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BIOMIMETIC SYNTHESIS OF 2,3-DIOXABICYCLO [4,4,0] DECANES AS PLANT GROWTH REGULATORS

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Key Word Index—*Eucalyptus grandis*; plant growth regulators; G-regulators; biological control.

Abstract—Naturally occurring derivatives of 2,3-dioxabicyclo [4,4,0] decane from *Ecucalyptus grandis* have been reported to possess a wide range of biological control in various plants including the parent one. The biogenetic type synthesis of these compounds have been discussed in this Paper.

INTRODUCTION

Naturally occurring derivatives (1–3) of 2,3-dioxabicyclo [4,4,0] decane from *Eucalyptus grandis*, termed as G-regulators [1] exercise control over a wide range of physiological functions [2, 3] in plants which include root strike in cuttings, water uptake, membrane permeability, frost resistance and inhibition of electron transport in photosynthesis. These compounds have been shown to possess promotory auxin-like activity at a concentration of about 5×10^{-6} M while an inhibitory abscissic acid type of activity is demonstrated at a concentration of 5×10^{-5} M. The presence of these biologically active compounds has also been confirmed in some other myrtaceous genera in addition to *Eucalyptus grandis*. A careful study of the structures (1–3) and the lack of optical purity at position C-4, together with the presence of the peroxyhemiacetal structure, creates a doubt about them being artefacts rather than natural products. However, by using labelled oxygen ($^{18}O_2$), it was proved that they are really natural products [4]. Some work has been reported [4, 5] about the synthetic aspects of these compounds but in one of the approaches the authors failed to obtain these compounds while in another report [6] the yields were poor and also the intermediates were not characterized properly. We have loosely modelled the chemical synthesis on the basis of their biosynthesis (Scheme I) and achieved the synthesis in almost quantitative yields and explained the various aspects of biosynthesis [7] in detail. The results are presented in this paper.

RESULTS AND DISCUSSION

The step I in the synthesis of G-regulators (1–3) involves a classical Knoevenagel condensation of the appropriate aldehyde with syncarpic acid [1]. The main problem in this type of condensation is the Michael addition of syncarpic acid on the alkylidene (5) to yield the undesired bis-adduct (8). To avoid the formation of 8 we have opted for a new method [11] to achieve the formation of 5 from syncarpic acid (4). When syncarpic acid in dry ether was treated with isobutyraldehyde in the presence of pyrrolidine at room temperature under nitrogen, it gave a white powdery solid which was identified as Mannich base (9) from its ^{1}H NMR spectral signals at δ0.89 (*t*, $J = 7$ Hz, 6H), 1.33 (*s*, 12H) and 4.43 (*d*, $J = 4$ Hz, 1H). The next step was the elimination of amine from the Mannich base which is best achieved by treatment with mineral acids but this yielded the adduct 8 on such a treatment. This may be attributed to the fact that the reaction is reversible [8] and the alkylidene produced undergoes Michael addition to the liberated syncarpic acid to yield 8. Mannich base on treatment with *p*-toluene sulphonic acid in dry dichloromethane yielded the corresponding alkylidene in quantitative yields which showed ^{1}H NMR spectral signals at δ1.15 (*d*, $J = 6.5$ Hz, 6H), 1.36 (*s*, 12H), 3.52 (*m*, 1H) and 7.28 (*d*, $J = 12$ Hz, 1H). The comparison of the NMR data of 9 and 5 revealed that the amine had been eliminated since the appearance of a signal at δ7.28 showed the presence of an α,β-unsaturated carbonyl system.

Equilibration of compounds 5 *and* 6

It was observed that after keeping the alkylidene at room temperature for several days in an open flask, it was transformed into the G_3(1). The ^{1}H NMR examination of the alkylidene (5) after some time in a sealed tube (sealed under N_2) showed the appearance of a new compound with additional signals appearing at δ1.48 (*s*, 12H), 1.68 (*br s*, 3H), 1.96 (*br s*, 3H), and 5.72 (*m*, 1H). This compound was identified as the dienol (6). The solid dienol (6) was treated with diazomethane and it yielded a liquid compound identified as the dienol ether (see Experimental). This change of alkylidene to dienol might be a heat-promoted sigma-tropic 1,4 hydride shift. To confirm this the reaction was studied by NMR monitoring at 70° in a sealed NMR tube. The data obtained did not fit into a first order equation. Similar studies at different temperatures supported the above conclusions. The possibility that the reaction might be light-promoted was discarded when it was found that the above conversion was feasible even when the alkylidene (5) was refluxed in benzene in the dark. Later it was found to be an acid catalysed reaction.

