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SYNTHESIS OF 2(3H)-BENZOFURANONE DERIVATIVES BY COPPER(I)-PROMOTED SUBSTITUTION REACTIONS OF ACTIVE METHYLENE CARBANIONS[1]

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ABSTRACT

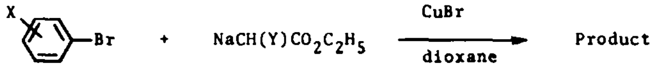
Activation of soft carbanions by copper(I) in the substitution reaction toward aryl halides and allyl halides was demonstrated. Derivatives of 2(3H)-benzofuranones (**2**, **14** - **18**) were prepared in a one-pot procedure by the reaction of copper(I) diethyl malonate with sodium o-bromophenoxide. 2-Hydroxybenzofuran (**4**) and its 2-amino derivative (**5**) were obtained by using copper(I) salts of ethyl acetoacetate and ethyl cyanoacetate. The reaction of sodium p-bromophenoxides with copper(I) diethyl malonate yielded p-1,1,2,2-tetracarboethoxyethylphenols (**7**, **8**). 3-Carboethoxy-3-β-methallyl-2-benzofuranone (**14**) was converted into spiro[2-benzofuranone-3,3'-(5',5'-dimethyl)-γ-butyrolactone] (**22**) under acidic conditions. The latter compound was further decarboxylated to give spiro[2-benzofuranone-3,1'-(2',2'-dimethyl)cyclopropane] (**23**) by the treatment with sodium ethoxide.

Coupling reactions between enolate anions and aryl halides have recently been developed as a direct synthetic method to α-aryl carbonyl compounds. Among these are an arylation of 2-methoxyallylnickel,[2] a Ni-catalyzed arylation of lithium enolate,[3] a Pd-catalyzed arylation of tin enolate,[4] and an Fe-initiated $S_{RN}1$ arylation of potassium enolate.[5] Softer carbanions such as active methylene carbanions have never been successfully utilized in these reactions, but they were found to undergo arylation under the influence of copper(I) salts.[3b,6] While it was shown that ethynylcopper(I) reagents could be used effectively for the synthesis of heterocyclic compounds such as benzofurans, thiobenzofurans, and indoles through the substitution of aryl halides followed by cyclization,[7] the utility of organocopper(I) reagents derived from active methylene carbanions has only recently been recognized for the construction of the indole nucleus.[8]

In the course of our study on these organocopper(I) reagents, we have found that copper(I) diethyl malonate reacts effectively with o- and p-bromophenoxide and this reaction can be applied to the synthesis of 2(3H)-benzofuranone derivatives. The reactivity of copper(I) diethyl malonate toward aryl, allyl and alkyl halides, and the convenient synthesis of 3-substituted 2(3H)-benzofuranones are described in this paper.

