# Furan Derivatives. Part 11 [1]. On Substituent Effects in the Synthesis of 3,4,5,6-Tetrahydrocyclohepta[*cd*]benzofurans



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Tetrahydrocyclohepta[*cd*]benzofurans **7a-e** were synthesized by the treatment of (5-oxo-tetrahydro-5*H*-benzocyclohepten-4-yloxy)acetic acids **5a-e** with sodium acetate in acetic anhydride or by heating of their esters **6a-e** with sodium hydroxide or sodium hydride in dioxane. The yield of furans **7** decreased as a substituent R of acids **5** or esters **6** was changed from hydrogen to a methyl, ethyl, or isopropyl group. When R was a phenyl group furan **7e** was always prepared in good yield. Sodium hydride was a useful base for synthesis of tetrahydrocyclohepta[*cd*]benzofurans.

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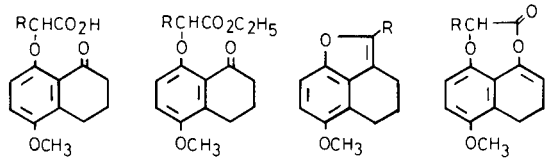
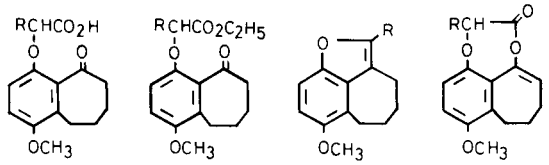
## Introduction.

Benzofurans may be readily synthesized by the treatment under reflux with sodium acetate in acetic anhydride [2] of 2-acylphenoxyacetic acids or by heating of their esters with bases such as potassium carbonate [3] or potassium hydroxide [4]. However, when naphthyloxyacetic acids **1** or their esters **2** in which the carbonyl group was fixed in the six-membered ring were used as the starting materials, naphthofurans **3** were not obtained in high yield because of formation of lactones **4** or saponification of the esters **2** to the corresponding carboxylic acids **1** [5]. Especially, when the substituent R of **1** or **2** was an isopropyl group the yield of naphthofuran **3d** was very low. The results were attributed to the carbonyl group in the six-membered ring which could not rotate freely and not take a favorable conformation for furan-ring formation [5]. Therefore, in the present paper we use acids **5** or esters **6** which have more flexible seven-membered carbonyl group and examine effects of the ring size and a kind of the substituent R(hydrogen, methyl, ethyl, isopropyl, or phenyl group) on synthesis of cyclohepta[*cd*]benzofurans **7** or lactones **8**. Cyclohepta[*cd*]benzofuran is uncommon ring system and described in a few literatures [6].

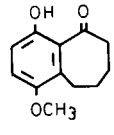
Formula 1




1 2 3 4




5 6 7 8




9

1 - 8
a ; R = H
b ; R = $CH_3$
c ; R = $C_2H_5$
d ; R = $CH(CH_3)_2$
e ; R = Ph

3, 7
f ; R = $CO_2H$
g ; R = $CO_2C_2H_5$

## Results and Discussion.

Starting acids **5** and esters **6** for synthesis of cyclohepta[*cd*]benzofurans **7** were prepared from 4-hydroxy-1-methoxybenzocyclohepten-5-one **9** [7] which was obtained by selective demethylation with aluminum chloride of 1,4-dimethoxy-6,7,8,9-tetrahydro-5*H*-benzocyclohepten-5-one [8]. When the compound **9** was allowed to react with ethyl bromoacetate in the presence of tripotassium phosphate

Table 1

Synthesis of Acids **5** and Esters **6** by the Reactions of **9** with Ethyl Bromoacetates $RCHBrCO_2C_2H_5$

| Substituent R | Compound (yield, %) | Compound (yield, %) |
|---|---|---|
| H | **5a** (96) | **6a** (79) |
| $CH_3$ | **5b** (96) | **6b** (80) |
| $C_2H_5$ | **5c** (48) | **6c** (75) |
| $CH(CH_3)_2$ | **5d** (73) | **6d** (88) |
| Ph | **5e** (51) | **6e** (79) |

followed by hydrolysis using potassium hydroxide, an acid **5a** was obtained in 96% yield. The acid **5a** was then ethylated to give the corresponding ester **6a** in 79% yield by refluxing in ethanol in the presence of sulfuric acid. Similarly, reaction of **9** with ethyl 2-bromopropionate, ethyl 2-bromobutyrate, ethyl 2-bromo-3-methylbutyrate, or ethyl 2-bromo-2-phenylacetate afforded the corresponding acids **5b-e** respectively after hydrolysis of the produced esters. Ethylation of the acids **5b-e** with ethanol proceeded smoothly to give esters **6b-e**. The results are summarized in Table 1.

