

Synthesis of Racemic [2-¹⁴C]Jasmonic Acid*

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(±)-[2-¹⁴C]Jasmonic Acid, Plant Growth Regulator

(±)-[2-¹⁴C]Jasmonic acid has been synthesized in nearly 50% yield *via* the route of the Michael addition starting from 2-(2Z-pentenyl)-2-cyclopenten-1-one and diethyl [2-¹⁴C]malonate followed by saponification and decarboxylation of the Michael products in one step.

Introduction

Jasmonic acid [(1*RS*,2*RS*)-3-oxo-2-(2*Z*-pentenyl)-cyclopentane-1-acetic acid] (**4**)* (Fig. 1) and its methyl ester are not only important substances in perfumery but the (–)-enantiomer of **4** and (–)-methyl jasmonate are also known to be endogenous plant growth regulators, widely distributed within the plant kingdom, and possessing phytohormone like properties [2, 3]. Both substances have received particular attention because of their physiological effects, like growth inhibition in rice seedlings, promotion of senescence in detached oat leaves, and inhibition of pollen germination etc. (for detailed references see [3, 4]). Senescence promotion by JA-Me in barley leaves is accompanied with degradations of chlorophyll and ribulose-1,5-bisphosphate carboxylase [5] and the induction of new polypeptides [6].

Further clarification of the physiological role of JA depends at least partly on the availability of radiolabelled JA for studies on uptake, transport, and metabolism in plants. Radiolabelled (±)-JA has been prepared by catalytic tritium exchange [7]. (±)-[2-¹⁴C]9,10-dihydro-JA has also been synthesized [8]. The present paper describes a simple two step synthesis for (±)-[2-¹⁴C]JA.

Materials and Methods

2-(2*Z*-Pentenyl)-2-cyclopenten-1-one was obtained from Firmenich SA, Geneva. Diethyl [2-¹⁴C]malonate (spec. radioactivity 437 MBq/mmol) was purchased from Central Institute of Nuclear Research of the Academy of Sciences of the GDR, Rossendorf, DDR-8051 Dresden.

Michael addition

180 mg (1.2 mmol) 2-(2*Z*-pentenyl)-2-cyclopenten-1-one (**1**) were dissolved in 1.2 ml absolute methanol and mixed with 147 mg (0.92 mmol) inactive and 13 mg (0.08 mmol) diethyl [2-¹⁴C]malonate (total radioactivity 35.7 MBq). The reaction was started by addition of 50 µl sodium methylate (2.15 mg Na) and allowed to proceed at room temperature under nitrogen for 1.5 h with magnetic stirring. The Michael addition was stopped by the addition of 7 µl HOAc, the mixture evaporated under reduced pressure, and bound to 0.5 g Florisil (Fluka AG, Switzerland). Chromatography on 100 g silica gel (Merck, FRG, 0.063–0.2 mm) using the solvent system *n*-hexane/EtOAc (8/2, v/v) gave 184.8 mg (0.6 mmol) **2** and **3** as a mixture (chemical and radiochemical yield 60%).

Decarboxylative saponification

60 mg of the mixture of **2** and **3** as well as 70 µl H₂O were heated at 225 °C for 18 h in a sealed tube (rinsing with nitrogen before tube sealing). The products were taken off in 0.1 M NaHCO₃ and extracted with chloroform to give the neutral fraction containing unreacted **1** and a distinct amount of the ethyl esters of **4** and **5** which were hydrolyzed to **4** and **5** by 0.5 M KOH (60 °C, 2 h, under nitrogen). Purification of **4** + **5** was performed by chromatogra-

Abbreviations: JA-jasmonic acid; JA-Me-methyl jasmonate.

* Part 60 of the series "Syntheses of radioactively labelled compounds". For part 59 see [1].

* The carbon atoms in **4** and **5** are numbered as shown in Figure 1 when used in connection with the trivial names.

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phy on 50 g silica gel (Merck, 0.063–0.2 mm) using solvent system A (see below). After acidification of the remaining aqueous phase the majority of **4** + **5** (9:1) was obtained in a pure form by chloroform extraction.

