

H. L. McPherson (1) and B. W. Ponder

Department of Chemistry, University of Alabama, University, Alabama 35486

Received December 12, 1975

Revised September 7, 1977

The Michael addition of ethyl acetoacetate to benzoquinone, toluquinone, and chlorobenzoquinone leads to formation of substituted 5-hydroxybenzofuran-3-carboxylates and linear benzo[1,2-*b*:4,5-*b'*]difurans. The previously reported structural proof for the benzodifurans obtained from chlorobenzoquinone and toluquinone, although correct in the conclusion, is shown to be invalid. Proof of the linear benzodifuran structures was obtained by comparison of the uv spectra with authentic angular benzo[1,2-*b*:4,3-*b'*]difurans.

J. Heterocyclic Chem., 15, 43 (1978)

During the course of some work in our laboratory to prepare a series of substituted 5-hydroxybenzofuran-3-carboxylic acid esters, which were to be screened for potential medicinal applications, it became apparent that some of the structures assigned to compounds of this type in the earlier literature were incorrect. In order to clarify some of these structural assignments, the Michael addition reaction of β -keto esters to several benzoquinones was reinvestigated.

The condensation of β -keto esters with benzoquinones has been reported by several investigators (2-9). The results of our investigations are summarized in Figure 1. The condensation of benzoquinone (1) and ethyl acetoacetate in alcoholic zinc chloride solution formed ethyl 5-hydroxy-2-methylbenzofuran-3-carboxylate (2) and 2,6-dimethylbenzo[1,2-*b*:4,5-*b'*]difuran-3,7-dicarboxylate (3).

Both the use of excess benzoquinone and/or the rapid addition of benzoquinone to the reaction mixture favors the formation of the difuran (3) (2,4,7,9-14).

The condensation of toluquinone (4) with ethyl acetoacetate has been reported to lead to a phenolic compound and a neutral compound (5) (tentative structure). Bernatek and coworker (15) indicated that the phenolic compound is ethyl 2,7-dimethyl-5-hydroxybenzofuran-3-carboxylate (6), although Grinev and coworkers (16) had earlier presented evidence, as outlined in Figure 2, that the phenolic compound is actually the 2,6-dimethyl isomer (7). Grinev's evidence consisted of two series of chemical reactions which led to compound 11, considered identical on the basis of a mixed melting point determination.

In order to resolve this discrepancy in structure assignment, the condensation of toluquinone and ethyl aceto-

Figure 1
Summary of Reactions of β -Keto Esters with Benzoquinones

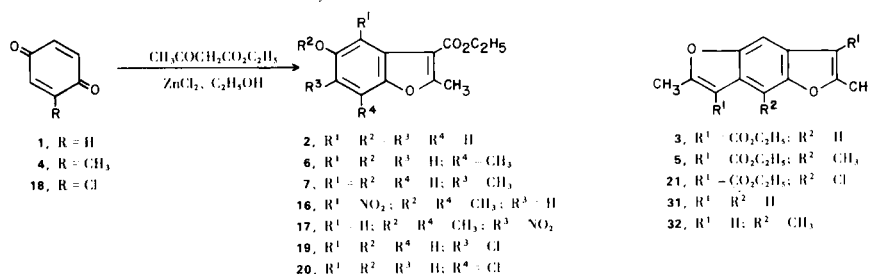
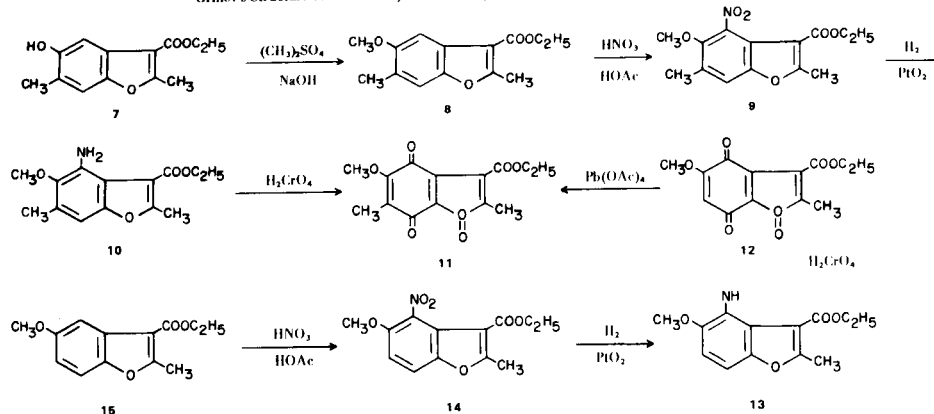


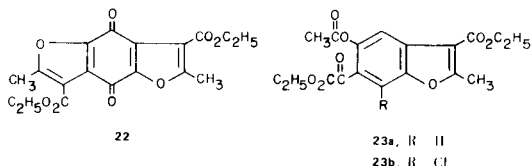
Figure 2
Grinev's Structure Proof for Ethyl 2,6-Dimethyl-5-hydroxybenzofuran-3-carboxylate (7)



acetate was repeated in our laboratory to yield, as reported before, a phenolic compound and a neutral compound. The nmr spectrum of both the acetate and the methyl ether derivative of the phenolic compound showed two doublets ($J = 2-3$ Hz) in the region δ 6.5-7.5, indicative of two *meta*-situated hydrogen atoms on the aromatic ring. Thus, it appears that Bernatek's assignment (structure **6**) is the correct one for this phenolic component. Grinev had reported that nitration of the methyl ether of the phenolic compound (structure **8** of Figure 2) gave a single nitro compound (**9**). However, when this nitration was repeated, we obtained material having a wide melting range, whose nmr spectrum indicated it to be an approximately 1:1 mixture of the 4-nitro- and 6-nitro substituted benzofuran rings, respectively (compounds **16** and **17**, Figure 1). This again locates the methyl substituent in the phenolic compound at C-7, as in Bernatek's structure (**6**).