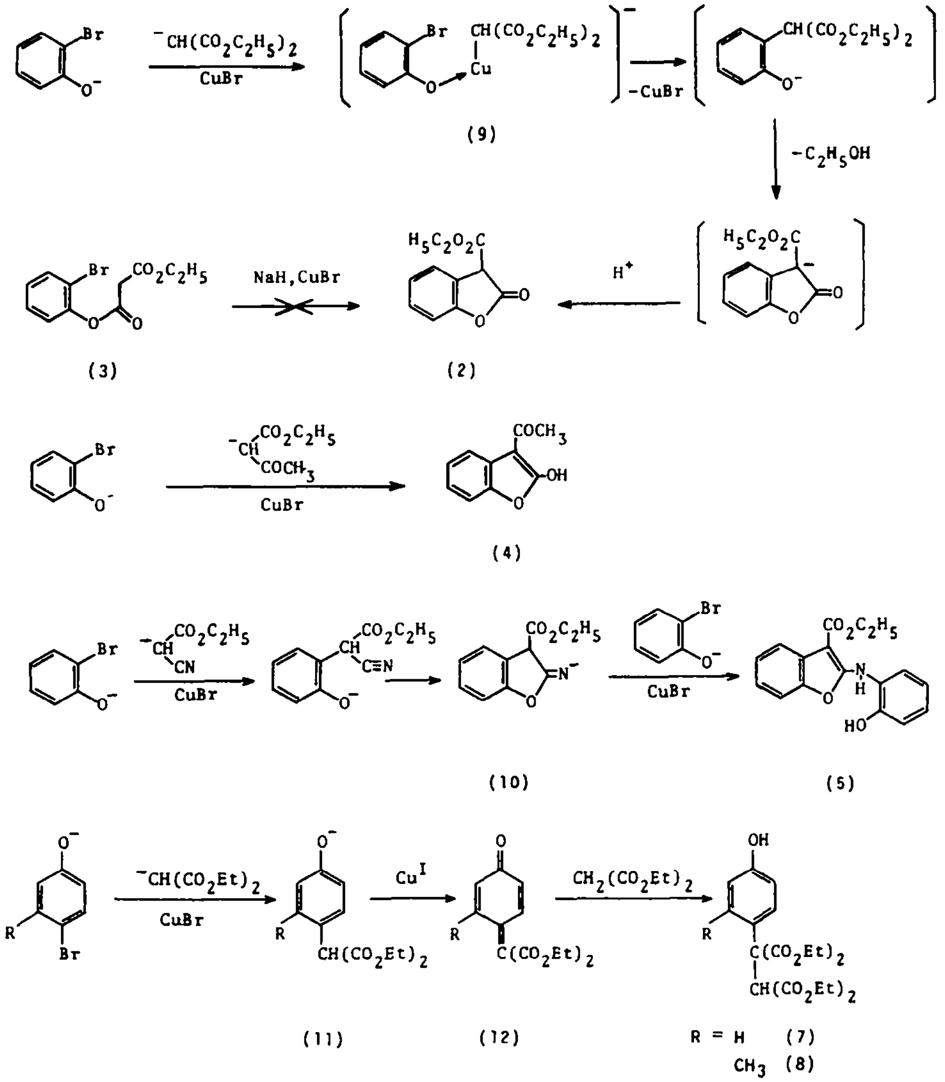
Addition of CuBr to sodium diethyl malonate in dioxane brought about a color change to yellow suggesting the formation of the organocopper species, copper(I) diethyl malonate, which is sensitive to air but stable up to 100°C under an inert atmosphere.[6b] When o-bromoanisole was allowed to react with 1.2 molar equivalents of copper(I) diethyl malonate for 5 hr at reflux in dioxane, 89 % yield (55 % conversion of o-bromoanisole) of the coupling product (1) was obtained (Table 1. entry 1). Formation of diethyl o-methoxyphenylmalonate[9] (**1**) which is more acidic than diethyl malonate resulted in the waste of the organocopper reagent. Although the treatment of o-bromophenol with copper(I) diethyl malonate (1.2 eq.) resulted in almost no substitution reaction, a good yield of 3-carboethoxy-2(3H)-benzofuranone (**2**) was obtained under much milder reaction conditions than those used for o-bromoanisole (Table 1. entry 2 and 3) when sodium o-bromophenoxide was used instead of o-bromophenol. The effectiveness of the reaction of sodium o-bromophenoxide compared with o-bromoanisole is not attributable to the prior formation of the mixed diester of malonic acid[10] (**3**), since the treatment of (**3**) with each equivalent of NaH and CuBr has failed to afford (**2**). Thus, o-bromophenoxide undergoes substitution by copper(I) diethyl malonate initially and lactonization occurs subsequently to give (**2**). The use of ethyl acetoacetate and ethyl cyanoacetate instead of diethyl malonate in the above procedure gave 3-acetyl-2-hydroxybenzofuran[11] (**4**) and 3-carboethoxy-2-o-hydroxyanilinobenzofuran(**5**) in 15 % and 34 % yield, respectively. The substitution reaction of ethyl cyanoacetate promoted by copper(I) was followed by the intramolecular attack of the phenoxide ion on the cyano group and the resulting imide anion (**10**) replaced a bromo anion from the second o-bromophenoxide to account for the formation of (**5**). A much higher reactivity of sodium p-bromophenoxide than p-bromoanisole has also been demonstrated (Table 1. entry 6 and 7). When sodium p-bromophenoxide was treated with copper(I) diethyl malonate (2 eq.) at 70°C for 3 hr, metallic copper deposited and p-1,1,2,2-tetracarboethoxyethylphenol (**7**) was obtained in 97 % yield (70 % conversion) probably with the intermediacy of an anionic diethyl p-hydroxyphenylmalonate (**11**) and a p-quinone methide (**12**). p-1,1,2,2-Tetracarboethoxyethyl-m-cresol (**8**) was also obtained by the same procedure in 100 % yield (63 % conversion).

Table 1. Copper(I)-Promoted Substitution Reaction of Active Methylene Carbanions with Bromophenol derivatives[a]



entry	X	Y	Temp. (°C)	Time (hr)	Product	Conversion[b] (%)	Yield[c] (%)
1	o-OCH_3	$CO_2C_2H_5$	100	5	(1)[d]	55	89
2	o-OH	$CO_2C_2H_5$	70	5	(2)	8	31
3	o-ONa	$CO_2C_2H_5$	70	5	(2)	85	93
4	o-ONa	$COCH_3$	80	5	(4)	-	15[e]
5	o-ONa	CN	80	5	(5)	-	34[e]
6	p-OCH_3	$CO_2C_2H_5$	100	5	(6)[f]	45	40
7	p-ONa	$CO_2C_2H_5$	70	3	(7)	70	97
8	p-ONa m-CH_3	$CO_2C_2H_5$	100	6	(8)	63[g]	100[g]

