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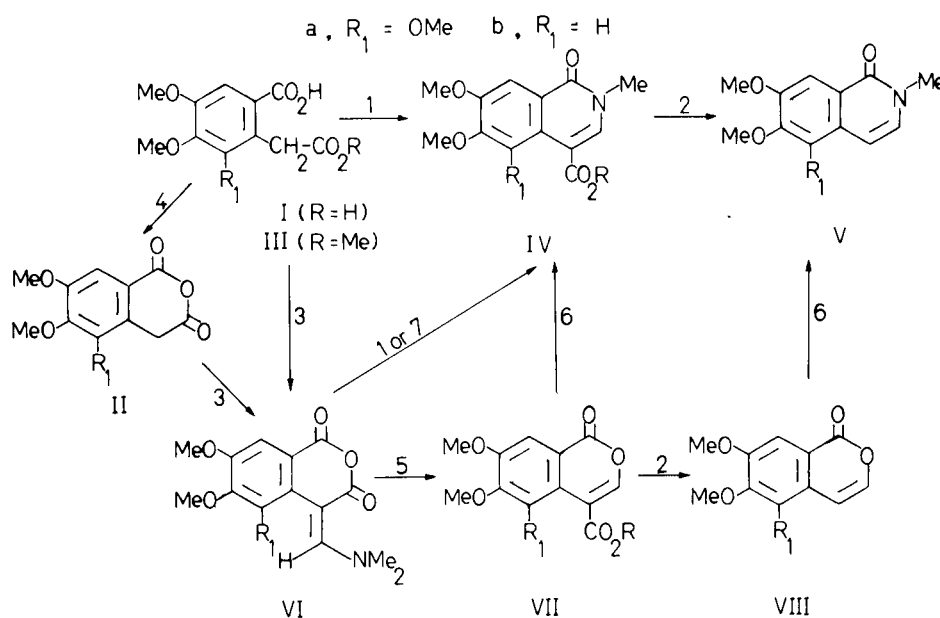
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The alkaloid thalactamine (*N*-methyl-5,6,7-trimethoxy-1(2*H*)isoquinolone) was synthesised in two steps from 4,5,6-trimethoxyhomophthalic acid (1a). Heating 1a with DMF/POCl₃ at 100° furnished thalactamine-4-carboxylic acid which was easily decarboxylated to give the alkaloid thalactamine. By the same two steps, the alkaloid *N*-methyl-6,7-dimethoxy-1(2*H*)isoquinolone is obtained from 4,5-dimethoxyhomophthalic acid. Synthesis for 1a from 2-bromogallic acid trimethyl ether was modified to give excellent yield. 5,6,7-Trimethoxy and 6,7-dimethoxyisocoumarin-4-carboxylic acid esters were synthesised from the homophthalic acids 1a and b by interacting them with DMF/phosphoryl chloride at 0°, to give corresponding 4-(*N,N*-dimethylaminoformylidene)isochroman-1,3-dione derivatives VIa and b and treating their alcoholic solutions with dry hydrogen chloride gas. The isocoumarins were converted into *N*-methyl-1(2*H*)isoquinolones by treating them with aqueous methylamine. The isochromandione VIa slowly changed into 3-chloro-4-formyl-5,6,7-trimethoxyisocoumarin during the working up of the reaction.

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The isolation of the alkaloid thalactamine was reported from the plant *Thalictrum minus* (1,2) and it was assigned the constitution of *N*-methyl-5,6,7-trimethoxy-1(2*H*)isoquinolone (Va) (1). We report an excellent synthesis for Va by making use of our new reaction (3) for synthesis of *N*-methyl-1(2*H*)isoquinolone by interaction of homophthalic acid with DMF/phosphoryl chloride. *N*-Methyl-

6,7-dimethoxy-1(2*H*)isoquinolone (Vb) was isolated recently as an alkaloid from the plant *Hernandia ovigera* L. (4,5), but its synthesis by oxidation of 6,7-dimethoxyisoquinoline was reported (6) long back. It was also obtained as degradation product of the natural alkaloids thalictarpine, thalmetatine (7,8), methyl papaverine (9), 2-nitropapaverine (10), 2-nitropapaveraldine (11). We



