H, m), 2.3-2.6 (2H, m), 3.02 (1H, t, J = 2.4 Hz, 4-H), 4.95 (1H, d, J = 2.4 Hz, 1'-H), 6.06 (1H, m, N-H), 7.28 (10H, m, Ar-H₁₀); ¹³C-nmr (50.3 MHz) δ 24.40 (t), 34.67 (t), 39.20 (t), 47.80 (d), 50.72 (d), 54.42 (d), 96.32 (s), 126.58 (d), 127.24 (d), 128.35 (2xd), 128.46 (2xd), 128.52 (2xd), 129.56 (2xd), 141.95 (s), 142.28 (s), 178.15 (s); ms m/z (rel intensity) 307 (M⁺, 29), 289 (6), 244 (1), 224 (62), 207 (24), 178 (14), 167 (100), 165 (64), 152 (34), 128 (10), 115 (14), 91 (6), 77 (6); hrms Calcd for C₂₀H₂₁N₀₂ 307.1572. Found 307.1580. Anal. Calcd for C₂₀H₂₁N₀₂: C, 78.15; H, 6.89; N, 4.56. Found: C, 77.93; H, 7.02; N, 4.53.

(±)-(1R*,4R*,5S*)-4-Phenyl-1-hydroxy-2-azabicyclo[3.3.0]octan-3-one (13). Compound (6) (5 g, 29.1 mmol) was treated according to the procedure described for (4). Column chromatography of the residue (hexane-EtOAc, 30:70) gave the carbinolamide (13) (3.92 g, 62 %): mp 145-147 °C (hexane); ir νmax 3615, 3440, 1705, 1603, 1500, 1457, 1400, 1080, 1010, 990 cm⁻¹; ¹H-nmr (200 MHz) δ 1.6-2.0 (5H, m), 2.18 (1H, m), 2.61 (1H, dt, J = 8.8, 3.8 Hz, 5-H), 3.34 (1H, d, J = 4.5 Hz, 4-H), 4.45 (1H, m, O-H), 6.68 (1H, m, N-H), 7.25 (5H, m, Ar-H₅); ¹³C-nmr (50.3 MHz) δ 24.68 (t), 33.43 (t), 40.37 (t), 55.00 (d), 56.79 (d), 96.42 (s),...
127.07 (d), 128.09 (2xd), 128.80 (2xd), 139.69 (s), 177.47 (s); ms m/s (rel intensity) 217 (M⁺, 71), 199 (37), 174 (100), 170 (35), 156 (14), 146 (33), 117 (53), 115 (70), 103 (21), 91 (59), 77 (21); hrms Calcd for C₁₃H₁₅NO₂: 217.1103. Found 217.1103. Analyt. Calcd for C₁₃H₁₅NO₂: C, 71.87; H, 6.96; N, 6.45. Found: C, 71.95; H, 7.04; N, 6.30.

Fragmentation of 4-Alkyl-1-hydroxy-2-azabicyclo[3.3.0]octan-3-one Derivatives (7-13): General Procedure. A solution of the carbinolamide (1 mmol) in CH₂Cl₂ (20 to 50 ml dried over 3-4 Å molecular sieves, in accord with the solubility of carbinolamide), containing (diacetoxyiodo)benzene (483 mg, 1.5 mmol) and I₂ (254 mg, 1 mmol), was irradiated with 2x100 W tungsten-filament lamps for the time and temperature stated in each case. The reaction mixture was then poured into aqueous sodium thiosulfate and extracted with CH₂Cl₂, dried over Na₂SO₄, concentrated, and the residue purified by chromatotron chromatography.

Fragmentation of (±)-(1R*,5S*)-1-Hydroxy-2-azabicyclo[3.3.0]octan-3-one (7). Carbinolamide (7) (242 mg, 1.72 mmol) in CH₂Cl₂ (86 ml) under Ar was treated with (diacetoxyiodo)benzene (831 mg, 2.58 mmol) and iodine (438 mg, 1.72 mmol) as described previously at 25 °C for 2 h, to give after chromatotron chromatography (hexane-EtOAc, 70:30) (±)-2-(3'-iodopropyl)succinimide (14) (110 mg, 24%) and (±)-3-iodoperhydroazocine-2,8-dione (15) (90 mg, 20%).

Compound (14): mp 93.5-95 °C (acetone-pentane); ir νmax 3404, 1786, 1709 cm⁻¹; ¹H-nmr (200 MHz) δ 1.68 (1H, m), 1.8-2.1 (3H, m), 2.41 (1H, dd, J = 8.3, 21.6 Hz, 2-H), 2.86 (1H, m, 3-H), 2.90 (1H, dd, J = 8.9, 21.3 Hz, 2-H), 3.19 (2H, m, 3'-H₂), 9.80 (1H, m, N-H); ¹³C-nmr (50.3 MHz) δ 5.24 (t), 30.45 (t), 31.94 (t), 35.49 (t), 40.26 (d), 177.07 (s), 180.24 (s); ms m/z (rel intensity) 268 (M⁺ + 1, 6), 155 (12), 140 (100), 127 (29), 97 (20), 69 (98); hrms Calcd for C₇H₁₄NO₂: 267.98346. Found 267.98429. Analyt. Calcd for C₇H₁₀NO₂: C, 31.48; H, 3.77; N, 7.34. Found: C, 31.60; H, 3.65; N, 5.28.

