

RUSCODIBENZOFURAN, A NEW DIBENZOFURAN FROM *RUSCUS ACULEATUS* L. (LILIACEAE)

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Abstract—The structure of ruscodibenzofuran, a new naturally occurring dibenzofuran from the roots of *Ruscus aculeatus* L. (Fam. Liliaceae), was determined by spectral means, the synthesis of model compounds and was confirmed by X-ray diffraction analysis.

Ruscus aculeatus L. (Liliaceae) has been used medicinally as a diuretic,¹ an anti-inflammatory² and to prevent atherosclerosis³ and circulatory insufficiency.⁴

In a previous communication⁵ we have reported the isolation of two new substances from the roots of the plant, the structure of one of which was proven to be 2,5 - diacetyl - 6 - hydroxybenzofuran, named euparone.⁶ The structural analysis of the other compound, designated as a phenolic substance, m.p. 168°, is the subject of this report and we now name it ruscodibenzofuran 1.

Ruscodibenzofuran 1, C₁₆H₁₄O₃ (high resolution mass spectrum) was isolated as rectangular crystals, m.p. 168°, and was optically inactive. The IR spectrum showed bonded hydroxyl and carbonyl absorptions (3420 and 1640 cm⁻¹, respectively). The bonded nature of the phenolic hydroxy was substantiated by a signal at δ 12.75 in the PMR spectrum.⁷ Evidence for the presence of only one phenolic hydroxyl group was shown by the formation of a monoacetate 2 and a monomethyl ether 3, with molecular formulas C₁₈H₁₆O₄ and C₁₇H₁₄O₄, respectively (mass spectra). In addition to the strongly bonded phenolic proton, the PMR spectrum of ruscodibenzofuran showed three methyl groups at δ 2.42 (s, 3H) and δ 2.59 (s, 6H) for aromatic methyls and/or methyl ketones. The aromatic region showed one downfield proton (δ 8.01, s) and three protons centered at δ 6.96.

When *O*-methylruscodibenzofuran was oxidized with sodium hypochlorite, the corresponding carboxylic acid 4 was obtained, C₁₆H₁₂O₄ (mass spectrum). The IR spectrum of the carboxylic acid showed only one carbonyl absorption (1700 cm⁻¹) indicating that ruscodibenzofuran contained only one carbonyl group in the form of a methyl ketone. Oxidation of the acid 4 with alkaline KMnO₄ resulted in the isolation of a tricarboxylic acid 5, the trimethyl ester of which 6 was prepared by treatment with diazomethane.

The trimethyl ester 6, C₁₉H₁₈O₆ (mass spectrum) showed four methoxy singlets in the PMR (δ 3.98, 4.03, 4.07, 4.09) along with four aromatic protons, three of which resonated downfield (δ 9.21, s, 1H) and δ 8.03 (s, 2H). One of these aromatic protons corresponds to that which was *ortho* to the acetyl function in ruscodibenzofuran and the other two must have been protons which were *ortho* to methyl groups, shifted downfield by conversion of the methyls to methoxycarbonyls.

These data suggested a dibenzofuran structure with one acetyl group, one phenolic function and two aromatic methyl groups. As the literature lacked compounds with appropriate substituents, it was necessary to prepare a few dibenzofurans with the required substitution for comparison with ruscodibenzofuran. Eight - acetyl - 2,4 - dimethyl - 7 - methoxydibenzofuran 7 was synthesized through a mixed Ulmann coupling⁸ of 2,4 - dimethyl - 6 - iodoanisole with 6-iodoresorcinol dimethyl ether, followed by reflux with HBr to yield 2,4 - dimethyl - 7 - hydroxydibenzofuran 8 as one of the products.

Treatment of 8 with dimethylsulphate and potassium carbonate followed by Friedel-Crafts acetylation (acetyl chloride and aluminum chloride) gave the desired product 7. A comparison of the physical and spectral data of 7 and *O*-methylruscodibenzofuran 3 is shown in Table 1. This comparison indicates that the two compounds were similar but not identical. In addition, the UV spectra of both compounds supported a dibenzofuran chromophore⁹ and the stability of dibenzofurans toward mass fragmentation¹⁰ was evident in both cases. Furthermore, the PMR spectra of both compounds were different in the aromatic and the methyl absorption regions. Finally, and of great importance, was the presence of an aromatic proton at δ 7.46 (s, 1H) assigned to H-1' in the PMR spectrum of 7 which was absent in that of *O*-methylruscodibenzofuran. This fact suggested that C-1 was substituted with a methyl group in ruscodibenzofuran. Thus, ruscodibenzofuran was assigned as either 10 or 1, and the synthesis of both compounds (or their methyl ethers) attempted.