Initially, reactions of acids **5** with sodium acetate in acetic anhydride were examined. It seems that furans **7** are produced by attack of an anion **10** on the carbonyl carbon of the seven-membered ring and lactones **8** are formed by attack of an enolate ion **11** on the carbonyl carbon of the acid anhydride [5]. Therefore, flexibility of the seven-membered ring [9] of **5** would favour furan-ring formation. The results ars shown in Table 2 along with yields of naphthofuran synthesis. When the acid **5a** (R = H) was refluxed with sodium acetate in acetic anhydride, furan **7a** was obtained in 88% yield and lactone **8a** was a small amount (3%). In the case of **5b** (R = $CH_3$) the yield of furan **7b** decreased to 52% and lactone formation increased up to 35%. Using the acid **5c** (R = $C_2H_5$) the ratio of furan **7c** (31%) and lactone **8c** (59%) was reversed. When the acid **5d** (R = $CH(CH_3)_2$) was employed lactone formation (81%) was much more favorable than furan formation (3%). On the other hand, in the case of the acid **5e** (R = Ph) furan formation (91%) was very easy. The results suggest that a steric effect of the substituent R is not important and electron-releasing substituents prevent furan-ring formation because the anion **10** become unstable and difficult to produce. The trend is similar to results of naphthofuran synthesis [5] from naphthyloxyacetic acids **1** having six-membered carbonyl group. However, Table 1 shows that seven-membered cyclic ketone is more favorable than six-membered cyclic ketone for furan-ring formation. The yield of furans **7** did not become much better as would be expected.

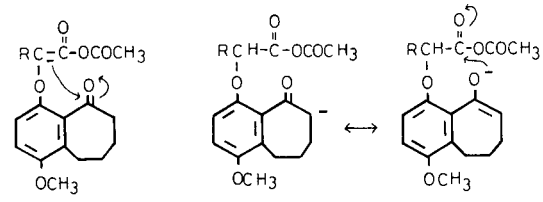
Table 2

Reactions of Acids **5** with Sodium Acetate in Acetic Anhydride [a]

| Run | Compound [b] | Product (yield, %) [c] | |
|---|---|---|---|
| 1 | **5a** {**1a**} | **7a** (88) {**3a** (43)} | **8a** ( 3) {**4a** (42)} [d] |
| 2 | **5b** {**1b**} | **7b** (52) {**3b** (25)} | **8b** (35) {**4b** (71)} |
| 3 | **5c** {**1c**} | **7c** (31) {**3c** (16)} | **8c** (59) {**4c** (82)} |
| 4 | **5d** {**1d**} | **7d** ( 3) {**3d** ( 3)} | **8d** (81) {**4d** (95)} |
| 5 | **5e** {**1e**} | **7e** (91) {**3e** (64)} | **8e** (0) {**4e** ( 6)} |

[a] A mixture of 5 (2.00 mmoles), sodium acetate (2.30 g, 28.0 mmoles), and acetic anhydride (7.5 ml) was heated at 150° for 1 hour. [b] Number in brace shows the starting material in naphthofuran synthesis. [c] The yields of napthofuans **3a-e** and lactones **4a-e** are shown in brace. [d] Lactone **8a** was hydrolyzed to the starting material **5a** during isolation procedure.

Formula 2



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Secondly, reactions of esters **6** with potassium hydroxide in dioxane were examined. In the reactions, furan formation and saponification of esters are competing. The results are summarized in Table 3. When the ester **6a** was allowed to react with potassium hydroxide, furans **7a** and **7f** were obtained in good yield (96%). However, as the substituent R was changed from a methyl group (55%) to an ethyl (34%) or isopropyl group (6%) the yields of furans **7** decreased rapidly. Synthesis of **7d** (R = $CH(CH_3)_2$) was difficult under the conditions. In the case of **6e** (R = Ph) furan **7e** was obtained in good yield (87%). The trend is similar to the results of naphthofuran synthesis from the reactions of ethyl naphthyloxyacetates **2** with potassium hydroxide. However, the yield of cyclohepta[*cd*]benzofurans **7** was a little lower than that of naphthofurans **3** because esters **6** were prone to suffer from saponification under the conditions. It was the unexpected result.