Compound (15): mp 119-121 °C (acetone-pentane); ir νmax 3351, 1686 cm⁻¹; ¹H-nmr (200 MHz) δ 1.8-2.05 (2H, m, 4-H, 5-H), 2.05-2.25 (2H, m, 4-H, 5-H), 2.80 (1H, dd, J = 7.3, 10.7, 14.0 Hz, 6-H), 3.07 (1H, dd, J = 4.8, 13.6, 14.0 Hz, 6-H), 3.06 (1H, dd, J = 7.1, 14.8 Hz, 2-H), 3.71 (1H, dd, J = 10.2, 14.8 Hz, 2-H), 4.62 (1H, m, 3-H); ¹³C-nmr (50.3 MHz) δ 21.68 (d), 22.49 (t), 30.45 (t), 31.94 (t), 48.33 (t), 169.56 (s), 172.50 (s); ms m/z (rel intensity) 267 (M⁺, 13), 140 (31), 127 (35), 122 (6), 112 (11), 98 (79), 97 (75), 69 (100); hrms Calcd for C₇H₁₄NO₂: 266.97563. Found 266.97585. Analyt. Calcd for C₇H₁₀NO₂: C, 31.48; H, 3.77; N, 5.24. Found: C, 31.51; H, 3.86; N, 5.12.

Fragmentation of (±)-(1R*,4S*,5S*)-4-(2'-Phenylethyl)-1-hydroxy-2-azabicyclo[3.3.0]octan-3-one (8). A solution of carbinolamide (8) (0.5 g, 2.04 mmol), (diacetoxyiodo)benzene (985 mg, 3.06 mmol) and iodine (518 mg, 2.04 mmol) in CH₂Cl₂ (50 ml) was allowed to react according to the general method. After 30 min at 20 °C and usual work-up, the residue gave, after column chromatography (hexane-EtOAc, 90:10), (±)-(2R*,3R*)-2-(2'-phenylethyl)-3-iodoperhydroazocine-2,8-dione (17) (242 mg, 32 %) and a polar fraction which was separated by fractional crystallization from EtOAc to give (±)-(25S*,35*)-2-(2'-phenylethyl)-3-(3'-iodopropyl)succinimide (16) (295 mg, 39 %) and (±)-(2R*,3S*)-2-(2'-phenylethyl)-3-iodoperhydroazocine-2,8-dione (18) (68 mg, 9 %).

Compound (16): mp 95-96 °C (EtOAc); ir νmax 3395, 3087, 3060, 1770, 1720, 1705, 1595, 1487, 1445, 1340, 1170, 695 cm⁻¹; ¹H-nmr (200 MHz) δ 1.6-2.1 (5H, m), 2.1-2.3 (1H, m), 2.54 (2H, m, 2-H, 3-H), 2.80 (2H, t, J = 7.8 Hz, 2'-H₂), 3.17 (2H, t, J = 6.3 Hz, 3'-H₂), 7.23 (5H, m, Ar-H₅), 8.93 (1H, m, N-H); ¹³C-nmr...
(20.1 MHz) δ 5.35 (t), 29.91 (t), 31.58 (t), 32.30 (t), 32.52 (t), 45.78 (d), 46.05 (d), 126.05 (d), 128.13 (2xd), 128.32 (2xd), 140.22 (s), 179.25 (s), 179.40 (s); ms m/z (rel intensity) 371 (M⁺, 4), 267 (40), 244 (46), 140 (100), 123 (13), 112 (33), 105 (23), 98 (39), 91 (97), 77 (14); hrms Calcd for C₁₅H₁₈NO₂: 371.0384. Found 371.0338. Anal. Calcd for C₁₅H₁₈NO₂: C, 48.53; H, 4.89; N, 3.77. Found: C, 48.57; H, 4.75; N, 3.83.

Compound (17): mp 133-135 °C (pentane); ir νmax 3335, 3080, 3055, 1685, 1595, 1485, 1400, 1350, 1320, 1250, 1155, 1140, 700 cm⁻¹; ¹H-nmr (200 MHz) δ 1.6-2.9 (10H, m), 3.27 (1H, dt, J = 9.9, 2.7 Hz, 2-H), 4.22 (1H, dt, J = 10.8, 1.7 Hz, 3-H), 7.24 (5H, m, Ar-H₅); ¹³C-nmr (50.3 MHz) δ: 23.39 (t), 33.13 (t), 33.36 (t), 33.89 (q), 34.27 (t), 35.16 (t), 53.61 (d), 126.27 (d), 128.42 (2xd), 128.54 (2xd), 140.56 (s), 170.34 (s), 172.33 (s); ms m/z (rel intensity) 371 (M⁺, 6), 244 (13), 227 (1), 216 (2), 199 (3), 181 (5), 171 (3), 155 (3), 140 (100), 123 (72), 117 (45), 112 (55), 105 (16), 104 (29), 95 (46), 91 (98), 77 (32); hrms Calcd for C₁₅H₁₈NO₂: 371.0384. Found 371.0377. Anal. Calcd for C₁₅H₁₈NO₂: C, 48.53; H, 4.89; N, 3.77. Found: C, 48.72; H, 4.63; N, 3.79.

