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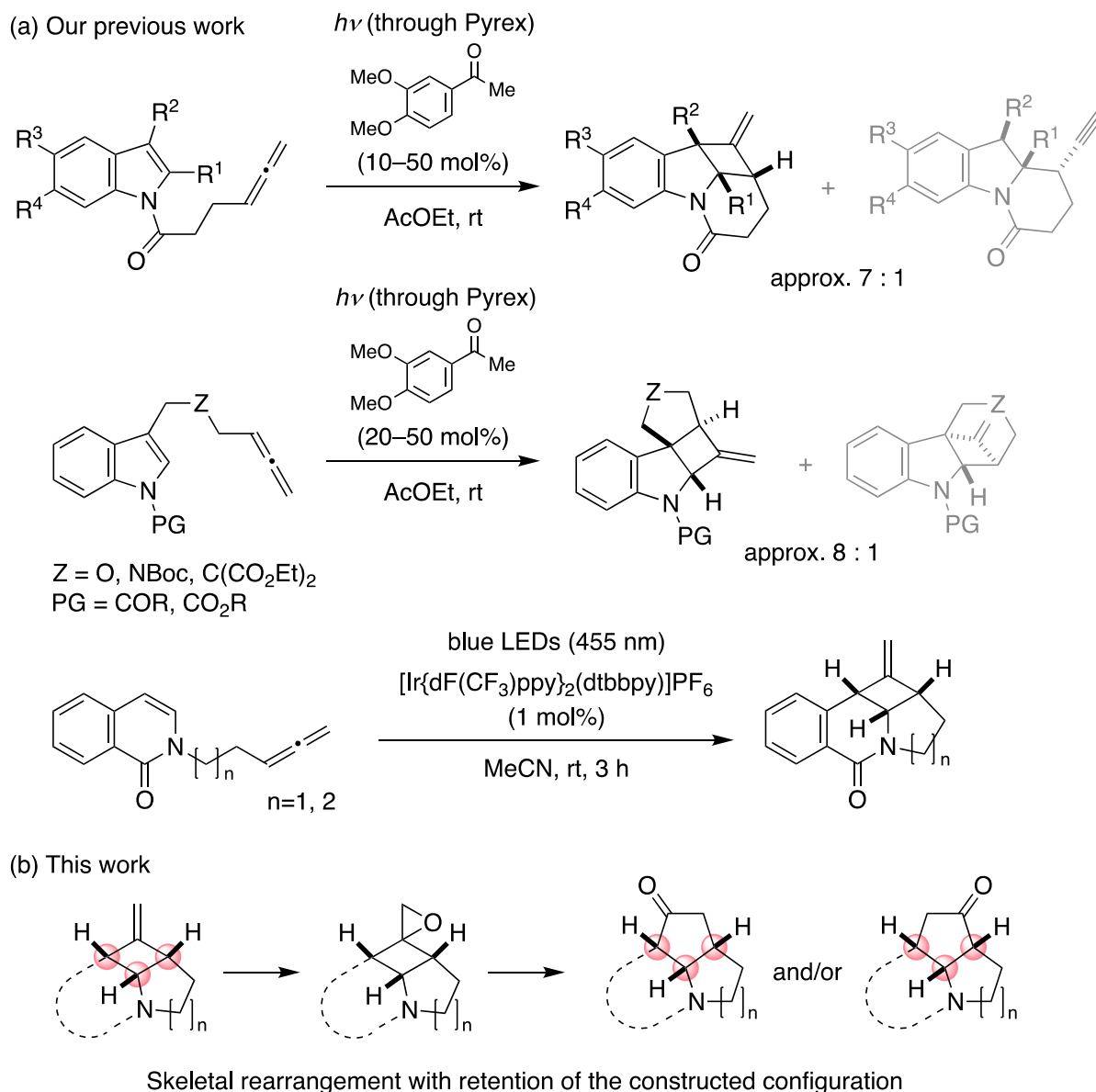
## STEREOSPECIFIC SKELETAL REARRANGEMENT OF EPOXIDES DERIVED FROM METHYLENECYCLOBUTANE-FUSED N- HETEROCYCLES

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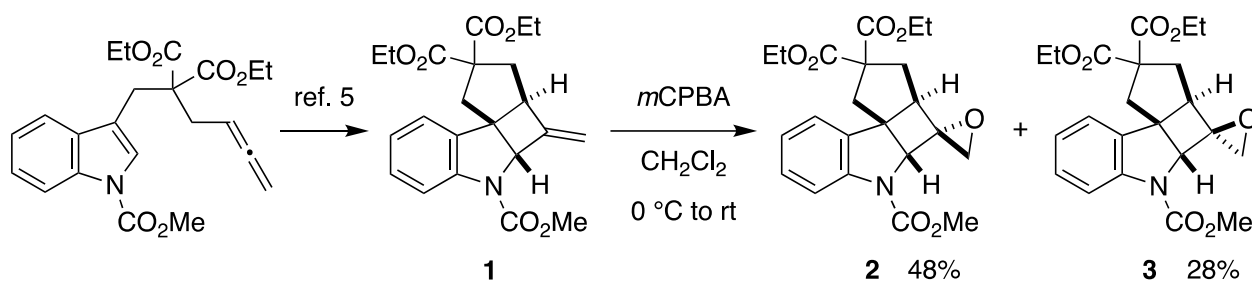
**Abstract** – Irradiation of indole or isocarbostyryl derivatives with allenyl side chain under appropriate conditions gave the corresponding methylenecyclobutane-fused N-heterocycles stereoselectively in high yields through intramolecular [2+2] cycloaddition. These addition products could be transformed to ring-expanded compounds without loss of the configuration by using a sequence of epoxidation and skeletal rearrangement.

Alkaloids constitute a large family of natural products exhibiting a wide range of structural diversity and biological activity.<sup>1</sup> Over the years, much effort has been dedicated toward development of effective synthetic methodologies to obtain this important class of compounds.<sup>2</sup> In this context, stereoselective construction of nitrogen-containing fused-ring frameworks remains a key methodology in the research field and attracts much attention of researchers. In our continuing work on the photochemistry of heteroaromatic compounds,<sup>3</sup> we recently found that 1-( $\omega$ -allenyl)indoles or 3-( $\omega$ -allenyl)indoles show an excellent reactivity in the intramolecular [2+2] photocycloaddition sensitized by 3',4'-dimethoxyacetophenone, which is a sensitizer of choice in this kind of reactions, to afford the corresponding methylenecyclobutane-fused N-heterocycles in good yields stereoselectively.<sup>4-6</sup> These reactions could be successfully extended to a visible-light (455 nm) promoted [2+2] cycloaddition of isocarbostyryls (Scheme 1a).<sup>7</sup> The most important feature of this [2+2] cycloaddition between N-heterocycles and allene is that the products have methylene group on the cyclobutane ring that can play a role as the next starting point for further molecular transformations.<sup>8</sup> As a synthetic application of these unique photoadducts, we would like to present here a stereospecific ring expansion of the cyclobutane-fused compounds by a sequence of epoxidation and Lewis acid catalyzed skeletal rearrangement (Scheme 1b).