Table 3

Reactions of Ester **6** with Potassium Hydroxide in Dioxane [a]

| Run | Compound [b] | Product (yield, %) [c] | |
|---|---|---|---|
| 1 | **6a** {**2a**} | **7a** (82) {**3a** (71)} | **5a** ( 0) {**1a** ( 0)} [d] |
| | | **7f** (14) {**3f** (22)} [e] | |
| 2 | **6b** {**2b**} | **7b** (55) {**3b** (84)} | **5b** (28) {**1b** (11)} |
| 3 | **6c** {**2c**} | **7c** (34) {**3c** (42)} | **5c** (60) {**1c** (53)} |
| 4 | **6d** {**2d**} | **7d** ( 6) {**3d** (13)} | **5d** (89) {**1d** (86)} |
| 5 | **6e** {**2e**} | **7e** (87) {**3e** (90)} | **5e** ( 0) {**1e** ( 8)} [d] |

[a] A mixture of **6** (1.80 mmoles), potassium hydroxide (0.504 g, 9.00 mmoles), and dioxane (10.0 ml) was refluxed for 1 hour. [b] Number in brace shows the starting material in naphthofuran synthesis. [c] The yields of naphthofurans **3a-e** and carboxylic acids **1a-e** in naphthofuran systhesis are shown in brace. [d] Acids **5a** and **5e** were not obtained. [e] Using **6a** as the starting material, acid **7f** was obtained along with **7a**.

Thirdly, reactions of esters **6** with sodium hydride [10] in dioxane were examined. The results are shown in Table

4. In the reactions furan formation and saponification of esters **6** are competing. Reaction of **6a** (R = H) with sodium hydride gave furans **7a**, **7f** and **7g** in high yield (97%). Similarly, esters **6b** (R = $CH_3$) and **6c** (R = $C_2H_5$) afforded furans **7b** and **7c** in good yields (86 and 70%) respectively. In the case of **6d** (R = $CH(CH_3)_2$) furan **7d** was obtained in medium yield (48%), which was because of partial decomposition of ester **6d** under the reaction conditions. When R was a phenyl group furan **7e** was produced easily (96%). Sodium hydride is a useful base in furan-ring formation from esters having cyclic carbonyl group, because sodium hydride is basic enough to give the anion **10** and does not saponify esters.

Table 4

Reactions of Esters 6 with Sodium Hydride in Dioxane [a]

| Run | Compound | Product (yield, %) | |
|---|---|---|---|
| 1 | **6a** | **7a** (46) | **5a** ( 0) [b] |
| | | **7f** (21) [c] | |
| | | **7g** (30) [c] | |
| 2 | **6b** | **7b** (86) | **5b** (14) |
| 3 | **6c** | **7c** (70) | **5c** (19) |
| 4 | **6d** | **7d** (48) [d] | **5d** (15) |
| 5 | **6e** | **7e** (96) | **5e** ( 0) [b] |

[a] A mixture of **6** (1.80 mmoles), 60% sodium hydride (0.360 g, 9.00 mmoles), and dioxane (10.0 ml) was refluxed for 1 hour. [b] Acids **5a** and **5e** were not obtained. [c] Using **6a** as the starting material, acid **7f** and ester **7g** were obtained by dehydration along with **7a**. The dehydration is not possible for compounds **6a-e** [d] The yield was not good because the starting material **6d** was partly decomposed during the reaction.

Thus, furan-ring formation is largely affected by a kind of substituent R. Electron-releasing substituents make furan-ring formation difficult. However, a strong base of sodium hydride is particularly useful for synthesis of cyclohepta[*cd*]benzofurans.

## EXPERIMENTAL

The melting points are uncorrected. Column chromatography was performed on silica gel (Wakogel C-200). Unless otherwise stated anhydrous sodium sulfate was employed as the drying agent. Ether refers to diethyl ether. 1,4-Dioxane was dried by refluxing with sodium. The ir spectra were determined on a Hitachi Model 270-30 ir spectrometer. The $^1H$ and $^{13}C$ nmr spectra were determined at 90 MHz on a JEOL JNM-FX 90Q FT NMR spectrometer, using tetramethylsilane as the internal standard.

(1-Methoxy-5-oxo-6,7,8,9-tetrahydro-5*H*-benzocyclohepten-4-yloxy)acetic Acid (**5a**).

