Synthesis of novel spiro[oxirane-pyrrolizin] derivatives by epoxidation of α,β-unsaturated pyrrolizinone with cyclohexylidenebishydroperoxide

Leilei Yang, Xiaofang Li*, Xiaolian Hu and Zhenqiang Tang

School of Chemistry and Chemical Engineering, Hunan University of Science and Technology, Xiangtan, Hunan 411201, P.R. China

A simple epoxidation of *E*-2-(arylmethylidene)-2,3-dihydro-1*H*-pyrrolizin-1-ones was accomplished using cyclohexylidenebishydroperoxide as the oxygen source. A number of 3-arylspiro[oxirane-2,2'-pyrrolizin]-1'(3'*H*)-ones were obtained in moderate to good yields.

Keywords: epoxidation, α,β-unsaturated carbonyl compounds, pyrrolizinone, cyclohexylidenebishydroperoxide, spiro[oxirane-pyrrolizin] derivatives

Epoxidation of olefins has attracted considerable attention in recent years due to the fact that epoxide products are significant building blocks in organic synthesis.[1-3] Numerous strategies for epoxidation of olefins have been developed and various oxidants have been successfully used for epoxidation, including oxygen,[4] dioxiranes,[5] hypervalent iodine reagents,[6] hydrogen peroxide[7-13] and hydroperoxide.[14-17] Among these oxidants, hydrogen peroxide is probably the most environmentally benign with the remarkable advantage of producing water as the only by-product. Unfortunately, hydrogen peroxide is usually used together with a catalyst in epoxidation reactions because its oxidant power is too low to oxidise some organic compounds.[13] By contrast, hydroperoxides have similar structures and stronger oxidant power. These are also useful oxidants for the epoxidation of α,β-unsaturated carbonyl compounds in excellent yields under simple and mild reaction conditions.[15]

Most recently, our group reported a simple method to synthesise a series of α,β-unsaturated carbonyl compounds containing the interesting building block pyrrolizinone.[18] Pyrrolizinones are an important type of heterocycle compound both in synthetic medicines and natural pharmacologically relevant alkaloids.[10,20] Past research has shown that pyrrolizinone compounds have broad biological activities, including psychostimulant,[21] analgesic,[22] antitubulin[23] and antidiabetic[24] effects and asneurokinin-1 (NK1) antagonists.[25] In this context, we have tried to introduce an oxirane ring structure into the pyrrolizine compound to synthesise new pyrrolizine derivatives for further preparations of products which may be useful. We report here the synthesis of 3-arylspiro[oxirane-2,2'-pyrrolizin]-1'(3'*H*)-ones by an epoxidation reaction between *E*-2-(arylmethylidene)-2,3-dihydro-1*H*-pyrrolizin-1-ones (**1a–i**) and cyclohexylidenebishydroperoxide (Scheme 1).

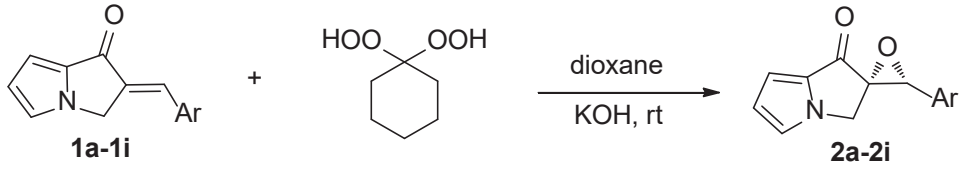
Results and discussion

At ambient temperature, *E*-2-(arylmethylidene)-2,3-dihydro-1*H*-pyrrolizin-1-ones reacted with cyclohexylidenebishydroperoxide in the presence of aqueous KOH in dioxane to afford the desired 3-arylspiro[oxirane-2,2'-pyrrolizin]-1'(3'*H*)-ones in moderate to good yields (Table 1). The reaction progress was monitored by TLC and the target products were purified by flash column chromatography on silica gel with petroleum ether:ethyl acetate as eluent. In order to understand the scope of this reaction, we studied various *E*-2-(arylmethylidene)-2,3-dihydro-1*H*-pyrrolizin-1-ones and the results are summarised in Table 1. It is clear that the yield of compounds containing electron-withdrawing substituents in the aryl group was higher than electron-donating groups. For example, those containing *E*-2-(2,4-dichlorobenzylidene)-2,3-dihydro-1*H*-pyrrolizin-1-one yielded the desired product (**2e**) in the highest yield (88%, entry 5) while the epoxide of *E*-2-(3,4-dimethoxybenzylidene)-2,3-dihydro-1*H*-pyrrolizin-1-one (**2i**) formed the product in the lowest yield (47%, entry 9). A similar trend has been shown in other epoxidations of α,β-unsaturated carbonyl compounds with hydrogen peroxide.[26]