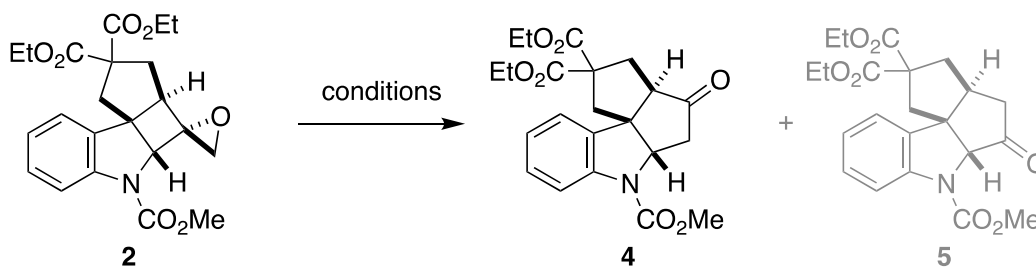
**Scheme 1.** Construction of N-heterocyclic fused-ring frameworks through photochemical [2+2] cycloaddition

Our investigation commenced with conventional epoxidation of photoadduct **1**. Treatment of the tetracyclic indoline **1**, which is the product of the intramolecular [2+2] photocycloaddition of 3-( $\omega$ -allenyl)indole,<sup>5</sup> with *m*CPBA gave the corresponding epoxides **2** and **3** in moderate combined yield (Scheme 2).<sup>9</sup> The preference of the formation of **2** is easily interpreted as the approach of *m*CPBA from the less hindered side of the methylene  $\pi$  plane. These diastereomers could be separated by careful preparative thin layer chromatography. The relative configuration of the products was determined by <sup>1</sup>H NMR NOE experiments.



With pure epoxide **2** in hand, the ring expansion of the cyclobutane moiety was investigated next. We were able to find several examples of similar ring expansion of spirocyclic epoxides in the literature,<sup>10</sup> including the synthesis of 2-arylcyclopentanones through epoxidation of benzylidenecyclobutanes and subsequent epoxide rearrangement reported by Shi and collaborators.<sup>11</sup> Though their reaction would be promoted by an aryl group that stabilizes a transition state or an intermediate of the reaction, our investigation began with modifying their reaction conditions.

**Table 1.** Ring expansion of epoxide **2**



entry	conditions	<b>4</b> (%) <sup>a</sup>	<b>5</b> (%)
1	Et <sub>2</sub> AlCl (25 mol%), toluene, -78 °C, 3 h	0	0
2	LiI (16 mol%), CH <sub>2</sub> Cl <sub>2</sub> , rt, 14 h	< 28 <sup>b</sup>	0
3	LiI (1 eq.), CH <sub>2</sub> Cl <sub>2</sub> , rt, 26 h	92	0
4	LiI (2.2 eq.), CH <sub>2</sub> Cl <sub>2</sub> , rt, 26 h	88	0

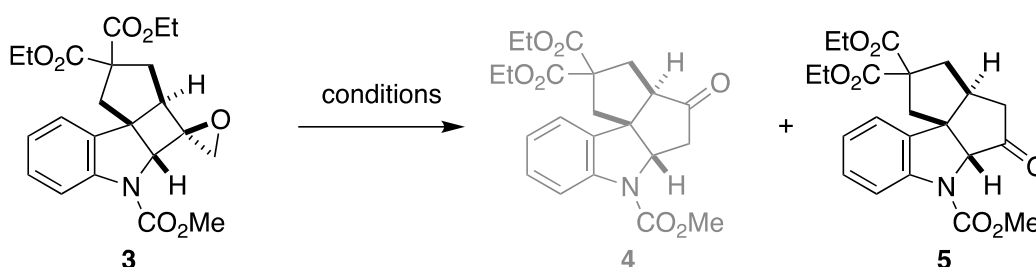
<sup>a</sup> Yields of the isolated product. <sup>b</sup> 72% recovery of **2**.

The results are shown in Table 1. At beginning, epoxide **2** was treated with Et<sub>2</sub>AlCl according to the Shi's report, but the reaction did not proceed at all and unreacted **2** was recovered (entry 1). This result would come from the difference between whether or not the compound has an aryl group that stabilizes developing positive charge at the epoxide carbon. Gratifyingly, treatment with LiI in dichloromethane, the other Shi's procedure, gave small amounts of the ring expanded product **4** (entry 2). The yield of **4** was significantly improved by increasing the amount of LiI (entry 3). Excess use of LiI did not show further improvement of the yield (entry 4). It is worth to mention that the relative configuration of chiral carbons that did not

take part in the rearrangement was completely retained. To our surprise, the other possible product **5** was not detected in  $^1\text{H}$  NMR analysis of the crude mixture in the slightest in all cases.

Prompted by this interesting result, the reaction of epoxide **3** (diastereomer of **2**) was investigated under the same reaction conditions (Table 2). In marked contrast to the reaction of **2**, ketone **5**, which is the regioisomer of **4**, was predominantly produced in this case (entry 1). A small amount of **4** (less than 10%) was also formed but it could not be separated by chromatography. Excess use of LiI did not improve the yield as observed in the reaction of **2** (entry 2). This stereospecific skeletal rearrangement suggests the synthetic potential of the [2+2] photocycloaddition of allene/epoxidation/ring-expansion sequence for the stereo- and regioselective preparation of angular type ring-fused indoline frameworks.