A mixture of **9** [7] (5.00 g, 24.3 mmoles), ethyl bromoacetate (20.0 g, 120 mmoles), tripotassium phosphate (20.0 g, 94.3 mmoles), and dioxane (80 ml) was refluxed for 1 hour. After removal of the tripotassium phosphate by filtration, the solution was extracted with ether. The extract was washed, dried and evaporated. The residue was dissolved in ethanol (25.0 ml) and hydrolyzed by adding a 1*M* aqueous potassium hydroxide solution. The alkaline solution was acidified with 6*M* hydrochloric acid and the resulting precipitate was extracted with ether. The extract was washed, dried and evaporated to give **5a** (6.15 g, 96%); it formed colorless needles from acetone, mp 120-121°; ir (potassium bromide): 1730 ($CO_2H$), 1690 $cm^{-1}$ (CO); $^1H$ nmr (deuteriochloroform): δ 1.65-1.89 (m, 4H, $C_7$-$H_2$ and $C_8$-$H_2$), 2.59-2.96 (m, 4H, $C_6$-$H_2$ and $C_9$-$H_2$), 3.80 (s, 3H, $OCH_3$), 4.70 (s, 2H, $CH_2CO_2H$), 6.84 (d, J = 9 Hz, 1H, $C_2$-H or $C_3$-H), 6.98 (d, J = 9 Hz, 1H, $C_2$-H or $C_3$-H), 10.21 (broad s, 1H, $CO_2H$); $^{13}C$ nmr (deuteriochloroform): δ 21.6 (t), 23.2 (t), 24.1 (t), 41.7 (t), 56.5 (q), 68.4 (t), 114.2 (d), 115.0 (d), 129.5 (s), 130.4 (s), 148.5 (s), 152.1 (s), 171.0 (s), 209.5 (s).

*Anal.* Calcd. for $C_{14}H_{16}O_5$: C, 63.62; H, 6.10. Found: C, 63.42; H, 5.93.

2-(1-Methoxy-5-oxo-6,7,8,9-tetrahydro-5*H*-benzocyclohepten-4-yloxy)propionic Acid (**5b**).

Compound **5b** (96%) was prepared from the reaction (refluxing for 1.5 hours) of **9** with ethyl 2-bromopropionate in a manner similar to synthesis of **5a**; it formed colorless prisms from benzene-hexane, mp 83-84°; ir (potassium bromide): 1760 ($CO_2H$), 1660 $cm^{-1}$ (CO); $^1H$ nmr (deuteriochloroform): δ 1.59 (d, J = 7 Hz, 3H, $CH_3CH$), 1.60-1.95 (m, 4H, $C_7$-$H_2$ and $C_8$-$H_2$), 2.29-3.25 (m, 4H, $C_6$-$H_2$ and $C_9$-$H_2$), 3.78 (s, 3H, $OCH_3$), 4.79 (q, J = 7 Hz, 1H, $CH_3CH$), 6.88 (s, 2H, $C_2$-H and $C_3$-H), 10.45 (broad s, 1H, $CO_2H$); $^{13}C$ nmr (deuteriochloroform): δ 18.8 (q), 21.4 (t), 23.1 (t), 24.0 (t), 41.5 (t), 56.4 (q), 76.0 (d), 114.3 (d), 115.1 (d), 129.4 (s), 130.1 (s), 148.0 (s), 151.9 (s), 173.7 (s), 209.8 (s).

*Anal.* Calcd. for $C_{15}H_{18}O_5$: C, 64.73; H, 6.52. Found: C, 64.89; H, 6.42.

2-(1-Methoxy-5-oxo-6,7,8,9-tetrahydro-5*H*-benzocyclohepten-4-yloxy)butyric Acid (**5c**).

Compound **5c** was prepared from the reaction (refluxing for 3 hours) of **9** with ethyl 2-bromobutyrate in a manner similar to synthesis of **5a**. The product was chromatographed and eluted with benzene(2)-ether(1) to give a colorless viscous oil (48%); ir (neat): 1760 ($CO_2H$), 1670 $cm^{-1}$ (CO); $^1H$ nmr (deuteriochloroform): δ 1.08 (t, J = 7 Hz, 3H, $CH_3CH_2$), 1.55-2.13 (m, 6H, $C_7$-$H_2$, $C_8$-$H_2$, and $CH_3CH_2$), 2.19-3.36 (m, 4H, $C_6$-$H_2$ and $C_9$-$H_2$), 3.80 (s, 3H, $OCH_3$), 4.78 (t, J = 6 Hz, 1H, $CHCO_2H$), 6.91 (s, 2H, $C_2$-H and $C_3$-H), 9.47 (broad s, 1H, $CO_2H$); $^{13}C$ nmr (deuteriochloroform): δ 9.4 (q), 21.5 (t), 23.1 (t), 24.0 (t), 26.2 (t), 41.4 (t), 56.4 (q), 80.5 (d), 114.2 (d), 115.0 (d), 129.3 (s), 130.0 (s), 148.1 (s), 151.8 (s), 173.2 (s), 209.9 (s).