Structural elucidation of the 3-arylspiro[oxirane-2,2'-pyrrolizin]-1'(3'*H*)-ones **2a–i** was unambiguously accomplished by various spectroscopic techniques (NMR, IR and HRMS). The high resolution mass spectrum of 3-phenylspiro[oxirane-2,2'-pyrrolizin]-1'(3'*H*)-one (**2a**) contained a peak at *m/z*

Table 1 Synthesis of spiro[oxirane-pyrrolizin] derivatives

Entry	Ar	Product	Time/h	Yield/%
1	C_6H_5	**2a**	5.0	63
2	4-FC_6H_4	**2b**	6.0	53
3	4-ClC_6H_4	**2c**	4.0	72
4	2-ClC_6H_4	**2d**	4.5	78
5	2,4-$Cl_2C_6H_4$	**2e**	6.0	88
6	4-$CH_3C_6H_4$	**2f**	5.5	54
7	4-$CH_3SC_6H_4$	**2g**	6.5	56
8	4-$CH_3OC_6H_4$	**2h**	5.0	60
9	3,4-$(OCH_3)_2C_6H_3$	**2i**	8.0	47



Ar: a, C_6H_5; **b**, 4-FC_6H_4; **c**, 4-ClC_6H_4; **d**, 2-ClC_6H_4; **e**, 2,4-$Cl_2C_6H_3$;
f, 4-$CH_3C_6H_4$; **g**, 4-$CH_3SC_6H_4$; **h**, 4-$CH_3OC_6H_4$; **i**, 3,4-$(OCH_3)_2C_6H_3$;

Scheme 1

* Correspondent. E-mail: lixiaofang@iccas.ac.cn

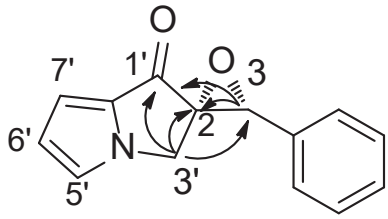


Fig. 1 Partial HMBC diagram of **2a**.

226.0865 ([M +H]$^+$), which indicated the existence of **2a** (calculated value 226.0863). The IR spectrum of **2a** revealed the presence of a carbonyl stretching vibration band at 1707 cm^{-1}, which was assigned to the carbonyl group of the pyrrolizinone moiety. The ^{1}H NMR spectrum of **2a** revealed two doublets at δ_H 4.05 ppm (J = 13.0 Hz) and 4.31 ppm (J = 13.0 Hz), which were assigned to the protons of methylene (H_2C-3') and one singlet at δ_H 4.56, which was assigned to the proton of CH (HC-3) in the oxirane ring (for numbering see Fig. 1). There was a singlet at δ_H 6.57 ppm, which was assigned to the proton of HC-6' in the pyrrolizinone ring. The doublet at δ_H 6.82 ppm (d, J = 3.5 Hz) and the singlet at δ_H 7.08 ppm were assigned to the proton of HC-7' and that of HC-5' respectively in the pyrrolizinone ring.

The ^{13}C NMR spectrum of the product **2a** exhibited the presence of carbonyl carbon at δ_C 183.1 ppm (C-1'). The signal at δ_C 44.8 ppm was assigned to the carbons of CH_2 (H_2C-3'), which existed in the pyrrolizine ring [based on Heteronuclear Singular Quantum Correlation (HSQC)]. The signal at δ_C 61.7 ppm was assigned to the carbons of CH (HC-3) present in the oxirane ring (based on HSQC). The signals at δ_C 110.1, 117.2 and 125.0 ppm represented the carbons of HC-7', HC-6' and HC-5', respectively. The signal at δ_C 68.9 ppm was assigned to the spiro carbons of C-2.

