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**Short Communication**

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# A Novel Synthesis of (±)-Munduserone *via* Acetylenic Intermediates

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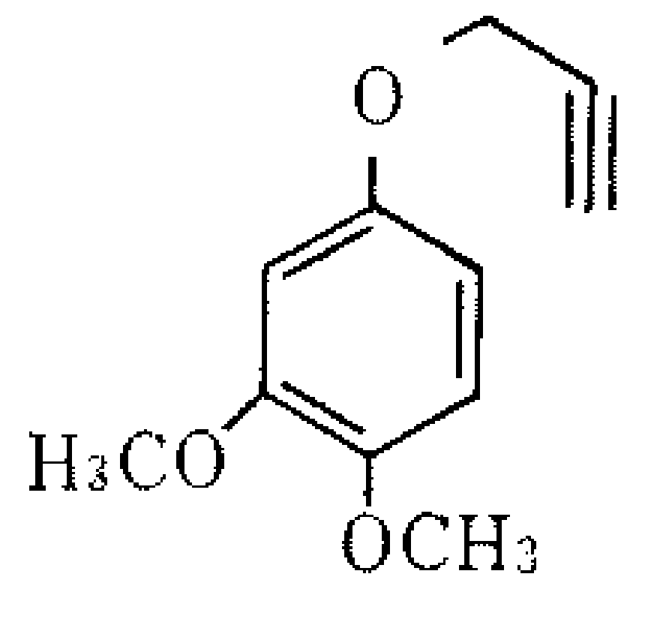
The first total synthesis of rotenone was accomplished by Miyano *et al.* by the use of Hoesh condensation via dehydrorotenone.[1] Since that time many synthetic works of rotenoids have been carried out by several different procedures. Those are: i) use of Hoesh condensation,[1,2] ii) utilization of isoflavone as an intermediate,[3] iii) enamine synthesis,[4] iv) thermal condensation of 4-carbethoxy-3-chromene with polyphenol,[5] and v) use of polyphosphoric acid in the acylation of phenols.[6] Among these five methods, the sodium borohydride reduction of dehydrorotenoids and succesive Oppenauer oxidation are the key reactions in their final steps. Recently Crombie *et al.* devised a new method, an one carbon insertion reaction using dimethylsulfonium methylide, which did not pass through dehydrorotenoids as an intermediate, and isorotenone was synthesized by this method.[7] Although this method is very interesting, the difficulty of obtaining isoflavone intermediates and the lack of generality were encountered.

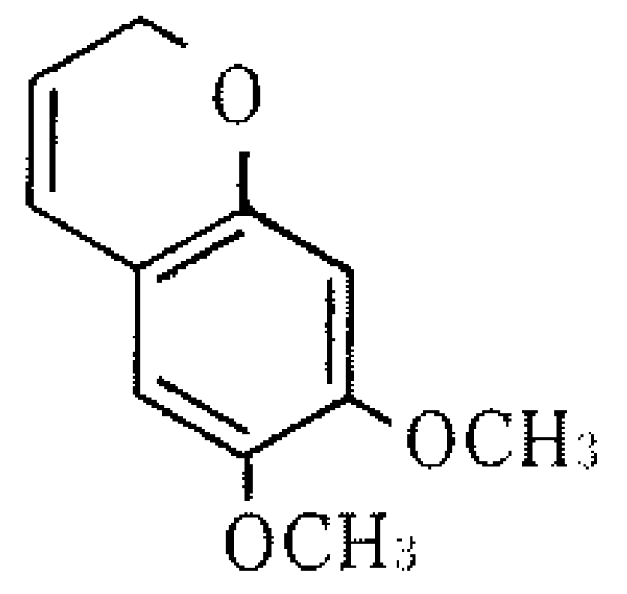
Here the authors wish to report a novel synthetic method of munduserone, the simplest rotenoid, *via* acetylenic intermediates. This method does not pass through dehydrorotenone-type intermediates, and starting materials can be obtained easier than that of the other methods.