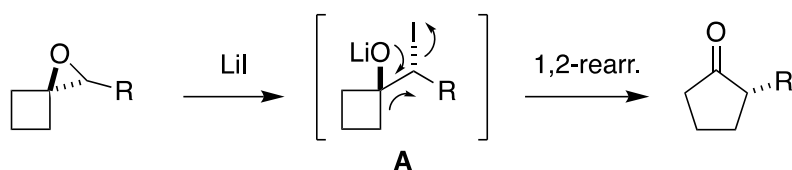
**Table 2.** Ring expansion of epoxide **3**



entry	conditions	<b>4</b> (%)	<b>5</b> (%) <sup>a</sup>
1	LiI (1 eq.), $\text{CH}_2\text{Cl}_2$ , rt, 26 h	<sup>b</sup>	85
2	LiI (2.6 eq.), $\text{CH}_2\text{Cl}_2$ , rt, 26 h	<sup>b</sup>	81

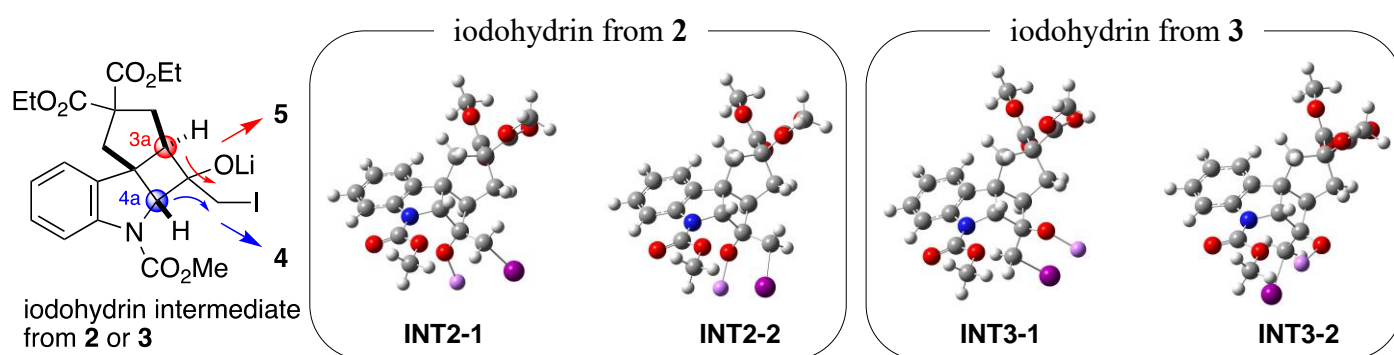
<sup>a</sup> Yields of the isolated product. A small amount of inseparable **4** was contained. <sup>b</sup> Not isolated. The isolated **5** contained a small amount of **4** (approximately 10%) judging from  $^1\text{H}$  NMR analysis (see the Supporting Information).

To obtain some insight into this stereospecific rearrangement, approximate consideration based on theoretical calculations was carried out, though detailed discussion on the reaction mechanism revealing the precise character of the transition states should be made in future study. It is proposed that the rearrangement with LiI likely proceeds via iodohydrin intermediate **A** accompanied with double inversion (Scheme 3).<sup>11a</sup> Accordingly, Gibbs free energies of four possible intermediates that lead to the formation of **4** or **5** from the substrates **2** or **3** were estimated by theoretical calculations. To save the computational resources, the compounds were simplified by replacing ethyl ester moiety with methyl ester. Each conformer was optimized using B3LYP DFT functional with 6-31+G(d,p) basis set for light atoms and the LanL2DZ ECP basis for iodine with the SMD model (dichloromethane), and frequency calculations for the stationary points were carried out to obtain the Gibbs free energy (298.15 K, 1.0 atm) in Gaussian 09.<sup>12</sup>



**Scheme 3.** Plausible reaction pathway for the epoxide rearrangement<sup>11a</sup>

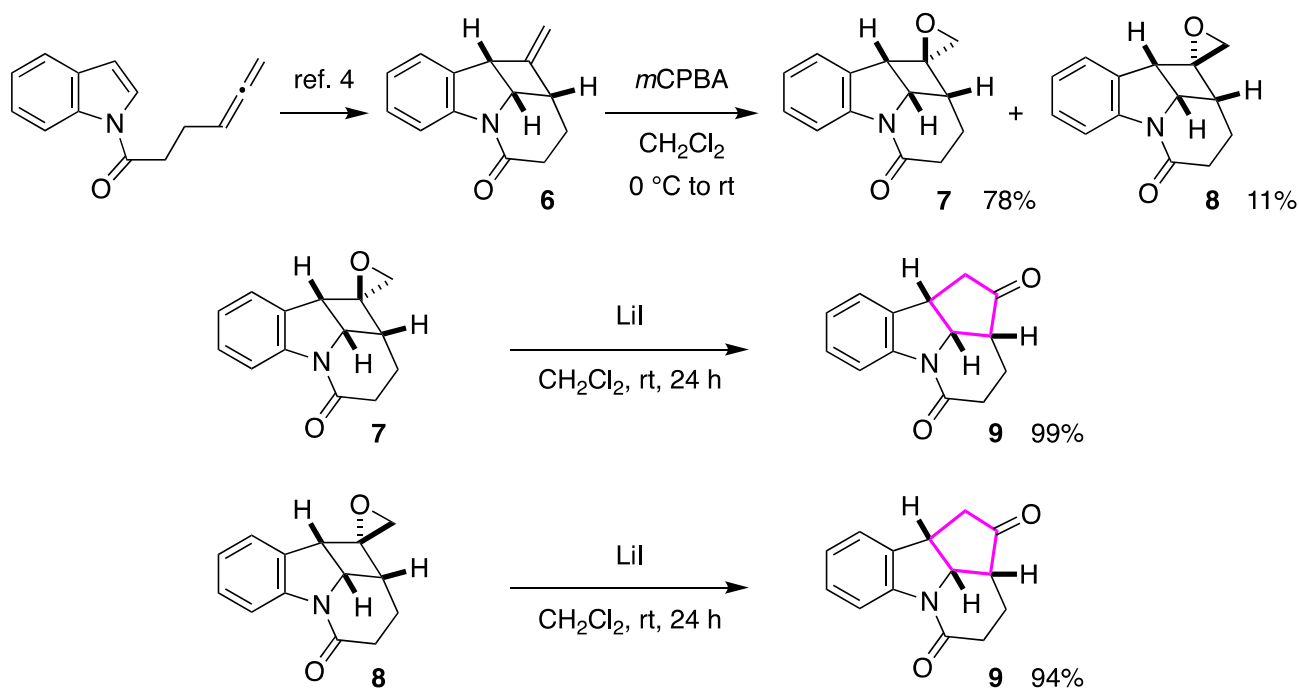
As shown in Figure 1, **INT2-1** and **INT2-2** are iodohydrin from epoxide **2**, and **INT3-1** and **INT3-2** are those from **3**. According to the well-known stereoelectronic theory,<sup>13</sup> the C–C bond that is located at the *anti*-periplanar position to the C–I bond is expected to participate in the rearrangement. Thus, **INT2-1** and **INT3-1** (the C–I bond is located at the *anti*-periplanar position to C4–C4a bond) are suitable to the formation of ketone **4** and **INT2-2** and **INT3-2** (the C–I bond is located at the *anti*-periplanar position to C4–C3a bond) lead to **5**. As a result of the calculation, **INT2-1** is more stable than **INT2-2** by 2.5 kcal/mol, whereas the difference between **INT3-1** and **INT3-2** is only 0.53 kcal/mol. Though the difference between migrating ability of C3a and C4a in **2** or **3** would be marginal, C3a is probably more prone to migrate in this case, and this property would give **5** from **3** that produces energetically close intermediates **INT3-1** and **INT3-2**. In the case of **2**, the energetic preference of **INT2-1** over **INT2-2**, which leads to the formation of **4**, would overcome the migratory tendency of C3a over C4a.



