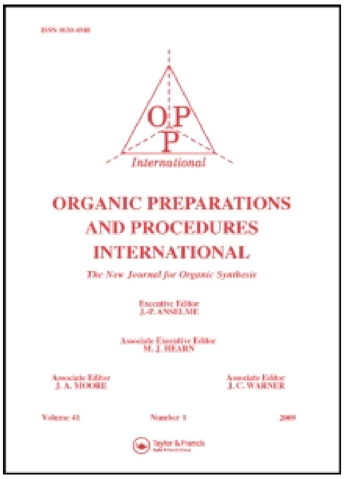

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5,6-DIMETHOXY-2-ISOPROPENYLBENZOFURAN AND 2-ISOPROPENYL-5,6-METHYLENEDIOXYBENZOFURAN

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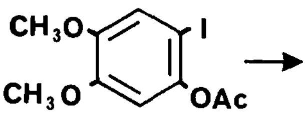
5,6-Dimethoxy-2-isopropenylbenzofuran(I), one of the simplest naturally occurring benzofurans,[1] was first obtained from Ligularia stenocephala (Compositae) and identified by Takahashi and coworkers.[2] Shortly thereafter, Fukui et al.[3] synthesized the methylenedioxy analogue(II) in anticipation of natural isolation. We have recently shown[4] that the readily available, stable copper(1) isopropenylacetylide(III) is an excellent reagent for the construction of 2-isopropenylbenzofurans by coupling with an o-halogenophenol, a general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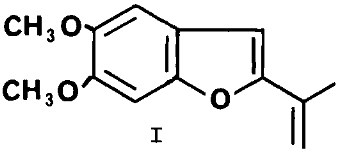
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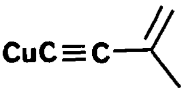
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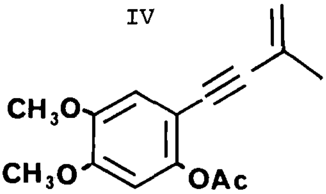
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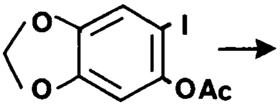
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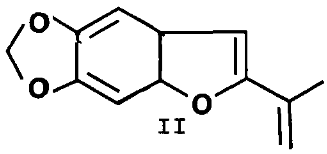
II

procedure introduced by Castro.[5] A simple synthesis of the title compounds employing (III) was accordingly sought. For this purpose, we examined the reaction of (III) with the readily obtained 4,5-dimethoxy-2-iodophenyl acetate (IV). It was hoped that the aryl iodide function would permit coupling to the acetoxy en-yne (V), which could be subsequently cyclized under appropriate conditions to yield the desired benzofuran (I). In fact, examination of the NMR spectrum of the crude reaction mixture revealed that (I) was formed directly along with (V) in a 4:1 ratio. Separation was readily accomplished by base treatment of the mixture whereby (V) would be converted to the phenol which would form the benzofuran (I) or be removed as the water-soluble salt.[6] In agreement, the neutral fraction was solely the natural product, 5,6-dimethoxy-2-isopropenylbenzofuran, isolated in 60% yield.

The synthesis of the methylenedioxy analogue (II) was similarly effected. The commercially available sesamol was acetylated and treated with iodine monochloride-silver acetate to give the iodophenyl acetate (VI), which after refluxing in pyridine solution with (III) and base hydrolysis yielded 2-isopropenyl-5,6-methylenedioxybenzofuran.

We believe that this method has distinct advantages for those cases in which the free o-halophenol is inherently unstable or difficult to prepare.

EXPERIMENTAL

P.m.r. spectra are reported for $CDCl_3$ solutions.

4,5-Dimethoxy-2-iodophenyl Acetate (IV). — To a stirred solution of 3,4-dimethoxyphenyl acetate[7] (5.06 g) in acetic anhydride (25 ml) was added silver acetate (4.32 g) followed by a solution of iodine monochloride (4.25 g) in acetic acid (25 ml). The mixture was stirred at room temp. for 1 hour, filtered, and the filtrate poured into ice-water. The resultant precipitate (cream solid, 6.60 g) was crystallized from aqueous methanol as white needles (6.25 g), m.p. 74.5-75.5°, δ 2.32 (s, OAc), 3.82 (s, OMe), 6.68 (s, H-6) and 7.22 (s, H-3).

Anal. Calcd. for $C_{10}H_{11}IO_4$: C, 37.29; H, 3.44

Found : C, 37.02; H, 3.44.