As a preliminary experiment, 3,4-dimethoxyphenyl propargyl ether (I) was heated in diethylaniline for 2.5 hr under nitrogen. The product was proved to be the chromene (II) by its IR and NMR spectra. Based on this result and the previous observation that 6a, 12a-dehydrorotenol (III) was cyclized to mutarotenone (IV) by sodium acetate,[8] the authors expected to obtain rotenoids from acetylenic ketone by intramolecular cyclization. Therefore the authors tried to synthesize munduserone by this route.

4-Methoxysalicylaldehyde was condensed with the lithium salt of I in liquid ammonia.



(I)



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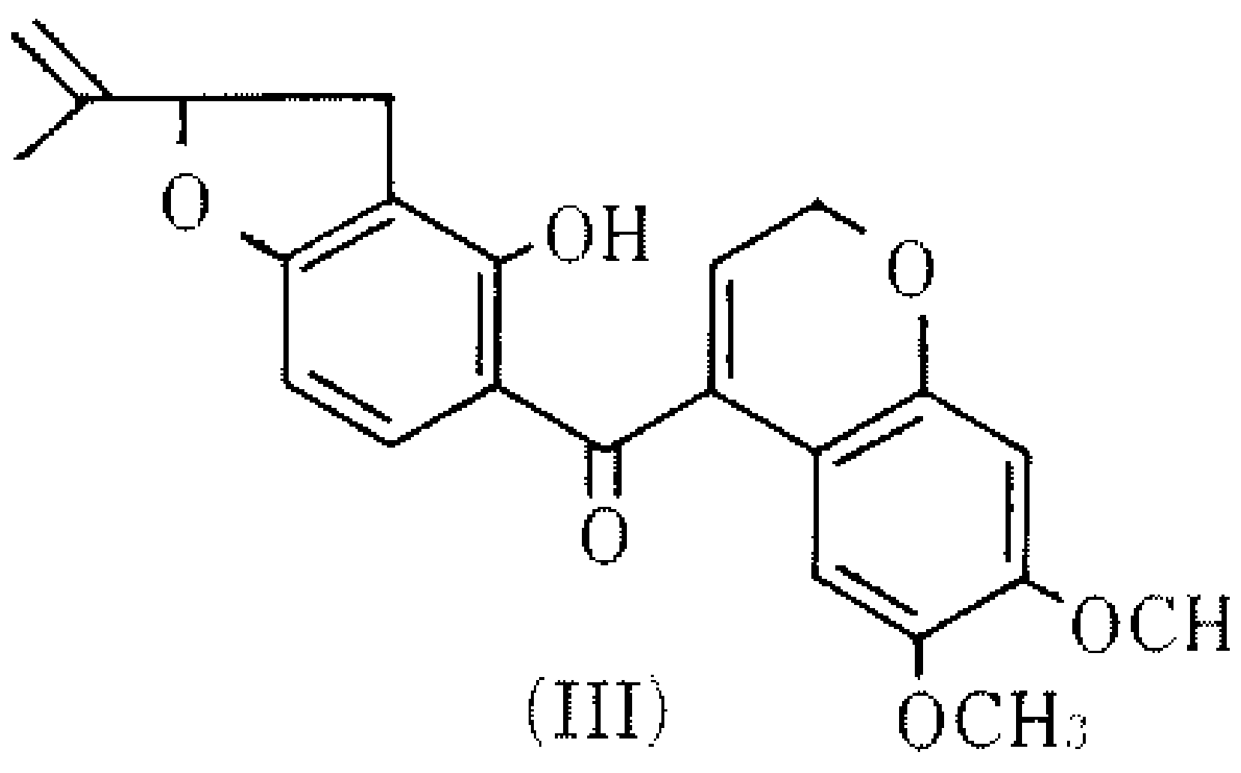