The condensation of chlorobenzoquinone (**18**) with ethyl acetoacetate in alcoholic zinc chloride solution has been shown by our work to give three compounds in low yields. Giza and Hinman (7) reported the isolation of ethyl 6-chloro-5-hydroxy-2-methylbenzofuran-3-carboxylate (**19**) in 17% yield with a melting point range of 172-174°. Starting from compound **2**, they could also isolate the same chlorobenzoquinone derivative in 8% yield. When Giza's procedure was repeated in our laboratory, two phenolic compounds were isolated, one being identical with that reported by Giza (compound **19**), and the second having a melting point of 209-210°. The nmr spectrum of this second phenolic compound, as its acetate derivative, showed doublets at δ 7.00 and 7.51 (1 H each, $J = 3$ Hz) which are indicative of *meta*-situated hydrogens, *i.e.* structure **20**. The nmr spectrum of the third compound isolated (m.p. 135-136°) had singlets at δ 2.66 (CH₃), 2.77 (CH₃), and 7.67 (1H) and two sets of triplets and quartets, assigned to two ethyl groups, and suggests structure **21**.

Grinev and coworkers (17) reported that rapid addition of chlorobenzoquinone to an alcoholic zinc chloride solution of ethyl acetoacetate resulted in formation of diethyl 4-chloro-2,6-dimethylbenzo[1,2-*b*:4,5-*b'*]difuran-3,7-dicarboxylate, **21** (m.p. 164-165°). Grinev's assignment of a linear structure for this benzodifuran compound (**21**), as well as for the other benzodifurans **3** and **5**, was based on the observation that their oxidation by chromium trioxide-acetic acid solution led to the same colorless

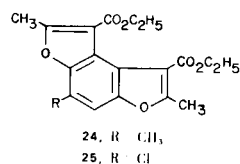


compound for which structure **22** was proposed. The oxidation products from compounds **3**, **5**, and **21** were considered to be identical on the basis of mixed melting

point determinations using an analyzed sample from compound **3** as a standard.

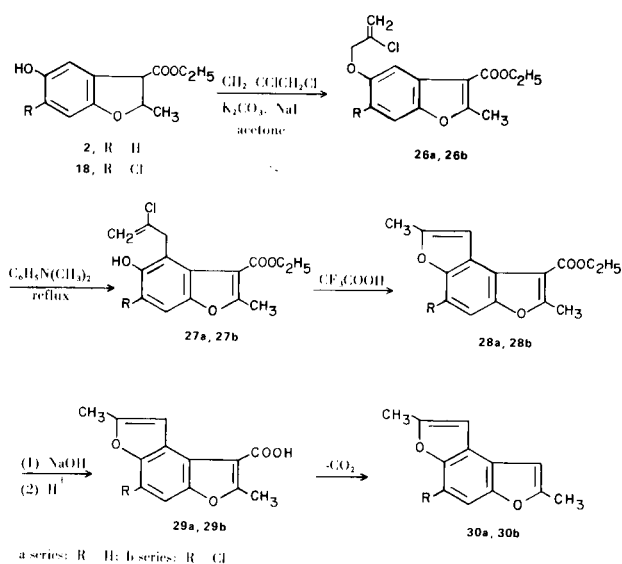
Repetition of this oxidation reaction on compound **3** in our laboratories gave the same *colorless* material as isolated by Grinev. However, the nmr spectrum of this oxidation product had singlets at δ 7.69 and 7.94 (1 H each), 2.33 and 2.76 (1 CH₃ each), and two sets of triplets and quartets for two ethyl groups. This suggests structure **23a**, which is the same compound obtained by Bernatek (13) by cleavage of the 2,3-double bond in compound **3** with ozone. Thus, this observation of oxidative cleavage of one of the furan rings of compound **3** by the action of chromium trioxide-acetic acid serves to invalidate Grinev's assignment of a linear structure for compounds **5** and **21**.

It should be pointed out that the structures for compounds previously assigned as **5** and **21** could equally well be represented by the angular benzo[1,2-*b*:4,3-*b'*]difuran isomers, **24** and **25**, respectively. Therefore, in an attempt to resolve the problem of linear *vs* angular benzodifuran



structures for the 1:2 adducts, a number of angular benzodifurans were prepared to serve as model compounds. The synthetic route to these angular isomers is shown in Figure 3. The Claisen rearrangement of compound **26a**

Figure 3
Synthetic Scheme for Angular Benzodifurans



formed by alkylation of compound **2** with 2,3-dichloro-1-propene (**18**) gave the 4-substituted derivative **27a**. The nmr spectrum of **27a** or its acetate derivative had two doublets ($J = 8.5-9$ Hz) in the region δ 6.95-7.35 indicating two *ortho* situated hydrogen atoms. Nmr spectra of crude

Table I

Ultraviolet Absorption Maxima of Substituted Benzodifurans,
 λ max (methanol) (log ϵ)

Compound	Compound	Compound	
3	228 (4.47)	28a 220 (4.71)	30b 225 (4.35)
	285 (4.23)	269 (3.34) s	270 (4.32) s
	292 (4.28)	278 (4.12)	278 (4.49)
	297 (4.30)	288 (3.08) s	289 (4.28)
	303 (4.38)		301 (3.92)
5(a)	212 (4.50)	28b 220 (3.90)	31(a) 230 (4.26)
	230 (4.46)	278 (3.86)	268 (4.19) s
	291 (4.28)	289 (3.78)	278 (4.40)
	301 (4.30)	299 (3.68)	287 (4.07)
			293 (4.17)
21	229 (4.58)	30b 221 (4.04)	32 229 (4.29)
	292 (4.35)	265 (4.16)	279 (4.41)
	303 (4.37)	273 (4.29)	292 (4.29) s
		285 (4.17)	298 (4.20) s
		295 (3.60)	303 (4.04)

(a) Ethyl alcohol was used as the solvent; s = shoulder.