Fragmentation of (±)-(1R*,4S*,5S*)-4-(1'-Methylthyl)-1-hydroxy-2-azabicyclo[3.3.0]octan-3-one (9). Carbinolamide (9) (410 mg, 2.24 mmol) in CH₂Cl₂ (75 ml) was irradiated in the presence of (dioxacyclo-iodo)benzene (1.15 g, 3.58 mmol) and I₂ (0.57 g, 2.24 mmol) for 45 min at 25 °C as described previously to give, after chromatography (hexane-EtOAc; 85:15), (±)-(25*,35*)-2-(1'-isopropyl)-3-(3'-iodopropyl)-succinimide (19) (408 mg, 59 %), (±)-(2R*,3R*)-(2-(1'-isopropyl)-3-ido-perhydroazocine-2,8-dione (20) (14 mg, 2 %), and (±)-(2R*,3S*)-2-(1'-isopropyl)-3-ido-perhydroazocine-2,8-dione (21) (45 mg, 6.5 %).

Compound (19): amorphous; ir νmax 3395, 1775, 1725, 1700, 1460, 1170 cm⁻¹; ¹H-nmr (200 MHz) δ 0.98 (3H, d, J = 7.0 Hz, 1'-Me), 1.04 (3H, d, J = 7.0 Hz, 1'-Me), 1.7-2.1 (4H, m, 1''-H₂, 2''-H₂), 2.25 (1H, m, 1''-H), 2.47 (1H, t, J = 4.2 Hz, 2-H), 2.59 (1H, dt, J = 4.2, 6.7 Hz, 3-H), 3.20 (2H, t, J = 6.4 Hz, 3''-H₂), 9.18 (1H, m, N-H); ¹³C-nmr (50.3 MHz) δ 5.81 (t), 18.12 (q), 19.59 (q), 28.99 (d), 30.05 (t), 32.60 (t), 42.11 (d), 52.76 (d), 179.57 (s), 180.18 (s); ms m/z (rel intensity) 309 (M⁺, 1), 294 (1), 266 (2), 237 (1), 223 (1), 194 (2), 182 (100), 155 (6), 140 (9), 127 (6), 111 (30); hrms Calcd for C₁₀H₁₆NO₂: 309.0228. Found 399.09228. Anal. Calcd for C₁₀H₁₆NO₂: C, 38.85; H, 5.22; N, 4.53. Found: C, 38.98; H, 5.36; N, 4.32.

Compound (20): mp 144-146 °C (hexane); ir νmax 3340, 1690, 1455, 1445, 1360, 1295, 1146 cm⁻¹; ¹H-nmr (200 MHz) δ 1.08 (3H, d, J = 7.0 Hz, 1'-Me), 1.16 (3H, d, J = 7.0 Hz, 1'-Me), 1.7-2.1 (2H, m, 4-H, 5-H), 2.15-2.4 (3H, m, 1'-H, 4-H, 5-H), 2.76 (1H, dd, J = 6.1, 13.5 Hz, 6-H), 3.16 (1H, dd, J = 6.7, 14.0 Hz, 6-H), 3.34 (1H, dd, J = 11.6, 4.0 Hz, 2-H), 4.51 (1H, d, J = 11.5 Hz, 3-H), 8.02 (1H, m, N-H); ¹³C-nmr (50.3 MHz) δ 15.47 (q), 20.81 (q), 23.49 (t), 31.51 (d), 31.86 (d), 33.51 (t), 35.53 (t), 57.00 (d), 170.52 (s), 172.34 (s); ms m/z (rel intensity) 309 (M⁺, 5), 214 (3), 182 (100), 165 (66), 154 (18), 137 (46), 127 (14), 123 (11), 109 (25), 98 (30), 95 (56); hrms Calcd for C₁₀H₁₆NO₂: 309.0228. Found 309.0200. Anal. Calcd for:
C_{10}H_{16}NO_2I: C, 38.85; H, 5.22; N, 4.52. Found: C, 38.89; H, 5.19; N, 4.41.