The same procedure described for the synthesis of 7 was utilized for the synthesis of *O*-methyl 10 starting

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Table 1. Comparison of the physical and spectroscopic data of *O*-methylruscobenzofuran 3 and 8-acetyl-2,4-dimethyl-7-methoxydibenzofuran 7

MeIR MAX	147-9°	155°
ν_{max} (cm ⁻¹)	297 (s), 161, 140 (4.5%), 165 (4.7%), 197 (sh), 118, 107 (sh), 113 and 101 (3.5%)	296 (3.9%), 241 (3.8%), 260 (4.1%), 296 (sh), 120 and 131 (3.1%)
δ_{max} (ppm)	2.41 (s) (3H), 2.47 (s) (3H), 2.62 (s) (3H), 3.24 (s) (3H), 3.31 (s) (3H), 2.46 (s) (3H), 1.68 (s) (3H), and 1.00 (s) (3H)	2.55 (s) (3H), 2.67 (s) (3H), 2.70 (s) (3H), 3.98 (s) (3H), 3.43 (s) (3H), 1.09 (s) (3H), 1.02 (s) (3H), and 1.00 (s) (3H)
M ⁺ , m/e (Intensity)	M ⁺ 268 (43), 253 (100), 238 (7), 225 (5), 119 (3), 105 (4), 106.5 (4) and 119 (3). Molecular formula C ₁₇ H ₁₆ O ₂	M ⁺ 265 (60), 251 (100), 238 (4), 225 (4), 210 (4), 194 (6), 106.5 (5), and 119 (7). Molecular formula C ₁₇ H ₁₆ O ₂
M ⁺ , m/e (Fragmentation Process)	239 (calc), 238.84 (M ⁺ → 253) 224 (calc), 223.89 (M ⁺ → 238)	239 (calc), 238.84 (M ⁺ → 253) 224 (calc), 223.89 (M ⁺ → 238)

8-Acetyl-2,4-dimethyl-7-methoxy-dibenzofuran 7

O-Methylruscobenzofuran 3

from 3,5 - dimethyl - 6 - iodoanisole. The intermediate product 11 was isolated and characterized (MS, PMR, UV, IR, m.p.) and its *O*-methyl ether 12 prepared. Friedel-Craft's acetylation of 12 did not result in the isolation of the required product. Instead, two diacetylated compounds 13 and 14 were formed (MS, PMR) and direct comparison with either ruscodibenzofuran or its methyl ether was not possible. However, acetylation (Friedel-Crafts) of ruscodibenzofuran afforded an acetyl derivative 15, C₁₈H₁₈O₄ (MS), which was clearly different from 13. The PMR of 2-acetyl-ruscodibenzofuran 15 showed that one aromatic proton was shifted downfield (δ 7.55) by the introduction of the new acetyl group indicating that there was an aromatic proton at C-3. This fact, in conjunction with all other data, indicated that ruscodibenzofuran should be represented as 1. The synthesis of 1 was unsuccessful because of the failure of 6 - bromo - 2,5 - dimethyl anisole to couple with 4-iodoresorcinoldimethylether under the reaction conditions for mixed Ullmann coupling previously used. Attempts for its synthesis using other reaction conditions are currently under investigation.

Concurrently with the synthetic effort, X-ray diffraction analysis of ruscodibenzofuran confirmed its structure as 1. A crystal of ruscodibenzofuran was ground into a sphere of radius 0.15 mm. The crystal was found to belong to the monoclinic space group P2₁/C and room temperature cell dimensions were obtained from a least-squares fit to 15 medium and high angle reflections yielding $a = 8.359(3)$, $b = 6.865(3)$, $c = 21.958(11)$ Å, $\beta = 92.58(3)^\circ$. Intensity data for $2\theta < 140^\circ$ were collected on a Syntex P2, diffractometer using the $\theta:2\theta$ scan technique and graphite monochromatized CuK α radiation ($\lambda = 1.54178$ Å). A total of 2352 independent reflections were measured and 1979 had intensities greater than $3\sigma(I)$. The structure was solved by direct methods using MULTAN.¹² Anisotropic least-squares refinement yielded an R value of 0.056 using all 2352 reflections. Hydrogen atom positions were obtained from a difference map and their contributions to the structure factors were included in the calculation.