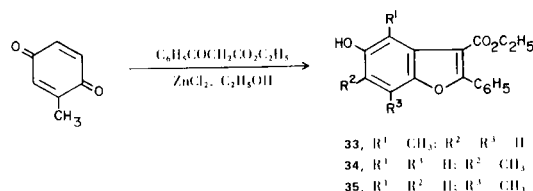
samples of **27a** failed to reveal any contamination by Claisen rearrangement to position 6.

Treatment of **27a** (preferably crude) with trifluoroacetic acid (20°) gave ring closure-elimination to form **28a**. Alkaline hydrolysis of **28a** followed by decarboxylation gave 2,7-dimethylbenzo[1,2-*b*:4,3-*b'*]difuran (**30a**). The same sequence of steps was used to convert compound **19** to 4-chloro-2,7-dimethylbenzo[1,2-*b*:4,3-*b'*]difuran (**30b**). Likewise, the alkaline hydrolysis and decarboxylation of compounds **3** and **5** gave the previously assigned tentative structures **31** and **32**, respectively.

The uv spectra of the angular benzo[1,2-*b*:4,3-*b'*]difuran derivatives prepared above (**28a**, **28b**, **30a**, and **30b**), and the known linear benzo[1,2-*b*:4,5-*b'*]difuran derivatives (**3** and **31**) are listed in Table I. A careful comparison of the absorption values in the table with those of compounds **5**, **21**, and **32** indicates that these latter compounds are linear benzodifurans.

Prior to obtaining the uv evidence for the linear structures for compounds **5**, **21**, and **32**, compound **21** had been subjected to oxidation with chromium trioxide in acetic acid, as mentioned previously. The product resulting from this oxidation, C₁₈H₁₇ClO₈, revealed a singlet in the nmr for an aromatic hydrogen at δ 7.67. According to published shielding parameters (19), replacing one of the two aromatic hydrogens of structure **23a** with a chlorine atom should result in a shielding effect (\sim 0.04 ppm) of the remaining hydrogen. This shielding effect is exhibited when comparing the two compounds **23a** and **23b** - the hydrogen atom at C-4 in **23b** is shifted upfield by 0.02 ppm from its position in compound **23a**.

Grinev and coworkers (20) reported that the condensation of toluquinone and ethyl benzoylacetate in alcoholic zinc chloride solution gave two products, as shown below, for which structures **33** (m.p. 143-144°; methyl ether, m.p. 77-78°) and **34** (m.p. 188-189°; methyl ether, m.p. 72-73°) were proposed without any proof. A repetition of this condensation reaction in our laboratories gave



two phenolic materials, m.p. 155-156° (methyl ether, m.p. 84-85°), and m.p. 186.5-188° (methyl ether, m.p. 77-78°). The nmr spectrum of the methyl ether of m.p. 77-78° showed a singlet at δ 7.22 (1H), which indicates structure **34**. The nmr of the methyl ether of m.p. 84-85° showed a doublet at δ 6.65 (1H, J = 3 Hz, additional fine splitting) which indicates structure **35** for this material.

EXPERIMENTAL

Spectra were determined on a Perkin Elmer 337 (ir), Varian A60A, EM 360 or Hitachi-Perkin Elmer R20B 60 MHz (nmr) with tetramethylsilane as an internal standard and a Cary 14 instrument (uv). Infrared spectra were measured as mineral oil mulls on sodium chloride plates. Melting points were determined using a Thomas Hoover Unimelt or a Fisher-Johns m.p. apparatus and are uncorrected. Analyses were performed in the analytical units of Ohio University, University of Alabama or Atlantic Microlab, Inc.

Ethyl 5-Hydroxy-2-methylbenzofuran-3-carboxylate (**2**) and Diethyl 2,6-Dimethylbenzo[1,2-*b*:4,5-*b'*]difuran-3,7-dicarboxylate (**3**).

The condensation of benzoquinone and ethyl acetoacetate in alcoholic zinc chloride (80-90°) gave the ether or alcohol soluble compound **2**, m.p. 143-144° (ethyl alcohol or benzene) in 25% yield; ir: 3310 and 1660 cm⁻¹; nmr (deuteriochloroform): δ 1.40 (t CH₃, J = 7 Hz), 2.71 (s CH₃), 4.38 (q CH₂, J = 7 Hz), 6.34 (s OH) and 6.68-7.58 (m 3H). Lit. m.p. 137° (10); 143.5-144° (7).

The ether or alcohol insoluble compound **3** was obtained (17%) as colorless needles, m.p. 188.0-188.5° (chloroform); ir: 1705 cm⁻¹; nmr (deuteriochloroform): δ 1.47 (t 2CH₃, J = 7.5 Hz), 2.77 (s 2CH₃), 4.39 (q 2CH₂, J = 7.5 Hz) and 7.87 (s 2H). Lit. m.p. 184° (10).