*Anal.* Calcd. for $C_{16}H_{20}O_5$: C, 65.74; H, 6.90. Found: C, 65.51; H, 6.75.

2-(1-Methoxy-5-oxo-6,7,8,9-tetrahydro-5*H*-benzocyclohepten-4-yloxy)-3-methylbutyric Acid (**5d**).

Compound **5d** was prepared from the reaction (refluxing for 8 hours) of **9** with ethyl 2-bromo-3-methylbytyrate in a manner similar to synthesis of **5a**. The product was chromatographed and eluted with benzene(2)-ether(1) to give a colorless viscous oil (73%); ir (neat): 1750 ($CO_2H$), 1660 $cm^{-1}$ (CO); $^1H$ nmr (deuteriochloroform): δ 1.04 (d, J = 7 Hz, 3H, $CH_3CH$), 1.12 (d, J = 7 Hz,

3H, $CH_3CH$), 1.63-1.97 (m, 4H, $C_7$-$H_2$ and $C_8$-$H_2$), 2.03-3.31 (m, 5H, $C_6$-$H_2$, $C_9$-$H_2$, and $CH_3CH$), 3.78 (s, 3H, $OCH_3$), 4.70 (d, J = 6 Hz, 1H, $CHCO_2H$), 6.91 (s, 2H, $C_2$-H and $C_3$-H), 10.53 (broad s, 1H, $CO_2H$); $^{13}C$ nmr (deuteriochloroform): δ 17.1 (q), 18.8 (q), 21.5 (t), 23.1 (t), 24.0 (t), 31.7 (d), 41.4 (t), 56.4 (q), 83.8 (d), 114.0 (d), 115.1 (d), 129.4 (s), 130.0 (s), 148.2 (s), 151.8 (s), 172.8 (s), 210.1 (s).

*Anal.* Calcd. for $C_{17}H_{22}O_5$: C, 66.65; H, 7.24. Found: C, 66.65; H, 7.45.

2-(1-Methoxy-5-oxo-6,7,8,9-tetrahydro-5*H*-benzocyclohepten-4-yloxy)-2-phenylacetic Acid (**5e**).

Compound **5e** (52%) was prepared from the reaction (stirring for 6 hours at room temperature) of **9** with ethyl 2-bromo-2-phenylacetate in a manner similar to synthesis of **5a**; it formed colorless prisms from benzene-hexane, mp 67.5-68.5°; ir (potassium bromide): 1720 ($CO_2H$), 1670 $cm^{-1}$ (CO); $^1H$ nmr (deuteriochloroform): δ 1.56-1.90 (m, 4H, $C_7$-$H_2$ and $C_8$-$H_2$), 2.34-3.30 (m, 4H, $C_6$-$H_2$ and $C_9$-$H_2$), 3.75 (s, 3H, $OCH_3$), 5.71 (s, 1H, $CHCO_2H$), 6.88 (s, 2H, $C_2$-H and $C_3$-H), 7.16-7.60 (m, 5H, Ph), 8.30 (broad s, 1H, $CO_2H$); $^{13}C$ nmr (deuteriochloroform): δ 21.4 (t), 23.2 (t), 24.0 (t), 41.6 (t), 56.3 (q), 81.4 (d), 114.6 (d), 115.0 (d), 127.0 (d), 128.8 (d), 129.0 (d), 129.7 (s), 130.3 (s), 135.3 (s), 147.7 (s), 152.2 (s), 171.2 (s), 209.8 (s).

*Anal.* Calcd. for $C_{20}H_{20}O_5$: C, 70.57; H, 5.92. Found: C, 70.83; H, 6.15.

Ethyl (1-Methoxy-5-oxo-6,7,8,9-tetrahydro-5*H*-benzocyclohepten-4-yloxy)acetate (**6a**).