The chemical and radiochemical purity was proved by TLC. Radiograms were obtained on a Berthold Scanner LB II. Solvent systems: A = *n*-hexane/EtOAc/HOAc (60/40/1, v/v/v), R_f **4** = 0.4, R_f **5** = 0.35; B = chloroform/EtOAc/HOAc (14/6/1, v/v/v), R_f **4** + **5** = 0.7; C = *n*-hexane/acetone (6/4, v/v), R_f **4** + **5** = 0.6.

Solvent system A allows the detection of **4** and **5** as a 9:1 mixture. The total chemical and radiochemical yield of **4** + **5** was 83.1%, their specific radioactivity 35.4 MBq/mmol.

Results and Discussion

The Michael addition has been realized several times as a basic reaction for the synthesis of JA and JA-like compounds [9–12]. Under the conditions of this reaction 2-(2*Z*-pentenyl)-2-cyclopenten-1-one (**1**) reacts with diethyl malonate under the formation of two racemic stereoisomers **2** and **3** (Fig. 1), separable by chromatographic methods. Attempts to decarboxylate **2** and **3** by heating in dimethyl sulfox-

ide in the presence of H₂O and NaCl [13] gave, under small scale conditions applied, only low yields of JA-Et. Apparently, the retro Michael addition forming the starting compound **1** is favoured. Therefore, the method of decarboxylative saponification by heating with water under high pressure [9] was adapted to radiochemical work. Under the conditions chosen, **2** as well as **3** gave a 9:1 mixture of (±)-jasmonic acid (**4**) and (±)-7-*iso*-jasmonic acid (**5**)*, a well known ratio for **4/5** preparations [12, 14]. For this reason a separation of the Michael products **2** + **3** has not been further achieved. The overall yield of about 50% for **4** + **5** related to the diethyl malonate used may be regarded as a good result as the Michael reaction has been achieved with a nearly 1:1 mixture of starting compounds. Generally, excess of the diester is used in this reaction.

In conclusion, a short, simple, and efficient synthesis of (±)-[2-¹⁴C]jasmonic acid has been established providing a specific radioactivity equal that chosen for the diethyl [2-¹⁴C]malonate.

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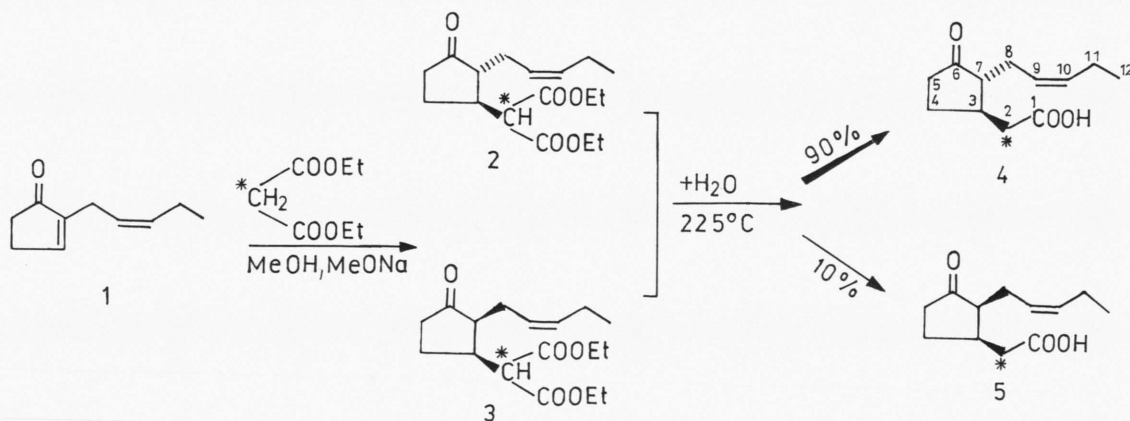


Fig. 1. Synthesis of (±)-[2-¹⁴C]jasmonic acid.

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