Methylation of compound **2** (dimethyl sulfate-sodium hydroxide-dioxane) gave the methyl ether **15** (distilled *in vacuo*), m.p. 40-41°; ir: 3125, 3060 and 1720 cm⁻¹; nmr (deuteriochloroform): δ 1.42 (t CH₃, J = 7.5 Hz), 2.71 (s CH₃), 3.83 (s CH₃), 4.38 (q CH₂, J = 7.5 Hz) and 6.8-7.5 (m 3H). Lit. m.p. 46-47° (16).

Diethyl 2,4,6-Trimethylbenzo[1,2-*b*:4,5-*b'*]difuran-3,7-dicarboxylate (**5**) and Ethyl 2,7-Dimethyl-5-hydroxybenzofuran-3-carboxylate (**6**).

The condensation of toluquinone and ethyl acetoacetate in alcoholic zinc chloride solution (80-90°) gave low yields (<16%)

of compound **6** which melted at 175-178° after repeated recrystallization from ethyl alcohol; ir: 3350, 3050 and 1670 cm^{-1} . Lit. m.p. 173° (4,16).

Extraction of crude compound **6** with a small volume of chloroform followed by chromatography of the extract (Alcoa F-20 alumina) gave up to 13% of compound **5**, m.p. 133-135° (ethyl alcohol); ir: 1720 and 1710 cm^{-1} ; nmr (deuteriochloroform): δ 1.43 and 1.45 (t 2CH₃, J = 7 Hz), 2.68 (s CH₃), 2.77 (s CH₃), 4.37 (q 2CH₂, J = 7 Hz) and 7.70 (s H). Lit. m.p. 120-122° (10); 133° (4).

Acetylation (acetic anhydride-trace of sulfuric acid) of compound **6** gave the acetate derivative, m.p. 95-96° (ethyl alcohol); ir: 1760 and 1700 cm^{-1} ; nmr (deuteriochloroform): δ 1.40 (t CH₃, J = 7.5 Hz), 2.27 (s CH₃), 2.36 (s CH₃), 2.71 (s CH₃), 4.36 (q CH₂, J = 7.5 Hz), 6.73 (d H, J = 3 Hz) and 7.41 (d H, J = 3 Hz). Lit. m.p. 96° (4).

Methylation of compound **6** (dimethyl sulfate-sodium hydroxide) gave the methyl ether, m.p. 129-130° (ethyl alcohol); ir: 3120, 3060 and 1695 cm^{-1} ; nmr (deuteriochloroform): δ 1.42 (t CH₃, J = 7.5 Hz), 2.42 (s CH₃, slightly broadened), 2.72 (s CH₃), 3.83 (s CH₃), 4.38 (q CH₂, J = 7.5 Hz), 6.65 (d H, J = 2 Hz, finely split) and 7.26 (d H, J = 2 Hz). Lit. m.p. 123-124° (16).

Ethyl 2,7-Dimethyl-5-methoxy-4- and 6-nitrobenzofuran-3-carboxylates (**16** and **17**).

Nitration of the methyl ether of compound **6** with nitric-acetic acids (steam cone) gave a 78% yield of yellow needles, m.p. 115-132° (ethyl alcohol) of an approximately 1:1 mixture of compounds **16** and **17**; ir: 1710, 1700 and 1600 cm^{-1} ; nmr (deuteriochloroform): δ 1.37 and 1.46 (t 2CH₃, J = 7.5 Hz), 2.40 and 2.48 (s 2CH₃), 2.71 and 2.74 (s 2CH₃), 3.89 and 3.91 (s 2CH₃), 4.30 and 4.32 (q 2CH₂, J = 7.5 Hz), 6.80 (s H) and 7.40 (s H). Lit. m.p. 112-113° (16).

Diethyl 4-Chloro-2,6-dimethylbenzo[1,2-*b*:4,5-*b'*]difuran-3,7-dicarboxylate (**21**), Ethyl 6-Chloro-5-hydroxy-2-methylbenzofuran-3-carboxylate (**19**), and Ethyl 7-Chloro-5-hydroxy-2-methylbenzofuran-3-carboxylate (**20**).

To a hot solution (oil bath at 80-90°) of anhydrous zinc chloride (40 g.), absolute ethyl alcohol (50 ml.) and ethyl acetoacetate (39.00 g., 0.30 mole) was rapidly added (ca. 5 minutes) a solution of chlorobenzoquinone (42.6 g., 0.30 mole) in 400 ml. of dry ether. The ether was removed by distillation during the addition. After a further three hours of heating, the hot, brown mixture was poured into cold water. The sticky brown lumps were filtered and heated with benzene (azeotropic drying). After cooling, the benzene mixture was filtered to provide an off-white powder, m.p. 170-195°. The material was sublimed at 130-135°/0.1 mm for 1 day. The white sublimate (7.09 g.), m.p. 168-180°, was recrystallized from ethyl alcohol to provide 2.70 g. (3.5%) of compound **19**. A sample which had been repeatedly recrystallized from ethyl alcohol had m.p. 184-186°. Lit. m.p. 182.0-182.5° (7); ir: 3290, 3250 and 1670 cm^{-1} .

The light yellowish sublimation residue (10.12 g.), m.p. 195-204°, was recrystallized from ethyl alcohol to provide 3.73 g. (4.9%) of compound **20**, m.p. 207-209°. A further recrystallization from ethyl alcohol gave m.p. 209-210°; ir: 3360 and 1680 cm^{-1} .

Anal. Calcd. for C₁₂H₁₁ClO₄: C, 56.59; H, 4.35. Found: C, 56.45; H, 4.40.