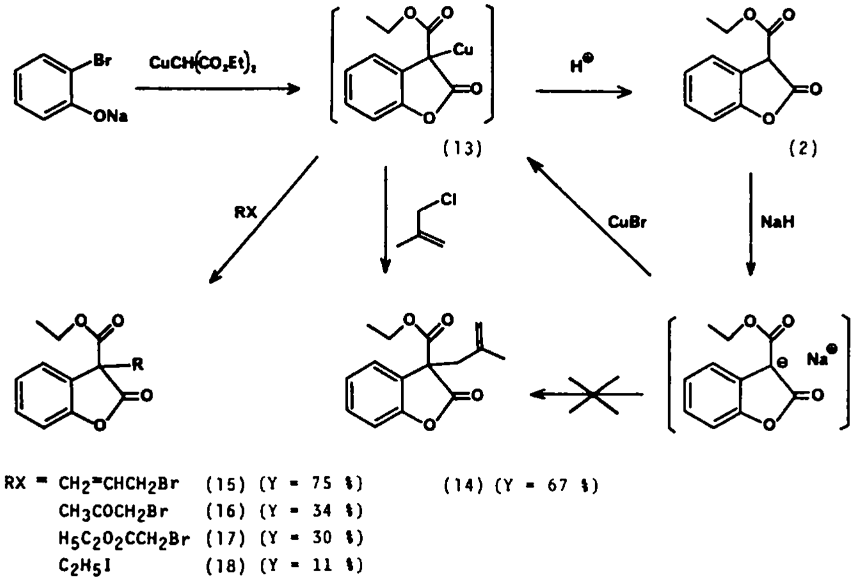
a) 1.2-Fold molar carbanion was used except for the last two rows where two-fold molar was used. b) Mol-% based on the charged aryl halide (GLC analysis). c) Product yield based on the converted aryl halide (GLC analysis). d) Diethyl o-methoxyphenylmalonate. e) Isolated yield. f) Diethyl p-methoxyphenylmalonate. g) Determined by HPLC.



Scheme 1. Reactions of copper(I) diethyl malonate, ethyl acetoacetate, and ethyl cyanoacetate with sodium o- and p-bromophenoxides.

We have pointed out that the reactivity of aryl halides towards copper(I) diethyl malonate decreases with increasing tne electron-donating power of their substituents.[6b] Therefore, it is noteworthy that o- and p-bromophenoxide react effectively under much milder reaction conditions than o- and p-bromoanisole do. Copper(I) diethyl malonate generated in situ is responsible for the activation of aromatic C-X bond through the electron transfer, as generally noted in the reactions of organocopper(I) species.[12] As the addition of an equivalent of sodium phenoxide to a reaction mixture of sodium diethyl malonate, phenyl bromide, and CuBr in dioxane did not cause a considerable rate enhancement, it is unlikely that the coordination of phenoxide may augment the reactivity of copper(I) diethyl malonate with respect to an intermolecular electron transfer to aryl halides. However, a complex between bromophenoxide and copper(I) such as (9) in Scheme 1 seems to facilitate an intramolecular metal-to-ligand electron transfer irrespective of whether the aromatic C-X bond is at the ortho or at the para position.

As this reaction to afford (2) is a coupling of two anionic reactants with one equivalent of bromide ion being replaced, the final reaction mixture should contain one equivalent of base. When β-methallyl chloride (1.2 eq.) was added to the reaction mixture instead of quenching with acid after the completion of the coupling reaction, 3-carboethoxy-3-β-methallyl-2-benzofuranone (**14**) was obtained in 67 % yield based on the converted o-bromophenol (79 %). This fact shows that the reaction of sodium o-bromophenoxide and copper(I) diethyl malonate generates an anionic (at the 3-position) species of 3-carboethoxy-2(3H)-benzofuranone under the reaction conditions. Although the treatment of (**2**) with an equimolar amount of NaH in dioxane under nitrogen and subsequently with β-methallyl chloride for 2 hr at reflux did not give (**14**) at all, the addition of CuBr to this reaction mixture resulted in the formation of (**14**) in a similar yield. Therefore, 3-(3-carboethoxy-2-benzofuranonyl)copper(I) (**13**) is considered to be an active species responsible for the allylation of (**2**). 3-Substituted-3-carboethoxy-2-benzofuranones (**15** - **18**) were also obtained conveniently through the one-pot procedure using allyl bromide, bromoacetone, ethyl bromoacetate and ethyl iodide, respectively (Scheme 2). As the reactivity of organocopper(I) species of active methylene carbanion toward alkyl and allyl halides has never been studied so far, the rates of the reactions, with ethyl iodide and β-methallyl chloride, of copper(I) diethyl malonate was compared with those of sodium diethyl malonate under the same reaction conditions by monitoring the amounts of the coupling products with time by GLC analysis. The second order rate constants (k) for the formation of diethyl β-methallylmalonate from copper(I) diethyl malonate and sodium diethyl malonate were 3.3×10^{-4} $M^{-1}s^{-1}$ and 1.5×10^{-5} $M^{-1}s^{-1}$ at 38°C, respectively, when the initial concentrations of diethyl malonate and β-methallyl chloride in dioxane are 3.2×10^{-1} M and 3.5×10^{-1} M, respectively. Under similar conditions as above, the rate constants for the formation of diethyl ethylmalonate from copper(I) diethyl malonate and the corresponding sodium salt were 4.5×10^{-4} $M^{-1}s^{-1}$ and 4.8×10^{-4} $M^{-1}s^{-1}$ respectively. Thus, copper(I) diethyl malonate proved to be especially effective in the substitution reaction toward allyl halides, but the reaction toward alkyl halides is not accelerated by copper(I). This result is



Scheme 2. Formation and reaction of 3-(3-carboethoxy-2-benzofranonyl)copper(I).