In the ^{1}H–^{13}C heteronuclear multiple bond correlation (HMBC) map of **2a** (Fig. 1), protons of H_2C-3' present in the pyrrolizine ring and HC-3 in the oxirane ring correlated with the spiro carbon C-2 (68.9 ppm), protons of H_2C-3' correlated with the carbon C-3 (61.7 ppm) and carbonyl carbon C-1' (183.1 ppm). Furthermore, the correlation between the proton of HC-3 and carbonyl carbon C-1' also supported the structural assignment.

Experimental

All chemicals and solvents were of reagent-grade quality and used without further purification. 2,3-Dihydro-1*H*-pyrrolizin-1-one[18] and cyclohexylidenebishydroperoxide[26] were prepared according to the reported procedures. NMR spectra were recorded on a Bruker AV-II 500 MHz NMR spectrometer, operating at 500 MHz for ^{1}H, and 125 MHz for ^{13}C. TMS was used as an internal reference for ^{1}H and ^{13}C chemical shifts and $CDCl_3$ was used as solvent. HRMS were obtained on a Thermo EXACTIVE spectrometer and the HRMS *m/z* values for **2c**, **2d** and **2e** refer to the ion containing only the ^{35}Cl isotope. IR spectra were recorded on a PE-2000 spectrometer in KBr pellets and are reported in cm^{-1}. Melting points were measured with a Yanaco MP500 melting point apparatus and are uncorrected. The analytical TLCs were performed with silica gel 60 F254 plates. Column chromatography was carried out by using silica gel 60 (200–300 mesh ASTM).

Synthesis of (E)*-2-arylmethylidene-2,3-dihydro-1*H*-pyrrolizin-1-ones* (**1a–i**)*; general procedure*

The aromatic aldehyde (10 mmol) was added to a stirring mixture of 2,3-dihydro-1*H*-pyrrolizin-1-one (10 mmol) in ethanol (10 mL) and sodium hydroxide (20 mmol) in water (10 mL). The mixture was stirred at 45°C and completion of the reaction was evidenced by TLC analysis (R_f = 0.3–0.4) using petroleum ether (60–80 °C)-ethyl acetate (V:V = 5:1) as eluent. The reaction mixture was then cooled and filtered and the product was recrystallised from ethanol to give **1a–i**.

*(*E*)-2-Benzylidene-2,3-dihydro-1*H*-pyrrolizin-1-one* (**1a**): Pale yellow solid; yield 58%; m.p. 132–133°C (lit.[18] 132–133°C).

*(*E*)-2-(4-Fluorobenzylidene)-2,3-dihydro-1*H*-pyrrolizin-1-one* (**1b**): Pale yellow solid; yield 58%; m.p. 169–170°C; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 5.16 (d, J = 2.0 Hz, 2H), 6.55 (dd, J_1 = 4.0 Hz, J_2 = 2.0 Hz, 1H), 6.88 (dd, J_1 = 4.0 Hz, J_2 = 1.0 Hz, 1H), 7.12–7.13 (m, 1H), 7.15 (t, J = 8.5 Hz, 2H), 7.44–7.47 (m, 2H), 7.15 (t, J = 2.5 Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) : δ 47.5, 108.9, 116.3, 116.4, 116.9, 122.2, 130.3, 130.7, 130.8, 132.0, 132.1, 134.36, 134.38, 134.42, 162.3, 164.3, 179.2; IR (KBr) ν 1696 cm^{-1}; ESI-HRMS calcd for[$C_{14}H_{11}FNO$]$^+$, [M + H]$^+$: m/z = 228.0819; found: 228.0812.

*(*E*)-2-(4-Chlorobenzylidene)-2,3-dihydro-1*H*-pyrrolizin-1-one* (**1c**): Pale yellow solid; yield 62%; m.p. 228–220°C (lit.[18] 218–220°C).

*(*E*)-2-(2-Chlorobenzylidene)-2,3-dihydro-1*H*-pyrrolizin-1-one* (**1d**): Pale yellow solid; yield 58%; m.p. 195–196°C (lit.[18] 195–196°C).

*(*E*)-2-(2,4-Dichlorobenzylidene)-2,3-dihydro-1*H*-pyrrolizin-1-one* (**1e**): Pale yellow solid; yield 48%; m.p. 201–202°C (lit.[18] 201–202°C).

*(*E*)-2-(4-Methylbenzylidene)-2,3-dihydro-1*H*-pyrrolizin-1-one* (**1f**): Pale yellow solid; yield 56%; m.p. 176–178°C (lit.[18] 177–178°C).