Reagents: 1 DMF/POCl₃ (ca 100°) 2 Heat 3 DMF/POCl₃ (ca 0°)
 4 Ac₂O 5 ROH/HCl 6 Aq. MeNH₂ 7 POCl₃

Scheme - 1

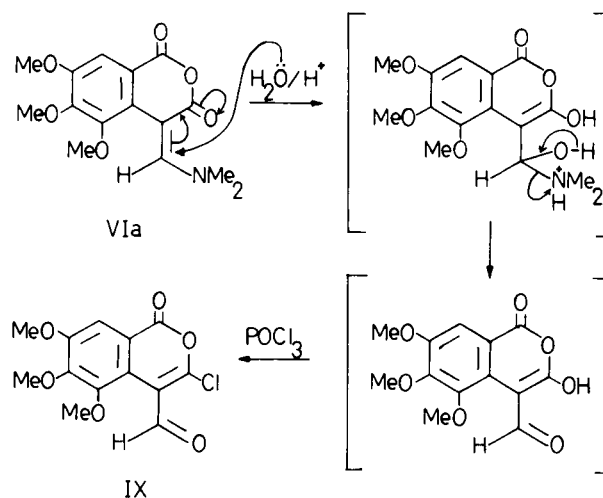
now report for it, a new and more simple synthesis by making use of the reaction (3) mentioned above.

4,5,6-Trimethoxyhomophthalic acid (Ia) with DMF/phosphoryl chloride at *ca.* 100° furnished thalactamine-4-carboxylic acid (IVa) in excellent yield and 4,5-dimethoxyhomophthalic acid (Ib) by the same reaction gave *N*-methyl-6,7-dimethoxy-1(2*H*)isoquinolone-4-carboxylic acid (IVb). The carboxylic acids IVa and b were decarboxylated smoothly to furnish thalactamine (Va) and *N*-methyl-6,7-dimethoxy-1(2*H*)isoquinolone (Vb) respectively, identical in all respects *viz.*, m.p. uv, ir and nmr spectra with the reported (1) natural product.

A modification of the reaction between homophthalic acid and DMF/phosphoryl chloride to give isocoumarin-4-carboxylic acid ester that was recently reported by us (12) was applied to 4,5,6-trimethoxy Ia and 4,5-dimethoxyhomophthalic acids (Ib) to give VIIa (R = Me and Et) and VIIb (R = Me and Et), respectively, in very good yield. It consists of isolating the intermediate 4-(*N,N*-dimethylaminoformylidene)isochroman-1,3-dione VI by carrying out the reaction at 0° and converting this intermediate VI into isocoumarin-4-carboxylic acid ester VII by simply treating its solution in the desired alcohol with dry hydrogen chloride gas. The reaction involves rearrangement and elimination of dimethylamine as explained before (12). The isocoumarins VIIb (R = H) and VIIIb (R = Me and Et) were obtained in good yields from the ester VIIb (R = Me or Et). The esters VIIa (R = Et) and VIIb (R = Me and Et) are described in literature (13,14) but were obtained in low yields by Claisen condensation of the diethyl ester of the same homophthalic acids (Ia and b, respectively) with ethyl formate. The isocoumarins VIIb (R = H) (14) and VIIIb (14,15,16,17) are also known and have been obtained by more than one method but all involve a number of steps, some of which are pretty difficult.

There is, however, a difference observed when the reaction of DMF/phosphoryl chloride at 0° was applied to 4,5,6-trimethoxyhomophthalic acid (Ia). The intermediate 4-(*N,N*-dimethylaminoformylidene)isochroman-1,3-dione (VIa) which in other cases separated from the reaction mixture, did not separate in this particular case, nor a solid separated out on pouring the reaction mixture on crushed ice. It formed a clear solution. The VIa could be precipitated from it only after adding sodium acetate and bringing the pH to 6-6.5. A further novel finding that was made was if the separated VIa was not immediately filtered (within 2 hours) but left aside in the refrigerator for 12 hours or more the product obtained was 3-chloro-4-formyl-5,6,7-trimethoxyisocoumarin (IX). In other words the initially separated VIa slowly changed into IX and transformation was nearly quantitative. The transformation is brought by the media of the reaction work up and it may be formulated as given below:

It is a slow hydrolysis leading to elimination of di-

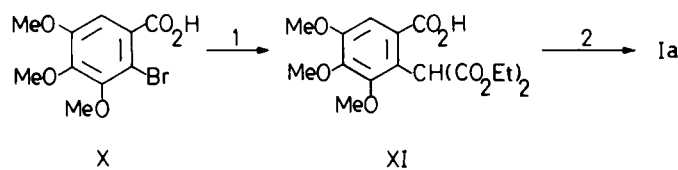


Scheme - 2

methylamine brought by nucleophilic attack of water at the olefinic double bond, the site of attack being highly electron deficient due to conjugation with C=O and due to an electron attracting NMe_2^+ group in the vicinity. The replacement of enolic -OH by Cl that takes place is probably brought out by the unchanged phosphoryl chloride and it is promoted by sodium acetate in the work up. Transformation of this type is not observed in the case of other 4-(*N,N*-dimethylaminoformylidene)isochroman-1,3-diones (3,20) VI during the work up but conditions are now being investigated to convert VI into corresponding 3-chloro-4-formylisocoumarins.

The constitution of 3-chloro-4-formyl-5,6,7-trimethoxyisocoumarin (IX) was established by its elemental analysis, uv, ir and nmr spectra. Its ir spectra gave two C=O bands one at 1760 cm^{-1} for lactonic C=O and another at 1680 cm^{-1} for aldehyde C=O. A little higher frequency for C=O of lactone is due to presence of electronegative Cl in its vicinity. The nmr spectrum gave singlets at δ 3.88 (3H, s), 4.03 (3H, s), 4.07 (3H, s) for the protons of the three methoxy groups, singlets at 7.63 (1H, s) and 10.3 (1H, s) for the aromatic and aldehyde protons, respectively.

Scheme 1 gives the synthesis of the alkaloids, of the isocoumarins and the interconversions of isocoumarins into *N*-methyl-1(2*H*)isoquinolones that were effected by aqueous methylamine. The interconversions which are easy to carry out and give quantitative yields, involve replacement of lactonic oxygen of the isocoumarin by NMe, the mechanism of which was explained before (18). Unlike 3-substituted isocoumarin-4-carboxylic acids (18, 19) which give corresponding isoquinolones with decarboxylation, no decarboxylation took place in case of VII and the same was the observation (20) in case of



Reagents: 1 $\text{H}_2\text{C}(\text{CO}_2\text{Et})_2$, NaH/CuBr 2 HCl(18%)

Scheme - 3

6,7-methylenedioxyisocoumarin-4-carboxylic acid, thus supporting the explanation given earlier (20).

4,5,6-Trimethoxyhomophthalic acid (Ia) was obtained (Scheme 3) from 2-bromogallic acid trimethyl ether (X) by modifying the synthesis (21) described earlier. The modification consists of using sodium hydride and cuprous bromide for condensation of X with diethylmalonate. The original synthesis (21) which used metallic sodium gave very poor yield of XI due to formation of much resinous material. With the modification, the present synthesis for Ia turns out to be far superior to the other reported (22,23). The other synthesis (22) for Ia is from gallic acid which involves chloral hydrate condensation and is accomplished in three steps. It can be profitably used for synthesis of 4,5,6-trihydroxyhomophthalic acid but methylation of it with dimethyl sulfate and alkali gives Ia (23) in very poor yield with the formation of a black sticky mass. Use of trimethyl ether of gallic acid in place of gallic acid in the synthesis lead to demethylation during the course of the reaction. 4,5-Dimethoxyhomophthalic acid (Ib) was obtained (24) from veratric acid.

EXPERIMENTAL

Uv spectra were measured with Zeiss VSU2P spectrophotometer. Ir spectra were recorded on Beckmann Infrared spectrophotometer. Nmr spectra were measured on Varian Associates A-60 and T-60 instruments and are given parts per million (δ) downfield from an internal TMS standard. The purity of compounds was tested by tlc. Microanalyses were carried out by Mrs. J. A. Patankar and Mr. D. S. More. Uv and ir spectra were recorded by Dr. P. M. Dhadke and Mr. D. G. Joshi.