In some preparations digestion of the crude adducts with a small amount of chloroform followed by chromatography over basic alumina, resulted in up to 4% of compound **21**, colorless needles, m.p. 135-136°; ir: 1710 cm^{-1} ; nmr (deuteriochloroform): δ 1.43 (t 2CH₃, J = 7.5 Hz, slightly broadened), 2.66 and

2.77 (s 2CH₃), 4.37 and 4.41 (q 2CH₂, J = 7.5 Hz) and 7.67 (s H).

Anal. Calcd. for C₁₈H₁₇ClO₆: C, 59.27; H, 4.70. Found: C, 59.25; H, 4.72.

The acetate of compound **19** (acetic anhydride-pyridine) had m.p. 107-109° (ethyl alcohol); ir: 3120, 1760 and 1710 cm^{-1} ; nmr (carbon tetrachloride-deuteriochloroform): δ 1.43 (t CH₃, J = 7.5 Hz), 2.37 and 2.74 (s 2CH₃), 4.39 (q CH₂, J = 7.5 Hz), 7.51 (s H) and 7.66 (s H).

Anal. Calcd. for C₁₄H₁₃ClO₅: C, 56.66; H, 4.44. Found: C, 56.60; H, 4.46.

The acetate derivative of compound **20** (acetic anhydride-sodium acetate) had m.p. 113-114° (ethyl alcohol); ir: 3120, 3090, 1755 and 1710 cm^{-1} ; nmr (carbon tetrachloride): δ 1.41 (t CH₃, J = 7.5 Hz), 2.24 and 2.78 (s 2CH₃), 4.33 (q CH₂, J = 7.5 Hz), 7.00 (d H, J = 3 Hz) and 7.51 (d H, J = 3 Hz).

Anal. Calcd. for C₁₄H₁₃ClO₅: C, 56.66; H, 4.44. Found: C, 56.62; H, 4.45.

Ethyl 5-Acetoxy-3-carbomethoxy-2-methylbenzofuran-6-glyoxylate (**23a**).

To a boiling solution of compound **3** (40.4 g., 0.123 mole) in 788 ml. of acetic acid was added a solution of chromium trioxide (98.8 g., 0.99 mole) in 738 ml. of acetic acid and 64 ml. of water. After the addition was completed (1 hour) the green mixture was cooled, diluted with water and the precipitate filtered. The cream colored powder was recrystallized from ethyl alcohol to afford 18.8 g. of compound **23a** (42%), m.p. 99-101°. Two further recrystallizations from ethyl alcohol gave colorless needles, m.p. 106-107°; ir: 1785, 1735, 1710 and 1670 cm^{-1} ; nmr (deuteriochloroform): δ 1.39 and 1.42 (t 2CH₃, J = 7.5 Hz), 2.33 (s CH₃), 2.76 (s CH₃), 4.42 (q 2CH₂, J = 7.5 Hz), 7.69 (s H-4) and 7.94 (s H-7). Lit. m.p. 99° (13); 106-107° (16).

Ethyl 5-Acetoxy-3-carbomethoxy-7-chloro-2-methylbenzofuran-6-glyoxylate (**23b**).

Oxidation of compound **21** with chromium trioxide in acetic acid gave a 20% yield of compound **23b**, colorless needles, m.p. 136-137° (ethyl alcohol-chloroform); ir: 3115, 1765, 1725 and 1700 cm^{-1} ; nmr (deuteriochloroform): δ 1.39 and 1.43 (t 2CH₃, J = 7 Hz), 2.26 and 2.82 (s 2CH₃), 4.40 (q 2CH₂, J = 7 Hz, finely split) and 7.67 (s H-4).

Anal. Calcd. for C₁₈H₁₇ClO₈: C, 54.49; H, 4.32. Found: C, 54.20; H, 4.30.

Ethyl 5-(2-Chloroallyloxy)-2-methylbenzofuran-3-carboxylate (**26a**).

A mixture of compound **2** (20.96 g., 0.10 mole), 2,3-dichloro-1-propene (15 ml., 0.16 mole), sodium iodide (15 g.), anhydrous potassium carbonate (40 g.) and dry acetone (400 ml.) was heated and stirred for 17 hours. The mixture was cooled and the acetone was partially evaporated. The residue was diluted with water, extracted with isopropyl ether, and the extract dried (calcium chloride), and evaporated. Vacuum distillation gave compound **26a** (85%) as a pale red liquid (m.p. 40-42°) which was further purified by evaporative distillation to afford colorless crystals, m.p. 43-44°; ir: 3140, 3090, 1705 and 1640 cm^{-1} ; nmr (carbon tetrachloride): δ 1.40 (t CH₃, J = 7.5 Hz), 2.66 (s CH₃), 4.42 (q CH₂, J = 7.5 Hz), 4.57 (s 2H, finely split), 5.41 (d H, J = 1.5 Hz, finely split), 5.60 (d H, J = 1.5 Hz, finely split) and 6.6-7.4 (m 3H).

Anal. Calcd. for C₁₅H₁₅ClO₄: C, 61.13; H, 5.13. Found: C, 61.34; H, 5.23.

Ethyl 4-(2-Chloroallyl)-5-hydroxy-2-methylbenzofuran-3-carboxylate (**27a**).

A solution of compound **26a** in *N,N*-dimethylaniline was boiled for 5 hours. The compound was isolated as a pale yellow solid in

60% yield, m.p. 135-138°. Successive recrystallizations from ethyl alcohol, and benzene-petroleum ether gave nearly colorless needles, m.p. 139-140°; ir: 3400 and 1660 cm^{-1} ; nmr (deuterioacetone): δ 1.40 (t CH_3 , $J = 7.5$ Hz), 2.63 (s CH_3), 4.32 (s 2H), 4.38 (q 2H, $J = 7.5$ Hz), 4.73 (d H, finely split), 5.07 (d H, finely split), 6.96 (d H, $J = 8.5$ Hz), 7.28 (d H, $J = 8.5$ Hz), and 8.33 (s OH).