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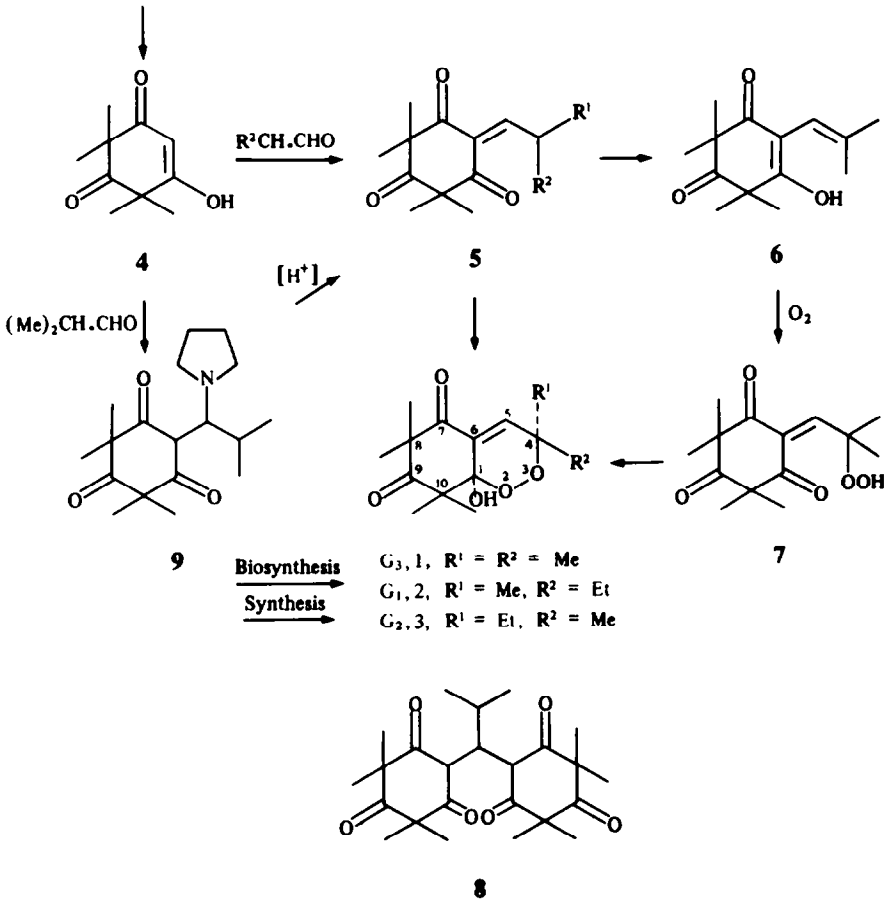

4 5 6 7 8 9

Uptake of oxygen and formation of a peroxyhemiacetal linkage

The next step is the reaction of dienol with oxygen. This can be achieved by the reaction of dienol with singlet oxygen to yield the required product either via Diels–Alder addition or the nucleophilic attack of oxygen at position C-4, thereby, creating chirality at C-4. However, when the reaction of dienol was performed with singlet oxygen produced by different methods [Rose Bengal or $Ca(OCl_2)_2$ and H_2O_2 etc.] the uptake of oxygen was not affected when compared to the reaction of dienol with ordinary oxygen in benzene. This observation proves that in this reaction triplet oxygen is involved rather than singlet oxygen which is also supported by the fact that the G's lack chirality at position C-4. Thus the reaction may be similar to that of ordinary enols with oxygen via radicals [9] to yield 7. The intermediate 7, which could not be isolated, may undergo ring closure to yield the desired compounds. Similarly by using other aldehydes G_2 and G_3 were synthesized. No attempts were made to purify the intermediates because of their labile nature since the Mannich bases decompose on silica gel while the alkylidenes or dienols react with oxygen to yield the corresponding G's during chromatography. In the final step a mixture of G_1 and G_2 was obtained in the ratio 4:5. This mixture was separated by two phase thin layer chromatography to yield the two pure compounds which showed IR and NMR spectra superimposable with those of authentic samples.

EXPERIMENTAL

Mps. uncorr. The NMR spectra were obtained on a 100 MHz instrument fitted with a temp. control system and TMS was used as the int. standard. To study the order of reaction an automatic integration of the disappearing signal at δ7.28 due to the olefinic proton of the alkylidene (5) and the appearance of a signal at 5.72 due to the olefinic proton of the dienol (6) was done by the computer on an FT-NMR machine while the data fitting to study the order of reaction was done manually.

Syncarpic acid (4) was synthesized from phloroglucinol by a previously reported method [10].