Diethyl (2-Carboxy-4,5,6-trimethoxyphenyl)malonate (XI).

A solution of 2-bromogallic acid trimethyl ether (25) (X) (5 g., 0.017 mole) and diethyl malonate (16.5 ml., 0.103 mole) in tetrahydrofuran (THF) (15 ml.) was added dropwise to a well stirred ice cold (*ca.* 0°) solution of sodium hydride (3.84 g., 0.103 mole) in THF (10 ml.). Cuprous bromide (0.46 g., 0.001 mole) was then added and the reaction mixture was heated at 75-80° for 4 hours and then poured on crushed ice. The solution (filtered if necessary to remove organic impurities) was shaken with ether. The aqueous layer on acidification with concentrated hydrochloric acid, gave first an oil that slowly solidified on cooling. It was filtered after leaving it in the refrigerator overnight. It crystallised from petroleum ether (b.p. 60-80°) as shining silky white needles (5 g.), m.p. 105-106° [Lit. 106° (21)]; ν max (potassium chloride): 3000 (OH of

CO_2H), 1740, 1690 ($\text{C}=\text{O}$ of ester and of CO_2H), 1600, 1580, 1500 cm^{-1} (aromatic); nmr (60 MHz) (deuteriochloroform): 1.26 (6H, m, $\text{CH}_2\cdot\text{CH}_3$), 3.93, 3.96, 3.98 (each 3H, s, OCH_3), 4.28 (4H, m, CH_2Me), 5.72 (1H, s, CH), 7.55 (1H, s, H-3), 10 (1H, s, CO_2H).

Anal. Calcd. for $\text{C}_{17}\text{H}_{22}\text{O}_9$: C, 55.13; H, 5.95. Found: C, 54.8; H, 6.3.

4,5,6-Trimethoxyhomophthalic Acid (Ia).

This compound was obtained by heating XI (1.7 g.) with hydrochloric acid (40 ml. 18%) on boiling water bath for 2.5 hours and the resulting solution was extracted with ether. Removal of the ether from the extract gave a gummy mass which on treatment with benzene in the cold gave a cream colored crystalline solid. It recrystallised from benzene-acetone as light cream colored needles (0.85 g.), m.p. 148-149° [Lit. m.p. 149° (21,22), 146° (23)]. Mixed m.p. with authentic specimen (22,23) was 149°; ν max (potassium bromide): *ca.* 3000 (OH of CO_2H), 1710, 1690 ($\text{C}=\text{O}$ of CO_2H), 1600 cm^{-1} (aromatic).

4,5,6-Trimethoxyhomophthalic Anhydride (IIa).

Compound Ia (2.5 g.) was refluxed with acetic anhydride (2 ml.) and cooled when it crystallised out. It was crystallised from benzene-light petroleum as shining needles (2 g.), m.p. 129-130° [Lit. m.p. 121° (22), 124-125° (23)].

Anal. Calcd. for $\text{C}_{12}\text{H}_{12}\text{O}_6$: C, 57.15; H, 4.7. Found: C, 57.05; H, 4.6.

Methyl 2-Carboxy-4,5,6-trimethoxyphenylacetate (IIIa).

This compound was obtained by refluxing methanolic solution of IIa (0.6 g. in 25 ml.) for 1.5 hours. It crystallised from benzene-light petroleum to afford 0.5 g. of shining needles, m.p. 114-115°; ν max (potassium bromide): *ca.* 3000 (OH of CO_2H), 1730, 1690 ($\text{C}=\text{O}$ of ester and of CO_2H), 1600, 1570, 1495 cm^{-1} (aromatic).

Anal. Calcd. for $\text{C}_{13}\text{H}_{16}\text{O}_6$: C, 54.93; H, 5.63. Found: C, 55.2; H, 5.8.

4-(*N,N*-Dimethylaminoformylidene)-5,6,7-trimethoxyisochroman-1,3-dione (VIa).