Figure 1 shows an ORTEP¹¹ drawing of the molecule while bond distances and angles are listed in Tables 2 and 3, respectively. A least-square plane fitted to all

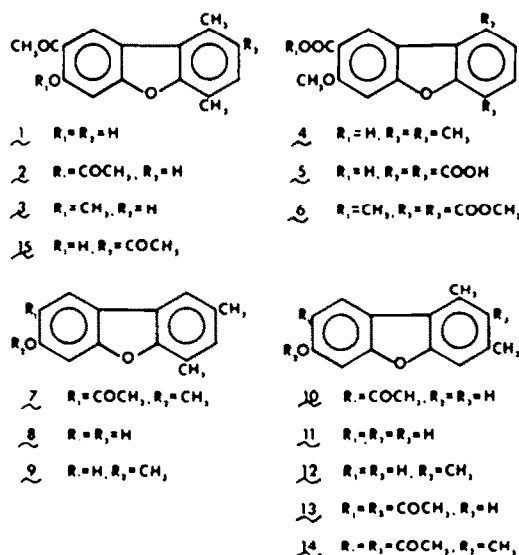


Table 2. Intramolecular bond distances with estimated standard deviations in parentheses

Atom	DISTANCE, Å
C1-C2	1.384 (14)
C2-C3	1.388 (14)
C3-C4	1.390 (14)
C4-C5	1.391 (14)
C5-C6	1.390 (14)
C6-C7	1.386 (14)
C7-C8	1.380 (14)
C8-C9	1.380 (14)
C9-C10	1.376 (14)
C10-C11	1.369 (14)
C11-C12	1.371 (14)
C12-C13	1.372 (14)
C13-C14	1.370 (14)
C14-C15	1.370 (14)
C15-C16	1.370 (14)
C16-C17	1.371 (14)
C17-C18	1.371 (14)
C18-C19	1.371 (14)
C19-C20	1.371 (14)
C20-C21	1.371 (14)
C21-C22	1.371 (14)
C22-C23	1.371 (14)
C23-C24	1.371 (14)
C24-C25	1.371 (14)
C25-C26	1.371 (14)
C26-C27	1.371 (14)
C27-C28	1.371 (14)
C28-C29	1.371 (14)
C29-C30	1.371 (14)
C30-C31	1.371 (14)
C31-C32	1.371 (14)
C32-C33	1.371 (14)
C33-C34	1.371 (14)
C34-C35	1.371 (14)
C35-C36	1.371 (14)
C36-C37	1.371 (14)
C37-C38	1.371 (14)
C38-C39	1.371 (14)
C39-C40	1.371 (14)
C40-C41	1.371 (14)
C41-C42	1.371 (14)
C42-C43	1.371 (14)
C43-C44	1.371 (14)
C44-C45	1.371 (14)
C45-C46	1.371 (14)
C46-C47	1.371 (14)
C47-C48	1.371 (14)
C48-C49	1.371 (14)
C49-C50	1.371 (14)
C50-C51	1.371 (14)
C51-C52	1.371 (14)
C52-C53	1.371 (14)
C53-C54	1.371 (14)
C54-C55	1.371 (14)
C55-C56	1.371 (14)
C56-C57	1.371 (14)
C57-C58	1.371 (14)
C58-C59	1.371 (14)
C59-C60	1.371 (14)
C60-C61	1.371 (14)
C61-C62	1.371 (14)
C62-C63	1.371 (14)
C63-C64	1.371 (14)
C64-C65	1.371 (14)
C65-C66	1.371 (14)
C66-C67	1.371 (14)
C67-C68	1.371 (14)
C68-C69	1.371 (14)
C69-C70	1.371 (14)
C70-C71	1.371 (14)
C71-C72	1.371 (14)
C72-C73	1.371 (14)
C73-C74	1.371 (14)
C74-C75	1.371 (14)
C75-C76	1.371 (14)
C76-C77	1.371 (14)
C77-C78	1.371 (14)
C78-C79	1.371 (14)
C79-C80	1.371 (14)
C80-C81	1.371 (14)
C81-C82	1.371 (14)
C82-C83	1.371 (14)
C83-C84	1.371 (14)
C84-C85	1.371 (14)
C85-C86	1.371 (14)
C86-C87	1.371 (14)
C87-C88	1.371 (14)
C88-C89	1.371 (14)
C89-C90	1.371 (14)
C90-C91	1.371 (14)
C91-C92	1.371 (14)
C92-C93	1.371 (14)
C93-C94	1.371 (14)
C94-C95	1.371 (14)
C95-C96	1.371 (14)
C96-C97	1.371 (14)
C97-C98	1.371 (14)
C98-C99	1.371 (14)
C99-C100	1.371 (14)
C100-C101	1.371 (14)
C101-C102	1.371 (14)
C102-C103	1.371 (14)
C103-C104	1.371 (14)
C104-C105	1.371 (14)
C105-C106	1.371 (14)
C106-C107	1.371 (14)
C107-C108	1.371 (14)
C108-C109	1.371 (14)
C109-C110	1.371 (14)
C110-C111	1.371 (14)
C111-C112	1.371 (14)