Conversion of syncarpic acid (4) *to Mannich base* (9). To a cooled stirred soln of syncarpic acid (4, 1.82 g, 10 mmol) and pyrrolidine (850 mg, 1.2 mmol) in dry Et_2O (50 ml) under N_2 was added dropwise a soln of isobutyraldehyde (900 mg, 1.25 mmole) in dry Et_2O (5 ml) over a period of 10 mins. After 5 min a suspension of white powder appeared and it was filtered under vacuum and washed with cold Et_2O to remove any traces of unreacted aldehyde or amine. It was vacuum dried to yield 3.05 g of pure compound, mp 140°. ($C_{18}H_{29}O_3N$ requires C, 70.32; H, 9.50. Found C, 70.34; H, 9.49%). IR ν_{max}^{Nujol} cm^{-1} 1590, 1550, 1240, 1150. ^1H NMR: δ0.89 (*t*, J=7 Hz, 6H), 1.33 (*s*, 12H), 4.43 (*d*, J=4 Hz, 1H).

Reaction of compound 9 *with* p-TsOH. To a stirred soln of Mannich base (9, 3 g, 0.1 mol) in dry CH_2Cl_2 (50 ml) at room temp., was added *p*-TsOH (1.8 g, 0.104 mmol). After stirring for 10 min, it was washed with cold H_2O and the H_2O layer was extracted with CH_2Cl_2, (3 × 15 ml) and the combined organic extracts were made neutral by repeated washing with H_2O and

dried. Evaporation of the solvent yielded a thick liquid (2.2 g, 86%). ($C_{14}H_{20}O_3$ requires: C, 71.15; H, 8.53; Found C, 71,17; H, 8.51%). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1680, 1460, 1380, 1360, 1310, 1290, 1060. ^1H NMR: δ1.15 (*d*, J = 6.5 Hz, 6H), 1.36 (*s*, 12H), 3.52 (*m*, 1H), 7.28 (*d*, J = 1 Hz, 1H).

Conversion of alkylidene **5** *to dienol* **6**. The alkylidene (2 g) was dissolved in benzene (50 ml) and refluxed under N_2 for 1 hr. Evaporation of the C_6H_6 under red. pres. on a rotavapor under N_2 yielded a white solid (2 g), mp 71°. ($C_{14}H_{20}O_3$ requires C, 71.15; H, 8.53. Found C, 71.10; H, 8.55%). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3450, 1680, 1640, 1590, 1460, 1380, 1360, 1320, 1230, 1210, 1080, 1010. ^1H NMR: δ1.48 (*s*, 12H), 1.68 (*br s*, 3H), 1.96 (*br s*, 3H), 5.72 (*m*, 1H).

Reaction of dienol (**6**) *with diazomethane*. The dienol (1 g) was treated with an excess of an ethereal soln of CH_2N_2 and, after 30 min at 0°, the evaporation of solvent yielded a thick yellow liquid (1 g). ($C_{15}H_{22}O_3$ requires C, 71.97; H, 8.86. Found C, 71.95; H, 8.88%). IR ν_{max}^{Nujol} cm^{-1}: 1680, 1646, 1585, 1455. ^1H NMR: δ1.44 (*s*, 3H), 1.93 (*s*, 3H), 1.56 (*br s*, 3H), 1.92 (*br s*, 3H), 3.8 (*s*, 3H), 5.84 (*m*, 1H).

Reaction of dienol (**6**) *with oxygen*. A soln of dienol (2 g) in C_6H_6 (50 ml) was stirred under an atmosphere of O_2. After 30 min, the evapn of solvent gave a white crystalline solid which showed IR, NMR and mass spectra superimposable with those of an authentic sample of G_3 ($R_1 = R_2 =$ Me). By this method were also obtained G_1 (R_1 = Me, R_2 = Et) and G_2 (R_1 = Et, R_2 = Me).

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ACYLRESORCINOLS FROM SEED KERNELS OF *MYRISTICA DACTYLOIDES*

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Key Word Index—*Myristica dactyloides*; Myristicaceae; seeds; polyketides; ^{13}C NMR.

Abstract—A new polyketide 1-(2,6-dihydroxyphenyl)-9-(4-hydroxy-3-methoxyphenyl)nonan-1-one and five other polyketides 1-(2,6-dihydroxyphenyl)tetradecan-1-one and malabaricones A–D have been isolated from *Myristica dactyloides* seeds. ^{13}C NMR of the first and the second mentioned compounds are also reported for the first time.

INTRODUCTION

Myristica dactyloides is used in native medicine [1] in Sri Lanka and its seeds and aril are used as adulterants to *M. fragrans* (nutmeg). Previously only myoinositol [2], malabaricone A (**2**) and 1-(2,6-dihydroxyphenyl)tetradecan-1-one (**1**) [3] have been isolated from the bark of *M. dactyloides*. We now report the isolation of six acylresorcinols (**1**–**6**) from seeds of *M. dactyloides*.

RESULTS AND DISCUSSION

Column chromatography of an acetone seed extract of *M. dactyloides* yielded six phenols. All six compounds had similar UV spectra, showed bathochromic shifts with alkali and gave a violet colouration with fast blue B salt, thus confirming their phenolic nature.

The peak around 3360 cm^{-1} in the IR spectrum confirmed the presence of a hydrogen-bonded hydroxyl.