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2',-3'DİHİDRO-2'-HİDROKSİİZOPROPİL-3'-METOKSİ FURANOKUMARİN (VII) IN TOTAL SENTEZİ.

THE TOTAL SYNTHESIS OF 2',3'-DIHYDRO-2'-HYRDOXYISOPROPYL-3'-METHOXYFURANOCOUMARIN (VII).

Solmaz DOĞANCA*

SUMMARY

In this study the total synthesis of 2',3'-dihydro-2'-hydroxyisoproply-3'-methoxyfuranocoumarin (VII) was performed in seven steps. Elucidation of the structures in each step were achieved by spectral and chemical methods.

ÖZET

Bu çalışmada 2',3'-dihidro-2'-hidroksiizopropil-3'-metoksifuranokumarin (VII) in 7 adımda total sentezi yapıldı. Her adımda meydana gelen yapıların aydınlatılmasında spektral yöntemler ve kimyasal reaksiyonlardan yararlanıldı.

INTRODUCTION

In our previous study, Hippomarathrum cristatum (DC.) Boiss., (Umbelliferae) was investigated for coumarin type compounds and (+) — Peucedanol Methyl Ether was isolated. Its structure was elucidated by using spectral methods (IR, UV, NMR, Mass, CD) and chemical reactions (1). In order to have further knowledge about this type coumarins, a total coumarin synthesis was performed in seven steps and its constitution was established as

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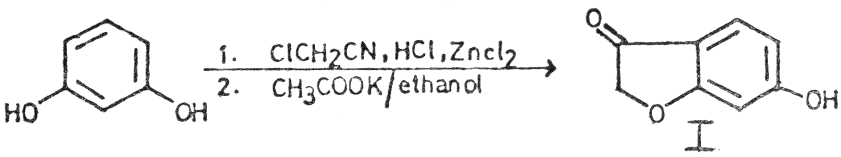
2′,3′-dihydro-2′-hydroxyisopropyl 3′-methoxyfuranocoumarin (VII) by using spectral methods (IR, UV, NMR, Mass) and chemical reactions.

EXPERIMENTAL

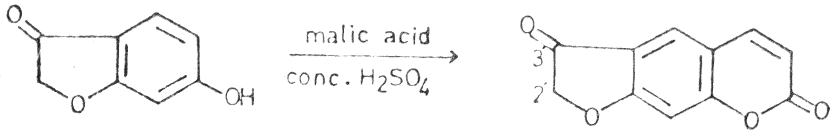
Three starting steps of this synthesis were performed according to literature (2,3).

6-Hydroxycoumaran-3-on (I) (2):



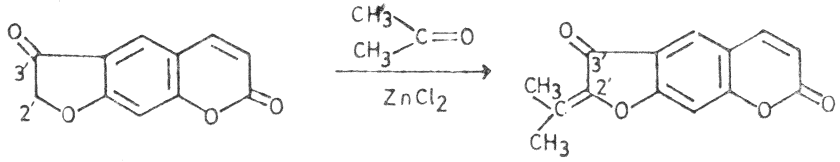
I

2′,3′-dihydro-3′-oxofuranocoumarin (II) (3):



I II

2′,3′-dihydro-2′-isopropyliden-3′-oxofuranocoumarin (III) (3):



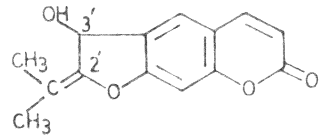
II III

The last four steps were developed from general chemical reactions, the procedures were altered for this compound as follows.

2′,3′-dihydro-2′-isopropyliden-3′-hydroxyfuranocoumarin (IV):

300 mg 2′,3′-dihydro-2′-isopropyliden-3′-oxofuranocoumarin (III) was dissolved in 60 ml of hot MeOH. 750 mg of $NaBH_4$ was added

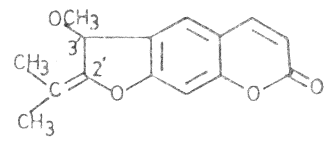
to the solution and heated under a reflux for 3 hrs (4). After cooling the mixture was acidified with 3N HC1 and kept at room temperature for 24 hrs., extracted with ether. After removal of the solvent a compound was obtained, the IR spectrum (KBr ν_{max} cm^{-1}) of the compound gave the newly added hydroxyl group at 3350.