C112-C113	1.371 (14)
C113-C114	1.371 (14)
C114-C115	1.371 (14)
C115-C116	1.371 (14)
C116-C117	1.371 (14)
C117-C118	1.371 (14)
C118-C119	1.371 (14)
C119-C120	1.371 (14)
C120-C121	1.371 (14)
C121-C122	1.371 (14)
C122-C123	1.371 (14)
C123-C124	1.371 (14)
C124-C125	1.371 (14)
C125-C126	1.371 (14)
C126-C127	1.371 (14)
C127-C128	1.371 (14)
C128-C129	1.371 (14)
C129-C130	1.371 (14)
C130-C131	1.371 (14)
C131-C132	1.371 (14)
C132-C133	1.371 (14)
C133-C134	1.371 (14)
C134-C135	1.371 (14)
C135-C136	1.371 (14)
C136-C137	1.371 (14)
C137-C138	1.371 (14)
C138-C139	1.371 (14)
C139-C140	1.371 (14)
C140-C141	1.371 (14)
C141-C142	1.371 (14)
C142-C143	1.371 (14)
C143-C144	1.371 (14)
C144-C145	1.371 (14)
C145-C146	1.371 (14)
C146-C147	1.371 (14)
C147-C148	1.371 (14)
C148-C149	1.371 (14)
C149-C150	1.371 (14)
C150-C151	1.371 (14)
C151-C152	1.371 (14)
C152-C153	1.371 (14)
C153-C154	1.371 (14)
C154-C155	1.371 (14)
C155-C156	1.371 (14)
C156-C157	1.371 (14)
C157-C158	1.371 (14)
C158-C159	1.371 (14)
C159-C160	1.371 (14)
C160-C161	1.371 (14)
C161-C162	1.371 (14)
C162-C163	1.371 (14)
C163-C164	1.371 (14)
C164-C165	1.371 (14)
C165-C166	1.371 (14)
C166-C167	1.371 (14)
C167-C168	1.371 (14)
C168-C169	1.371 (14)
C169-C170	1.371 (14)
C170-C171	1.371 (14)
C171-C172	1.371 (14)
C172-C173	1.371 (14)
C173-C174	1.371 (14)
C174-C175	1.371 (14)
C175-C176	1.371 (14)
C176-C177	1.371 (14)
C177-C178	1.371 (14)
C178-C179	1.371 (14)
C179-C180	1.371 (14)
C180-C181	1.371 (14)
C181-C182	1.371 (14)
C182-C183	1.371 (14)
C183-C184	1.371 (14)
C184-C185	1.371 (14)
C185-C186	1.371 (14)
C186-C187	1.371 (14)
C187-C188	1.371 (14)
C188-C189	1.371 (14)
C189-C190	1.371 (14)
C190-C191	1.371 (14)
C191-C192	1.371 (14)
C192-C193	1.371 (14)
C193-C194	1.371 (14)
C194-C195	1.371 (14)
C195-C196	1.371 (14)
C196-C197	1.371 (14)
C197-C198	1.371 (14)
C198-C199	1.371 (14)
C199-C200	1.371 (14)
C200-C201	1.371 (14)
C201-C202	1.371 (14)
C202-C203	1.371 (14)
C203-C204	1.371 (14)
C204-C205	1.371 (14)
C205-C206	1.371 (14)
C206-C207	1.371 (14)
C207-C208	1.371 (14)
C208-C209	1.371 (14)
C209-C210	1.371 (14)
C210-C211	1.371 (14)
C211-C212	1.371 (14)
C212-C213	1.371 (14)
C213-C214	1.371 (14)
C214-C215	1.371 (14)
C215-C216	1.371 (14)
C216-C217	1.371 (14)
C217-C218	1.371 (14)
C218-C219	1.371 (14)
C219-C220	1.371 (14)
C220-C221	1.371 (14)
C221-C222	1.371 (14)
C222-C223	1.371 (14)
C223-C224	1.371 (14)
C224-C225	1.371 (14)
C225-C226	1.371 (14)
C226-C227	1.371 (14)
C227-C228	1.371 (14)
C228-C	

