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A short access to highly strained spiranic compounds from ethyl 3-cyclobutylprop-2-enoate

Hani Salim, Olivier Piva *

Institut de Chimie et de Biochimie Moléculaires et Supramoléculaires (ICBMS), UMR CNRS 5246, Université Lyon 1, 43, Bd du 11 novembre 1918, F-69622 Villeurbanne, France
Université de Lyon, F-69622 Villeurbanne, France

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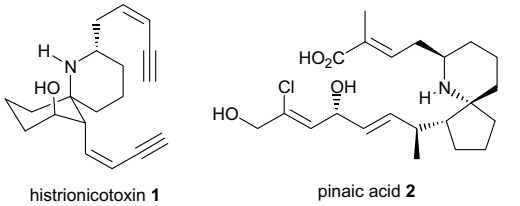
Abstract

UV irradiation of ethyl 3-cyclobutylpropen-2-oate delivered the β,γ-unsaturated isomer in high yield. Its C=C double bond was submitted to epoxidation and cyclopropanation to deliver the corresponding spiro[3.2]hexane derivatives. Alternatively, the same substrate treated by TMS–I or by OsO_4 allowed an easy access to two spiranic butyrolactones.

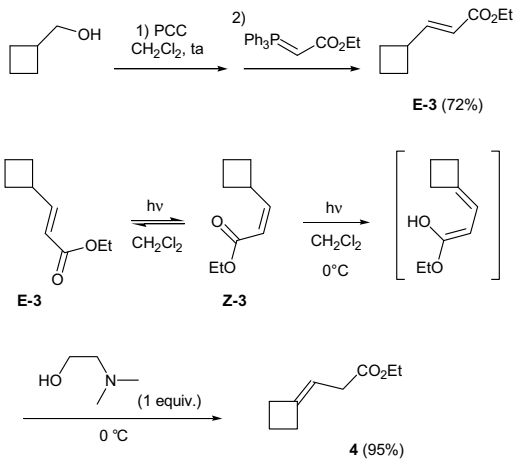
Keywords: Photochemistry; Isomerization; Cyclopropanation; Epoxidation; Lactone

Spiranic compounds due to their atypical topologies have always attracted the attention of synthetic chemists.[1] It is noteworthy that some of them possess important biological activities like histrionicotoxin **1** which exhibits neuro-physiological properties[2] or pinnaic acid **2** which possess anti-inflammatory properties[3,4] (Scheme 1). In contrast, more strained structures in which the spiranic centre is connected either to a three or to a four-membered ring are rarely found in Nature. Nevertheless, their synthesis has been considered in the context of energy storage[5,6] or as prodrugs.[7,8]

In connection with our interest into photochemical processes, we already reported the direct formation of spiranic β-lactams by irradiation of 3-carboxamido-cyclohex-2-enones.[9] Alternatively, larger spiranic lactones and lactams were conveniently obtained by the selective cleavage of cyclobutane derivatives.[10] Here, we wish to describe the synthesis of heterocyclic spirocompounds possessing a cyclobutane ring directly connected to a second 3 or 5-membered ring. Our strategy is based on the functionalization of ethyl



Scheme 1.



Scheme 2.

* Corresponding author. Tel./fax: +33 472 448 136.
E-mail address: piva@univ-lyon1.fr (O. Piva).

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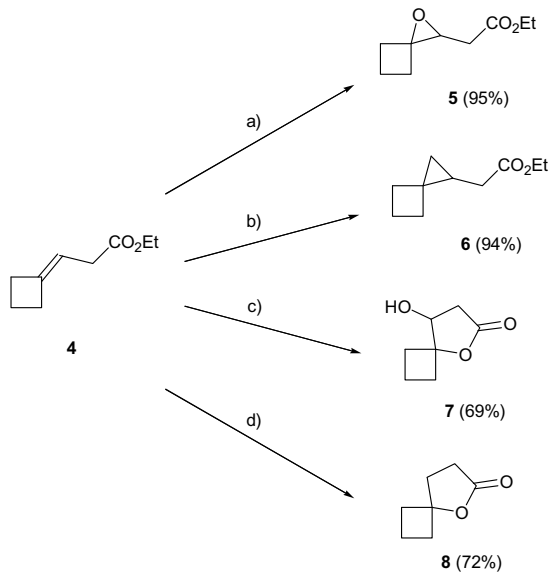

Scheme 3. Reagents and conditions: (a) *m*-CPBA, CH_2Cl_2, 0 °C; (b) (i) Et_2Zn, CH_2Cl_2, 0 °C, 10 min; (ii) CH_2I_2, 0 °C then rt; (c) OsO_4, NMO, acetone/H_2O (1:1), t.a., overnight; (d) TMS–Cl, NaI, CH_3CN, reflux.