**Figure 1.** Possible conformers of intermediary iodohydrins (simplified models)

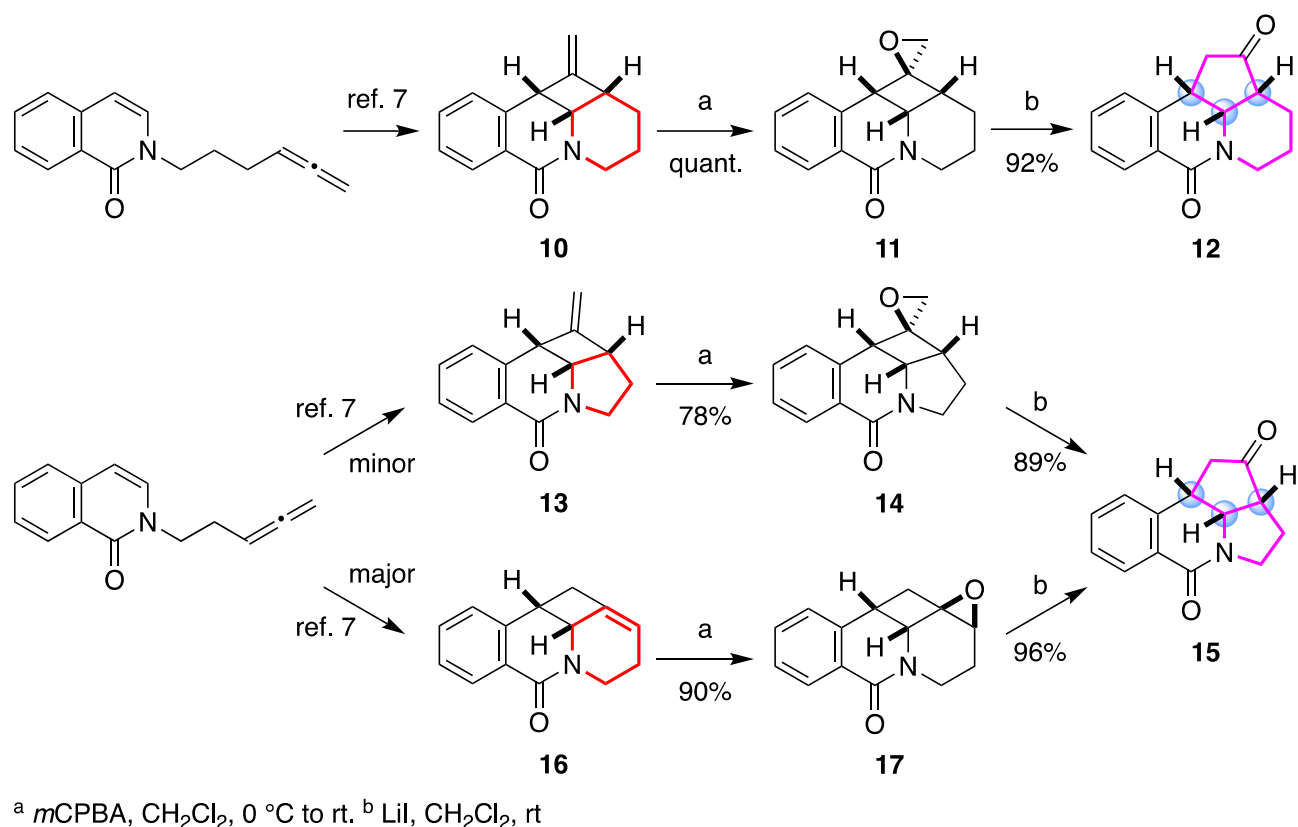
In order to show the versatility of this method for the construction of fused indoline frameworks, we attempted a reaction with the photoadduct **6** next (Scheme 4). Similarly, the reaction of **6** with *m*CPBA gave the corresponding epoxides **7** and **8** with preference for the formation of **7** via approach of *m*CPBA from the less hindered convex side. Treatment of epoxide **7** with LiI under the conditions shown in Table 1, entry 3, afforded the rearranged ketone **9** almost quantitatively. But, in contrast to the reactions of **2** and **3**, the stereoisomeric epoxide **8** also gave the same ketone **9** in high yield. In this case, the conformers of plausible intermediate iodohydrins likely located in relatively narrow energy range. This made the rapid

interconversion between conformers possible, and benzylic carbon that has migrating ability much higher than the other carbon translocated preferentially.<sup>14</sup>



**Scheme 4.** Ring expansion of the photoadduct **6** via epoxidation/rearrangement sequence

This rearrangement was applicable not only to indoline derivatives but to isoquinolone derivatives (Scheme 5). Substrates **10** with 6-membered ring fusion and **13** with 5-membered ring fusion were investigated. Epoxidation of these compounds under the same conditions described above gave the corresponding epoxides **11** or **14** as a single diastereomer in good yield. Sterically unfavorable approach from the concave side did not occur at all in these cases. Rearrangement of **11** and **14** promoted by LiI afforded ketones **12** and **15** in excellent yields with complete retention of configuration of the carbons existing on the 4-membered ring. In the photoreaction to prepare *exo*-methylene-type substrate **13**, it has already been found that **13** was a minor product and that the reaction gave *endo*-alkene **16** predominantly.<sup>7</sup> However, the compound **16** turned out to converge into the ketone **15**, which is the same product as **13** gave, via the epoxidation/rearrangement sequence in excellent overall yield. This result indicates that the problem of regioselectivity in the photochemical [2+2] cycloaddition of allene is not important in this case to obtain the rearranged ketone.



**Scheme 5.** Ring expansion of the photoadduct **10** and **13** via epoxidation-rearrangement sequence

In summary, a method for the construction of fused N-heterocyclic frameworks has been developed through the stereoselective [2+2] photochemical cycloaddition reaction of allene-tethered indole or isocarbostyryl derivatives followed by epoxidation/LiI-promoted rearrangement sequence. The relative configuration of the photoadduct was completely retained through the transformation, giving the rearranged ketones in excellent yields. These findings provide an efficient route to unique nitrogen heterocyclic scaffolds that are otherwise difficult to prepare, generating molecular complexity from readily available starting materials.