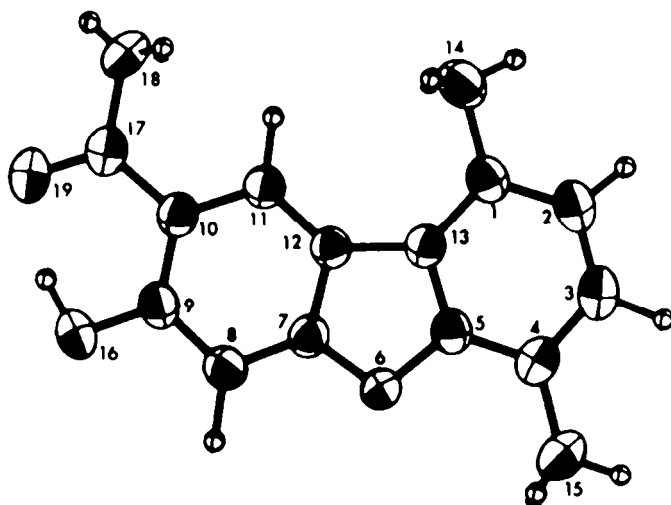


Fig. 1. An ORTEP drawing of ruscodibenzofuran 1.

Table 3. Bond angles, with estimated standard deviation in parentheses

ANGLE, °	ANGLE, °
C1-C2-C3	120.6 (4)
C2-C3-C4	121.5 (5)
C3-C4-C5	121.9 (5)
C4-C5-C6	120.6 (5)
C5-C6-C7	124.6 (5)
C6-C7-C8	120.9 (5)
C7-C8-C9	120.7 (5)
C8-C9-C10	120.7 (5)
C9-C10-C11	121.5 (5)
C10-C11-C12	121.5 (5)
C11-C12-C13	121.5 (5)
C12-C13-C14	121.5 (5)
C13-C14-C15	121.5 (5)
C14-C15-C16	121.5 (5)
C15-C16-C17	121.5 (5)
C16-C17-C18	121.5 (5)
C17-C18-C19	121.5 (5)
C18-C19-C20	121.5 (5)
C19-C20-C21	121.5 (5)
C20-C21-C22	121.5 (5)
C21-C22-C23	121.5 (5)
C22-C23-C24	121.5 (5)
C23-C24-C25	121.5 (5)
C24-C25-C26	121.5 (5)
C25-C26-C27	121.5 (5)
C26-C27-C28	121.5 (5)
C27-C28-C29	121.5 (5)
C28-C29-C30	121.5 (5)
C29-C30-C31	121.5 (5)
C30-C31-C32	121.5 (5)
C31-C32-C33	121.5 (5)
C32-C33-C34	121.5 (5)
C33-C34-C35	121.5 (5)
C34-C35-C36	121.5 (5)
C35-C36-C37	121.5 (5)
C36-C37-C38	121.5 (5)
C37-C38-C39	121.5 (5)
C38-C39-C40	121.5 (5)
C39-C40-C41	121.5 (5)
C40-C41-C42	121.5 (5)
C41-C42-C43	121.5 (5)
C42-C43-C44	121.5 (5)
C43-C44-C45	121.5 (5)
C44-C45-C46	121.5 (5)
C45-C46-C47	121.5 (5)
C46-C47-C48	121.5 (5)
C47-C48-C49	121.5 (5)
C48-C49-C50	121.5 (5)
C49-C50-C51	121.5 (5)
C50-C51-C52	121.5 (5)
C51-C52-C53	121.5 (5)
C52-C53-C54	121.5 (5)
C53-C54-C55	121.5 (5)
C54-C55-C56	121.5 (5)
C55-C56-C57	121.5 (5)
C56-C57-C58	121.5 (5)
C57-C58-C59	121.5 (5)
C58-C59-C60	121.5 (5)
C59-C60-C61	121.5 (5)
C60-C61-C62	121.5 (5)
C61-C62-C63	121.5 (5)
C62-C63-C64	121.5 (5)
C63-C64-C65	121.5 (5)
C64-C65-C66	121.5 (5)
C65-C66-C67	121.5 (5)
C66-C67-C68	121.5 (5)
C67-C68-C69	121.5 (5)
C68-C69-C70	121.5 (5)
C69-C70-C71	121.5 (5)
C70-C71-C72	121.5 (5)
C71-C72-C73	121.5 (5)
C72-C73-C74	121.5 (5)
C73-C74-C75	121.5 (5)
C74-C75-C76	121.5 (5)
C75-C76-C77	121.5 (5)
C76-C77-C78	121.5 (5)
C77-C78-C79	121.5 (5)
C78-C79-C80	121.5 (5)
C79-C80-C81	121.5 (5)
C80-C81-C82	121.5 (5)
C81-C82-C83	121.5 (5)
C82-C83-C84	121.5 (5)
C83-C84-C85	121.5 (5)
C84-C85-C86	121.5 (5)
C85-C86-C87	121.5 (5)
C86-C87-C88	121.5 (5)
C87-C88-C89	121.5 (5)
C88-C89-C90	121.5 (5)
C89-C90-C91	121.5 (5)
C90-C91-C92	121.5 (5)
C91-C92-C93	121.5 (5)
C92-C93-C94	121.5 (5)
C93-C94-C95	121.5 (5)
C94-C95-C96	121.5 (5)
C95-C96-C97	121.5 (5)