3-cyclobutenyliden-3-propenoate **4** which could be obtained by photoisomerization of α,β-unsaturated ester **3**[11,12] (Scheme 2).

Irradiation of *E*-ethyl 3-cyclobutylpropen-2-oate **3** at 254 nm in dichloromethane and in the presence of *N*,*N*-dimethylaminoethanol afforded the corresponding β,γ-unsaturated ester **4** in a very high yield. It is worth to note that the presence of the β-aminoalcohol is crucial to promote the protonation of the photodienol intermediate.

Compound **4** was first submitted to the action of *m*-CPBA to give in 95% yield the corresponding ethyl (6-[5-oxaspiro[3,2]hexanyl)acetate **5** which was plenty characterized according to ^{1}H NMR and MS spectroscopy.[13] Similarly, cyclopropanation of **4** was conveniently achieved in a similar yield by using diiodomethane and diethylzinc according to a well-established procedure[14] (Scheme 3).

The synthesis of spiro[4,3] octane derivatives was also investigated. Dihydroxylation of **4** furnished directly the parent β-hydroxylactone **7** in 69% yield. Action of TMS–I[15,16] easily generated in situ delivered in 72% yield, the known butyrolactone **8**.[17]

In conclusion, we have demonstrated the easy conversion of ethyl 3-cyclobutylidenpropanoate into different highly strained spiranic compounds which could be of interest as building blocks in organic synthesis.

Acknowledgements

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13. Selective data for new isolated compounds. Compound **4**: ^{1}H NMR (300 MHz): 1.25 (3H, t, $J = 7.1$ Hz), 1.85–2.05 (2H, m), 2.58–2.73 (4H, m), 2.89 (2H, d, $J = 6.0$ Hz), 4.21 (2H, q, $J = 7.1$ Hz), 5.15–5.25 (1H, m). ^{13}C NMR (75 MHz): 14.4, 17.0, 29.4, 31.1, 33.9, 60.7, 112.2, 144.5, 172.7. Compound **5**: ^{1}H NMR (300 MHz): 1.25 (3H, t, $J = 7.1$ Hz), 1.55–2.61 (8H, m), 3.19 (1H, t, $J = 6.0$ Hz), 4.19 (2H, q, $J = 7.1$ Hz). ^{13}C NMR (75 MHz): 13.1, 14.4, 28.6, 31.1, 36.3, 57.1, 61.1, 63.7, 170.7. IR: 2934, 2857, 1738, 1489, 1448, 1369, 1174, 823 cm^{-1}. HRMS: calcd for $C_9H_{14}O_3$, 170.8634; found, 170.8639. Compound **6**: ^{1}H NMR (300 MHz): 0.13 (1H, dd, $J = 1.3$ and 5.1 Hz), 0.63 (1H, ddd, $J = 1.7$, 5.1 and 8.5 Hz), 0.84–0.97 (1H, m), 1.25 (3H, t, $J = 7.2$ Hz), 1.90–2.05 (6H, m), 2.14 (2H, dd, $J = 1.7$ and 7.1 Hz); 4.13 (2H, q, $J = 7.1$Hz). ^{13}C NMR (75 MHz): 14.5, 17.5, 18.2, 18.3, 23.7, 26.6, 30.2, 36.2, 60.5, 173.7. IR: 2929, 2857, 1738, 1492, 1448, 1369, 1176, 820 cm^{-1}. HRMS: calcd for $C_{10}H_{16}O_2$, 168.1150; found, 168.1145. Compound **7**: ^{1}H NMR (300 MHz): 1.55–2.17 (5H, m), 2.27–2.60 (m, 4H), 2.77 (1H, dd, $J = 5.2$ and 18.0 Hz), 4.39 (1H, dd, $J = 1.7$ and 5.3 Hz). ^{13}C NMR (75 MHz): 12.2, 27.8, 32.7, 37.8, 72.4, 88.6, 176.8. IR: 3434, 2929, 2942, 1765, 1494, 1403, 1300, 1055, 875 cm^{-1}. HRMS: calcd for $C_7H_{10}O_3$, 142.0630; found, 142.0630. Compound **8**: ^{1}H NMR (300 MHz): 1.60–2.10 (6H, m), 2.27 (2H, t, $J = 8.0$ Hz), 2.52 (2H, t, $J = 8.0$ Hz). ^{13}C NMR (75 MHz): 12.3, 28.9, 33.7, 34.8, 85.4, 176.8. IR: 2986, 2942, 2880, 1775, 1422, 1292, 1182, 1146, 1107, 955, 909 cm^{-1}.
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