## EXPERIMENTAL

NMR spectra were obtained on JEOL JNM-ECS400 and JNM-ECZ400S spectrometers. Proton multiplicity was described as follows: singlet, s; doublet, d; triplet, t; broadened, br. Carbon multiplicity was assigned by a DEPT experiment and described as follows: methyl, CH<sub>3</sub>; methylene, CH<sub>2</sub>; methine, CH; quaternary, C. Silica gel column chromatography was performed with Fuji Silysia PSQ60B. Preparative thin-layer chromatography (TLC) was carried out with Wako Gel B-5F (FUJIFILM Wako Pure Chemical Industries). Solvents and reagents were used as received unless otherwise noted. Mass spectrometry was carried out at the Instrumental Analysis Division, Global Facility Center, Creative Research Institution, Hokkaido University.

## Starting Materials

The starting materials **1**,<sup>5</sup> **6**,<sup>4</sup> **10**,<sup>7</sup> **13**,<sup>7</sup> and **16**<sup>7</sup> were prepared according to our previous reports.

## General procedure for the epoxidation/rearrangement and physical data of the products

The reaction of **2** is representative. (Table 1, entry 3)

To a solution of **1** (89.1 mg, 0.223 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (2 mL) at 0 °C was added *m*-chloroperbenzoic acid (wet, 70% (w/w), 164.4 mg, 0.67 mmol) with stirring. After the addition, the solution was allowed to warm to room temperature and stirred for 46 h. The reaction was stopped by the addition of saturated aqueous solution of sodium hydrogencarbonate and the mixture was extracted with CH<sub>2</sub>Cl<sub>2</sub> for four times. After drying over anhydrous sodium sulfate, the solvent was evaporated under reduced pressure. The crude material was purified by silica gel thin layer chromatography (hexane/AcOEt = 4/1, developed three times) to give the product **2** (44.3 mg, 0.107 mmol, 48%) and **3** (26.1 mg, 0.0628 mmol, 28%) both as colorless oil.

**rac-2,2-Diethyl 5-methyl (3aR,4S,4aR,9bS)-3,3a-dihydrospiro[cyclopenta[2,3]cyclobuta[1,2-b]indole-4,2'-oxirane]-2,2,5(1H,4aH)-tricarboxylate (2)**: colorless oil; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>, 50 °C) δ 7.94 (br s, 1H), 7.23 (t, *J*=7.7 Hz, 1H), 7.17 (d, *J*=7.5 Hz, 1H), 7.00 (t, *J*=7.5 Hz, 1H), 4.88 (br s, 1H), 4.37–4.20 (m, 4H), 3.70 (br s, 3H), 3.03–3.01 (m, 1H), 2.94 (d, *J*=14.4 Hz, 1H), 2.73–2.51 (m, 5H), 1.33 (t, *J*=7.1 Hz, 3H), 1.28 (t, *J*=7.1 Hz, 3H); <sup>13</sup>C{<sup>1</sup>H} NMR (100 MHz, CDCl<sub>3</sub>, 20 °C) δ 171.4 (C), 170.9 (C), 153.0 (C), 144.0 (C), 133.2 (C), 128.7 (CH), 122.9 (CH), 122.2 (CH), 115.1 (CH), 67.7 (CH), 62.9 (C), 62.0 (CH<sub>2</sub>), 61.92 (C), 61.85 (CH<sub>2</sub>), 56.1 (CH), 53.8 (C), 52.4 (CH<sub>3</sub>), 50.7 (CH<sub>2</sub>), 40.8 (CH<sub>2</sub>), 36.6 (CH<sub>2</sub>), 14.01 (CH<sub>3</sub>), 13.97 (CH<sub>3</sub>); HRMS (ESI<sup>+</sup>) *m/z* 438.1514 (M+Na<sup>+</sup>), calcd for C<sub>22</sub>H<sub>25</sub>NNaO<sub>7</sub>: 438.1523.

**rac-2,2-Diethyl 5-methyl (3aR,4R,4aR,9bS)-3,3a-dihydrospiro[cyclopenta[2,3]cyclobuta[1,2-b]indole-4,2'-oxirane]-2,2,5(1H,4aH)-tricarboxylate (3)**: colorless oil; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>, 50 °C) δ 7.87 (br s, 1H), 7.28–7.24 (m, 2H), 7.03 (t, *J*=7.5 Hz, 1H), 4.94 (br s, 1H), 4.36–4.19 (m, 4H), 3.77 (br s, 3H), 3.15 (dd, *J*=8.1, 4.7 Hz, 1H), 2.99 (d, *J*=14.4 Hz, 1H), 2.87 (d, *J*=5.3 Hz, 1H), 2.73–2.63 (m, 2H), 2.55–2.52 (m, 2H), 1.35–1.27 (m, 6H); <sup>13</sup>C{<sup>1</sup>H} NMR (100 MHz, CDCl<sub>3</sub>, 50 °C) δ 171.6 (C), 171.0 (C), 152.9 (C), 143.3 (C), 133.5 (C), 128.7 (CH), 123.3 (CH, overlapped), 115.4 (CH), 70.5 (CH), 63.5 (C), 62.3 (C), 61.92 (CH<sub>2</sub>), 61.85 (CH<sub>2</sub>), 54.8 (CH), 53.8 (C), 52.6 (CH<sub>3</sub>), 50.2 (CH<sub>2</sub>), 43.4 (CH<sub>2</sub>), 35.2 (CH<sub>2</sub>), 14.1 (CH<sub>3</sub>), 14.0 (CH<sub>3</sub>); HRMS (ESI<sup>+</sup>) *m/z* 438.1511 (M+Na<sup>+</sup>), calcd for C<sub>22</sub>H<sub>25</sub>NNaO<sub>7</sub>: 438.1523.

In a screw-capped test tube, **2** (21.0 mg, 0.0505 mmol), LiI•*n*H<sub>2</sub>O (contains LiI 82% (w/w), 8.8 mg, 0.054 mmol), and Teflon-coated stirring tip were charged. Air present in the flask was replaced with argon by several rapid evacuation/Ar introduction cycles. CH<sub>2</sub>Cl<sub>2</sub> (0.2 mL) was transferred into the flask by a syringe. The screw-cap was tightly closed, and the test tube was wrapped with a sheet of aluminum foil. The suspension was vigorously stirred for 26 h at room temperature. After stopping the reaction by the addition



of water, the mixture was extracted with  $\text{CH}_2\text{Cl}_2$  for three times. The combined extracts were dried over anhydrous sodium sulfate. After removal of the solid by filtration, the solvent was evaporated under reduced pressure. The crude material was purified by silica gel thin layer chromatography (hexane/AcOEt = 3/1) to give the product **4** (19.3 mg, 0.0465 mmol, 92%) as colorless oil.