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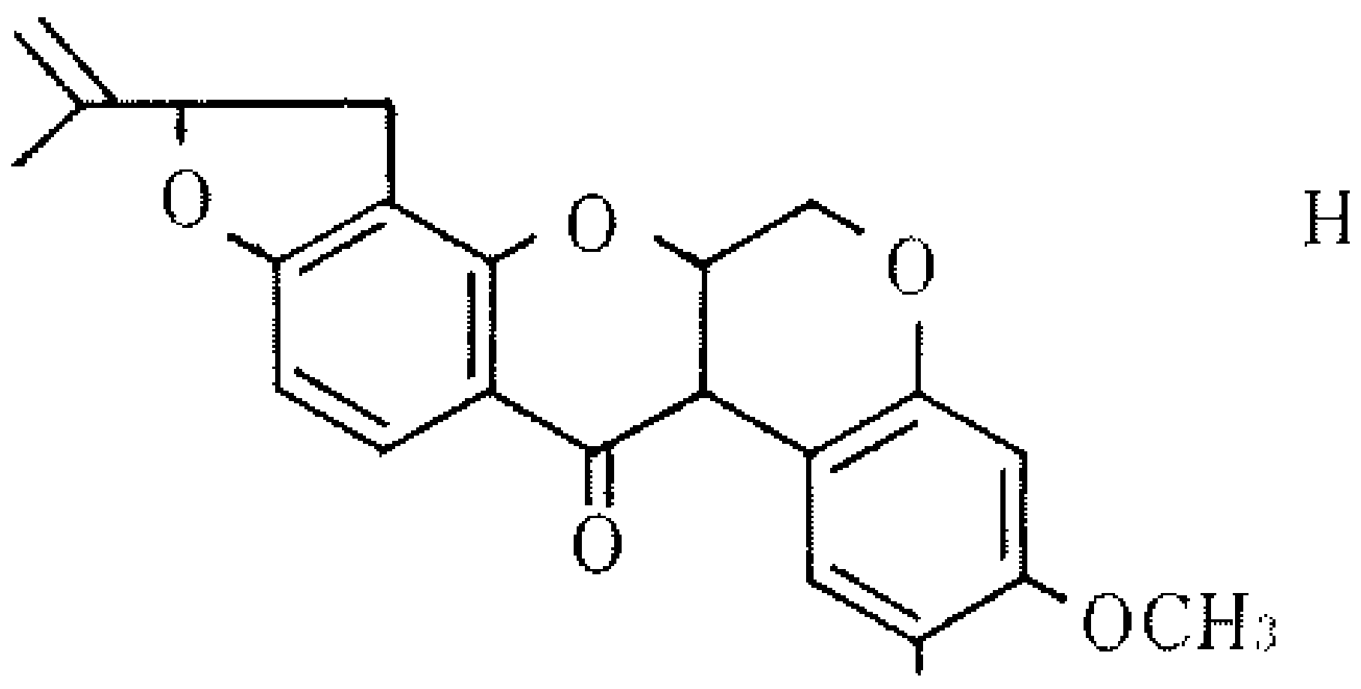