Compound (21): mp 167-169 °C (acetone-hexane); ir v_{max} 3330, 1690, 1600, 1455, 1375, 1360, 1280, 1160, 1110 cm⁻¹; \(^{1}^H\)-nmr (200 MHz) δ 0.98 (3H, d, J = 6.4 Hz, 1'-Me), 1.01 (3H, d, J = 6.5 Hz, 1'-Me), 1.7-2.1 (3H, m, 4-H, 5-H2), 2.25 (1H, m, 1'-H), 2.33 (1H, dd, J_{2,1} = 8.9, J_{2,3} = 4.1 Hz, 2-H), 2.67 (1H, dq, J = 4.6, 15.1 Hz, 4-H), 2.93 (1H, dd, J = 8.3, 14.5 Hz, 6-H), 3.07 (1H, dd, J = 8.8, 11.7 Hz, 6-H), 4.32 (1H, dt, J = 4.7, 12.6 Hz, 3-H), 8.28 (1H, m, N-H); \(^{13}C\)-nmr (50.3 MHz) δ 18.89 (q), 21.40 (q), 24.59 (t), 30.56 (d), 32.20 (d), 36.68 (t), 38.06 (t), 55.29 (d), 170.13 (s), 171.55 (s); ms m/z (rel intensity) 309 (M⁺, 28), 266 (1), 182 (100), 165 (60), 154 (46), 139 (19), 137 (48), 127 (36), 123 (15), 109 (38), 98 (43), 95 (98); hrmrs Calcd for C_{10}H_{16}NO_2I 309.0228. Found 309.0237. Anal. Calcd for C_{10}H_{16}NO_2I: C, 38.85; H, 5.22; N, 4.52. Found: C, 38.76; H, 5.17; N, 4.58.

Fragmentation of (±)-(1R*,4S*,5S*,1'S*)-4-(1'-Phenylethyl)-1-hydroxy-2-azabicyclo[3.3.0]octan-3-one (10). Carbinolamide (10) (2.02 g, 8.24 mmol) in CH₂Cl₂ (162 ml) was irradiated in the presence of (diacetoxyiodo)benzene (4 g, 12.4 mmol) and I₂ (2.1 g, 8.24 mmol) as above for 40 min at 25 °C to give, after chromatography (hexane-EtOAc, 95:5), (±)-(2S*,3S*,1'S*)-(2-(1'-phenylethyl)-3-(3'-iodopropyl)succinimide (22) (1.71 g, 55.9 %), (±)-(2R*,3R*,1'S*)-2-(1'-phenylethyl)-3-iodoperhydroazocine-2,8-dione (24) (60 mg, 2 %), and (±)-(2R*,3S*,1'S*)-2-(1'-phenylethyl)-3-iodoperhydroazocine-2,8-dione (25) (93 mg, 3 %).

Compound (22): mp 86-88 °C (acetone); ir v_{max} 3410, 3070, 1780, 1725, 1065, 1455, 1350, 1180, 705 cm⁻¹; \(^{1}^H\)-nmr (200 MHz) δ 1.51 (3H, d, J = 7.0 Hz, 1'-Me), 1.6-1.9 (4H, m), 2.55 (1H, dt, J = 3.9, 6.5 Hz, 3-H), 2.71 (1H, dd, J = 3.4, 7.0 Hz, 2-H), 3.06 (2H, dt, J = 2.7, 6.3 Hz, 3'-H2), 3.34 (1H, dq, J = 7.0, 6.6 Hz, 1'-H), 7.27 (5H, m, Ar-Hs), 8.23 (1H, m, N-H); \(^{1}^H\)-nmr (200 MHz, C₆D₆) δ 1.19 (3H, d, J = 7.7 Hz, 1'-Me), 1.1-1.4 (4H, m), 2.15 (2H, m, 2-H, 3-H), 2.45 (2H, dt, J = 1.2, 6.6 Hz, 3'-H2), 2.85 (1H, qui, J = 6.9 Hz, 1'-H), 7.0 (6H, m, N-H, Ar-Hs); \(^{13}C\)-nmr (50.3 MHz) δ 5.49 (t), 18.63 (q), 29.48 (t), 31.84 (t), 40.16 (d), 43.22 (d), 52.70 (d), 126.70 (d), 127.24 (2xd), 128.16 (2xd), 141.33 (s), 178.40 (s), 179.10 (s); ms m/z (rel intensity) 372 (M⁺+1, 7), 244 (44), 173 (3), 145 (5), 140 (6), 128 (7), 117 (7), 105 (100), 91 (14), 77 (21); hrmrs Calcd for C_{15}H_{19}NO_{2}I 372.0464. Found 372.0458. Anal. Calcd for C_{15}H_{19}NO_{2}I: C, 48.53; H, 4.89; N, 3.77. Found: C, 48.71; H, 4.75; N, 3.69.