Anal. Calcd. for $\text{C}_{15}\text{H}_{15}\text{ClO}_4$: C, 61.13; H, 5.13. Found: C, 61.33; H, 5.23.

The acetate derivative of compound **27a** was prepared (30%) by conducting the Claisen rearrangement of compound **26a** in acetic anhydride and *N,N*-dimethylaniline, m.p. 63-65° (carbon tetrachloride-petroleum ether); ir: 3100, 1755 and 1715 cm^{-1} ; nmr (carbon tetrachloride): δ 1.39 (t CH_3 , $J = 7.5$ Hz), 2.25 and 2.63 (s 2 CH_3), 4.13 (s 2H, finely split), 4.36 (q 2H, $J = 7.5$ Hz), 4.65 (d H, $J = 1.5$ Hz), 5.08 (d H, $J = 1.5$ Hz), 6.96 (d H, $J = 9$ Hz) and 7.33 (d H, $J = 9$ Hz).

Anal. Calcd. for $\text{C}_{17}\text{H}_{17}\text{ClO}_5$: C, 60.63; H, 5.09. Found: C, 60.63; H, 5.10.

Ethyl 2,7-Dimethylbenzo[1,2-*b*:4,3-*b'*]difuran-1-carboxylate (**28a**).

A solution of compound **26a** (5.50 g., 0.0187 mole) in 45 ml. of *N,N*-dimethylaniline was boiled for 5.5 hours. The solution was cooled, diluted with cold, dilute hydrochloric acid and the brown oil which eventually solidified was washed with water. The dry lumps were dissolved in 35 ml. of trifluoroacetic acid. After three hours the trifluoroacetic acid was allowed to evaporate. The black residue was washed with water and recrystallized from ethyl alcohol to afford tan rods (59%), m.p. 93-95°. Further recrystallizations from ethyl alcohol gave colorless needles, m.p. 94.5-95.0°; ir: 1690 cm^{-1} ; nmr (deuteriochloroform): δ 1.42 (t CH_3 , $J = 7.5$ Hz), 2.47 (d CH_3 -7, $J = 1.5$ Hz), 2.70 (s CH_3), 4.41 (q 2H, $J = 7.5$ Hz), 7.08 (s H-4, finely split), 7.23 (s H) and 7.25 (s H, finely split).

Anal. Calcd. for $\text{C}_{15}\text{H}_{14}\text{O}_4$: C, 69.76; H, 5.46. Found: C, 69.95; H, 5.49.

2,7-Dimethylbenzo[1,2-*b*:4,3-*b'*]difuran-1-carboxylic Acid (**29a**).

Alkaline hydrolysis of compound **28a** followed by acidification gave **29a** (94%), m.p. 253-254° (ethyl alcohol); ir: 3200-2400 and 1665 cm^{-1} .

Anal. Calcd. for $\text{C}_{13}\text{H}_{10}\text{O}_4$: C, 67.80; H, 4.38. Found: C, 67.60; H, 4.50.

2,7-Dimethylbenzo[1,2-*b*:4,3-*b'*]difuran (**30a**).

Pyrolysis of the potassium salt of compound **29a** gave **30a**, m.p. 107.5-108.5° (petroleum ether); ir: 3130, 1590, 1280, 1270, 1260, 1225, 1150, 1125, 1035, 990, 965, 930, 805, 800, 790, 780 and 775 cm^{-1} ; nmr (carbon tetrachloride): δ 2.40 (d 2 CH_3 , $J = 1$ Hz), 6.32 (s 2H; finely split) and 7.18 (s 2H).

Anal. Calcd. for $\text{C}_{12}\text{H}_{10}\text{O}_4$: C, 77.40; H, 5.41. Found: C, 77.13; H, 5.50.

Ethyl 6-Chloro-5-(2-chloroallyloxy)-2-methylbenzofuran-3-carboxylate (**26b**).

Alkylation of compound **19** with 2,3-dichloro-1-propene gave **26b** (93%), m.p. 93-94° (carbon tetrachloride-petroleum ether); ir: 3120, 3100 and 1700 cm^{-1} ; nmr (carbon tetrachloride): δ 1.42 (t CH_3 , $J = 7.5$ Hz), 2.67 (s CH_3), 4.32 (q 2H, $J = 7.5$ Hz), 4.60 (s 2H, finely split), 5.46 (d H, $J = 1$ Hz), 5.71 (d H, $J = 1$ Hz) and 7.32 (s 2H).

Anal. Calcd. for $\text{C}_{15}\text{H}_{14}\text{Cl}_2\text{O}_4$: C, 54.73; H, 4.29. Found: C, 54.80; H, 4.31.

Ethyl 6-Chloro-4-(2-chloroallyl)-5-hydroxy-2-methylbenzofuran-3-carboxylate (**27b**).

The material, which readily becomes purple, had m.p. 75-79°

(sublimed); ir: 3550, 3115 and 1720 cm^{-1} ; nmr (carbon tetrachloride): δ 1.40 (t CH_3 , $J = 7.5$ Hz), 2.63 (s CH_3), 4.23 (s 2H, finely split), 4.39 (q 2H, $J = 7.5$ Hz), 4.71 (d H, finely split), 5.07 (d H, finely split), 5.61 (s OH) and 7.32 (s H).