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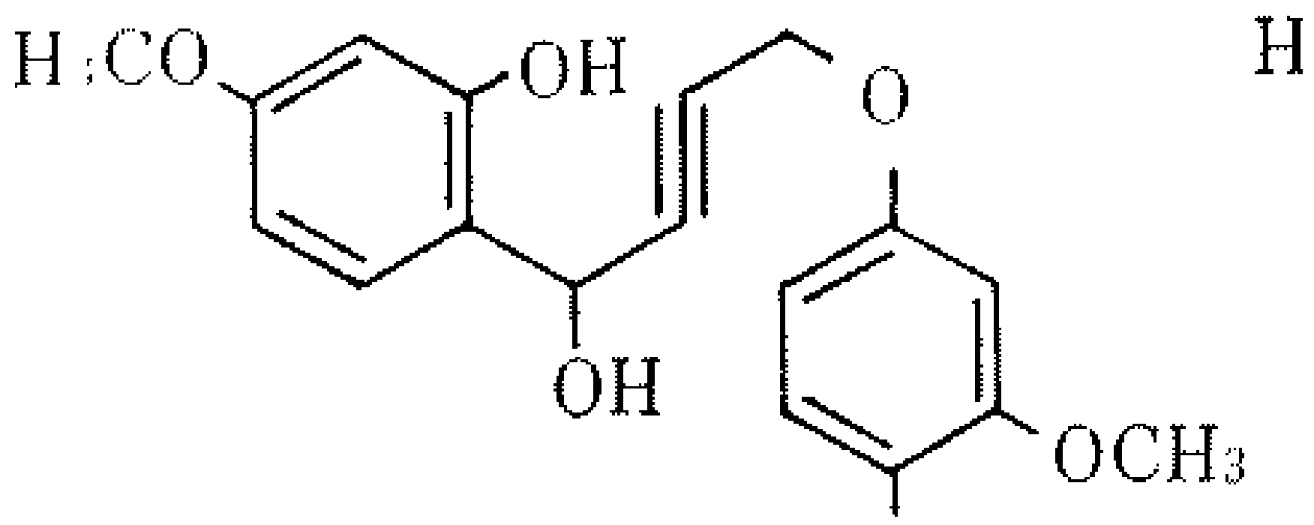

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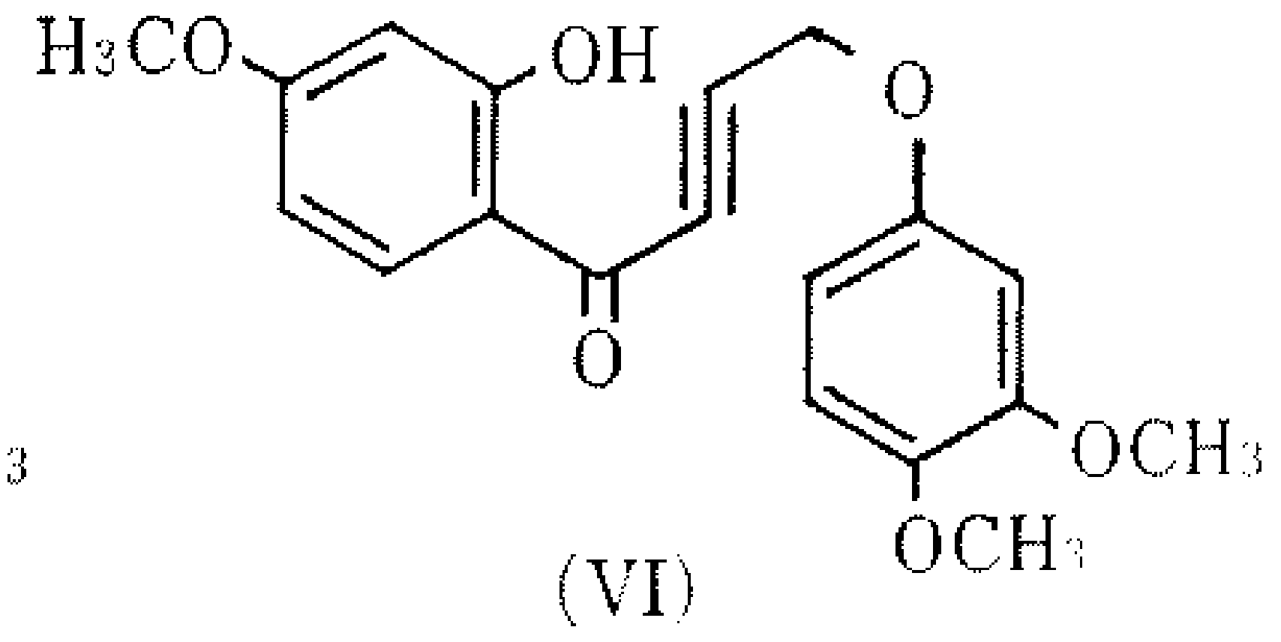