Phosphoryl chloride (1 ml., 0.01 mole) was added dropwise to a well stirred solution of Ia (1.35 g., 0.005 mole) in DMF (4 ml., 0.5 mole) cooled in ice. The stirring was continued further for 45 minutes at 0° and then at room temperature for 1 hour, when a clear solution was obtained. It was poured over crushed ice and sodium acetate was added to bring the pH to 6-6.5. It was allowed to stand in the refrigerator for 2 hours, when a yellow crystalline solid separated out. It was filtered and crystallised from benzene-light petroleum as bright yellow colored needles (0.8 g.), m.p. 147-148°; ν max (potassium bromide): 1715, 1670 (twin bands of anhydride $\text{C}=\text{O}$), 1600, 1550 cm^{-1} (aromatic); ν max (methanol): nm ($\log \epsilon$) 205 (3.67), 260 (3.64); nmr (60 MHz) (deuteriochloroform): 3.35 (6H, s, $\text{N}(\text{CH}_3)_2$), 3.78, 3.95, 4.03 (each 3H, s, OCH_3), 7.5 (1H, s, H-8), 8.63 (1H, s, $\text{CH}\cdot\text{NMe}_2$).

Anal. Calcd. for $\text{C}_{15}\text{H}_{17}\text{O}_6\text{N}$: C, 58.64; H, 5.54; N, 4.56. Found: C, 59.0; H, 5.6; N, 4.7.

Compound VIa was also obtained by using anhydride IIa (1.25 g.) in place of Ia in the above reaction.

3-Chloro-4-formyl-5,6,7-trimethoxyisocoumarin (IX).

The reaction was carried out as above. After decomposing the reaction mixture on crushed ice and adding sodium acetate to bring the pH to 6-6.5, it was kept for 12 hours in the refrigerator and filtered. The initially separated solid changed its appearance to yellow silky needles during this period. It crystallised from

benzene-light petroleum as clusters of yellow silky needles (0.8 g.), m.p. 162-163°; ν max (potassium bromide): 2960 (br), 1760, 1680, 1590, 1470, 1400, 1350, 1100, 945, 800 cm^{-1} ; $\nu\lambda$ max (methanol): nm (log ϵ) 215 (3.62), 250 (3.54); nmr (60 MHz) (deuteriochloroform): 3.88, 4.03, 4.07, (each 3H, s, OCH_3), 7.63 (1H, s, H-8), 10.3 (1H, s, CHO).

Anal. Calcd. for $\text{C}_{13}\text{H}_{11}\text{ClO}_6$: C, 52.7; H, 4.2. Found: C, 52.26; H, 3.68.

The D.N.P. derivative had 184-185° dec.

Anal. Calcd. for $\text{C}_{19}\text{H}_{15}\text{ClO}_9\text{N}_4$: N, 11.7. Found: N, 11.4.

4-(*N,N*-Dimethylaminoformylidene)-6,7-dimethoxyisochroman-1,3-dione (VIb).

The reaction of DMF (7.3 ml., 0.1 mole)/phosphoryl chloride (1.82 ml., 0.02 mole) on Ib (2.4 g., 0.01 mole) and IIb (2.2 g., 0.01 mole) gave the same product VIb. The reactions were carried out as described under VIa. A yellow product separated out from the reaction mixtures in both cases, crushed ice was added to it and the solid was filtered. It crystallised from acetone (2.4 g.) as bright yellow needles, m.p. 238-240°; ν max (potassium bromide): 1715, 1680 (twin bands of anhydride C=O), 1600, 1575 cm^{-1} (aromatic); $\nu\lambda$ max (dioxane): nm (log ϵ) 235 (3.67), 265 (3.44).

Anal. Calcd. for $\text{C}_{14}\text{H}_{15}\text{O}_5\text{N}$: C, 60.6; H, 5.4; N, 5.05. Found: C, 61.0; H, 5.6; N, 5.2.

4-Carbomethoxy-5,6,7-trimethoxyisocoumarin (VIIa, R = Me).