A mixture of **5a** (2.00 g, 7.58 mmoles), ethanol (50.0 ml), and a few drops of concentrated sulfuric acid was refluxed for 6 hours. After evaporation of the ethanol the residue was extracted with ether. The extract was washed with a 1*M* aqueous potassium carbonate solution, then with water, dried and evaporated to give **6a** (2.24 g, 79%); it formed colorless prisms from ethanol, mp 55.5-56.5°; ir (potassium bromide): 1760 ($CO_2C_2H_5$), 1700 $cm^{-1}$ (CO); $^1H$ nmr (deuteriochloroform): δ 1.27 (t, J = 7 Hz, 3H, $CH_2CH_3$), 1.62-1.92 (m, 4H, $C_7$-$H_2$ and $C_8$-$H_2$), 2.50-2.90 (m, 4H, $C_6$-$H_2$ and $C_9$-$H_2$), 3.77 (s, 3H, $OCH_3$), 4.21 (q, J = 7 Hz, 2H, $CH_2CH_3$), 4.60 (s, 2H, $CH_2CO_2$), 6.74 (d, J = 9 Hz, 1H, $C_2$-H or $C_3$-H), 6.82 (d, J = 9 Hz, 1H, $C_2$-H or $C_3$-H); $^{13}C$ nmr (deuteriochloroform): δ 14.1 (q), 22.9 (t), 23.5 (t), 24.6 (t), 42.1 (t), 56.3 (q), 61.0 (t), 68.4 (t), 113.2 (d), 114.2 (d), 127.7 (s), 133.2 (s), 148.3 (s), 151.5 (s), 169.1 (s), 206.8 (s).

*Anal.* Calcd. for $C_{16}H_{20}O_5$: C, 65.74; H, 6.90. Found: C, 65.60; H, 7.06.

Ethyl 2-(1-Methoxy-5-oxo-6,7,8,9-tetrahydro-5*H*-benzocyclohepten-4-yloxy)propionate (**6b**).

Compound **6b** (80%) was prepared from the reaction of **5b** with ethanol in a manner similar to synthesis of **6a**; it formed colorless plates from ethanol-hexane, mp 59-60°; ir (potassium bromide): 1760 ($CO_2C_2H_5$), 1705 $cm^{-1}$ (CO); $^1H$ nmr (deuteriochloroform): δ 1.25 (t, J = 7 Hz, 3H, $CH_2CH_3$), 1.55 (d, J = 7 Hz, 3H, $CH_3CHCO_2$), 1.60-1.92 (m, 4H, $C_7$-$H_2$ and $C_8$-$H_2$), 2.48-3.20 (m, 4H, $C_6$-$H_2$ and $C_9$-$H_2$), 3.76 (s, 3H, $OCH_3$), 4.19 (q, J = 7 Hz, 2H, $CH_2CH_3$), 4.64 (q, J = 7 Hz, 1H, $CH_3CHCO_2$), 6.79 (s, 2H, $C_2$-H and $C_3$-H); $^{13}C$ nmr (deuteriochloroform): δ 14.1 (q), 18.4 (q), 23.0 (t), 23.5 (t), 24.7 (t), 42.2 (t), 56.3 (q), 61.0 (t), 76.0 (d), 113.1 (d), 115.3 (d), 127.5 (s), 133.6 (s), 148.0 (s), 151.5 (s), 172.3 (s), 206.7 (s).

*Anal.* Calcd. for $C_{17}H_{22}O_5$: C, 66.65; H, 7.24. Found: C, 66.94; H, 7.29.

Ethyl 2-(1-Methoxy-5-oxo-6,7,8,9-tetrahydro-5*H*-benzocyclohepten-4-yloxy)butyrate (**6c**).

Compound **6c** (75%) was prepared as a colorless oil from the reaction of **5c** with ethanol in a manner similar to synthesis of **6a**, bp 174-175° (0.9 Torr); ir (neat): 1760 ($CO_2C_2H_5$), 1705 $cm^{-1}$ (CO); $^1H$ nmr (deuteriochloroform): δ 1.03 (t, J = 7 Hz, 3H, $CH_3CH_2CH$), 1.24 (t, J = 7 Hz, 3H, $CO_2CH_2CH_3$), 1.60-2.10 (m, 6H, $C_7$-$H_2$, $C_8$-$H_2$ and $CH_3CH_2CH$), 2.30-3.18 (m, 4H, $C_6$-$H_2$ and $C_9$-$H_2$), 3.75 (s, 3H, $OCH_3$), 4.18 (q, J = 7 Hz, 2H, $CO_2CH_2CH_3$), 4.48 (t, J = 6 Hz, 1H, $CHCO_2$), 6.67 (d, J = 9 Hz, 1H, $C_2$-H or $C_3$-H), 6.71 (d, J = 9 Hz, 1H, $C_2$-H or $C_3$-H); $^{13}C$ nmr (deuteriochloroform): δ 9.4 (q), 14.2 (q), 23.2 (t), 23.5 (t), 24.7 (t), 26.1 (t), 42.2 (t), 56.3 (q), 60.8 (t), 80.1 (d), 113.0 (d), 113.9 (d), 127.4 (s), 133.1 (s), 148.1 (s), 151.1 (s), 171.6 (s), 206.5 (s).