*(*E*)-2-(4-(Methylthio)benzylidene)-2,3-dihydro-1*H*-pyrrolizin-1-one* (**1g**): Pale yellow solid; yield 41%; m.p. 193–194°C (lit.[18] 192–193).

*(*E*)-2-(4-Methoxybenzylidene)-2,3-dihydro-1*H*-pyrrolizin-1-one* (**1h**): Pale yellow solid; yield 71%; m.p. 182–184°C (lit.[18] 182–184°C).

*(*E*)-2-(3,4-Dimethoxybenzylidene)-2,3-dihydro-1*H*-pyrrolizin-1-one* (**1i**): Pale yellow solid; yield 82%; m.p. 208–209°C; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 3.93 (s, 3H), 3.94 (s, 3H), 5.15 (d, J = 1.5 Hz, 2H), 6.54 (dd, J_1 = 3.5 Hz, J_2 = 2.0 Hz, 1H), 6.86 (dd, J_1 = 4.5 Hz, J_2 = 1.0 Hz, 1H), 6.94 (d, J = 8.5 Hz, 1H), 6.96 (d, J = 2.0 Hz, 1H), 7.07 (dd, J_1 = 4.5 Hz, J_2 = 1.0 Hz, 1H), 7.12 (d, J = 1.5 Hz, 1H), 7.15 (s, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) : δ 47.5, 55.97, 55.99, 108.5, 111.4, 113.2, 116.6, 122.0, 123.7, 127.4, 131.6, 132.6, 134.6, 149.2, 150.6, 179.5; IR (KBr) ν 1698 cm^{-1}; ESI-HRMS calcd for[$C_{16}H_{16}NO_3$]$^+$, [M + H]$^+$: m/z = 270.1125; found: 270.1131.

*Synthesis of 3-arylspiro[oxirane-2, 2'-pyrrolizin]-1'(3'*H*)-ones* (**2a–i**); *general procedure*

A solution containing the *E*-2-(arylmethylidene)-2,3-dihydro-1*H*-pyrrolizin-1-one **1**, cyclohexylidenebishydroperoxide (1 mmol) and aqueous KOH (1.0 M, 1.0 mL) in 5 mL of dioxane was stirred at room temperature. Completion of the reaction was evidenced by TLC analysis (R_f = 0.4–0.5) using petroleum ether (60–80°C):ethyl acetate (V:V = 5:1) as eluent. Then, the reaction mixture was diluted with ethyl acetate (15 mL) and washed with water (4 mL). The organic layer was dried over $MgSO_4$ and then the solvent was evaporated under reduced pressure. The crude product was subjected to column chromatography using petroleum ether (60–80 °C):ethyl acetate (V:V = 5:1) as eluent to afford the corresponding **2**.

*3-Phenylspiro[oxirane-2,2'-pyrrolizin]-1'(3'*H*)-one* (**2a**): White solid; yield 63%; m.p. 152–153°C; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 4.05 (d, J = 13.0 Hz, 1H, H_2C-3'), 4.31 (d, J = 13.0 Hz, 1H, H_2C-3'), 4.56 (s, 1H, HC-3), 6.57 (s, 1H), 6.82 (d, J = 3.5 Hz, 1H), 7.08 (s, 1H), 7.29 (d, J = 7.0 Hz, 2H), 7.36–7.43 (m, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) : δ 44.8, 61.7, 68.9, 110.1, 117.2, 125.0, 126.0, 128.8, 128.9, 131.8, 133.9, 183.1; IR (KBr) ν 1707 cm^{-1}; ESI-HRMS calcd for[$C_{14}H_{12}NO_2$]$^+$, [M + H]$^+$: m/z = 226.0863; found: 226.0865.

*3-(4-Fluorophenyl)spiro[oxirane-2,2'-pyrrolizin]-1'(3'*H*)-one* (**2b**): White solid; yield 53%; m.p. 165–166°C; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 4.03 (d, J = 12.5 Hz, 1H, H_2C-3'), 4.30 (d, J = 12.5 Hz, 1H, H_2C-3'), 4.54 (s, 1H, HC-3), 6.58 (s, 1H), 6.89 (s, 1H), 7.09 (s, 1H), 7.20 (d, J = 8.5 Hz, 2H), 7.27–7.20 (m, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) : δ 44.7, 61.0, 68.8, 110.1, 115.9, 116.1, 117.2, 125.0, 127.75, 127.82, 129.73, 129.76, 131.8, 162.0, 164.0, 182.7; IR (KBr) ν 1703 cm^{-1}; ESI-HRMS calcd for[$C_{14}H_{11}FNO_2$]$^+$, [M + H]$^+$: m/z = 244.0768; found: 244.0773.

