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Short Note

(±)-Methyl 1,1a,2,7b-Tetrahydro-2-oxocyclopropa[*c*] Chromene-1a-carboxylate

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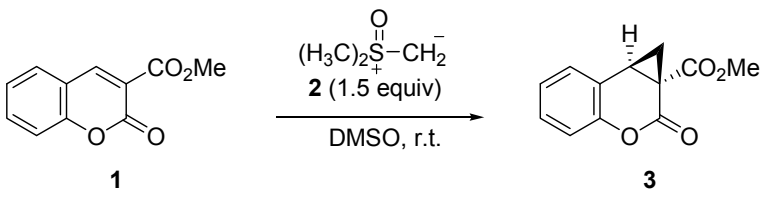
Abstract: A novel method for the preparation of (±)-methyl 1,1a,2,7b-tetrahydro-2-oxocyclopropa[*c*] chromene-1a-carboxylate has been developed. The cyclopropanation of methyl coumarin-3-carboxylate provided title compound in moderate yield by dropwise treatment with 1.5 equiv. of dimethylsulfoxonium methylide over 6 h. The structure of the newly synthesized compound was determined using ^{1}H-, ^{13}C-NMR, IR and mass spectral data.

Keywords: cyclopropanation; coumarin; dimethylsulfoxonium methylide

1. Introduction

The cyclopropane is the ubiquitous subunit in many natural products and bioactive compound. And this scaffold serves as key intermediates for many useful organic syntheses because of its unique combination of reactivity and structural properties [1–3]. Consequently, a considerable attention has been directed towards the stereoselective construction of these three-membered carbocyclic ring systems over the past few decades [4]. Recently, among diverse cyclopropane compounds, donor-acceptor (D-A) cyclopropane has attracted many organic chemists due to its special character containing donor and acceptor substituents at vicinal positions [5,6].

In continuation of our research interest in the stereoselective synthesis of diarylalkane derivatives using D-A cyclopropane [7,8], we considered the D-A cyclopropane of coumane type that would possibly be synthesized from coumarin-3-carboxylate [9]. Ethyl 1,1a,2,7b-tetrahydro-2-oxocyclopropa[*c*]chromene-1a-carboxylate was reported by Ohta and co-workers from the reaction of dimethylsulfoxonium methylide and ethyl coumarin-3-carboxylate [10]. However, the desired cyclopropylcoumarine was obtained in only 28% yield and cyclopentabenzofuran product was mainly obtained [11]. We found that title compound can be obtained in moderate yield (45% yield) by adding dimethylsulfoxonium methylide dropwise over 6h (Scheme 1). The reaction of methyl coumarin-3-carboxylate (**1**) was carried out in DMSO at room temperature. To the reaction mixture the pre-synthesized dimethylsulfoxonium methylide (**2**) from the mixture of trimethylsulfoxonium iodide and sodium hydride was added dropwise using syringe pump over 6 h and gave the desired product in moderate yield. The structure of compound **3** was confirmed by ^{1}H- and ^{13}C-NMR, IR, mass spectral data, and all data are in accordance with the assumed structure.



Scheme 1. Synthesis of (±)-methyl 1,1a,2,7b-tetrahydro-2-oxocyclopropa[*c*]chromene-1a-carboxylate (**3**).

2. Experimental Section

2.1. General Information

All reagents were used as received without further purification. Chromatographic purification of the title compound **3** was accomplished using forced-flow chromatography on ICN 60 32-64 mesh silica gel 63 (Merck, Darmstadt, Germany). Thin-layer chromatography (TLC) (Merck, Darmstadt, Germany) was performed on EM Reagents 0.25 mm silica gel 60-F plates. Developed chromatograms were visualized by fluorescence quenching and anisaldehyde stain.^{1}H- and ^{13}C-NMR spectra were recorded on 400 MHz instrument (Bruker BioSpin GmbH, Karlsruhe, Germany) as noted, and are internally referenced to residual protio solvent signals. Data for ^{1}H NMR are reported as follows: chemical shift (δ ppm), multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet), integration, coupling constant (Hz) and assignment (Supplementary Materials). Data for ^{13}C-NMR are reported in terms of chemical shift. IR spectra were recorded on Perkin-Elmer 1600 FT-IR spectrometer (Bruker Optics GmbH, Ettlingen, Germany), and reported in terms of frequency of absorption (cm^{-1}). High-resolution mass spectrometry data was recorded on a JEOL JMS-700 M Station mass spectrometer (JEOL, Tokyo, Japan).