**rac-2,2-Diethyl 6-methyl (3aR,5aS,10bS)-4-oxo-3a,4,5,5a-tetrahydropentaleno[1,6a-b]indole-2,2,6(1H,3H)-tricarboxylate (4)**: colorless oil;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ , 55 °C)  $\delta$  7.78 (br s, 1H), 7.28–7.24 (m, 1H), 7.18 (d,  $J=7.3$  Hz, 1H), 7.06 (d,  $J=7.4$  Hz, 1H), 4.82 (t,  $J=7.5$  Hz, 1H), 4.26–4.17 (m, 4H), 3.86 (s, 3H), 3.09 (dd,  $J=18.8, 8.2$  Hz, 1H), 2.93–2.88 (m, 2H), 2.80 (obscured d,  $J=14$  Hz, 1H), 2.68 (dd,  $J=14.0, 10.4$  Hz, 1H), 2.51–2.40 (m, 2H), 1.30–1.24 (m, 6H);  $^{13}\text{C}\{^1\text{H}\}$  NMR (100 MHz,  $\text{CDCl}_3$ , 55 °C)  $\delta$  214.8 (C), 172.0 (C), 170.5 (C), 153.4 (C), 141 (C\*), 136.7 (C\*), 128.9 (CH), 124.0 (CH), 123.3 (CH), 115.3 (CH), 66.7 (CH), 62.1 ( $\text{CH}_2$ ), 61.8 ( $\text{CH}_2$ ), 61.4 (C), 59.8 (CH), 58.9 (C), 52.7 ( $\text{CH}_3$ ), 50.1 ( $\text{CH}_2$ ), 46.8 ( $\text{CH}_2$ ), 37.4 ( $\text{CH}_2$ ), 14.0 ( $\text{CH}_3$ ), 13.8 ( $\text{CH}_3$ ) (\* These quaternary carbons were hardly detected in the 1D spectrum likely due to the slow rotation of the carbamate moiety, but they were clearly detected in the HMBC spectrum); HRMS (ESI<sup>+</sup>)  $m/z$  438.1514 ( $\text{M}+\text{Na}^+$ ), calcd for  $\text{C}_{22}\text{H}_{25}\text{NNaO}_7$ : 438.1523.

Physical data of the other products were as follows:

**rac-2,2-Diethyl 6-methyl (3aS,5aR,10bS)-5-oxo-3a,4,5,5a-tetrahydropentaleno[1,6a-b]indole-2,2,6(1H,3H)-tricarboxylate (5)**: 17.9 mg (0.0431 mmol, 85%, containing a small amount (approx. 10%) of inseparable **4**); conditions: **3**, 21.1 mg (0.0508 mmol),  $\text{Li}\cdot n\text{H}_2\text{O}$ , 8.3 mg (0.051 mmol),  $\text{CH}_2\text{Cl}_2$ , 0.2 mL, rt, 26 h; colorless oil;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ , 55 °C)  $\delta$  7.74 (br s, 1H), 7.26–7.21 (m, 1H), 7.18 (d,  $J=7.3$  Hz, 2H), 7.05 (dt,  $J_d=1.0$  Hz,  $J_t=7.6$  Hz, 1H), 4.62 (s, 1H), 4.30–4.18 (m, 4H), 3.88 (s, 3H), 3.02–2.85 (m, 3H), 2.67 (d,  $J=14.9$  Hz, 1H), 2.44–2.39 (m, 1H), 2.28 (dd,  $J=18.8, 8.2$  Hz, 1H), 2.17 (dd,  $J=13.8, 9.3$  Hz, 1H), 1.31–1.26 (m, 6H);  $^{13}\text{C}\{^1\text{H}\}$  NMR (100 MHz,  $\text{CDCl}_3$ , 55 °C)  $\delta$  213.1 (C), 171.6 (C, overlapped), 153.8 (C), 141.5 (C\*), 134 (C\*), 129.0 (CH), 124.1 (CH), 123.1 (CH), 115.5 (CH), 71.6 (CH), 62.0 ( $\text{CH}_2$ ), 61.9 ( $\text{CH}_2$ ), 61.1 (C), 58.9 (C), 52.9 ( $\text{CH}_3$ ), 47.4 ( $\text{CH}_2$ ), 44.6 (CH), 42.0 ( $\text{CH}_2$ ), 41.8 ( $\text{CH}_2$ ), 14.02 ( $\text{CH}_3$ ), 13.96 ( $\text{CH}_3$ ) (\* These quaternary carbons were hardly detected in the 1D spectrum likely due to the slow rotation of the carbamate moiety, but they were clearly detected in the HMBC spectrum); HRMS (ESI<sup>+</sup>)  $m/z$  438.1514 ( $\text{M}+\text{Na}^+$ ), calcd for  $\text{C}_{22}\text{H}_{25}\text{NNaO}_7$ : 438.1523.

**rac-(1S,1aR,9bS,9cS)-2,3,9b,9c-Tetrahydrospiro[benzo[*b*]cyclobuta[*hi*]indolizine-1,2'-oxiran]-4(1aH)-one (7)**: 42.4 mg (0.187 mmol, 78%); conditions: **6**, 50.2 mg (0.238 mmol), *m*CPBA, 124.7 mg (0.506 mmol),  $\text{CH}_2\text{Cl}_2$ , 2.5 mL, 0 °C to rt, 24 h; colorless solid;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.84 (d,  $J=7.9$  Hz, 1H), 7.20 (t,  $J=7.4$  Hz, 1H), 7.04–6.97 (m, 2H), 4.74 (t,  $J=6.9$  Hz, 1H), 4.01 (d,  $J=6.9$  Hz, 1H), 3.53–3.47 (m, 1H), 2.54–2.46 (m, 2H), 2.33–2.25 (m, 2H), 2.17–2.09 (m, 1H), 1.62–1.52 (m, 1H);  $^{13}\text{C}\{^1\text{H}\}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  170.8 (C), 145.3 (C), 130.7 (C), 128.1 (CH), 124.2 (CH), 123.7 (CH), 117.5

(CH), 69.1 (C), 56.7 (CH), 48.4 (CH), 47.3 (CH<sub>2</sub>), 39.8 (CH), 34.4 (CH<sub>2</sub>), 21.6 (CH<sub>2</sub>); HRMS (ESI<sup>+</sup>) *m/z* 250.0833 (M+Na<sup>+</sup>), calcd for C<sub>14</sub>H<sub>13</sub>NNaO<sub>2</sub>: 250.0839.