Anal. Calcd. for $\text{C}_{15}\text{H}_{14}\text{Cl}_2\text{O}_4$: C, 54.73; H, 4.29. Found: C, 54.64; H, 4.30.

Ethyl 5-Chloro-2,7-dimethylbenzo[1,2-*b*:4,3-*b'*]difuran-1-carboxylate (**28b**).

Treatment of crude compound **27b** with trifluoroacetic acid gave compound **28b** (60%), m.p. 155-156° (ethyl alcohol); ir: 3150, 3075, 3055 and 1695 cm^{-1} ; nmr (deuteriochloroform): δ 1.47 (t CH_3 , $J = 7.5$ Hz), 2.53 (d CH_3 -7, $J = 1$ Hz), 2.72 (s CH_3), 4.43 (q 2H, $J = 7.5$ Hz), 7.09 (d H-8, $J = 1$ Hz) and 7.25 (s H-4).

Anal. Calcd. for $\text{C}_{15}\text{H}_{13}\text{ClO}_4$: C, 61.55; H, 4.48. Found: C, 61.74; H, 4.58.

5-Chloro-2,7-dimethylbenzo[1,2-*b*:4,3-*b'*]difuran-1-carboxylic Acid (**29b**).

Alkaline hydrolysis of compound **28b** followed by acidification and digestion with ethyl alcohol gave compound **29b** as a yellow powder (84%), m.p. 317-320°; ir: 3300-2500 and 1675 cm^{-1} .

Anal. Calcd. for $\text{C}_{13}\text{H}_9\text{ClO}_4$: C, 59.00; H, 3.43. Found: C, 58.98; H, 3.47.

4-Chloro-2,7-dimethyl[1,2-*b*:4,3-*b'*]difuran (**30b**).

Decarboxylation (quinoline, cupric oxide) of compound **29b** gave **30b** as colorless needles (17%), m.p. 110-111° (petroleum ether); ir: 3125, 3110, 1670, 1595, 1270, 1190, 1170, 1155, 1085, 1015, 990, 983, 895, 795, 775, 742, 708, 675 and 600 cm^{-1} ; nmr (carbon tetrachloride): δ 2.42 (s CH_3), 2.48 (s CH_3), 6.33 (s H, finely split), 6.39 (s H, finely split) and 7.20 (s H).

Anal. Calcd. for $\text{C}_{12}\text{H}_{11}\text{ClO}_2$: C, 65.32; H, 4.11. Found: C, 65.46; H, 4.10.

2,6-Dimethylbenzo[1,2-*b*:4,5-*b'*]difuran (**31**).

Alkaline hydrolysis of compound **3** followed by acidification and subsequent boiling of the crude dicarboxylic acid with quinoline and cupric oxide, gave compound **31** as colorless thin scales, m.p. 115-116° (petroleum ether); ir: 3125, 1860, 1700, 1605, 1290, 1185, 1165, 1120, 1035, 1000, 930, 860, 852, 807, 790, 705, 610, and 600 cm^{-1} ; nmr (deuteriochloroform): δ 2.43 (s 2 CH_3 , finely split), 6.34 (s 2H, slightly broadened), and 7.35 (s 2H). Lit. m.p. 113-114° (10).

2,4,6-Trimethylbenzo[1,2-*b*:4,5-*b'*]difuran (**32**).

Alkaline hydrolysis of compound **5** followed by acidification and subsequent boiling of the crude dicarboxylic acid with quinoline and cupric oxide gave after chromatography (basic alumina) and sublimation, **36**, m.p. 75-76° (ethyl alcohol); ir: 3110, 1655, 1605, 1310, 1280, 1215, 1185, 1165, 1140, 1070, 1035, 995, 935, 860, 825, 800, 785, 745, 710, 695, 615 and 605 cm^{-1} ; nmr (carbon tetrachloride): δ 2.40 (t 2 CH_3 , $J = <1$ Hz), 2.52 (s CH_3), 6.27 (s 2H, finely split), and 7.16 (s H). Lit. m.p. 70-71.5° (10).

Ethyl 5-Hydroxy-6-methyl-2-phenylbenzofuran-3-carboxylate (**34**) and Ethyl 5-Hydroxy-7-methyl-2-phenylbenzofuran-3-carboxylate (**35**).

To a hot (80-90°), stirred solution of anhydrous zinc chloride (7.0 g.), absolute ethyl alcohol (10 ml.) and ethyl benzoylacetate (9.6 g., 0.050 mole) was added dropwise a solution of toluquinone (6.1 g., 0.050 mole) in 250 ml. of dry ether. The ether was removed by distillation and the mixture heated a further 21 hours. The mixture was cooled and the brown paste filtered and washed with cold ethyl alcohol to afford a light tan powder, m.p. 168-179°. Further recrystallizations from ethyl alcohol gave colorless

needles (13%) of compound **34**, m.p. 185-187°. The analytical sample melted at 186.5-188°; ir: 3350 and 1665 cm^{-1} ; nmr (deuterioacetone): δ 1.36 (t CH_3 , $J = 7.5$ Hz), 2.46 (s CH_3), 4.38 (q 2H, $J = 7.5$ Hz) and 7.3-8.4 (m 8H). Lit. m.p. 188-189° (20).

Anal. Calcd. for $\text{C}_{18}\text{H}_{16}\text{O}_4$: C, 72.96; H, 5.44. Found: C, 72.83; H, 5.46.