Compound (24): mp 148.5-149 °C (EtOAc-hexane); ir v_{max} 3330, 3100, 3080, 1690, 1600, 1490, 1460, 1405, 1360, 1340, 1285, 1140, 700 cm⁻¹; \(^{1}^H\)-nmr (200 MHz) δ 1.57 (3H, d, J = 7.0 Hz, 1'-Me), 1.7-2.3 (4H, m), 2.69 (1H, dd, J = 6.0, 13.2, 6-H), 3.07 (1H, dt, J = 6.5, 13.8 Hz, 6-H), 3.51 (1H, dq, J = 4.3, 7.2 Hz, 1'-H), 3.66 (1H, dd, J = 4.3, 11.4 Hz, 2-H), 4.57 (1H, dm, J = 11.5 Hz, 3-H), 7.23 (5H, m, Ar-Hs), 7.77 (1H, m, N-H); \(^{13}C\)-nmr (50.3 MHz) δ 13.18 (q), 23.56 (t), 31.80 (d), 33.57 (t), 35.51 (t), 42.34 (d), 58.62 (d), 128.60 (d), 128.04 (2xd), 128.47 (2xd), 143.36 (s), 170.07 (s), 171.87 (s); ms m/z (rel intensity) 371 (M⁺, 40), 244 (77), 227 (28), 216 (21), 199 (22), 181 (13), 145 (22), 129 (31), 117 (17), 115 (18), 105 (100), 91 (28), 77 (23); hrmrs Calcd for C_{15}H_{19}NO_{2}I 371.0384. Found 371.0389. Anal. Calcd for C_{15}H_{19}NO_{2}I: C, 48.53; H, 4.89; N, 3.77. Found: C, 48.37; H, 5.03; N, 3.79.

Compound (25): ir v_{max} 3340, 3080, 3060, 1704, 1694, 1600, 1490, 1460, 1440, 1400, 1380, 1370, 1360, 1270, 1160, 1070, 1015, 702 cm⁻¹; \(^{1}^H\)-nmr (200 MHz) δ 1.33 (3H, d, J = 6.7 Hz, 1'-Me), 1.60 (1H, m), 1.90 (1H, m), 2.20 (1H, m), 2.45 (1H, m), 2.96 (1H, dd, J = 9.0, 14.5 Hz, 6-H), 3.06 (1H, dd, J = 4.1, 9.7 Hz, 2-H), 3.13 (1H, m, 6-H), 3.32 (1H, dq, J = 9.7, 6.6 Hz, 1'-H), 3.69 (1H, ddd, J = 4.1, 5.9, 13.4 Hz, 3-H), 7.32
(5H, m, Ar-Hs), 8.24 (1H, m, N-H); 13C-nmr (50.3 MHz) δ 21.32 (q), 24.12 (t), 31.43 (d), 36.84 (t), 37.97 (t), 43.14 (d), 53.95 (d), 127.16 (d), 127.85 (2xd), 128.99 (2xd), 142.44 (s), 169.65 (s), 171.48 (s); ms m/z (rel intensity) 371 (M+, 44), 244 (25), 227 (25), 216 (24), 199 (29), 183 (22), 157 (21), 145 (41), 129 (44), 115 (23), 105 (100), 91 (35), 77 (30); h rms Calcd for C15H18NO2I 371.0384. Found. 371.0381. Anal. Calcd for C15H18NO2I: C, 48.53; H, 4.89; N, 3.77. Found: C, 48.67; H, 4.75; N, 3.83. X-ray analysis: C15H18NO2I, orthorhombic, space group P21/c, Z = 4, a = 17.508(3), b = 7.192, c = 11.931 Å; β = 95.01 (5)°. Crystal size: 0.2x0.3x0.05 mm. The data were measured on a Philips PW-1100 four-circle automatic diffractometer operating with Cu-Kα radiation (λ = 1.5418 Å) monochromated by graphite. The orientation matrix of the crystal was calculated from the angular setting of 25 randomly distributed reflections found in the range 10°<θ<25°.

The structure was solved by means of direct methods and refined with isotropic factors. Owing to the small size of the crystal and the small number of reflections above the 2σ background level, only the iodine atom was refined anisotropically. Most of the hydrogen atoms (64 % of the total) were located on successive Fourier-difference maps, and introduced with a fixed isotropic thermal factor equal to that of the bonded carbon. The others were imposed at their theoretical places. An important decomposition was found during the data collection and the crystal life-time is about 10 min, the crystal turning brown upon I2 release. Only one crystal was used in the data collection. A very high-speed recording technique was adopted: no background measurements during the data collection. A very high-speed recording technique was adopted: no background measurements during the data collection and a 15 sec scanning time per reflection. The background was a extrapolated curve of stationary counts (time = 30 s) obtained at different θ angles. The intensities, measured up to θ = 65°, were merged and averaged after scaling as usual with an overall Rsymm = 7.6 % for 2321 measured reflections. They were reduced to F structural factors by means of standard Lorentz and polarization corrections and considered as observed above the 2σ background level. The unique data set contains 1394 reflections of which 828 are above the 2σ background level.

Fragmentation of (±)-(1R*,4S*,5S*,1'R*)-4-(1'-Phenylethyl)-1-hydroxy-2-azabicyclo[3.3.0]octan-3-one (11). Carbinolamide (11) (0.6 g, 2.45 mmol) in CH2Cl2 (60 ml) was irradiated in the presence of (diacetoxyido)benzene (1.18 g, 3.7 mmol) and I2 (0.62 g, 2.45 mmol) as above, at 25 °C for 50 min, to give, after chromatography (hexane-EtOAc, 90:10), (±)-(2S*,3S*,1'R*)-2-(1'-phenylethyl)-3-(3"-iodopropyl)succinimide (23) (554 mg, 61 %), (±)-(2R*,3R*,1'R*)-2-(1'-phenylethyl)-3-iodoperhydroazocine-2,8-dione (26) (27 mg, 3 %), and (±)-(2R*,3S*,1'R*)-2-(1'-phenylethyl)-3-iodoperhydroazocine-2,8-dione (27) (91 mg, 10 %).