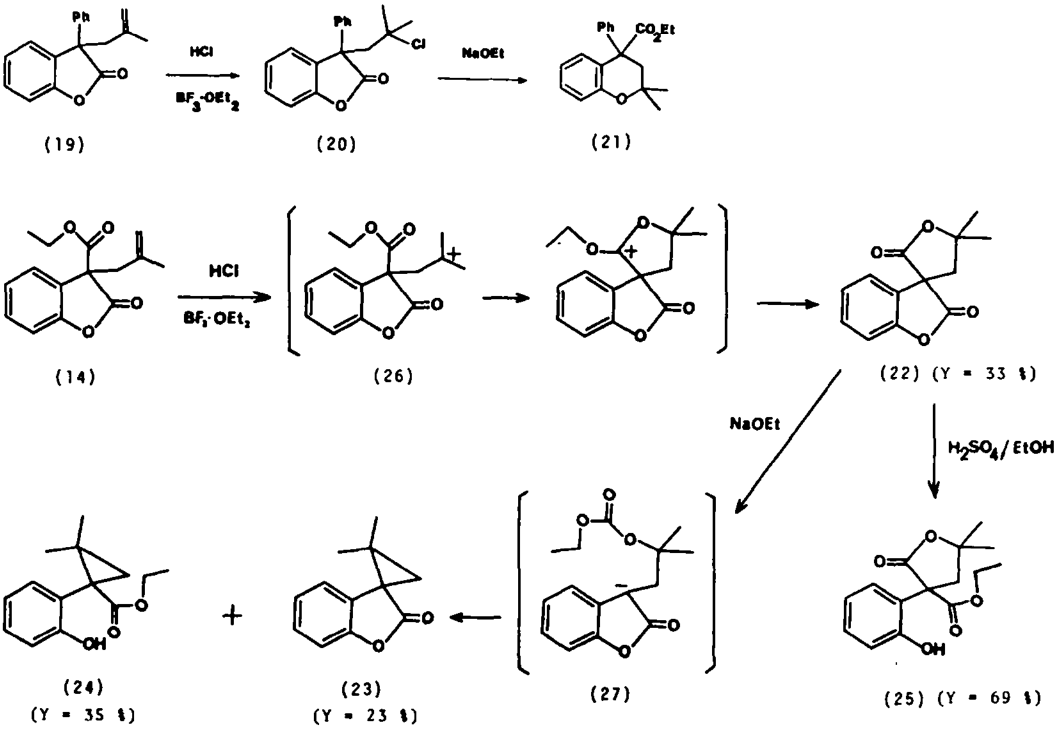
Table 2. Second Order Rate Constants for the Substitution Reactions of Copper(I) and Sodium Diethyl Malonate with β-Methallyl Chloride and Ethyl Iodide in Dioxane at 38°C.

$$MCH(CO_2C_2H_5)_2 + RX \xrightarrow{k} RCH(CO_2C_2H_5)_2$$

M	RX	$k(M^{-1}s^{-1})$	k_{Cu}/k_{Na}
Cu	$CH_2{=}C(CH_3)CH_2Cl$	3.3×10^{-4}	22
Na	$CH_2{=}C(CH_3)CH_2Cl$	1.5×10^{-5}	
Cu	CH_3CH_2I	4.5×10^{-4}	0.94
Na	CH_3CH_2I	4.8×10^{-4}	

consistent with the observation that (**13**) gave only 11 % yield of the ethylated product (**18**) even after prolonged heating.

It was reported that 3-β-methallyl-3-phenyl-2-benzofuranone (**19**) was converted into 2,2-dimethyl-4-carboethoxy-4-phenylchroman (**21**) via HCl addition to the olefinic moiety of (**19**) followed by a ring-opening - recyclization sequence under basic conditions.[13] When (**14**) was treated with dry HCl, the corresponding HCl addition reaction did not take place, but the neighboring carboethoxy group reacted with the tertiary carbonium ion intermediate (**26**) to give spiro[2-benzofuranone-3,3'-(5',5'-dimethyl)-γ-butyrolactone] (**22**) in 33 % yield after hydrolysis. Furthermore, the treatment of (**22**) with sodium ethoxide brought about decarboxylation to give spiro[2-benzofuranone-3,1'-(2',2'-dimethyl)cyclopropane] (**23**) in 23 % yield and its lactone ring-opened product (**24**) in 35 % yield, whereas ethanolysis of (**22**) under acidic conditions resulted in an effective benzofuranone



Scheme 3. Reaction of 3-β-methallyl-2-benzofuranones.

ring opening to yield 3-carboethoxy-3-(o-hydroxyphenyl)-5,5-dimethyl-γ-butyrolactone (**25**) in 69 % yield. The formation of (**23**) is explainable in terms of the C-C bond cleavage between the carbonyl carbon and the α-carbon followed by replacement of ethyl carbonate ion (Scheme 3). The 2(3H)-benzofuranone structure of (**2**, **14-18**, **22**, **23**) was best evidenced by the strong absorptions due to C=O stretching vibrations at around 1800 cm^{-1} in their IR spectra. ^1H-NMR spectra of (**22**) and (**23**) show the ring methylene protons as a pair of AB doublets with the geminal coupling constants of 14 Hz and 6 Hz, clearly indicating that these methylenes are involved in the 5-membered and 3-membered ring system respectively. (**24**) and (**25**) also show a pair of AB doublets with the coupling constants of 14 Hz and 5 Hz respectively.