C96-C97-C98	121.5 (5)
C97-C98-C99	121.5 (5)
C98-C99-C100	121.5 (5)
C99-C100-C101	121.5 (5)
C100-C101-C102	121.5 (5)
C101-C102-C103	121.5 (5)
C102-C103-C104	121.5 (5)
C103-C104-C105	121.5 (5)
C104-C105-C106	121.5 (5)
C105-C106-C107	121.5 (5)
C106-C107-C108	121.5 (5)
C107-C108-C109	121.5 (5)
C108-C109-C110	121.5 (5)
C109-C110-C111	121.5 (5)
C110-C111-C112	121.5 (5)
C111-C112-C113	121.5 (5)
C112-C113-C114	121.5 (5)
C113-C114-C115	121.5 (5)
C114-C115-C116	121.5 (5)
C115-C116-C117	121.5 (5)
C116-C117-C118	121.5 (5)
C117-C118-C119	121.5 (5)
C118-C119-C120	121.5 (5)
C119-C120-C121	121.5 (5)
C120-C121-C122	121.5 (5)
C121-C122-C123	121.5 (5)
C122-C123-C124	121.5 (5)
C123-C124-C125	121.5 (5)
C124-C125-C126	121.5 (5)
C125-C126-C127	121.5 (5)
C126-C127-C128	121.5 (5)
C127-C128-C129	121.5 (5)
C128-C129-C130	121.5 (5)
C129-C130-C131	121.5 (5)
C130-C131-C132	121.5 (5)
C131-C132-C133	121.5 (5)
C132-C133-C134	121.5 (5)
C133-C134-C135	121.5 (5)
C134-C135-C136	121.5 (5)
C135-C136-C137	121.5 (5)
C136-C137-C138	121.5 (5)
C137-C138-C139	121.5 (5)
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C147-C148-C149	121.5 (5)
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C188-C189-C190	121.5 (5)
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C328-C329-C330	121.5 (5)
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C337-C338-C339	121.5 (5)
C338-C339-C340	121.5 (5)
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C344-C345-C346	121.5 (5)
C345-C346-C347	121.5 (5)
C346-C347-C348	121.5 (5)
C347-C348-C349	121.5 (5)
C348-C349-C350	121.5 (5)
C349-C350-C351	121.5 (5)
C350-C351-C352	121.5 (5)
C351-C352-C353	121.5 (5)
C352-C353-C354	121.5 (5)
C353-C354-C355	121.5 (5)
C354-C355-C356	121.5 (5)
C355-C356-C357	121.5 (5)
C356-C357-C358	121.5 (5)
C357-C358-C359	121.5 (5)
C358-C359-C360	121.5 (5)
C359-C360-C361	121.5 (5)
C360-C361-C362	121.5 (5)
C361-C362-C363	121.5 (5)
C362-C363-C364	121.5 (5)
C363-C364-C365	121.5 (5)
C364-C365-C366	121.5 (5)
C365-C366-C367	121.5 (5)
C366-C367-C368	121.5 (5)
C367-C368-C369	121.5 (5)
C368-C369-C370	121.5 (5)
C369-C370-C371	121.5 (5)
C370-C371-C372	121.5 (5)
C371-C372-C373	121.5 (5)
C372-C373-C374	121.5 (5)
C373-C374-C375	121.5 (5)
C374-C375-C376	121.5 (5)
C375-C376-C377	121.5 (5)
C376-C377-C378	121.