Compound (23): mp 100-101 °C (acetone-hexane); ir νmax 3395, 1775, 1720, 1600, 1450, 1355, 1345, 1170, 650 cm⁻1; 1H-nmr (200 MHz) δ 1.36 (3H, d, J = 7.2 Hz, 1'-Me), 1.3-1.6 (4H, m), 2.59 (1H, dt, J = 4.3, 5.7 Hz, 3-H), 2.81 (1H, dd, J = 4.2, 4.2 Hz, 2-H), 2.93 (2H, t, J = 6.3 Hz, 3"-H2), 3.55 (1H, dq, J = 7.2, 4.2 Hz, 1'-H), 7.31 (5H, m, Ar-Hs), 8.29 (1H, m, N-H); 13C-nmr (200 MHz, C6D6) δ 1.12 (3H, d, J = 7.2 Hz, 1'-Me), 0.9-1.3 (4H, m), 2.33 (1H, m, 3-H), 2.4-2.7 (3H, m, 2-H and 3"-H2), 3.37 (1H, m, 1'-H), 7.04 (5H, m, Ar-Hs), 9.50 (1H, m, N-H); 13C-nmr (50.3 MHz) δ 5.22 (t), 14.14 (q), 29.69 (t), 32.14 (t), 38.61 (d), 41.59 (d), 53.80 (d), 127.25 (3xd), 128.80 (2xd), 141.70 (s), 178.60 (s), 179.67 (s); ms m/z (rel intensity) 371 (M+, 10), 244 (94), 216 (2), 173 (5), 145 (18), 129 (7), 117 (8), 105 (100), 91 (13), 77 (17); h rms Calcd for C15H18NO2I 371.0384. Found. 371.0391. Anal. Calcd for C15H18NO2I: C, 48.53; H, 4.89; N, 3.77. Found: C, 48.71; H, 4.93; N, 3.65.
Compound (26): amorphous; ir νmax 3340, 1690, 1600, 1450, 1400, 1340, 1265, 1150, 1125, 905, 650 cm⁻¹; ¹H-nmr (200 MHz) δ 1.49 (3H, d, J = 7.0 Hz, 1'-Me), 1.7 (1H, m), 1.9-2.15 (2H, m), 2.3 (1H, m), 2.76 (1H, dm, J = 14.6 Hz, 6-H), 3.20 (1H, dt, J = 5.9, 14.3 Hz, 6-H), 3.59 (1H, dq, J = 5.7, 7.0 Hz, 1'-H), 3.63 (1H, dd, J = 5.7, 15.8 Hz, 2-H), 4.16 (1H, m, 3-H), 7.31 (3H, m, Ar-H₃), 7.63 (2H, m, Ar-H₂), 7.87 (1H, m, N-H); ¹³C-nmr (50.3 MHz) δ 19.97 (q), 24.82 (t), 32.20 (d), 33.23 (t), 35.04 (t), 41.50 (d), 59.16 (d), 127.01 (d), 128.00 (2xd), 129.70 (2xd), 141.31 (s), 170.19 (s), 172.31 (s); ms m/z (rel intensity) 371 (M⁺, 30), 244 (71), 227 (21), 216 (20), 199 (20), 171 (10), 157 (12), 145 (24), 129 (33), 115 (19), 105 (100), 91 (32), 77 (26); hrmrs Caled for C₁₅H₁₈NO₂I 371.0384. Found 371.0379. Anal. Caled for C₁₅H₁₈NO₂I: C, 48.53; H, 4.89; N, 3.77. Found: C, 48.73; H, 4.95; N, 3.50.

Compound (27): mp 194.5-196 °C (acetone-hexane); ir νmax 3340, 1700, 1600, 1360, 1330, 1280, 1160 cm⁻¹; ¹H-nmr (200 MHz) δ 1.29 (3H, d, J = 7.0 Hz, 1'-Me), 1.8-2.1 (2H, m), 2.3 (1H, m), 2.75 (1H, m), 2.75-3.2 (3H, m), 3.33 (1H, dd, J = 9.8, 7.1 Hz, 1'-H), 4.46 (1H, dt, J = 4.4, 12.5 Hz, 3-H), 7.25 (5H, m, Ar-H₅), 7.86 (1H, m, N-H); ¹³C-nmr (50.3 MHz) δ 19.14 (q), 24.71 (t), 30.11 (d), 36.80 (t), 38.17 (t), 43.45 (d), 54.12 (d), 126.73 (d), 127.59 (2xd), 128.71 (2xd), 144.47 (s), 168.86 (s), 171.07 (s); ms m/z (rel intensity) 371 (M⁺, 75), 244 (23), 226 (27), 216 (26), 199 (13), 183 (10), 171 (7), 157 (12), 145 (45), 131 (10), 129 (29), 115 (18), 105 (100), 91(30), 77(32); hrmrs Caled for C₁₅H₁₈NO₂I 371.0384. Found 371.0387. Anal. Caled for C₁₅H₁₈NO₂I: C, 48.53; H, 4.89; N, 3.77. Found: C, 48.64; H, 4.87; N, 3.50.