In conclusion, copper(I) diethyl malonate is effective in the substitution reaction toward aryl and allyl halides but not toward alkyl halides, and the reaction with o-bromophenoxide can serve as a very convenient tool for new classes of 2(3H)-benzofuranone derivatives which are not accessible directly by known methods.[14]

Experimental

Melting points were taken on a micro melting point apparatus and are uncorrected. IR spectra were measured on a Shimadzu IR-420 spectrometer. ^1H- and ^{13}C-NMR spectra were recorded on JEOL MH-100 and JEOL FX-60Q spectrometers with chemical shifts given on the δ scale from tetramethylsilane as an internal standard. Mass spectra were obtained on a Shimadzu GCMS-9000 spectrometer. Elemental Analyses were performed on a Yanaco MT2 CHN corder. Kieselgel 60 F_{254} silica gel plates (Merck) and Wakogel C-300 silica gel (Wako Junyaku) were used for TLC and column chromatography.

3-Carboethoxy-2(3H)-benzofuranone (2)

To a suspension of sodium hydride (0.88 g of 60 % suspension in mineral oil was washed with petroleum ether, 22 mM) in dioxane (10 mL) was added o-bromophenol (1.73 g, 10 mM) and diethyl malonate (1.92 g, 12 mM) successively under an atmosphere of nitrogen. After the mixture was stirred for 30 min at room temperature, cuprous bromide (1.72 g, 12 mM) was added under a stream of nitrogen and the resulting mixture was heated at 70°C for 5 hr with stirring. The reaction mixture was cooled and then partitioned between benzene and 3 % HCl aqueous solution. The organic layer was washed with water repeatedly, dried over anhydrous magnesium sulfate, and concentrated under reduced pressure. The residual oil was fractionally distilled to give 3-carboethoxy-2(3H)-benzofuranone (**2**) at 180°C / 7 mmHg. Isolated yield was 1.21 g (59 %). GLC yield (93 % based on 85 % conversion of o-bromophenol) was determined by using diphenyl as an internal standard: IR (NaCl) 1840, 1830, 1810 cm^{-1}; ^1H-NMR ($CDCl_3$) δ 7.10(m, 4H, Ar-H), 4.45(s, 1H, CH), 4.18(q, 2H, CH_2), 1.29(t, 3H, CH_3); mass spectrum, m/e 206(M). Anal. Calcd for $C_{11}H_{10}O_4$: C, 64.07; H, 4.89. Found: C, 64.26; H, 4.95.

3-Acetyl-2-hydroxybenzofuran (4)

A mixture of ethyl acetoacetate (1.56 g, 12 mM), o-bromophenol (1.73 g, 10 mM), NaH (22 mM), and CuBr (1.72 g, 12 mM) in dioxane (10 mL) was heated at 80°C for 5 hr similarly to the above procedure. This was partitioned between chloroform and 3 % HCl. The organic layer was washed, dried and evaporated to give a residue which was treated with petroleum ether. The formed precipitate was recrystallized from benzene - n-hexane to give white crystals of 3-acetyl-2-hydroxybenzofuran (**4**) in 15 % yield (0.26 g): mp 137°C; IR (KBr) 1730, 1710 cm^{-1}; ^1H-

NMR ($CDCl_3$) δ 7.10(m, 4H, Ar-H), 2.41(s, 3H, CH_3); mass spectrum, m/e 176(M). Anal. Calcd for $C_{10}H_8O_3$: C, 68.18; H, 4.58. Found: C, 68.11; H, 4.72.

3-Carboethoxy-2-o-hydroxyanilinobenzofuran (5)

A mixture of ethyl cyanoacetate (1.36 g, 12 mM), o-bromophenol (1.73 g, 10 mM), NaH (22 mM), and CuBr (1.72 g, 12 mM) in dioxane (10 mL) was allowed to react and worked up as described above. The crude product was treated with chilled benzene and the precipitate was collected and recrystallized from benzene - n-hexane to give 3-carboethoxy-2-o-hydroxyanilinobenzofuran (5) in 34 % yield (0.50 g): mp 183°C; IR (KBr) 3400, 3350, 1660, 1625 cm^{-1}; ^1H-NMR ($CDCl_3$ + d_6-DMSO) δ 9.50(br s, 1H, NH), 7.83(m, 1H, Ar-H), 7.65(m, 1H, Ar-H), 7.34(s, 1H, OH), 7.25 - 6.84(m, 6H, Ar-H), 4.37(q, 2H, CH_2), 1.44(t, 3H, CH_3); mass spectrum, m/e 297(M). Anal. Calcd for $C_{17}H_{15}NO_4$: C, 68.68; H, 5.09; N, 4.71. Found: C, 68.38; H, 4.89; N, 4.76.

p-1,1,2,2-Tetracarboethoxyethylphenol (7)