removed by passing SO_2 into the solution with the formation of a yellow precipitate. The precipitate was filtered, washed with water followed by ethanol and dried to give 12 mg of 5. Methylation of 5 using ethereal diazomethane (5 ml) (prepared from *N*-methyl-*N'*-nitroso-*p*-toluenesulphonamide and potassium hydroxide¹¹) followed by crystallization from methanol yielded pale yellow crystals of 6 (12 mg), m.p. 169°; UV (MeOH): 236 (4.30), 282 (3.90) and 351 (3.70) nm; IR (KBr): 1725, 1633, 1280, 1145 and 1085 cm^{-1} ; PMR (CDCl_3): δ 3.98 (3H, s), 4.03 (3H, s), 4.07 (3H, s), 4.10 (3H, s), 7.25 (1H, s), 8.03 (2H, s) and 9.21 (1H, s); MS: $M^+ m/e$ 372 (82%) ($\text{C}_{18}\text{H}_{14}\text{O}_6$), 311 (9), 295 (8), 281 (8), 251 (11), 221 (11) and 155 (18).

4-Iodoresorcinoldimethylether 16. An ice cold solution of 2,4-dimethoxyaniline (5 g) in 10% sulphuric acid (50 ml) was treated with sodium nitrite (3 g, added in portions). Potassium iodide (5 g) was then added in small amounts and the deep brown precipitate was extracted with chloroform (3 \times 100 ml). The chloroform extract was washed with 10% sodium thiosulphate solution (3 \times 10 ml), followed by water (2 \times 50 ml), dried and evaporated to dryness. The brown oily residue (8 g) was chromatographed over silicic acid (30 g) and eluted with chloroform. Evaporation of the fraction containing the first yellow zone afforded a yellow oil (4 g) which crystallized on standing in the refrigerator into needles of 16; m.p. 40–41°; UV (MeOH): 211 (4.40), 237 (4.21), 284 (3.60) and 292 (sh, 3.57) nm; IR (KBr): 3030, 1580, 1310, 1214, 1055 and 790 cm^{-1} ; PMR (CDCl_3): δ 3.75 (3H, s, OCH_3), 3.80 (3H, s, OCH_3), 6.23 (1H, dd, $J = 9$ Hz and 3 Hz, H-6), 6.37 (1H, d, $J = 3$ Hz, H-2) and 7.54 (1H, d, $J = 9$ Hz, H-5); MS: $M^+ m/e$ 264 (100%) ($\text{C}_{10}\text{H}_8\text{IO}_2$), 249 (5), 221 (8) and 127 (20).

2,4-Dimethyl-6-iodoanisole 17. A stirred solution of 2,4-dimethylphenol (5 g) in 10% aqueous ammonia was treated with a solution of iodine (10 g) in 30% potassium iodide (10 ml) by dropwise addition over a period of 30 min. The mixture was allowed to stir for one additional hour after which it was poured onto ice cold 10% sulphuric acid (50 ml). The resulting brown gummy precipitate was extracted with chloroform (3 \times 100 ml), the chloroform solution washed with 10% sodium thiosulphate (3 \times 50 ml), then with water (2 \times 50 ml), dried, filtered and evaporated to afford a brown oil (9.30 g). This oil was chromatographed over silicic acid (30 g) and eluted with chloroform. The residue (5.5 g) obtained after evaporation of the first fraction (500 ml) was methylated with dimethyl sulphate (5 ml) and anhyd. potassium carbonate (3 g) in refluxing acetone to yield after work-up a yellow orange oil of 17 (5.7 g); UV (MeOH): 217 (4.18), 230 (sh, 4.00), 277 (sh, 3.13) and 284 (sh, 3.12) nm; IR (KBr): 2950, 1600, 1470, 1275, 1230, 1124, 1010 and 853 cm^{-1} ; PMR (CDCl_3): δ 2.20 (3H, s), 2.27 (3H, s) for two aromatic methyls, 3.73 (3H, s, OCH_3), 6.92 (1H, br, s, H-3) and 7.38 (1H, br, s, H-5); MS: $M^+ m/e$ 262 (100) ($\text{C}_{10}\text{H}_{11}\text{IO}$).

2,4-Dimethyl-7-hydroxydibenzofuran 8. 4-Iodoresorcinoldimethylether 16 (1.2 g) and 2,4-dimethyl-6-iodoanisole 17 (0.4 g) were thoroughly mixed with finely powdered copper (10 g) and the mixture heated (oil bath) for 90 min at 220°. The product was cooled to room temperature, extracted with methylene chloride and filtered. Evaporation of the solvent afforded a dark brown viscous residue (0.61 g) which was partially purified by passing through a silicic acid column (10 g) and elution with methylene chloride. The solvent was evaporated and the residue (0.47 g) refluxed with hydrobromic acid (48%, 7.5 ml) for 6 h under nitrogen. The cooled reaction mixture was alkalized (pH 11) with 5N KOH and extracted with methylene chloride (3 \times 20 ml). The basic fraction was acidified (pH 2) with conc. HCl and extracted with methylene chloride (4 \times 30 ml). The combined extracts were washed with water (2 \times 20 ml), dried (anhyd. Na_2SO_4) and evaporated to dryness. The residue (0.29 g) was chromatographed over silicic acid (40 g) and eluted with methylene chloride in 10 ml fractions. Evaporation of fractions 13–15 and crystallization of the residue from chloroform-methanol (2:1) afforded 8 as light buff needles (40 mg), m.p. 119°; UV (MeOH): 220 (4.69), 229 (sh, 4.57), 240 (sh, 4.41), 259 (4.35), 300 (sh, 4.37) and 307 (4.41) nm; IR (KBr): 3300, 1631, 1594, 1388, 1252, 1132 and 942 cm^{-1} ; PMR (CDCl_3): δ 2.41 (3H, s), 2.49 (3H,

s), 5.47 (1H, br, s, phenolic OH), 6.76 (1H, dd, $J = 9, 3$ Hz, H-8), 6.96 (1H, s, H-3), 7.00 (1H, d, $J = 3$ Hz, H-6), 7.41 (1H, s, H-1) and 7.65 (1H, d, $J = 9$ Hz, H-9); MS: $M^+ m/e$ 212 (100%) ($\text{C}_{14}\text{H}_{12}\text{O}_3$), 211 (35), 198 (20), 197 (37), 149 (6) and 115 (5).