Fragmentation of (±)-(1R*,4R*,5S*)-4-Diphenylmethyl-1-hydroxy-2-azabicyclo[3.3.0]octan-3-one (12). Carbinolamide (12) (225 mg, 0.73 mmol) in CH₂Cl₂ (35 ml) was irradiated for 45 min at 25 °C as described previously to give, after chromatography (hexane-EtOAc, 98:2), (±)-(2S*,3S*)-2-diphenylmethyl-1-iodo-3-indolpropyloctahydrooxacine-2,8-dione (29) (22 mg, 7 %), and (±)-(2R*,3E*)-2-diphenylmethyl-1-iodoactazocine-2,8-dione (30) (26 mg, 8 %).

Compound (28): mp 124.5-126 °C (acetone-hexane); ir νmax 3398, 1782, 1727, 1601, 1500, 1453, 1345, 1170 cm⁻¹; ¹H-nmr (200 MHz) δ 1.7-1.8 (4H, m), 2.75 (1H, dt, J = 6.1, 3.8 Hz, 3-H), 3.05 (2H, m, 3'-H₂), 3.38 (1H, dd, J = 3.8, 7.0 Hz, 2-H), 4.43 (1H, d, J = 7.0 Hz, 1'-H), 7.31 (10H, m, Ar-H₁₀), 8.09 (1H, m, N-H); ¹³C-nmr (50.3 MHz) δ 5.41 (t), 29.68 (t), 32.40 (t), 44.61 (d), 51.31 (d), 52.58 (d), 127.16 (d), 127.33 (d), 128.28 (2xd), 128.55 (2xd), 128.66 (2xd), 128.82 (2xd), 140.21 (s), 140.56 (s), 177.49 (s), 178.78 (s); ms m/z (rel intensity) 433 (M⁺, 9), 306 (3), 278 (1), 207 (9), 167 (100), 152 (10), 128 (3), 115 (6), 91 (4), 77 (3); hrmrs Caled for C₂₀H₂₀N₂O₂ 433.0539. Found 433.0556. Anal. Caled for C₂₀H₂₀N₂O₂: C, 55.44; H, 4.65; N, 3.23. Found: C, 55.23; H, 4.73; N, 3.25.

Compound (29): mp 193-195 °C (acetone); ir νmax 3350, 1710, 1600, 1490, 1450, 1405, 1355, 1325, 1290, 1260, 1140, 695 cm⁻¹; ¹H-nmr (200 MHz) δ 1.85 (1H, m), 2.0-2.4 (3H, m), 2.80 (1H, dm, J = 14.7 Hz, 6-H), 3.28 (1H, dt, J = 14.4, 5.8 Hz, 6-H), 4.27 (2H, m, 2-H, 3-H), 4.29 (1H, s, 3-H), 4.75 (1H, d, J = 7.0 Hz, 1'-H), 7.28 (8H, m, Ar-H₈), 7.51 (2H, m, Ar-H₂), 7.78 (1H, m, N-H); ¹³C-nmr (50.3 MHz) δ 24.84 (t), 29.76 (d), 33.42 (t), 35.01 (t), 54.45 (d), 57.62 (d), 127.02 (d), 128.57 (2xd), 128.60 (2xd), 129.15 (2xd), 129.50 (2xd), 140.20 (s), 140.95 (s), 170.45 (s), 172.32 (s); ms m/z (rel intensity) 433 (M⁺, 11), 306 (M⁺-I, 7), 278 (9), 261 (5), 207 (46), 178 (3), 167 (100), 152 (26), 129 (20), 115 (26), 91 (22), 77 (12); hrmrs Caled for C₂₀H₂₀N₂O₂ 306.1494. Found 306.1487. Anal. Caled for C₂₀H₂₀N₂O₂: C, 55.44; H, 4.65; N, 3.23. Found: C, 55.47; H, 4.85; N, 3.11.
Fragmentation of $\pm$-(1R*,4R*,55*)-4-Phenyl-1-hydroxy-2-azabicyclo[3.3.0]octan-3-one (13). A solution of carbinolamide (13) (825 mg, 3.9 mmol) in CH$_2$Cl$_2$ (90 ml) was irradiated in the presence of (diacetoxyiodo)benzene (1.88 g, 5.85 mmol) and I$_2$ (0.99 g, 3.9 mmol) for 30 min at 25 °C as described previously to give, after chromatography (hexane-EtOAc, 80:20), $\pm$-(2R*,3S*)-2-phenyl-3-(3"-iodopropyl)succinimide (31) (834 mg, 64 %) and $\pm$-(2R*,3S*)-2-phenyl-3-iodoperhydroazocine-2,8-dione (32) (26 mg, 2 %).