*Anal.* Calcd. for $C_{18}H_{24}O_5$: C, 67.48; H, 7.55. Found: C, 67.21; H, 7.62.

Ethyl 2-(1-Methoxy-5-oxo-6,7,8,9-tetrahydro-5*H*-benzocyclohepten-4-yloxy)-3-methylbutyrate (**6d**).

Compound **6d** was prepared from the reaction of **5d** with ethanol in a manner similar to synthesis of **6a**. The product was chromatographed and eluted with benzene to give a colorless oil (88%); ir (neat): 1760 ($CO_2C_2H_5$), 1710 $cm^{-1}$ (CO); $^1H$ nmr (deuteriochloroform): δ 1.04 (d, J = 7 Hz, 6H, $(CH_3)_2CH$), 1.24 (t, J = 7 Hz, 3H, $CO_2CH_2CH_3$), 1.64-1.92 (m, 4H, $C_7$-$H_2$ and $C_8$-$H_2$), 2.00-3.24 (m, 5H, $C_6$-$H_2$, $C_9$-$H_2$ and $CHCHCO_2$), 3.75 (s, 3H, $OCH_3$), 4.18 (q, J = 7 Hz, 2H, $CO_2CH_2CH_3$), 4.31 (d, J = 5 Hz, 1H, $CHCHCO_2$), 6.64 (d, J = 9 Hz, 1H, $C_2$-H or $C_3$-H), 6.80 (d, J = 9 Hz, 1H, $C_2$-H or $C_3$-H); $^{13}C$ nmr (deuteriochloroform): δ 14.2 (q), 17.7 (q), 18.5 (q), 23.3 (t), 23.5 (t), 24.8 (t), 31.7 (d), 42.3 (t), 56.3 (q), 60.7 (t), 83.1 (d), 112.8 (d), 113.1 (d), 127.5 (s), 133.4 (s), 148.1 (s), 150.9 (s), 171.1 (s), 206.4 (s).

*Anal.* Calcd. for $C_{19}H_{26}O_5$: C, 68.24; H, 7.84. Found: C, 68.51; H, 8.01.

Ethyl 2-(1-Methoxy-5-oxo-6,7,8,9-tetrahydro-5*H*-benzocyclohepten-4-yloxy)-2-phenylacetate (**6e**).

Compound **6e** (79%) was prepared from the reaction of **5e** with ethanol in a manner similar to synthesis of **6a**; it formed colorless plates from ethanol-hexane, mp 68-69°; ir (potassium bromide): 1750 ($CO_2C_2H_5$), 1700 $cm^{-1}$ (CO); $^1H$ nmr (deuteriochloroform): δ 1.16 (t, J = 7 Hz, 3H, $CH_2CH_3$), 1.60-1.88 (m, 4H, $C_7$-$H_2$ and $C_8$-$H_2$), 2.48-3.00 (m, 4H, $C_6$-$H_2$ and $C_9$-$H_2$), 3.74 (s, 3H, $OCH_3$), 4.14 (q, J = 7 Hz, 2H, $CO_2CH_2CH_3$), 5.57 (s, 1H, $CHCO_2$), 6.74 (s, 2H, $C_2$-H and $C_3$-H), 7.24-7.60 (m, 5H, Ph); $^{13}C$ nmr (deuteriochloroform): δ 14.0 (q), 22.9 (t), 23.5 (t), 24.5 (t), 42.1 (t), 56.2 (q), 61.3 (t), 81.4 (d), 113.0 (d), 115.2 (d), 127.2 (d), 127.8 (s), 128.5 (d), 128.7 (d), 133.6 (s), 135.8 (s), 147.4 (s), 151.6 (s), 169.9 (s), 206.4 (s).

*Anal.* Calcd. for $C_{22}H_{24}O_5$: C, 71.72; H, 6.57. Found: C, 72.01; H, 6.70.