A mixture of diethyl malonate (1.60 g, 10 mM), p-bromophenol (0.865 g, 5 mM), NaH (15 mM), and CuBr (1.44 g, 10 mM) in dioxane (10 mL) was heated at 70 °C for 3 hr. The mixture was quenched with 3 % HCl solution and extracted with ether. Kugelrohr distillation at 230 °C / 1 mmHg afforded pure p-1,1,2,2-tetracarboethoxyethylphenol (7) in 55 % yield (1.13 g). GLC yield (97 % based on 70 % conversion of p-bromophenol) was determined by using diphenyl as an internal standard: IR (NaCl) 3410, 1730 cm^{-1}; ^1H-NMR ($CDCl_3$) δ 6.50(m, 4H, Ar-H), 6.16(s, 1H, OH), 4.14(s, 1H, CH), 3.98, 3.88(q×2, 4H×2, CH_2×4), 1.10, 1.06(t×2, 6H×2, CH_3×4); ^{13}C-NMR ($CDCl_3$) δ 168.9, 167.5, 155.8, 129.1, 126.0, 114.9, 63.3, 62.3, 61.7, 57.0, 13.6; mass spectrum, m/e 410(M). Anal. Calcd for $C_{20}H_{26}O_9$: C, 58.53; H, 6.39. Found: 58.79; H, 6.30.

p-1,1,2,2-Tetracarboethoxyethyl-m-cresol (8)

A mixture of diethyl malonate (1.60 g, 10 mM), p-bromo-m-cresol (0.935 g, 5 mM), NaH (15 mM), and CuBr (1.44 g, 10 mM) in dioxane 10 ml was heated at 100 °C for 6 hr and then worked up as described above. Isolated yield was 47 % (1.14 g). HPLC yield by using diphenyl was 100 % based on 63 % conversion of p-bromo-m-cresol: mp 131°C; IR (KBr) 3420, 1750, 1730, 1705 cm^{-1}; ^1H-NMR ($CDCl_3$) δ 6.68(m, 3H, Ar-H), 5.67(s, 1H, OH), 4.35(s, 1H, CH), 4.23, 4.08(q×2, 4H×2, CH_2×4), 2.17(s, 3H, CH_3), 1.23, 1.13(t×2, 6H×2, CH_3×4); ^{13}C-NMR ($CDCl_3$) δ 169.6, 167.4, 155.2, 137.7, 129.4, 126.0, 118.9, 112.5, 64.4, 62.3, 61.4, 54.9, 20.5, 13.5; mass spectrum, m/e 424(M). Anal. Calcd for $C_{21}H_{28}O_9$: C, 59.43; H, 6.65. Found: C, 59.71; H, 6.65.

3-Carboethoxy-3-β-methallyl-2-benzofuranone (14)

β-Methallyl chloride (1.09 g, 12 mM) was added after a mixture of diethyl malonate (1.92 g, 12 mM), o-bromophenol (1.73 g, 10 mM), NaH (22 mM), and CuBr (1.72 g, 12 mM) in dioxane (10 mL) was heated at reflux for 3 hr, and further 2 hr heating at reflux was continued. The reaction mixture was worked up as described above and fractional distillation at 145 - 158°C / 2 mmHg afforded 3-carboethoxy-3-β-methallyl-2-benzofuranone in 48 % yield (1.25 g). GLC yield (67 % based on 79 % conversion of o-bromophenol) was determined by using diphenyl as an internal standard: IR (NaCl) 1810, 1740, 1645, 900 cm^{-1}; ^1H-NMR (CCl_4) δ 7.49 - 6.89(m, 4H, Ar-H), 4.48 - 4.52(m, 2H, C=CH_2), 4.17, 4.13(q×2, 2H, OCH_2), 2.99(s, 2H, CH_2C=C), 1.42(s, 3H, CH_3), 1.20(t, 3H, CH_3); mass spectrum, m/e 260(M). Anal. Calcd for $C_{15}H_{16}O_4$: C, 69.22; H, 6.20. Found: C, 68.89; H, 6.20.

3-Allyl-3-carboethoxy-2-benzofuranone (**15**)

Allyl bromide (1.45 g, 12 mM) was added and heating was continued at reflux temperature for further 2 hr. Fractional distillation at 122 - 130°C / 3 mmHg afforded 3-allyl-3-carboethoxy-2-benzofuranone (**15**) in 53 % yield (1.30 g). GLC yield (75 % based on 81 % conversion of o-bromophenol) was determined by using diphenyl as an internal standard: IR (NaCl) 1810, 1730, 1640, 930 cm^{-1}; ^1H-NMR (CCl_4) δ 7.50 - 6.92(m, 4H, Ar-H), 5.78 - 4.78(m, 3H, $CH_2{=}CH$), 4.13, 4.08(q×2, 2H, OCH_2), 2.91(d, 2H, $CH_2C{=}C$), 1.17(t, 3H, CH_3); mass spectrum, m/e 246(M). Anal. Calcd for $C_{14}H_{14}O_4$: C, 68.28; H, 5.73. Found: C, 68.31; H, 5.83.

3-Acetonyl-3-carboethoxy-2-benzofuranone (**16**)

Bromoacetone (1.64 g, 12 mM) was added and heating was continued at reflux temperature for further 1.5 hr. Kugelrohr distillation followed by crystallization from diethyl ether gave 3-acetonyl-3-carboethoxy-2-benzofuranone (**17**) in 26 % yield (0.68 g). GLC yield (34 % based on 94 % conversion of o-bromophenol) was determined relative to diphenyl as an internal standard: mp 89 - 91°C; IR (KBr) 1805, 1745, 1710 cm^{-1}; ^1H-NMR ($CDCl_3$) δ 7.55 - 6.85(m, 4H, Ar-H), 4.15(q, 2H, OCH_2), 3.62, 3.56(s×2, 2H, $CH_2C{=}O$), 2.08(s, 3H, $CH_3C{=}O$), 1.14(t, 3H, CH_3); mass spectrum, m/e 262(M). Anal. Calcd for $C_{14}H_{14}O_5$: C, 64.12; H, 5.38. Found: C, 64.13; H, 5.40.