***rac*-(1*R*,1*aR*,9*bS*,9*cS*)-2,3,9*b*,9*c*-Tetrahydrospiro[benzo[*b*]cyclobuta[*hi*]indolizine-1,2'-oxiran]-4(1*aH*)-one (8)**: 6.2 mg (0.027 mmol, 11%); conditions: **6**, 50.2 mg (0.238 mmol), *m*CPBA, 124.7 mg (0.506 mmol), CH<sub>2</sub>Cl<sub>2</sub>, 2.5 mL, 0 °C to rt, 24 h; colorless solid; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.89 (d, *J*=8.1 Hz, 1H), 7.25–7.21 (m, 1H), 7.03–6.98 (m, 2H), 4.69 (t, *J*=6.0 Hz, 1H), 4.21 (d, *J*=6.0 Hz, 1H), 3.65–3.59 (m, 1H), 2.77 (d, *J*=4.6 Hz, 1H), 2.71 (d, *J*=4.6 Hz, 1H), 2.50 (dt, *J*<sub>d</sub>=14.2 Hz, *J*<sub>t</sub>=3.0 Hz, 1H), 2.26 (dt, *J*<sub>d</sub>=5.9 Hz, *J*<sub>t</sub>=14.2 Hz, 1H), 1.88–1.73 (m, 2H); <sup>13</sup>C{<sup>1</sup>H} NMR (100 MHz, CDCl<sub>3</sub>) δ 171.4 (C), 146.1 (C), 128.6 (C), 128.2 (CH), 124.6 (CH), 124.1 (CH), 117.2 (CH), 64.7 (C), 59.7 (CH), 48.9 (CH<sub>2</sub>), 47.5 (CH), 39.0 (CH), 34.1 (CH<sub>2</sub>), 17.5 (CH<sub>2</sub>); HRMS (ESI<sup>+</sup>) *m/z* 250.0832 (M+Na<sup>+</sup>), calcd for C<sub>14</sub>H<sub>13</sub>NNaO<sub>2</sub>: 250.0839.

***rac*-(2*aR*,10*bS*,10*cR*)-1,2*a*,2*a*1,3,4,10*b*-Hexahydrobenzo[*b*]cyclopenta[*hi*]indolizine-2,5-dione (9)**: 20.5 mg (0.0902 mmol, 99%); conditions: **7**, 20.7 mg (0.0911 mmol), LiI·*n*H<sub>2</sub>O, 15.1 mg (0.0925 mmol), CH<sub>2</sub>Cl<sub>2</sub>, 0.3 mL, rt, 24 h; colorless oil. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.06 (d, *J*=7.9 Hz, 1H), 7.27–7.23 (m, 2H), 7.09–7.05 (m, 1H), 4.87 (t, *J*=7.5 Hz, 1H), 3.94–3.88 (m, 1H), 3.07–3.00 (m, 1H), 2.94 (ddd, *J*=19.4, 11.1, 1.7 Hz, 1H), 2.53–2.30 (m, 3H), 2.19 (dd, *J*=19.4, 6.4 Hz, 1H), 2.10–1.99 (m, 1H); <sup>13</sup>C{<sup>1</sup>H} NMR (100 MHz, CDCl<sub>3</sub>) δ 215.7 (C), 170.0 (C), 141.5 (C), 134.1 (C), 128.3 (CH), 124.34 (CH), 124.32 (CH), 116.5 (CH), 64.0 (CH), 46.7 (CH), 43.2 (CH<sub>2</sub>), 39.1 (CH), 32.3 (CH<sub>2</sub>), 20.3 (CH<sub>2</sub>); HRMS (ESI<sup>+</sup>) *m/z* 250.0831 (M+Na<sup>+</sup>), calcd for C<sub>14</sub>H<sub>13</sub>NNaO<sub>2</sub>: 250.0839.

***rac*-(1*S*,1*aR*,10*bS*,10*cS*)-1*a*,2,3,4,10*b*,10*c*-Hexahydro-6*H*-spiro[benzo[*b*]cyclobuta[*ij*]quinolizine-1,2'-oxiran]-6-one (11)**: 18.8 mg (0.0779 mmol, 90%); conditions: **10** (containing an inseparable impurity (approx. 10%), likely a regioisomer), 19.4 mg (0.0861 mmol), *m*CPBA, 45.8 mg (0.186 mmol), CH<sub>2</sub>Cl<sub>2</sub>, 1 mL, 0 °C to rt, 26 h; colorless oil; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.12–8.09 (m, 1H), 7.40–7.32 (m, 2H), 7.00–6.97 (m, 1H), 4.78–4.75 (m, 1H), 4.30 (distorted t, *J*=6.4 Hz, 1H), 3.87 (d, *J*=6.8 Hz, 1H), 3.14 (distorted t, *J*=6.3 Hz, 1H), 2.64 (d, *J*=4.6 Hz, 1H), 2.51–2.45 (m, 1H), 2.30 (d, *J*=4.6 Hz, 1H), 1.78–1.56 (m, 4H); <sup>13</sup>C{<sup>1</sup>H} NMR (100 MHz, CDCl<sub>3</sub>) δ 162.3 (C), 133.5 (C), 131.9 (CH), 128.8 (CH), 128.0 (C), 127.9 (CH), 126.8 (CH), 66.3 (C), 47.9 (CH), 46.5 (CH<sub>2</sub>), 42.6 (CH), 41.6 (CH), 40.3 (CH<sub>2</sub>), 22.5 (CH<sub>2</sub>), 20.0 (CH<sub>2</sub>); HRMS (ESI<sup>+</sup>) *m/z* 264.0991 (M+Na<sup>+</sup>), calcd for C<sub>15</sub>H<sub>15</sub>NNaO<sub>2</sub>: 264.0995.

***rac*-(2*aR*,11*bS*,11*cR*)-1,2*a*,4,5,11*b*,11*c*-Hexahydro-3*H*-benzo[*b*]cyclopenta[*ij*]quinolizine-2,7-dione (12)**: 17.3 mg (0.0717 mmol, 92%); conditions: **11**, 18.8 mg (0.0779 mmol), LiI·*n*H<sub>2</sub>O, 21.5 mg (0.13 mmol), CH<sub>2</sub>Cl<sub>2</sub>, 0.2 mL, rt, 48 h; faintly yellow solid. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.17 (dd, *J*=7.7, 1.4 Hz, 1H), 7.47 (dt, *J*<sub>d</sub>=1.5, *J*<sub>t</sub>=7.7 Hz, 1H), 7.39 (dt, *J*<sub>d</sub>=1.3, *J*<sub>t</sub>=7.4 Hz, 1H), 7.23–7.21 (m, 1H), 4.80–4.75 (m, 1H), 4.28 (t, *J*=4.8 Hz, 1H), 3.47 (ddd, *J*=11.7, 8.8, 4.6 Hz, 1H), 2.74 (dd, *J*=19.1, 8.8 Hz, 1H), 2.59 (t, *J*=4.8 Hz, 1H), 2.50 (dt, *J*<sub>d</sub>=2.5, *J*<sub>t</sub>=13.3 Hz, 1H), 2.38–2.33 (m, 1H), 2.32 (dd, *J*=19.1, 11.7 Hz, 1H), 1.75–

1.60 (m, 2H) 1.38–1.23 (m, 1H);  $^{13}\text{C}\{^1\text{H}\}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  214.3 (C), 163.8 (C), 138.6 (C), 132.2 (CH), 129.4 (CH), 127.7 (CH), 127.2 (CH), 126.8 (C), 57.6 (CH), 51.2 (CH), 43.5 ( $\text{CH}_2$ ), 40.5 ( $\text{CH}_2$ ), 37.2 (CH), 21.5 ( $\text{CH}_2$ ), 21.0 ( $\text{CH}_2$ ); HRMS ( $\text{ESI}^+$ )  $m/z$  264.0989 ( $\text{M}+\text{Na}^+$ ), calcd for  $\text{C}_{15}\text{H}_{15}\text{NNaO}_2$ : 264.0995.

