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Iron(III) catalysis of an intramolecular Michael reaction

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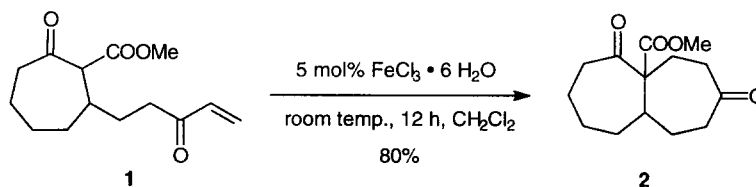
Abstract

Iron(III)chloride hexahydrate catalyzes intramolecular Michael reactions under mild and neutral conditions with excellent chemo- and stereoselectivity. © 1998 Elsevier Science Ltd. All rights reserved.

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Transition metal catalysis of the Michael reaction of 1,3-dicarbonyl compounds with acceptor activated olefins is known since the early 1980's [1] and it is a valuable alternative to the classic base catalysis of the reaction. Owing to the mild and neutral conditions, the chemoselectivity of these processes is superior to that offered by base catalysis, since the latter suffers from various unwanted side and subsequent reactions, such as aldol cyclizations, ester solvolyses or retro-Claisen type decompositions. Inspired by our results on the catalysis of *intermolecular* Michael reactions by $\text{FeCl}_3 \cdot 6 \text{H}_2\text{O}$ [2], we considered that this simple and readily available compound might also be an efficient and mild catalyst for chemo- and stereoselective *intramolecular* Michael reactions [3].

Precursor compound **1** cleanly converted within a few hours in diluted CH_2Cl_2 solution with 5 mol% $\text{FeCl}_3 \cdot 6 \text{H}_2\text{O}$ to the annulation product **2** (Scheme). The isolated yield after chromatography is good (80%), and no side products, *e. g.* dimers resulting from an intermolecular reaction, are detectable by GC-MS. Importantly, the reaction proceeds without any need for anhydrous or inert conditions. Moreover, the workup procedure is very simple: Filtration through a short column of silica gel removes all iron containing materials.



With respect to stereoselectivity, the racemic product **2**¹ was formed as a single diastereoisomer. The relative *trans* configuration was established by a *J*-resolved homonuclear correlation experiment. A *triplet-triplet* coupling pattern of the 7-H (methine) resonance in the ¹H-NMR spectrum represents a symmetrical environment of 7-H with two axial (*J* = 11 Hz) and two equatorial (*J* = 3 Hz) vicinal protons, which can only be realized in a *trans*-connection of the two seven membered rings. A complete assignment of all carbon and proton resonances was achieved with a number of homo- and heteronuclear 2D-NMR experiments.

The synthesis of precursor **1** was accomplished by introduction of the ω-alkenyl side chain by cuprate [4] addition to a cycloheptenone-2-carboxylate [5] followed by allylic oxidation with SeO₂-*t*BuO₂H [6,7] and PCC [8].

In summary, the Fe(III) catalysis of the Michael reaction of β-ketoesters and enones introduces the opportunity to perform intramolecular seven-membered ring annulations, which are highly chemo- and stereoselective. The relative configuration of the product was established to be *trans*.

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¹ *trans*-Methyl Bicyclo[5.5.0]dodecane-2,11-dione-1-carboxylate **2**. Compound **1** (89 mg, 0.35 mmol) and FeCl₃ · 6 H₂O (4.7 mg, 0.017 mmol) were stirred in CH₂Cl₂ (1 ml) for 12 h at ambient temperature. Subsequently, the reaction mixture was transferred onto the top of a silica gel column, and the product **2** was eluted with cyclohexane-*tert*-butyl methyl ether (1 : 2, *R_f* = 0.33) to yield 71 mg (80%) **2** as a colorless oil. Also, an amount of about 10 mg (11%) of the starting material **1** was recovered (*R_f* = 0.38). Spectral data: ¹H NMR (CDCl₃, 500 MHz): δ = 1.36 (m, 1 H; 5-H), 1.56 (m, 1 H; 4-H), 1.71 (tt, *J* = 11, 3 Hz, 1 H; 7-H), 1.71-1.81 (m, 2 H; 6-H, 8-H), 1.89-1.95 (m, 2 H; 4-H, 5-H), 2.08-2.22 (m, 3 H; 6-H, 8-H, 12-H), 2.27 (ddd, *J* = 15, 6, 3 Hz, 1 H; 12-H), 2.51 (ddd, *J* = 16, 6, 3 Hz, 1 H; 11-H), 2.54 (ddd, *J* = 15, 6, 4 Hz, 1 H; 9-H), 2.57 (m, 1 H; 3-H), 2.61 (m, 1 H; 9-H), 2.65 (ddd, *J* = 16, 12, 3 Hz, 1 H; 11-H), 2.70 (ddd, *J* = 13, 6, 5 Hz, 1 H; 3-H), 3.83 (s, 3 H; CH₃) ppm. ¹³C{¹H} NMR (CDCl₃, 50 MHz): δ = 24.36 (4-C), 28.44 (5-C), 29.51 (8-C), 31.20 (12-C), 36.17 (6-C), 39.47 (11-C), 41.49 (3-C), 42.57 (9-C), 46.11 (7-C), 52.02 (OCH₃), 66.14 (1-C), 171.84 (COOMe), 209.68 (2-C), 212.71 (10-C) ppm.