3-Carboethoxy-3-carboethoxymethyl-2-benzofuranone (**17**)

Ethyl bromoacetate (2.00 g, 12 mM) was added and the whole mixture was refluxed for further 18 hr. Kugelrohr distillation at 170°C / 0.2 mmHg followed by purification by GLC gave 3-carboethoxy-3-carboethoxymethyl-2-benzofuranone (**17**) in 18 % yield (0.53 g). GLC yield (30 % based on 96 % conversion of o-bromophenol) was determined by using diphenyl as an internal standard: IR (NaCl) 1810, 1730 cm^{-1}; ^1H-NMR (CCl_4) δ 7.55 - 6.90(m, 4H, Ar-H), 4.14, 3.97(q×2, 2H×2, OCH_2×2), 3.40(s, 2H, $CH_2C{=}O$), 1.19, 1.07(t×2, 3H×2, CH_3×2); mass spectrum, m/e 292(M). Anal. Calcd for $C_{15}H_{16}O_6$: C, 61.64; H, 5.52. Found: C, 61.92; H, 5.50.

3-Carboethoxy-3-ethyl-2-benzofuranone (**18**)

Ethyl iodide (1.87 g, 12 mM) was added and the whole mixture was refluxed for further 90 hr. Kugelrohr distillation at 165°C / 3 mmHg followed by purification with silica gel column chromatography (eluent: benzene) afforded 3-carboethoxy-3-ethyl-2-benzofuranone (**18**). GLC yield (11 % based on 89 % conversion of o-bromophenol) was determined by using diphenyl as an internal standard: IR (NaCl) 1810, 1740 cm^{-1}; ^1H-NMR (CCl_4) δ 7.58 - 6.98(m, 4H, Ar-H), 4.14, 4.11(q×2, 2H, OCH_2), 2.26(q, 2H, CH_2), 1.18(t, 3H, CH_3), 0.77(t, 3H, CH_3); mass spectrum, m/e 234(M). Anal. Calcd for $C_{13}H_{14}O_4$: C, 66.66; H, 6.02. Found: C, 68.89; H, 6.20.

Measurement of the second order rate constants for allylation and alkylation of diethyl malonate.

A mixture of sodium diethyl malonate (3.2×10^{-1} mol/L), β-methallyl chloride (3.5×10^{-1} mol/L), diphenyl (1.6×10^{-1} mol/L) and CuBr (7.0 mmol) in dioxane (20 mL) was maintained at 38°C with stirring. An aliquot (ca. 0.1 mL) was taken from the flask at every 20 minutes, quenched with acid, worked up ordinarily, and then β-methallyl diethyl malonate was quantitized by GLC using diphenyl as a standard. Taking A and B as the initial concentrations of diethyl malonate and β-methallyl chloride, and C as the concentration of the coupling product at the time T, $(A-B)^{-1}\log[BA^{-1}(C-A)(C-B)^{-1}]$ was plotted against T to show a fairly good linearity with the slope (k_{Cu}) of 3.3×10^{-4} $mol^{-1}Ls^{-1}$. k_{Na} (1.5×10^{-5} $mol^{-1}Ls^{-1}$) in the absence of CuBr was obtained under otherwise the same conditions. The progress of the reaction of sodium diethyl malonate (4.1 × 10^{-1} mol/L) and ethyl iodide (4.5 × 10^{-5} mol/L) in the presence of CuBr (9.0 mmol) in dioxane (20 mL) at 38°C was followed to give the slope (k_{Cu}) of 4.5 × 10^{-4} $mol^{-1}Ls^{-1}$. The progress of the reaction of sodium diethyl malonate (3.7 × 10^{-1} mol/L) and ethyl iodide (4.0 × 10^{-1} mol/L) in dioxane (20 mL) at 38°C was followed to give the slope (k_{Na}) of 4.8 × 10^{-4} $mol^{-1}Ls^{-1}$.

Spiro[2-benzofuranone-3,3'-(5',5'-dimethyl)-γ-butyrolactone] (**22**)

Dry hydrogen chloride was bubbled for 2 hr into a cyclohexane (15 mL) solution of 3-carboethoxy-3-β-methallyl-2-benzofuranone (**14**) (3.90 g, 15 mM) containing diphenylamine (39 mg) and boron trifluoride etherate (63 mg). After the solution was stirred for 48 hr at room temperature, cold water was added. Cyclohexane layer was separated and aqueous layer was extracted with ether. The combined organic later was dried over anhydrous $MgSO_4$, filtered and evaporated. The residue was chromatographed on silica gel with benzene to afford spiro[2-benzofuranone-3,3'-(5',5'-dimethyl)-γ-butyrolactone] (**22**) in 33 % yield (1.15 g). When a chloroform solution of (30 mL) of (**14**) (3.90 g, 15 mM) containing a few drops of conc. H_2SO_4 was refluxed for 12 hr and worked up as described above, the compound (**22**) was isolated in 38 % yield (1.32 g): mp 106 - 109°C; IR (KBr) 1800, 1750 cm^{-1}; ^1H-NMR ($CDCl_3$) δ 7.68 - 7.12(m, 4H, Ar-H), 2.91, 2.48(d×2, 2H, CH_2, J_{gem}= 14 Hz), 1.75, 1.68(s×2, 3H×2, CH_3×2); mass spectrum, m/e 188(M-44). Anal. Calcd for $C_{13}H_{12}O_4$: C, 67.23; H, 5.21. Found: C, 67.24; H, 5.01.

