

SYNTHESIS OF 1-METHYL-3- $\gamma$ , $\delta$ -DIMETHYLALLYL-4,6,8-  
TRIMETHOXY-2-QUINOLONE, AN ALKALOID FROM PTELEA  
TRIFOLIATA<sup>†</sup>

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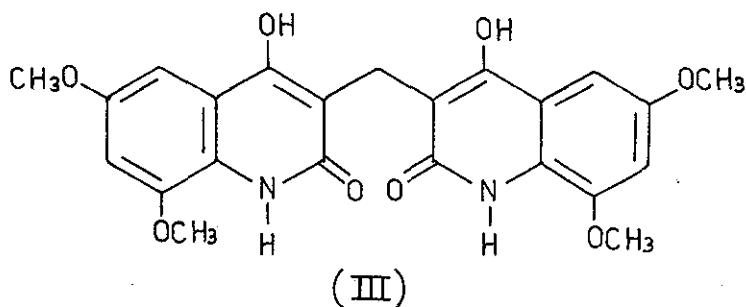
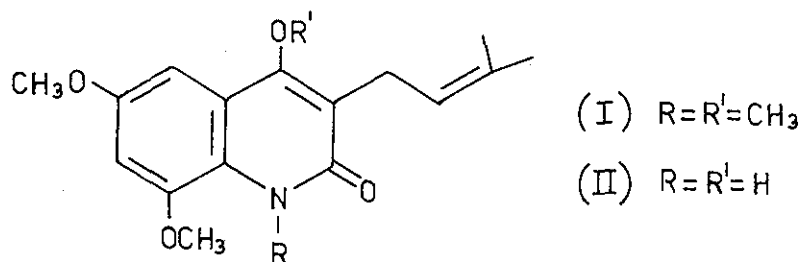
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1-Methyl-3- $\gamma$ , $\delta$ -dimethylallyl-4,6,8-trimethoxy-2-quinolone (I), an alkaloid extracted from Ptelea trifoliata, was synthesized by N,O-dimethylation of 3- $\gamma$ , $\delta$ -dimethylallyl-4-hydroxy-6,8-dimethoxy-2-quinolone (II). 3,3'-Methylenebis-4-hydroxy-6,8-dimethoxy-2-quinolone (III) was also obtained in the reaction of 2,4-dimethoxyaniline with diethyl 2-(3-methyl 2-butenyl) malonate.

The isolation of 1-methyl-3- $\gamma$ , $\delta$ -dimethylallyl-4,6,8-trimethoxy-2-quinolone, a component of Ptelea trifoliata.L (Rutaceae), has been described recently by Reisch et al.<sup>1</sup> who assigned the structure (I) mainly on the basis of spectroscopic data.

As a further contribution of our researches on the synthesis of quinoline alkaloids, we wish to report the synthesis of compound (I) by N,O-dimethylation of 3- $\gamma,\delta$ -dimethylallyl-4-hydroxy-6,8-dimethoxy-2-quinolone (II) using the procedure of Harnisch and Brack<sup>2,3</sup>.

The quinolone (II) has been obtained according to the general method of synthesis of 3- $\gamma,\delta$ -dimethylallyl-4-hydroxy-2-quinolones recently reinvestigated by Young et al.<sup>4</sup>. Reaction of 2,4-dimethoxyaniline with diethyl 2-(3-methylbut-2-enyl)malonate gave, in addition to the expected quinolone (II), a second product shown to be 3,3'-methylenebis-4-hydroxy-6,8-dimethoxy-2-quinolone (III).



Diethyl 2-(3-methyl 2-butenyl)malonate (4g) and 2,4-dimethoxyaniline (2.75 g) in diphenyl ether (40 ml) was refluxed under nitrogen for 2.5 hr. The reaction mixture was cooled and the separated product (III) was washed with ethanol and dried. The resultant orange powder (320 mg) was extremely insoluble in most solvents: m.p. 330° (Kofler), ir (nujol) 3350 (OH), 1650  $\text{cm}^{-1}$  (CO-NH); m/e 454 ( $\text{M}^+$ ) ( $\text{C}_{23}\text{H}_{22}\text{O}_8\text{N}_2$ ).

The structure of product III was confirmed by independent synthesis as follows. A suspension of 4-hydroxy-6,8-dimethoxy-2-quinolone<sup>3</sup> (200 mg) in boiling water (50 ml) was treated with 40% aqueous formaldehyde solution (3 ml) under stirring. The mixture was refluxed for 10 min., cooled and the separated product was washed with ethanol to give III, whose ir spectrum was superimposable upon that of the product from 2,4-dimethoxyaniline.

The diphenyl ether solution, diluted with petroleum ether, afforded further material (630 mg), which was treated with boiling ethanol giving the product (III) (300 mg) as ethanol-insoluble material.

The ethanol-soluble material yielded the expected 3- $\chi$ , $\chi$ -dimethylallyl-4-hydroxy-6,8-dimethoxy-2-quinolone (II) (200 mg) which was chromatographed on silica gel using an eluent as cyclohexane-chloroform (1:1), m.p. 173-175° (from ethyl acetate); ir (nujol) 1652  $\text{cm}^{-1}$  (CO-NH); uv (EtOH)  $\lambda_{\text{max}}$  (log  $\epsilon$ ) 223 nm (4.87), 253 (4.43), 288(4.0), 292(3.80), 320(3.65); nmr (60 MHz,  $\text{CD}_3\text{OD}$ )  $\delta$  1.70 and 1.80 (broad s, allylic Me), 3.30 (2 H, d, J 6.5 Hz,  $-\text{CH}_2-\text{CH}=\text{}$ ), 3.80 and 3.90 (2 s, 2  $\text{OCH}_3$ ), 5.20 (1 H, t, J 6.5 Hz,  $-\text{CH}_2-\text{CH}=\text{}$ ), 6.60 (1 H, d, J 2.5 Hz, H-7), 6.80 (1 H, d, J 2.5 Hz, H-5).

To a solution of (II) (150 mg) in dimethylformamide (8 ml),

powdered potassium hydroxide ( 500 mg) was added and then dimethyl sulphate ( 1 ml) was added with stirring. The solution was heated at 50-55° for 6 hr, poured into water and extracted with ether. The residue after evaporation of the solvent gave 1-methyl-3- $\gamma,\gamma$ - dimethylallyl-4,6,8-trimethoxy-2-quinolone ( I ) ( 115 mg), m.p.70-71° ( from petroleum ether); uv ( EtOH)  $\lambda$  max ( log  $\xi$  ) 235 (4.6), 282(4.0), 292(3.95), 343(3.74); m/e 317 ( M<sup>+</sup>); nmr ( 60 MHz, CDCl<sub>3</sub> )  $\delta$  1.75 and 1.85 ( broad s, allylic Me), 3.35 ( 2 H, d, J 6.7 Hz, -CH<sub>2</sub>-CH=), 3.88 ( 9 H, s, 3 OCH<sub>3</sub>), 3.90 ( 3 H, s, NCH<sub>3</sub>), 5.25 ( 1 H, t, J 6.7 Hz, -CH<sub>2</sub>-CH=), 6.25 ( 1 H, d, J 2.7 Hz, H-7), 6.88 ( 1 H, d, J 2.7 Hz, H-5).

The data are in agreement with those reported<sup>1</sup>, thus confirming the structure (I) proposed for the alkaloid.

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#### REFERENCES

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