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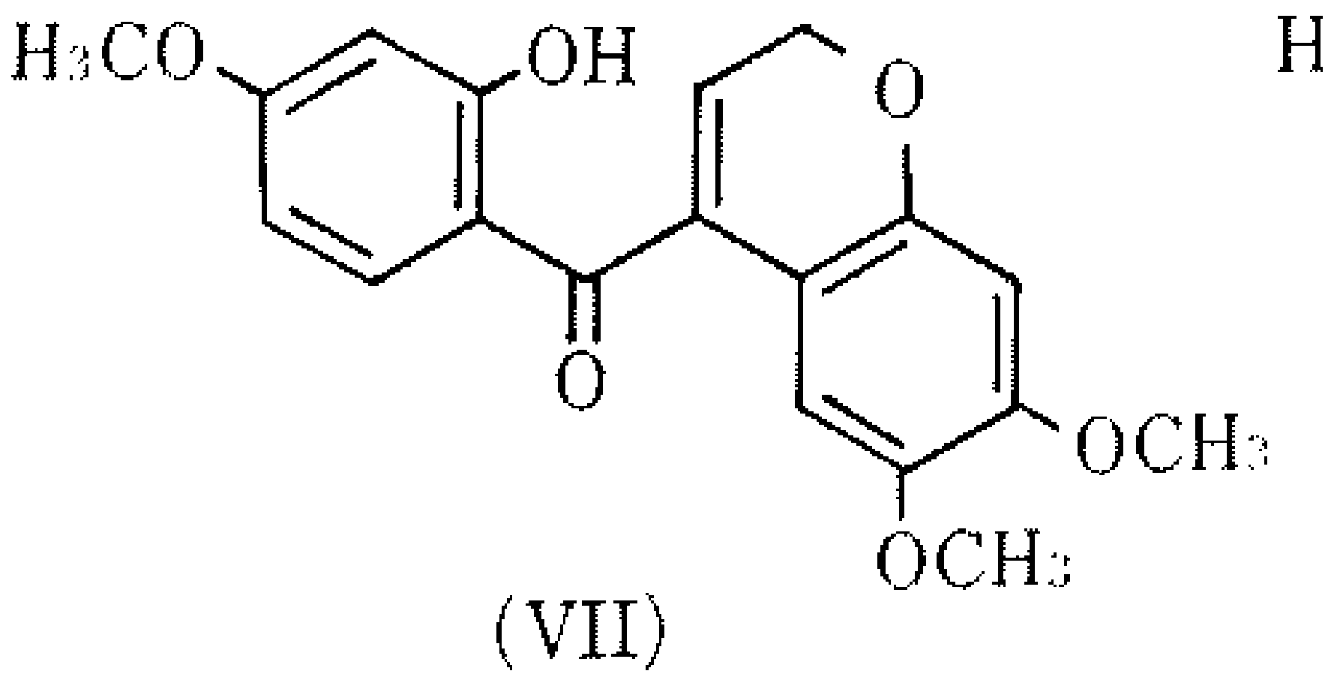
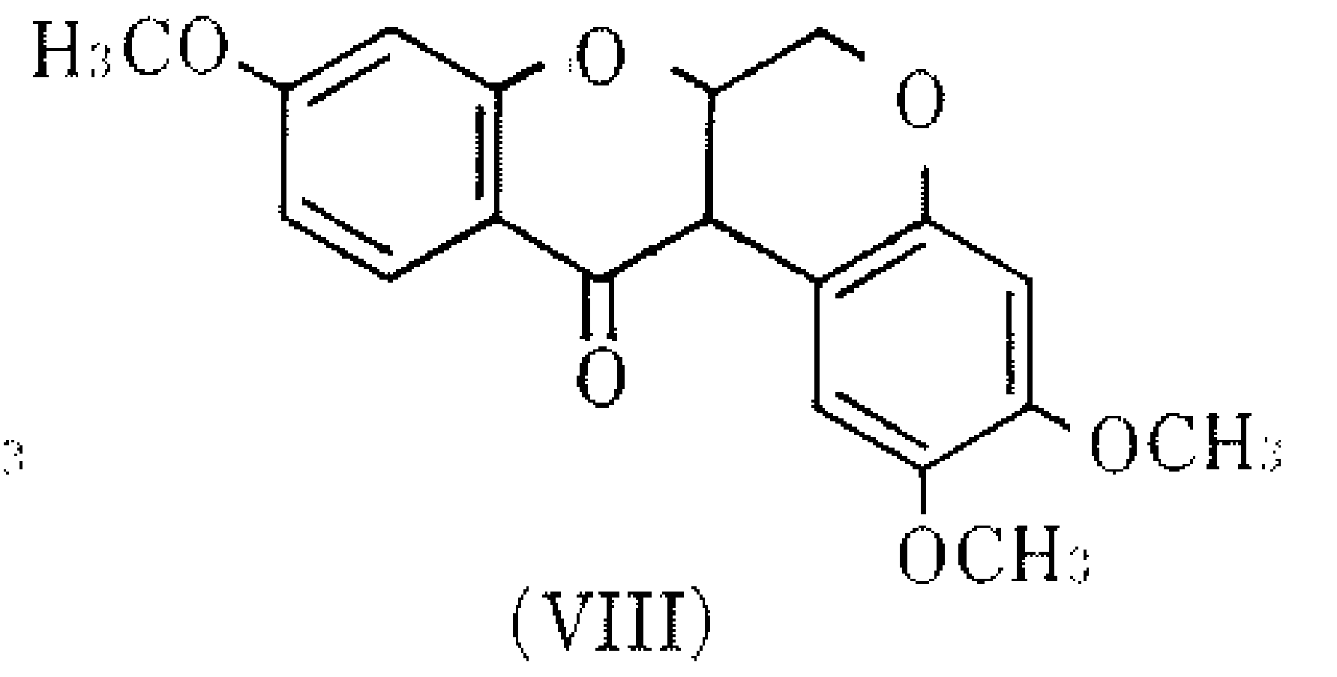