3-(4-Chlorophenyl)spiro[oxirane-2,2'-pyrrolizin]-1'(3'H)-one (**2c**): White solid; yield 72%; m.p. 173–174°C; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 4.03 (d, J = 13.0 Hz, 1H, H_2C-3'), 4.30 (d, J = 13.0 Hz, 1H, H_2C-3'), 4.54 (s, 1H, HC-3), 6.58 (s, 1H), 6.89 (d, J = 3.5 Hz, 1H), 7.09 (s, 1H), 7.24 (d, J = 8.5 Hz, 2H), 7.40 (d, J = 8.5 Hz, 2H); ^{13}C NMR

($CDCl_3$, 125 MHz) : δ 44.7, 61.0, 68.8, 110.2, 117.3, 125.0, 127.4, 129.1, 129.4, 131.2, 133.7, 132.5, 134.9, 182.5; IR (KBr) *v* 1714 cm^{-1}; ESI-HRMS calcd for$[C_{14}H_{11}ClNO_2]^+$, [M + H] $^+$: *m/z* = 260.0473; found: 260.0477.

*3-(2-Chlorophenyl)spiro[oxirane-2,2'-pyrrolizin]-1'(3'*H*)-one* (**2d**): White solid; yield 78%; m.p. 153–154°C; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 3.93 (d, *J* = 13.0 Hz, 1H, H_2C-3'), 4.15 (d, *J* = 13.0 Hz, 1H, H_2C-3'), 4.76 (s, 1H, HC-3), 6.59 (s, 1H), 6.92 (d, *J* = 4.0 Hz, 1H), 7.07 (s, 1H), 7.34 (s, 3H), 7.40 (t, *J* = 4.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) : δ 44.8, 59.6, 68.2, 110.2, 117.2, 124.9, 126.8, 127.2, 129.5, 130.0, 131.8, 132.4, 133.3, 182.4; IR (KBr) *v* 1711 cm^{-1}; ESI-HRMS calcd for$[C_{14}H_{11}ClNO_2]^+$, [M + H] $^+$: *m/z* = 260.0473; found: 260.0465.

*3-(2,4-Dichlorophenyl)spiro[oxirane-2,2'-pyrrolizin]-1'(3'*H*)-one* (**2e**): White solid; yield 88%; m.p. 187–188°C; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 3.94 (d, *J* = 13.0 Hz, 1H, H_2C-3'), 4.16 (d, *J* = 13.0 Hz, 1H, H_2C-3'), 4.71 (s, 1H, HC-3), 6.06 (s, 1H), 6.92 (d, *J* = 4.0 Hz, 1H), 7.09 (s, 1H), 7.28 (d, *J* = 8.0 Hz, 1H), 7.33 (d, *J* = 8.5 Hz, 1H), 7.43 (s, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) : δ 44.7, 59.1, 68.2, 110.4, 117.3, 125.1, 127.6, 127.7, 129.5, 131.1, 131.7, 133.9, 135.4 181.9; IR (KBr) *v* 1711 cm^{-1}; ESI-HRMS calcd for$[C_{14}H_{10}Cl_2NO_2]^+$, [M + H] $^+$: *m/z* = 294.0083; found: 294.0086.

*3-(*p*-Tolyl)spiro[oxirane-2,2'-pyrrolizin]-1'(3'*H*)-one* (**2f**): White solid; yield 54%; m.p. 154–155°C; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 2.37 (s, 3H, $^-CH_3$), 4.05 (d, *J* = 12.5 Hz, 1H, H_2C-3'), 4.29 (d, *J* = 12.5 Hz, 1H, H_2C-3'), 4.52 (s, 1H, HC-3), 6.57 (s, 1H), 6.88 (d, *J* = 4.0 Hz, 1H), 7.07 (s, 1H), 7.16 (d, *J* = 8.0 Hz, 2H), 7.33 (d, *J* = 8.0 Hz, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) : δ 21.3, 44.8, 61.8, 68.8, 109.9, 117.0, 124.8, 125.9, 129.5, 130.9, 131.8, 138.9, 183.1; IR (KBr) *v* 1712 cm^{-1}; ESI-HRMS calcd for$[C_{15}H_{14}NO_2]^+$, [M + H] $^+$: *m/z* = 240.1019; found: 240.1026.