Compound (30): mp 188-190 °C (acetone-hexane); ir $\nu_{max}$ 3347, 3090, 3060, 1770, 1600, 1494, 1452, 1375, 1362, 1318, 1278, 1232, 1158 cm$^{-1}$; $^1$H-nmr (200 MHz) $\delta$ 1.76 (1H, m), 2.00 (1H, m), 2.30 (1H, m), 2.60 (1H, m), 3.04 (1H, dd, $J$ = 8.9, 14.4 Hz, 6-H), 3.39 (1H, dd, $J$ = 11.2, 2.0, 9.1 Hz, 6-H), 3.85 (1H, dd, $J$ = 3.8, 10.3 Hz, 2-H), 3.92 (1H, m, 3-H), 4.52 (1H, d, $J$ = 10.3 Hz, 1'-H), 7.31 (10H, m, Ar-H$_{10}$), 8.08 (1H, m, N-H); $^{13}$C-nmr (50.3 MHz) $\delta$ 24.27 (t), 31.18 (d), 37.12 (t), 38.00 (t), 51.04 (d), 54.82 (d), 126.82 (d), 127.28 (2xd), 127.32 (d), 128.34 (2xd), 128.99 (2xd), 129.19 (2xd), 140.52 (s), 142.37 (s), 168.64 (s), 171.21 (s); ms m/z (rel intensity) 433 (M$^+$, 18), 306 (2), 278 (5), 266 (3), 224 (7), 207 (89), 178 (13), 167 (100), 165 (60), 152 (26), 129 (26), 115 (24), 105 (17), 91 (23), 77 (17); hrms Calcd for C$_{26}$H$_{20}$NO$_2$I 433.0539. Found 433.0546. Anal. Calcd for C$_{20}$H$_{20}$NO$_2$I: C, 55.44; H, 4.65; N, 3.23. Found: C, 55.48; H, 4.53; N, 3.37.

Compound (31): mp 110-111 °C (MeOH); ir $\nu_{max}$ 3440, 3025, 1790, 1730, 1603, 1500, 1460, 1355, 1340, 1160 cm$^{-1}$; $^1$H-nmr (200 MHz) $\delta$ 1.8-2.15 (4H, m), 3.01 (1H, dt, $J$ = 5.8, 7, 5 Hz, 3-H), 3.13 (2H, t, $J$ = 6.4 Hz, 3"-H$_2$), 3.71 (1H, d, $J$ = 5.9 Hz, 2-H), 7.31 (5H, m, Ar-H$_5$), 8.39 (1H, m, N-H); $^{13}$C-nmr (50.3 MHz) $\delta$ 5.58 (t), 30.12 (t), 31.23 (t), 48.97 (d), 53.69 (d), 127.73 (2xd), 127.96 (d), 129.12 (2xd), 136.20 (s), 177.72 (s), 178.96 (s); ms m/z (rel intensity) 343 (M$^+$, 5), 272 (14), 217 (51), 216 (100), 188 (7), 174 (21), 145 (90), 128 (23), 117 (91), 115 (95), 103 (24), 91 (87), 77 (34); hrms Calcd for C$_{13}$H$_{15}$NO$_2$I 344.0148. Found 344.0150. Anal. Calcd for C$_{13}$H$_{14}$NO$_2$I: C, 45.50; H, 4.11; N, 4.08. Found: C, 45.71; H, 4.08; N, 3.87.

Compound (32): mp 188-189 °C (acetone-hexane); ir $\nu_{max}$ 3375, 1705, 1602, 1500, 1452, 1410, 1365, 1340, 1310, 1290, 1190, 1145, 695 cm$^{-1}$; $^1$H-nmr (200 MHz) $\delta$ 1.9-2.2 (2H, m), 2.25-2.4 (2H, m), 2.90 (1H, dd, $J$ = 5.7, 15.8 Hz, 6-H), 3.35 (1H, dt, $J$ = 7.4, 15.9 Hz, 6-H), 4.70 (2H, m, 2-H, 3-H), 7.35 (5H, m, Ar-H$_5$), 8.03 (1H, m, N-H); $^{13}$C-nmr (50.3 MHz) $\delta$ 23.46 (t), 32.29 (t), 34.12 (d), 35.59 (t), 60.67 (d), 128.43 (2xd), 128.55 (d), 129.09 (2xd), 137.01 (s), 169.34 (s), 172.12 (s); ms m/z (rel intensity) 343 (M$^+$, 6), 216 (72), 188 (20), 173 (43), 155 (11), 145 (38), 130 (54), 129 (55), 117 (60), 115 (78), 106 (67), 98 (35), 91 (100), 77 (16); hrms Calcd for C$_{13}$H$_{15}$NO$_2$I 344.0148. Found 344.0144. Anal. Calcd for C$_{13}$H$_{14}$NO$_2$I: C, 45.50; H, 4.11; N, 4.08. Found: C, 45.39; H, 4.25; N, 4.05.

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REFERENCES AND NOTES


15. Atomic coordinates, bond lengths, and angles have been deposited at the Cambridge Crystallographic Data Centre.


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