The brown alcoholic filtrate and washings were combined, diluted with water and the mixture extracted with carbon tetrachloride. The extract was dried (calcium chloride), filtered and evaporated. The residue was repeatedly recrystallized from ethyl alcohol to provide compound **35** (9%), m.p. 155-156°; ir: 3380, 3060, and 1680 cm^{-1} ; nmr (deuterioacetone): δ 1.37 (t CH_3 , $J = 7.5$ Hz), 2.49 (s CH_3 , finely split), 4.36 (q 2H, $J = 7.5$ Hz), 6.81 (d H, finely split) and 7.3-8.3 (m 7H). Lit. m.p. 143-144° (20).

Anal. Calcd. for $\text{C}_{18}\text{H}_{16}\text{O}_4$: C, 72.96; H, 5.44. Found: C, 72.81; H, 5.39.

The methyl ether of compound **34** had m.p. 84-85° (petroleum ether); ir: 3060 and 1700 cm^{-1} ; nmr (deuteriochloroform): δ 1.34 (t CH_3 , $J = 7.5$ Hz), 2.31 and 3.86 (s CH_3), 4.34 (q 2H, $J = 7.5$ Hz), 7.22 (s H) and 7.3-8.2 (m 6H). Lit. m.p. 77-78° (20).

Anal. Calcd. for $\text{C}_{19}\text{H}_{18}\text{O}_4$: C, 73.53; H, 5.85. Found: C, 73.59; H, 5.84.

The methyl ether of compound **35** had m.p. 77-78° (petroleum ether-carbon tetrachloride); ir: 3065 and 1700 cm^{-1} ; nmr (deuteriochloroform): δ 1.33 (t CH_3 , $J = 7.5$ Hz), 2.44 and 3.80 (s 2 CH_3), 4.32 (q CH_2 , $J = 7.5$ Hz), 6.65 (d H, $J = 3$ Hz, finely split), 7.2-7.6 (m 4H) and 7.9-8.2 (m 2H). Lit. m.p. 72-73° (20).

Anal. Calcd. for $\text{C}_{19}\text{H}_{18}\text{O}_4$: C, 73.53; H, 5.85. Found: C, 73.64; H, 5.89.

REFERENCES AND NOTES

- (1) Taken in part from a dissertation to be submitted by H. L. McPherson in partial fulfillment of the requirements for the degree of Doctor of Philosophy at the University of Alabama.
- (2) H. Pechmann, *Chem. Ber.*, **21**, 3005 (1888).
- (3) M. Ikuta, *J. Prakt. Chem.*, **45**, 65 (1892).
- (4) C. Grabe and S. Levy, *Ann. Chem.*, **283**, 245 (1894).
- (5) F. Bergel, A. Jacob, A. R. Todd and T. S. Work, *J. Chem. Soc.*, 1375 (1938).
- (6) S. E. Fumagalli and C. H. Eugster., *Helv. Chim. Acta*, **54**, 959 (1971).
- (7) C. A. Giza and R. L. Hinman, *J. Org. Chem.*, **29**, 1453 (1964).
- (8) E. Bernatek, M. Johnsgard and T. Stenrud, *Acta Chem. Scand.*, **21**, 574 (1967) and other papers in the series.
- (9) A. N. Grinev and A. P. Terent'ev, *Vestnik Moskov. Univ., Ser. Mat. Mekh., Astron., Fiz., Khim.*, **12**, 147 (1957); *Chem. Abstr.*, **53**, 3187 (1959) and other papers in the series. An English translation is available from the British Library Lending Division, Boston Spa, United Kingdom as #RTS-2726.
- (10) A. P. Terent'ev, A. N. Grinev and P. Bon-Khvar, *Zhur. Obshch. Khim.*, **24**, 2050 (1954); *J. Gen. Chem. USSR.*, **24**, 2015 (1954); *Chem. Abstr.*, **49**, 13959 (1955).
- (11) A. N. Grinev, P. Bon-Khvar and A. P. Terent'ev, *Zhur. Obshch. Khim.*, **26**, 2928 (1956); *J. Gen. Chem. USSR*, **26**, 3255 (1956); *Chem. Abstr.*, **51**, 7349 (1957).
- (12) E. Bernatek and M. Hvatum, *Acta Chem. Scand.*, **14**, 836 (1960).
- (13) E. Bernatek and F. Thoresen, *ibid.*, **13**, 342 (1959).
- (14) E. Bernatek and S. Ramstad, *ibid.*, **7**, 1351 (1953).
- (15) E. Bernatek and I. Bo, *ibid.*, **13**, 337 (1959).
- (16) A. N. Grinev and A. P. Terent'ev, *J. Gen. Chem. USSR*, **28**, 80 (1958); *Chem. Abstr.*, **52**, 12830 (1958).
- (17) A. N. Grinev, P. Bon-Khvar, V. N. Frosin and A. P. Terent'ev, *J. Gen. Chem. USSR*, **26**, 603 (1956); *Chem. Abstr.*, **50**, 13860 (1956).
- (18) The method of converting a phenol to a 2-methylbenzofuran is that of W. K. Anderson and E. J. LaVoie, *Chem. Commun.*, 174 (1974).
- (19) M. Zanger, *Org. Magn. Reson.*, **4**, 1 (1972).
- (20a) A. N. Grinev, P. Bon-Khvar and A. P. Terent'ev, *Vestnik Moskov. Univ. 11, Ser. Fiz-Mat. i. Estestven. Nauk*, No. 2, 91 (1956); *Chem. Abstr.*, **50**, 16737 (1956); (b) A. N. Grinev, N. K. Venetseva and A. P. Terent'ev, *J. Gen. Chem. USSR*, **28**, 1850 (1958); *Chem. Abstr.*, **53**, 1296 (1959).