*3-(4-(Methylthio)phenyl)spiro[oxirane-2,2'-pyrrolizin]-1'(3'*H*)-one* (**2g**): White solid; yield 56%; m.p. 161–163°C; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 2.50 (s, 3H, $^-SCH_3$), 4.05 (d, *J* = 13.0 Hz, 1H, H_2C-3'), 4.29 (d, *J* = 13.0 Hz, 1H, H_2C-3'), 4.51 (s, 1H, HC-3), 6.57 (s, 1H), 6.88 (d, *J* = 4.0 Hz, 1H), 7.07 (s, 1H), 7.20 (d, *J* = 7.5 Hz, 1H), 7.26 (d, *J* = 7.5 Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) : δ 15.5, 44.8, 61.5, 68.9, 110.0, 117.1, 124.9, 126.4, 130.5, 131.8, 139.9, 182.9; IR (KBr) *v* 1712 cm^{-1}; ESI-HRMS calcd for$[C_{15}H_{14}NO_2S]^+$, [M + H]$^+$: *m/z* = 272.0740; found: 272.0736.

*3-(4-Methoxyphenyl)spiro[oxirane-2,2'-pyrrolizin]-1'(3'*H*)-one* (**2h**): White solid; yield 60%; m.p. 151–152°C; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 3.83 (s, 3H, $^-OCH_3$), 4.07 (d, *J* = 13.0 Hz, 1H, H_2C-3'), 4.30 (d, *J* = 13.0 Hz, 1H, H_2C-3'), 4.51 (s, 1H, HC-3), 6.57 (s, 1H), 6.89 (d, *J* = 4.0 Hz, 1H), 6.93 (d, *J* = 8.5 Hz, 2H), 7.07 (s, 1H), 7.21 (d, *J* = 8.5 Hz, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) : δ 44.8, 55.4, 61.7, 68.9, 109.9, 114.3, 117.0, 124.8, 125.8, 127.3, 131.9, 160.1, 183.2; IR (KBr) *v* 1710 cm^{-1}; ESI-HRMS calcd for$[C_{15}H_{14}NO_3]^+$, [M + H]$^+$: *m/z* = 256.0968; found: 256.0976.

*3-(3,4-Dimethoxyphenyl)spiro[oxirane-2,2'-pyrrolizin]-1'(3'*H*)-one* (**2i**): White solid; yield 47%; m.p. 158–160°C; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 3.89 (s, 3H, $^-OCH_3$), 3.90 (s, 3H, $^-OCH_3$), 4.06 (d, *J* = 13.0 Hz, 1H, H_2C-3'), 4.29 (d, *J* = 13.0 Hz, 1H, H_2C-3'), 4.52 (s, 1H, HC-3), 6.58 (s, 1H), 6.78 (s, 1H), 6.86–6.90 (m, 3H), 7.09 (s, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) : δ 44.8, 56.0, 61.7, 68.9, 108.6, 110.0, 111.3, 117.1, 118.6, 124.9, 126.3, 131.9, 140.3, 149.5, 183.1; IR (KBr) *v* 1707 cm^{-1}; ESI-HRMS calcd for$[C_{16}H_{16}NO_4]^+$, [M + H]$^+$: *m/z* = 286.1074; found: 286.1077.

Conclusion

We have successful developed a method for the synthesis of 3-arylspiro[oxirane-2,2'-pyrrolizin]-1'(3'*H*)-ones by the epoxidation of *E*-2-(arylmethylidene)-2,3-dihydro-1*H*-pyrrolizin-1-ones by cyclohexylidenebishydroperoxide under very mild reaction conditions. This simple and efficient method gives products that should now be able to be converted into useful products.