(VII)



(VIII)

Although a considerable amount of starting materials remained, the desired acetylenic carbinol (V) was observed on thin layer chromatogram. But the acetylenic carbinol (V) was so unstable that a part of them was polymerized during the course of column chromatography. Therefore, the crude reaction product was directly converted to acetylenic ketone (VI) by active manganese dioxide in methylene chloride at room temperature and the ketone (VI) was purified by silicagel column chromatography and successive recrystallization, mp 121.5∼122.0°C as yellow needles. The structure of VI was confirmed by the following spectral data; IR $\nu_{max}^{nujol}$ cm$^{-1}$: 2240 (–C≡C–), and 1640 (chelated unsaturated =CO); NMR $\delta_{Me_4Si}^{CDCl_3}$ (60 MH$_z$) 3.85, 3.87, 3.92 (each 3H, s, three $CH_3O$), 4.95 (2H, s, $-C{\equiv}C{-}CH_2-$), 11.85 (1H, s, –OH) and 6.3∼6.9, 7.66 (6H, aromatic protons). Yield of VI from I was *ca.* 30%. The acetylenic ketone (VI) was cyclized to a dehydrorotenol type compound (VII) by heating in diethylaniline to 180∼185°C for 2.5 hr under nitrogen. Treatment of the crude product with sodium acetate in 99% ethanol for 2.5 hr under refluxing afforded (±)-munduserone (VIII). The pure material was obtained easily after silicagel column chromatography and recrystallization. From 3.0 g of acetylenic ketone (VI) about 0.5 g of (±)-munduserone was obtained. The synthesized (±)-munduserone was identical to an authentic sample⁶⁾ in its IR, NMR, mp and mixed mp, and thin layer chromatographic behavior.

This method *via* acetylenic intermediates seems applicable to the general synthesis of rotenoids and further studies are now in progress.

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