2,4-Dimethyl-7-methoxydibenzofuran 9. Methylation of 8 (35 mg) using dimethyl sulphate (1 ml) and anhydrous potassium carbonate (500 mg) in anhydrous acetone resulted in the formation of a faint yellow oil (37 mg) of 9; MS: $M^+ m/e$ 226 (76%) for $\text{C}_{14}\text{H}_{14}\text{O}_3$; PMR showed a methoxy singlet at δ 3.81.

8-Acetyl-2,4-dimethyl-7-methoxydibenzofuran 7. Aluminum chloride (anhyd., 1 g) was added to a solution of 9 (36 mg) in methylene chloride (10 ml) and the mixture heated to reflux. Acetyl chloride (0.5 ml) in methylene chloride (5 ml) was added slowly from a pressure equalizing dropping funnel and reflux continued for 2 h. The reaction mixture was cooled to room temperature and partitioned with 10% HCl. The organic layer was washed with water (2 \times 15 ml), dried (anhyd. Na_2SO_4), filtered and evaporated to dryness. Crystallization of the residue from chloroform-ethanol afforded faint yellow prisms and large needles of 7 (30 mg), m.p. 147–149°. For physical and spectral data of 7 see Table I.

1,3-Dimethyl-7-hydroxydibenzofuran 11. Ullmann coupling of 16 (12.5 g) and 3,5-dimethyl-6-iodoanisole (2.5 g) following a procedure similar to that discussed under synthesis of 8 resulted in the formation of 11 (230 mg), m.p. 108–113°; UV (MeOH): 222 (4.79), 240 (sh, 4.47), 260 (4.36), 300 (4.42), 309 (4.29) and 340 (sh, 2.63) nm; IR (KBr): 3365, 2950, 1600, 1450, 1150 and 960 cm^{-1} ; PMR (CDCl_3): 2.43 (3H, s), 2.62 (3H, s), 5.52 (1H, br, s, phenolic OH), 6.70–7.10 (4H, m) and 7.66 (1H, d, $J = 9$ Hz, H-9); MS: $M^+ m/e$ 212 (100%) ($\text{C}_{14}\text{H}_{12}\text{O}_3$), 211 (51) and 197 (49).

2,8-Diacetyl-1,3-dimethyl-7-hydroxydibenzofuran 13. Methylation of 11 (75 mg) using dimethyl sulphate (1 ml) and anhyd. K_2CO_3 (500 mg) in refluxing acetone (20 ml) resulted in the formation of an oily product 12 (73 mg); PMR methoxy signal at δ 3.87. The crude 12 was acetylated as described under synthesis of 7 to give a product which showed one major spot on TLC (R_f 0.66) using benzene-ethyl acetate (9:1). Preparative-layer chromatography of the reaction product using the same system resulted in the isolation of 13 (R_f 0.66), 13 mg, m.p. 190–195° dec.; IR (KBr): 1675, 1640, 1615, 1255, 1147 and 1055 cm^{-1} ; PMR (CDCl_3): δ 2.48 (3H, s), 2.65 (3H, s), 2.70 (3H, s), 2.74 (3H, s), 6.77 (1H, s), 6.94 (1H, s), 8.06 (1H, s, H-9) and 12.81 (1H, s, strongly bonded phenolic OH); MS: $M^+ m/e$ 296 (54%) ($\text{C}_{16}\text{H}_{14}\text{O}_4$), 281 (76), 268 (77) and 253 (100).

2-Acetylresorcinodibenzofuran 15. Friedel Craft's acetylation of 1 (20 mg) in a similar manner as discussed under synthesis of 7 resulted in the formation of yellow product containing some unreacted material. The crude product was purified by preparative layer chromatography using benzene-ethyl acetate (3:1). Elution of the zone at R_f 0.65 and crystallization of the residue from chloroform-ethanol afforded faint yellow needles of 15 (12 mg), m.p. 170°; IR (KBr): 3440, 2920, 1670, 1640, 1250 and 1115 cm^{-1} ; PMR (CDCl_3): δ 2.56 (3H, s), 2.65 (3H, s), 2.75 (3H, s), 2.88 (3H, s), 7.10 (1H, s, H-6), 7.55 (1H, s, H-3), 8.38 (1H, s, H-9) and 12.80 (1H, s, bonded phenolic OH); MS: $M^+ m/e$ 296 (53%) ($\text{C}_{16}\text{H}_{14}\text{O}_4$), 281 (100) and 253 (10).

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