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References

1 H. Adolfsson and D. Balan, *Aziridines and epoxides in organic synthesis* ed. A. K. Yudin. Wiley VCH, Verlag GmbH & CoKaA, 2006, Chap. 6.
2 B. Wang, X.-Y. Wu, O. A. Wong, B. Nettles, M.-X. Zhao, D. Chen and Y. Shi, *J. Org. Chem.*, 2009, **74**, 3986.
3 O. Illa, M. Arshad, A. Ros, E. M. M. Garrigle and V. K. Aggarwal, *J. Am. Chem. Soc.*, 2013, **132**, 1828.
4 D. Enders, J. Zhu and G. Raabe, *Angew. Chem. Int. Ed.*, 1996, **35**, 1725.
5 Q.-H. Xia, H.-Q. Ge, C.-P. Ye, Z.-M. Liu and K.-X. Su, *Chem. Rev.*, 2005, **105**, 1603.
6 S. Lee and D. W. C. MacMillan, *Tetrahedron*, 2006, **62**, 11413.
7 M. Wu, C.-X. Miao, S. Wang, X. Hu, C. Xia, F. E.Küuhn and W. Sun, *Adv. Synth. Catal.*, 2011, **252**, 3014.
8 C. M. Reisinger, X. Wang and B. List, *Angew. Chem. Int. Ed.*, 2008, **47**, 8112.
9 M. Wu, B. Wang, S. Wang, C. Xia and W. Sun, *Org. Lett.*, 2009, **11**, 3622.
10 Y. Demizu, N. Yamagata, S. Nagoya, Y. Sato, M. Doi, M. Tanaka, K. Nagasawa, H. Okuda and M. Kurihara, *Tetrahedron*, 2011, **67**, 6155.
11 T. Ooi, D. Ohara, M. Tamura and K. Maruoka, *J. Am. Chem. Soc.*, 2004, **126**, 6844.
12 X. Wang, C. M. Reisinger and B. List, *J. Am. Chem. Soc.*, 2008, **130**, 6070.
13 B. S. Lane and K. Burgess, *Chem. Rev.*, 2005, **103**, 2457.
14 X. Lu, Y. Liu, B. Sun, B. Cindric and L. Deng, *J. Am. Chem. Soc.*, 2008, **130**, 8134.
15 K. Jakka, J. Liu and C.-G. Zhao, *Tetrahedron Lett.*, 2007, **48**, 139.
16 X. Wang, L. Shi, M. Li and K. Ding, *Angew. Chem. Int. Ed.*, 2005, **44**, 6362.
17 A. Lattanzi, *Adv. Synth. Catal.*, 2006, **348**, 339.
18 B. Liu, X. F. Li, L. Y. Du, Z. K. Li and R. J. Zeng. *J. Chem. Res.*, 2013, **36**, 774.
19 E. Lescot, R. Bureau, J. S. O. Santos, C. Rochais, V. Lisowski, J. Lancelot and S. Rault, *J. Chem. Inf. Model*, 2005, **45**, 708.
20 A. Padwa, M. N. Jacquez and A. Schmidt, *Org. Lett.*, 2001, **3**, 1781.
21 S. Rault, J. C. Lancelot, L. Bouyazza, M. Robba, M. A. Quermonne, B. Nammathao, J. Louchahi-Raoul and R. Marcy, *Eur. J. Med. Chem.*, 1991, **26**, 939.
22 H. Yu, F. Wang and S. F. Zhang, *Chin. Chem. Lett.*, 2003, **14**, 565.
23 V. Perri, C. Rochais, J. S. O. Santos, R. Legay, T. Cresteil, P. Dallemagne and S. Rault, *Eur. J. Med. Chem.*, 2010, **45**, 1146.
24 H. Sugihara, N. Matsumoto, Y. Hamuro and Y. Kawamatsu, *Arzneimittel-Forsch.*, 1974, **24**, 1560.
25 G. J. Morriello, G. Chicchi, T. Johnson, S. G. Mills, J. DeMartino, M. Kurtz, K. L. C. Tsao, S. Zheng, X. Tong, E. Carlson, K. Townson, A. Wheeldon, S. Boyce, N. Collinson, N. Rupniak and R. J. DeVita, *Bioorg. Med. Chem. Lett.*, 2010, **20**, 5925.
26 Y. Y. Chu, X. H. Liu, W. Li, X. L. Hu, L. L. Lin and X. F. Feng, *Chem. Sci.*, 2012, **3**, 1996.
27 K. Zÿmitek, M. Zupan, S. Stavber and J. Iskra, *Org. Lett.*, 2006, **8**, 2491.