Dry hydrogen chloride gas was bubbled through methanolic solution of VIa (2 g. in 80 ml.) for 4 hours at room temperature and then refluxed further for 2 hours. Methanol was removed by distillation and water was added to the residue and it was extracted with ether. Removal of the ether from the ethereal extract yielded a bright yellow oil. It distilled under reduced pressure to give an oil (1.5 g.) which solidified on standing, b.p. 205-207°/2.5 mm, m.p. 114-115°; ν max (dichloromethane): 1730 (C=O of lactone and ester), 1600, 1495 cm^{-1} (aromatic); nmr (60 MHz) (carbon tetrachloride): 3.5 (3H, s, CO_2CH_3), 3.7, 3.9 (9H, m, OCH_3), 5.58 (1H, s, H-3), 7.38 (1H, s, H-8).

Anal. Calcd. for $\text{C}_{14}\text{H}_{14}\text{O}_7$: C, 57.15; H, 4.76. Found: C, 56.9; H, 4.9.

4-Carboethoxy-5,6,7-trimethoxyisocoumarin (VIIa, R = Et).

This compound was prepared as above using an ethanolic solution of VIa (0.8 g. in 50 ml.). It gave an oil (0.6 g.) which distilled under reduced pressure, b.p. 220-225°/2 mm, m.p. 104-105° [Lit. (13) m.p. 105-106°]; ν max (dichloromethane): 1740 (C=O of lactone and of ester), 1600, 1495 cm^{-1} (aromatic); nmr (60 MHz) (carbon tetrachloride): 1.27 (3H, t, $\text{CH}_2\text{-CH}_3$), 3.91, 3.97 (9H, m, OCH_3), 4.25 (2H, m, CH_2CH_3), 5.75 (1H, s, H-3), 7.47 (1H, s, H-8).

Anal. Calcd. for $\text{C}_{15}\text{H}_{16}\text{O}_7$: C, 58.43; H, 5.19. Found: C, 58.1; H, 5.0.

4-Carbomethoxy-6,7-dimethoxyisocoumarin (VIIIb, R = Me).

This compound was prepared as above using a methanolic solution of VIb (2.4 g. in 100 ml.). The product crystallised from methanol as colorless silky needles (1.5 g.), m.p. 172-173° [Lit. (14) m.p. 175°]; ν max (potassium bromide): 1750, 1710 (C=O of ester and lactone), 1610, 1600, 1500 cm^{-1} (aromatic); $\nu\lambda$ max (methanol): nm (log ϵ) 245 (3.45), 280 (2.38), 320 (2.17).

Anal. Calcd. for $\text{C}_{13}\text{H}_{12}\text{O}_6$: C, 59.09; H, 4.56. Found: C, 59.2; H, 4.7.

4-Carboethoxy-6,7-dimethoxyisocoumarin (VIIIb, R = Et).

This compound was prepared as above using ethanolic solution of VIb (2.4 g. in 100 ml.) in the above reaction. It crystallised

from ethanol as colorless silky needles (1.2 g.), m.p. 150-151° [Lit. (14) m.p. 156°]; ν max (potassium bromide): 1725 (sh), 1710 (C=O of ester and lactone), 1600, 1500 cm^{-1} (aromatic); $\nu\lambda$ max (methanol): nm (log ϵ) 250 (3.93), 280 (3.03), 320 (2.38).

Anal. Calcd. for $\text{C}_{14}\text{H}_{14}\text{O}_6$: C, 60.43; H, 5.04. Found: C, 60.0; H, 5.8.

4-Carboxy-6,7-dimethoxyisocoumarin (VIIIb, R = H).

This compound was obtained from the esters (1 g.) by refluxing with a mixture of glacial acetic acid, concentrated hydrochloric acid and water as described in the literature (14), shining needles (0.8 g.) from acetic acid, m.p. 311-312° dec. [Lit. (14) m.p. 313°]; ν max (potassium bromide): ca. 3250 (br, OH of CO_2H), 1720, 1680 (C=O of lactone and of CO_2H), 1600, 1510 cm^{-1} (aromatic); $\nu\lambda$ max (ethanol): nm (log ϵ) 245 (3.79), 280 (2.92), 325 (2.94).