IV

2′,3′-dihydro-2′-isopropyliden-3′-methoxyfuranocoumarin (V):

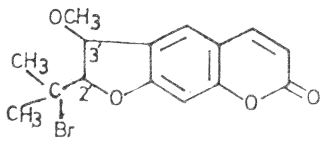
225 mg 2′,3′-dihydro-2′-isopropyliden-3′-hydroxyfuranocoumarin (IV) was dissolved in 150 ml of dry acetone. 1.5 g of non aqueous Na_2CO_3 and 15 ml of dimethylsulphate were added to the solution. The mixture was refluxed for 6 hrs., cooled and filtered, 150 ml of water was added to the filtrate. The solution was extracted with $CHC1_3$ and evaporated to dryness (5). The compound thus obtained contains the methoxy group, this is seen in IR spectrum (KBr ν_{max}) 1025 cm^{-1} and there is no hydroxyl group is left.



V

2′,3′-dihydro-2′-bromoisopropyl-3′-methoxyfuranocoumarin (VI):

180 mg 2′,3′-dihydro 2′-isopropyliden-3′-methoxyfuranocoumarin (V) was dissolved in 4.5 ml of gl. AcOH by heating and 0.6 ml AcOH (saturated with HBr) was added to the solution. After 1 hr. the compound (VI) precipitated (HBr was added to the isopropyliden group) (6). The precipitated compound was filtered, washed with water and dried. The adduct was controlled by $AgNO_3$ solution ($AgNO_3$ in EtOH) (7), the compound was heated with alcoholic $AgNO_3$ solution, turbidity showed the occurence of AgBr.



VI

2',3'-dihydro-2'-hydroxyisopropyl-3'-methoxyfuranocoumarin (VII):

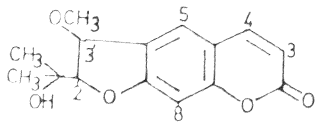
135 mg 2',3'-dihydro-2'-bromoisopropyl-3'-methoxyfuranocoumarin (VI) and 15 mg K_2CO_3 were heated with 60 ml of water for 2 hrs. (8,9). The mixture was cooled and filtered, extracted with $CHC1_3$, evaporated and crystallized from EtOH. m.p 139-140°C ; (Found: C, 65.60 H, 5.90 $C_{15}H_{16}O_5$ requires C, 65.21 : H, 5.79 %, M^+ 276 correlated this).

IR (KBr ν_{max} cm^{-1}): 3300 (OH), 1740 (lactone carbonyl), 1630 (α-pyrone), 1388 and 1370 (gem-dimethyl), 1280, 1025 (OCH_3). UV λ_{max} (logε) 206 (4.41), 218 (4.22), 223 (4.28), 253 (3.68), 300 sh, 331 (4.16) nm.

NMR spectrum ($CDC1_3$: TMS) showed methyl groups atδ 1.24 (3H, s), 1,28 (3H, s), a hydroxyl proton atδ 2.24 (1H, m) (D_2O exchange), a methoxy group atδ 3.60 (3H, s), well divided doublets atδ 6.20 (1H, d, C_3H) andδ 7.60 (1H, d, C_4H), Two peaks atδ 6.75 (1H, s) andδ 7.20 (1H, s) ppm showed the protons of C_5 anc C_8 respectively. Weil divided doublets atδ 3.00 (1H, d, C_3 H) andδ3.64 (1H, d, C_2' H) showed the protons of dihydrofuran ring.

RESULTS

The constitution of the synthesized compound (VII) was established as shown below by using spectral methods (IR, UV, NMR, Mass) and chemical reastions.



VII

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