***rac*-(1*S*,1*aR*,9*bS*,9*cS*)-2,3,9*b*,9*c*-Tetrahydrospiro[benzo[*f*]cyclobuta[*hi*]indolizine-1,2'-oxiran]-**

**5(1*aH*)-one (14)**: 14.8 mg (0.0651 mmol, 78%); conditions: **13**, 17.7 mg (0.0838 mmol), *m*CPBA, 61.0 mg (0.25 mmol),  $\text{CH}_2\text{Cl}_2$ , 1 mL, 0 °C to rt, 25 h; colorless oil;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.07–8.05 (m, 1H), 7.41–7.33 (m, 2H), 7.02–6.99 (m, 1H), 4.64–4.58 (m, 1H), 4.33 (t,  $J=6.0$  Hz, 1H), 3.86 (d,  $J=6.0$  Hz, 1H), 3.47–3.43 (m, 1H), 3.30–3.22 (m, 1H), 2.54 (d,  $J=4.5$  Hz, 1H), 2.18 (d,  $J=4.5$  Hz, 1H), 2.09–2.00 (m, 1H), 1.80–1.72 (m, 1H);  $^{13}\text{C}\{^1\text{H}\}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  163.4 (C), 134.2 (C), 132.1 (CH), 128.9 (CH), 128.2 (C), 128.1 (CH), 126.9 (CH), 70.3 (C), 53.6 (CH), 47.8 (CH), 47.1 ( $\text{CH}_2$ ), 46.9 ( $\text{CH}_2$ ), 40.5 (CH), 25.6 ( $\text{CH}_2$ ); HRMS ( $\text{ESI}^+$ )  $m/z$  250.0834 ( $\text{M}+\text{Na}^+$ ), calcd for  $\text{C}_{14}\text{H}_{13}\text{NNaO}_2$ : 250.0839.

***rac*-(2*aR*,10*bS*,10*cR*)-1,2*a*,3,4,10*b*,10*c*-Hexahydrobenzo[*f*]cyclopenta[*hi*]indolizine-2,6-dione (15)**:

20.8 mg (0.0915 mmol, 89%); conditions: **14**, 23.4 mg (0.103 mmol),  $\text{LiI}\cdot n\text{H}_2\text{O}$ , 17.7 mg (0.108 mmol),  $\text{CH}_2\text{Cl}_2$ , 0.2 mL, rt, 71 h; pale yellow solid;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.08 (d,  $J=7.6$  Hz, 1H), 7.47–7.43 (m, 1H), 7.40–7.36 (m, 1H), 7.24 (d,  $J=7.5$  Hz, 1H), 4.50 (t,  $J=4.9$  Hz, 1H), 3.84–3.76 (m, 1H), 3.65–3.51 (m, 2H), 3.01–2.98 (m, 1H), 2.75 (dd,  $J=19.4, 9.3$  Hz, 1H), 2.45–2.38 (m, 1H), 2.31–2.21 (m, 2H);  $^{13}\text{C}\{^1\text{H}\}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  216.7 (C), 162.4 (C), 138.8 (C), 132.1 (CH), 128.5 (CH), 127.9 (CH), 127.8 (CH), 127.6 (C), 62.2 (CH), 54.3 (CH), 44.1 ( $\text{CH}_2$ ), 42.9 ( $\text{CH}_2$ ), 36.2 (CH), 25.7 ( $\text{CH}_2$ ); HRMS ( $\text{ESI}^+$ )  $m/z$  250.0831 ( $\text{M}+\text{Na}^+$ ), calcd for  $\text{C}_{14}\text{H}_{13}\text{NNaO}_2$ : 250.0839.

***rac*-(1*aS*,9*bS*,10*aR*,10*bR*)-1*a*,2,9*b*,10*b*-Tetrahydro-3*H*,5*H*,10*H*-benzo[*g*]cyclobuta[*ij*]oxireno[2,3-*a*]quinolizin-5-one (17)**:

39.7 mg (0.175 mmol, 90%); conditions: **16**, 41.2 mg (0.195 mmol), *m*CPBA, 143.1 mg (0.58 mmol),  $\text{CH}_2\text{Cl}_2$ , 2 mL, 0 °C to rt, 24 h; colorless solid;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.16 (dd,  $J=7.9, 1.3$  Hz, 1H), 7.44 (dt,  $J_d=1.5, J_t=7.5$  Hz, 1H), 7.33 (t,  $J=7.3$  Hz, 1H), 7.11 (d,  $J=7.6$  Hz, 1H), 4.43 (d,  $J=11$  Hz, 1H), 4.32 (dd,  $J=13, 6.6$  Hz, 1H), 3.95 (dt,  $J_d=5.2, J_t=11$  Hz, 1H), 3.27 (dd,  $J=13.6, 11$  Hz, 1H), 3.07 (d,  $J=2.8$  Hz, 1H), 2.65 (ddd,  $J=13.6, 5.2, 1.5$  Hz, 1H), 2.40 (dt,  $J_d=4.3, J_t=13$  Hz, 1H), 2.23–2.14 (m, 1H), 1.94 (dd,  $J=15.5, 4.3$  Hz, 1H);  $^{13}\text{C}\{^1\text{H}\}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  162.5 (C), 139.0 (C), 132.4 (CH), 128.5 (CH), 127.9 (CH), 127.1 (CH), 126.6 (C), 62.8 (C), 58.3 (CH), 53.2 (CH), 37.9 ( $\text{CH}_2$ ), 37.1 ( $\text{CH}_2$ ), 26.9 (CH), 23.8 ( $\text{CH}_2$ ); HRMS ( $\text{ESI}^+$ )  $m/z$  250.0833 ( $\text{M}+\text{Na}^+$ ), calcd for  $\text{C}_{14}\text{H}_{13}\text{NNaO}_2$ : 250.0839.

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