*2.2. Syntheis of (±)-Methyl 1,1a,2,7b-Tetrahydro-2-oxocyclopropa[c]chromene-1a-carboxylate (**3**)*

Trimethylsulfoxonium iodide (396 mg, 1.8 mmol) was added to a suspension of NaH (60% in mineral oil, 60 mg, 1.5 mmol) in DMSO (5 mL) at room temperature and the whole was stirred for 40 min. The resulting mixture was added dropwise over 6 h using a syringe pump to the solution of methyl coumarin-3-carboxylate (**1**, 218 mg, 1.0 mmol) in DMSO (5 mL). After additional stirring 2 h, the reaction mixture was cooled to 0 °C and water was added for workup. The mixture was then extracted with CH_2Cl_2. The combined organic layer was washed with brine, dried over anhydrous $MgSO_4$, and concentrated in vacuo. The crude product was purified on silica gel column chromatography using ethyl acetate and hexane (1/10) as eluents to afford the desired title compound **3** (45%, 98 mg). White solid; m.p. 100–102 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 (dd, *J* = 7.5, 1.6 Hz, 1H), 7.32–7.24 (m, 1H), 7.14 (td, *J* = 7.5, 1.2 Hz, 1H), 7.04 (d, *J* = 8.2 Hz, 1H), 3.84 (s, 3H), 2.93 (dd, *J* = 9.1, 6.5 Hz, 1H), 2.48 (dd, *J* = 9.1, 5.0 Hz, 1H), 1.40 (dd, *J* = 6.5, 5.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.1, 162.4, 149.5, 128.6, 127.7, 124.7, 120.1, 117.2, 53.3, 29.3, 28.6, 21.3; IR (film) 3038, 2965, 2923, 1757, 1720, 1497, 1440, 1374, 1322, 1287, 1249, 1197, 1150, 1103, 1051 cm^{-1}; HRMS (EI) *m*/*z* calcd. for $[M]^+$ $C_{12}H_{10}O_4$: 218.0579 Found: 218.0551.

Supplementary Materials: Copies of the ^{1}H- and ^{13}C-NMR spectra for compound **3** are available online.

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Author Contributions: Both authors contributed equally to this work.

Conflicts of Interest: The authors declare no conflict of interest.

References

1. Donaldson, W.-A. Synthesis of cyclopropane containing natural products. *Tetrahedron* **2003**, *57*, 8587–8627. [CrossRef]
2. Brackmann, F.; Meijere, A. Natural occurrence, syntheses, and applications of cyclopropyl-group-containing α-amino acids. 1. 1-Aminocyclopropanecarboxylic acid and other 2,3-methanoamino acids. *Chem. Rev.* **2007**, *107*, 4493–4537. [CrossRef] [PubMed]
3. Chen, D.Y.-K.; Pouwer, R.H.; Richard, J.-A. Recent advances in the total synthesis of cyclopropane-containing natural products. *Chem. Soc. Rev.* **2012**, *41*, 4631–4642. [CrossRef] [PubMed]
4. Bartoli, G.; Bencivenni, G.; Dalpozzo, R. Asymmetric cyclopropanation reactions. *Synthesis* **2014**, *46*, 979–1029.
5. Reissig, H.-U.; Zimmer, R. Donor–acceptor-substituted cyclopropane derivatives and their application in organic synthesis. *Chem. Rev.* **2003**, *103*, 1151–1196. [CrossRef] [PubMed]

6. Schneider, T.F.; Kaschel, J.; Werz, D.B. A new golden age for donor-acceptor cyclopropanes. *Angew. Chem. Int. Ed.* **2014**, *53*, 5504–5523. [CrossRef] [PubMed]
7. Kim, A.; Kim, S.-G. Lewis acid-catalyzed Friedel–Crafts alkylation of donor–acceptor cyclopropanes with electron-rich benzenes to generate 1,1-diarylalkanes. *Eur. J. Org. Chem.* **2015**, 6419–6422. [CrossRef]
8. Sin, S.; Kim, S.-G. Stereoselective cascade reactions of donor–acceptor cyclopropanes with *m*-*N*,*N*-dialkylaminophenyl α,β-unsaturated carbonyls: Facile diastereoselective synthesis of *cis*- and *trans*-tetralins. *Adv. Synth. Catal.* **2016**, *358*, 2701–2706. [CrossRef]
9. Abdel-Wahab, B.F.; Mohamed, H.A.; Farhat, A.A. Ethyl coumarin-3-carboxylate: Synthesis and chemical properties. *Org. Commun.* **2014**, *7*, 1–27.
10. Yamashita, M.; Okuyama, K.; Kawajiri, T.; Takada, A.; Inagaki, Y.; Nakano, H.; Tomiyama, M.; Ohnaka, A.; Terayama, I.; Kawasaki, I.; et al. A novel tandem reaction of 3-substituted coumarins with two equivalents of dimethylsulfoxonium ylide to 2-substituted cyclopenta[*b*]benzofuran-3-ol derivatives. *Tetrahedron* **2002**, *58*, 1497–1505. [CrossRef]
11. Yamashita, M.; Okuyama, K.; Kawasaki, I.; Ohta, S. One-step synthesis of 2-substituted cyclopenta[*b*] benzofuran-3-ol derivatives from 3-substituted coumarins. *Tetrahedron Lett.* **1995**, *36*, 5603–5606. [CrossRef]

Sample Availability: Not available.