Anal. Calcd. for $\text{C}_{12}\text{H}_{10}\text{O}_6$: C, 57.61; H, 4.0. Found: C, 57.2; H, 4.2.

6,7-Dimethoxyisocoumarin (VIIIb).

This compound was obtained by decarboxylation of the acid VIIIb (R = H) by heating 0.5 g. of VIIIb at 310-325° with copper bronze as described in the literature (14), shining needles (0.3 g.) from benzene-*n*-hexane, m.p. 119-121° [Lit. m.p. 120° (14), 122-123° (15), 121-122° (16), 97° (17)]; ν max (potassium bromide): 1720 (br, C=O of lactone), 1640, 1600, 1555, 1500 cm^{-1} (aromatic); $\nu\lambda$ max (methanol): nm (log ϵ) 240 (3.58), 280 (3.05), 325 (2.92); nmr (60 MHz) (deuteriochloroform): 3.98, 4 (each 3H, s, OCH_3), 6.45 (1H, d, $-\text{CH}=\text{CH}-\text{O}$, J = 6 Hz), 6.83 (1H, s, H-5), 7.25 (1H, d, $-\text{CH}=\text{CH}-\text{O}$, J = 6 Hz), 7.65 (1H, s, H-8).

Anal. Calcd. for $\text{C}_{11}\text{H}_{10}\text{O}_4$: C, 64.07; H, 4.9. Found: C, 64.0; H, 4.7.

2-Methyl-5,6,7-trimethoxy-1(2H)isoquinolone-4-carboxylic Acid (IVa, R = H), Thalactamine-4-carboxylic Acid.

i) Action of DMF/Phosphoryl Chloride at 100° on Ia and IIa.

The reaction was carried out at 0° as described under VIa and then heated on a boiling water bath for 4 hours. After adding crushed ice, the product separated. It crystallised from ethyl acetate as shining silky needles (0.4 g.), m.p. 220-222° dec.; ν max (potassium chloride): ca. 3420 (OH of CO_2H), 1690, 1640 (C=O of CO_2H and of lactam), 1620, 1600, 1545 cm^{-1} (aromatic); $\nu\lambda$ max (methanol): nm (log ϵ) 235 (3.49), 250 (3.61), 295 (3.01), 340 (2.87); nmr (60 MHz) (trifluoroacetic acid): 3.98 (3H, s, N-CH_3), 4.02, 4.16, 4.23 (each 3H, s, OCH_3), 7.85 (1H, s, H-8), 7.93 (1H, s, H-3).

Anal. Calcd. for $\text{C}_{14}\text{H}_{15}\text{O}_6\text{N}$: C, 57.33; H, 5.12; N, 4.8. Found: C, 56.9; H, 5.1; N, 5.1.

Compound IVa (R = H) was also obtained by using anhydride IIa (1.26 g.) in place of Ia in the above reaction.

ii) Action of Phosphoryl Chloride on VIa.

A mixture of VIa (0.8 g.) and phosphoryl chloride (1 ml.) was heated on boiling water bath for 3 hours and then poured on crushed ice. The product was crystallised repeatedly first from benzene and then from ethyl acetate (0.2 g.), m.p. and mixed m.p. 220-222° dec.

iii) Action of Aqueous Methylamine on Isocoumarin Ester (VIIa, R = Me or Et).

A mixture of VIIa (R = Me or Et) (0.3 g.) and aqueous methylamine (30 ml.) and ethanol (10 ml.) was heated on boiling water bath for 3 hours and the solid that separated after acidification was crystallised as before (0.2 g.), m.p. and mixed m.p. 220-222° dec.

2-Methyl-6,7-dimethoxy-1(2H)isoquinolone-4-carboxylic Acid (IVb, R = H).

Compound IVb was obtained by carrying out the reaction of DMF/phosphoryl chloride at 100° on Ib and IIb with the addition of excess of DMF (7.3 ml., 0.1 mole), by heating VIb with phosphoryl chloride and by the action of aqueous methylamine on VIIb (R = Me and H) by the procedures described above, (under i, ii and iii respectively). The product crystallised from acetic acid as pale yellow needles (2.2 g.), m.p. 311-312° dec.; ν max (potassium chloride): ca. 3000 (OH of CO₂H), 1710, 1640 (C=O of CO₂H and of lactam) 1600, 1510 cm⁻¹ (aromatic); λ max (methanol): nm (log ϵ) 225 (3.57), 250 (3.83), 295 (3.0), 335 (3.02).