Spiro[2-benzofuranone-3,1'-(2',2'-dimethyl)cyclopropane] (**23**) and 1-carboethoxy-1-(o-hydroxyphenyl)-2,2-dimethylcyclopropane (**24**)

To a sodium ethoxide solution prepared from absolute ethanol (10 mL) and sodium (46 mg, 2 mM) was added spiro[2-benzofuranone-3,3'-(5',5'-dimethyl)-γ-butyrolactone] (22) (464 mg, 2 mM), and the solution was refluxed for 2 hr. 3% Aqueous HCl was added and the reaction mixture was extracted with ether. The organic layer was washed with water, dried over anhydrous $MgSO_4$, and evaporated. The residue was chromatographed on silica gel with n-hexane - ethylacetate (5 : 1). The first band gave spiro[2(3-benzofuranone-3,1'-(2',2'-dimethyl)cyclopropane] (**23**) in 23 % yield (86 mg) and the second band gave 1-carboethoxy-1-(o-hydroxyphenyl)-2,2-dimethylcyclopropane (**24**) in 35 % yield (164 mg). (**23**): mp 107 - 110°C; IR (KBr) 3010, 1770 cm^{-1}; ^1H-NMR ($CDCl_3$) δ 7.26 - 6.58(m, 4H, Ar-H), 1.92, 1.60(d×2, 2H, CH_2, J_{gem}= 6 Hz), 1.52, 1.40(s×2, 3H×2, CH_3×2); mass spectrum m/e 188(M). Anal Calcd for $C_{22}H_{12}O_2$: C, 76.57; H, 6.43. Found: C, 76.76; H, 6.79. (**24**): IR (NaCl) 3280, 3050, 1675 cm^{-1}; ^1H-NMR (CCl_4) δ 7.89(s, 1H, Ar-OH), 6.65 - 6.24(m, 4H, Ar-H), 4.12(q, 2H, OCH_2), 1.54, 1.07(d×2, 2H, CH_2, J_{gem}= 5 Hz), 1.25(t, 3H, CH_3), 1.26, 0.85(s×2, 3H×2, CH_3×2); mass spectrum, m/e 234(M). Anal. Calcd for $C_{14}H_{18}O_3$: C, 71.79; H, 7.74. Found: C, 71.40; H, 7.62.

3-Carboethoxy-3-(o-hydroxyphenyl)-5,5-dimethyl-γ-butyrolactone (**25**)

A mixture of spiro[2-benzofuranone-3,3'-(5',5'-dimethyl)-γ-butyrolactone (**22**) (230 mg, 1 mM), absolute ethanol (200 mL), and a few drops of conc. H_2SO_4 was refluxed for 24 hr with stirring. This was partitioned between ether and water. The ether layer was washed with water, dried over anhydrous $MgSO_4$ and evaporated to dryness. The residue was recrystallized from benzene to give 3-carboethoxy-3-(o-hydroxyphenyl)-5,5-dimethyl-γ-butyrolactone (**25**) in 69 % yield (192 mg): mp 157°C; IR (KBr) 3260, 1720 cm^{-1}; ^1H-NMR ($CDCl_3$) δ 7.39 - 6.55(m, 5H, Ar-H, and Ar-OH), 4.24(q, 2H, OCH_2), 3.09, 2.69(d×2, 2H, CH_2, J_{gem}= 14 Hz), 1.50, 1.39(s×2, 3H×2, CH_3×2), 1.24(t, 3H, CH_3); mass spectrum m/e 278(M). Anal. Calcd for $C_{15}H_{18}O_5$: C, 64.74; H, 6.52. Found: C, 64.59; H, 6.80.

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9. ^{1}H-NMR spectra of **(1)** and **(6)** are as follows: **(1)** δ 7.24 - 6.60(m, 4H, Ar-H), 4.88(s, 1H, Ar-CH), 4.10(q, 4H, OCH_2), 3.75(s, 3H, OCH_3), 1.22(t, 6H, CH_3); **(6)** δ 7.13 - 6.68(m, 4H, Ar-H). 4.35(s, 1H, Ar-CH), 4.06(q, 4H, OCH_2), 3.65(s, 3H, OCH_3), 1.20(t, 6H, CH_3).
10. o-Bromophenyl ethyl malonate was prepared from carboethoxyacetyl chloride and o-bromophenol in the presence of diethylaniline in dry ether: b.p. 120°C / 1 mmHg; ^{1}H-NMR (CCl_4) δ 7.50 - 6.80(m, 4H, Ar-H), 4.15(q, 2H, OCH_2), 3.50(s, 2H, CH_2), 1.25(t, 3H, CH_3).
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