It slowly decomposes on exposure to the atmosphere, but is relatively stable when stored in a stoppered vessel at 0°.

5,6-Dimethoxy-2-isopropenylbenzofuran (I). — A solution of the *o*-iodophenyl acetate (IV) (2.07 g) in pyridine (20 ml) was added to a suspension of cuprous isopropenylacetylide[4] (909 mg) in the same solvent (20 ml) and the mixture refluxed under nitrogen for 22 hr. It was cooled, diluted with diethyl ether (250 ml) and filtered through Celite. Evaporation of the washed and dried filtrate under reduced pressure gave a residual oil (1.32 g) whose NMR spectrum indicated a mixture of benzofuran(IV) and en-yne(V) in 4:1 ratio, unchanged by refluxing in pyridine under nitrogen for a further 4 hr.

A solution of this mixture (1.22 g) in methanol (40 ml) was refluxed with sodium hydroxide (200 mg) in water (3 ml) for 1 hr., filtered and concentrated under reduced pressure. Extraction with ether and evaporation of the washed and dried extract gave a residual dark crystalline solid (782 mg) whose NMR spectrum indicated the sole presence of (I). Crystallization from ligroin containing a few drops of pyridine yielded (I) as white needles, m.p. 70-72° (lit.[2] m.p. 72.5-73°); ν (Nujol) 1618, 1550, 1484, 1001, 953 and 890 cm^{-1}; λ_{max} (MeOH) 215.5, 278.5, 288.5, 315 and 326(sh.) nm (log 4.24, 4.09, 4.08, 4.27 and 4.20 respectively); δ 2.10 (br.s. MeC=C), 3.88 (s, two OMe), 5.02-5.17 (m, vinyl H), 5.65-5.75 (m, vinyl H), 6.52 (s, H-3), 6.95 (s, H-4) and 7.02 (s, H-7).

2-Iodo-4,5-methylenedioxyphenyl Acetate(VI). — A solution of iodine monochloride (3.84 g) in acetic acid (25 ml) was added to a solution of 3,4-methylenedioxyphenyl acetate[8] (4.18 g) and silver acetate (3.885 g) in acetic anhydride (25 ml). The mixture was stirred for 1 hr., filtered and the filtrate poured into ice-water to precipitate an oil which slowly solidified. The collected solid (5.80 g) was recrystallized from aqueous methanol to give the iodophenyl acetate (VI) as glistening flakes (2.33 g), m.p. 61-62°. Filtration of the black mother liquor residues in benzene through a short column of silica yielded a further 1.55 g of the same purity, δ 2.30 (s, OAc), 5.97 (s, OCH_2O), 6.63 (s, H-6) and 7.18 (s, H-3).

Anal. Calcd. for $C_9H_7IO_4$: C, 35.32; H, 2.31

Found : C, 35.23; H, 2.33

2-Isopropenyl-5,6-methylenedioxybenzofuran(II). — To a suspension of cuprous isopropenylacetylide (682 mg) in pyridine (15 ml) was added a solution of the iodophenyl acetate(VI) (1.58 g) in the same solvent (15 ml) and the mixture heated under reflux (nitrogen atmosphere) for 48 hr. It was then cooled, poured into ether (200 ml) and filtered through Celite. The washed ether extract was treated with charcoal, dried ($MgSO_4$), filtered and the solvent removed to give a dark brown mass (817 mg), (NMR spectrum analysis indicated a 1:1 mixture of benzofuran(II) and the related en-yne) which was dissolved in methanol (50 ml) and refluxed with sodium hydroxide (760 mg) in water (10 ml) under nitrogen for 1 hr. Work up as before gave 2-isopropenyl-5,6-methylenedioxybenzofuran (439 mg), obtained as a yellow white powder on sublimation (0.15 mm/100°) or yellow crystals, m.p. 96-97°, from aqueous methanol (lit.[3] m.p. 98-99°) ν (Nujol) 1617, 1547, 1496, 1030, 938 and 875 cm^{-1}; λ_{max}(EtOH) 222, 276, 289 sh., 322, 325 and 333 nm (log 4.10, 4.06, 3.92, 4.24, 4.24 and 4.20 respectively); δ 2.07 (d, J 1.5 Hz, MeC=C), 5.00-5.17 (m, vinyl H), 5.60-5.73 (m, vinyl H), 5.96 (s, OCH_2O), 6.52 (s, H-3), 6.88 (s, H-4) and 6.96 (s, H-7).

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