Anal. Calcd. for C₁₃H₁₃O₅N: C, 59.3; H, 4.94; N, 5.3. Found: C, 59.2; H, 4.9; N, 5.6.

4-Carbomethoxy-N-methyl-6,7-dimethoxy-1(2H)isoquinolone (IVb, R = Me).

Compound IVb was prepared by passing dry hydrogen chloride gas into a methanolic solution of IVb (R = H) (0.6 g. in 100 ml.) for 6 hours at room temperature and then refluxed for 2 hours. It crystallised from ethanol as clusters of silky needles (0.6 g.), m.p. 192-193°; ν max (nujol): 1725, 1640 (C=O of ester and of lactam), 1580, 1495 cm⁻¹ (aromatic).

Anal. Calcd. for C₁₄H₁₅NO₅: C, 60.4; H, 5.4; N, 5.04. Found: C, 60.7; H, 5.6; N, 5.3.

N-Methyl-5,6,7-trimethoxy-1(2H)isoquinolone (Va) (Thalactamine).

Decarboxylation of IVa (R = H) (0.3 g.) was carried out by heating in a metal bath above the m.p. (ca. 225°), until the evolution of carbon dioxide ceased (0.5 hour). The product was distilled under reduced pressure (ca. 200°/2.5 mm) and crystallised from light petroleum as silky needles (0.15 g.), m.p. 111-112° (Lit. (2) m.p. 112-114°); ν max (potassium bromide): 1650 (C=O of lactam), 1610, 1600 cm⁻¹ (aromatic); λ max (methanol): nm (log ϵ) 245 (3.78), 270 (3.09), 280 (3.17), 290 (3.16), 335 (2.92); nmr (60 MHz) (deuteriochloroform): 3.6 (3H, s, NCH₃), 4.9 (H, s, OCH₃), 6.7 (1H, d, -CH=CH-N, J = 7.5 Hz), 7 (1H, d, -CH=CH-N, J = 7.5 Hz), 7.66 (1H, s, H-8).

Anal. Calcd. for C₁₂H₁₃NO₃: C, 62.65; H, 6.02; N, 5.6. Found: C, 63.0; H, 5.7; N, 5.7.

N-Methyl-6,7-dimethoxy-1(2H)isoquinolone (Vb).

i) Decarboxylation of IVb (R = H).

Compound IVb was reacted by using the procedure as given above. The product crystallised from n-hexane as yellow prisms (0.4 g.), m.p. 109-110° [Lit. m.p. 109-110° (9), shrinks 102° melts 107° (10), 112° (11)]; pierate: m.p. 130-132° [Lit. 136-137° (9), 128-130° (11)]; ν max (potassium bromide): 1640 (C=O of lactam), 1590, 1490 cm⁻¹ (aromatic); λ max (methanol): nm (log ϵ) 245 (3.8), 270 (3.11), 280 (3.18), 290 (3.18), 335 (2.9); nmr (60 MHz) (deuteriochloroform): 3.6 (3H, s, N-CH₃), 3.98, 4.02 (each 3H, s, OCH₃), 6.42 (1H, d, -CH=CH-N, J = 7 Hz), 6.9 (1H, s, H-5), 7.05 (1H, d, -CH=CH-N, J = 7 Hz), 7.87 (1H, s, H-8).

Anal. Calcd. for C₁₂H₁₃O₃N: C, 65.77; H, 5.94; N, 6.39. Found: C, 65.4; H, 5.6; N, 6.1.

ii) Action of Aqueous Methylamine on Isocoumarin VIIIb.

Compound VIIIc (0.2 g.) was heated with aqueous methylamine (10 ml.) on a boiling water bath for 3 hours and then acidified. The product crystallised as above, m.p. and mixed m.p. 109-110°.

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