General Procedure for the Reactions of **5a-e** with Sodium Acetate in Acetic Anhydride.

A mixture of **5** (2.00 mmoles), sodium acetate (2.30 g, 28.0 mmoles), and acetic anhydride (7.5 ml) was heated at 150° for 1 hour. The mixture was poured into ice-water (200 ml), stirred for 5 minutes to decompose the excess of acetic anhydride, and extracted with ether. The extract was washed with a 1*M* aqueous potassium carbonate solution, then with water, dried and evapo-

rated. The residue was chromatographed and eluted with benzene. The first fraction gave furan **7** and the second fraction afforded lactone **8**.

General Procedure for the Reactions of **6** with Potassium Hydroxide in Dioxane.

A mixture of **6** (1.80 mmoles), powdered potassium hydroxide (0.504 g, 9.00 mmoles), and dry dioxane (10.0 ml) was refluxed for 1 hour. After adding water (10 ml) to the mixture, the solution was immediately poured into 2*M* hydrochloric acid (100 ml) and stirred for 15 minutes. The acidic solution was extracted with ether. The extract was washed three times with a 1*M* aqueous potassium carbonate solution (50 ml), then with water, dried and evaporated. The residue was chromatographed and eluted with benzene to give furan **7**. The alkaline solution was acidified with 6*M* hydrochloric acid and the resulting precipitate was extracted with ether. The extract was washed, dried and evaporated. The residue was chromatographed and eluted with benzene(2)-ether(1) to give acid **5**. Further elution with acetone afforded furan **7f**.

General Procedure for the Reactions of **6** with Sodium Hydride in Dioxane.

A mixture of **6** (1.80 mmoles), 60% sodium hydride (0.360 g, 9.00 mmoles), and dioxane (10.0 ml) was refluxed for 1 hour. After decomposition of the excess of sodium hydride with water (10 ml), the mixture was poured into 2*M* hydrochloric acid (100 ml) and extracted with ether. The extract was washed three times with a 1*M* aqueous potassium carbonate solution, then with water, dried and evaporated. The residue was chromatographed and eluted with benzene to give furan **7**. Further elution afforded ester **7g**. The alkaline solution was acidified with 6*M* hydrochloric acid and the resulting precipitate was extracted with ether. The extract was washed, dried and evaporated. The residue was chromatographed and eluted with benzene(2)-ether(1) to give carboxylic acid **5**. Further elution with acetone afforded furan **7f**.

7-Methoxy-3,4,5,6-tetrahydrocyclohepta[*cd*]benzofuran (**7a**).

This compound was obtained as a colorless oil, bp 104-105° (0.7 Torr); $^1$H nmr (deuteriochloroform): δ 1.76-2.10 (m, 4H, $C_4$-$H_2$ and $C_5$-$H_2$), 2.74-3.10 (m, 4H, $C_3$-$H_2$ and $C_6$-$H_2$), 3.85 (s, 3H, $OCH_3$), 6.86 (d, J = 9 Hz, 1H, $C_8$-H or $C_9$-H), 7.24 (d, J = 9 Hz, 1H, $C_8$-H or $C_9$-H), 7.35 (s, 1H, $C_2$-H); $^{13}$C nmr (deuteriochloroform): δ 26.4 (t), 28.0 (t), 28.6 (t), 29.6 (t), 57.0 (q), 108.1 (d), 108.8 (d), 120.9 (s), 124.1 (s), 128.3 (s), 141.3 (d), 150.9 (s), 152.5 (s).

*Anal.* Calcd. for $C_{13}H_{14}O_2$: C, 77.20; H, 6.98. Found: C, 76.98; H, 7.20.

7-Methoxy-2-methyl-3,4,5,6-tetrahydrocyclohepta[*cd*]benzofuran (**7b**).

This compound was obtained as colorless needles from methanol, mp 81.5-82.0°; $^1$H nmr (deuteriochloroform): δ 1.74-2.06 (m, 4H, $C_4$-$H_2$ and $C_5$-$H_2$), 2.29 (s, 3H, $CH_3$), 2.58- 2.78 (m, 2H, $C_3$-$H_2$ or $C_6$-$H_2$), 2.90-3.10 (m, 2H, $C_3$-$H_2$ or $C_6$-$H_2$), 3.79 (s, 3H, $OCH_3$), 6.71 (d, J = 9 Hz, 1H, $C_8$-H or $C_9$-H), 7.13 (d, J = 9 Hz, 1H, $C_8$-H or $C_9$-H); $^{13}$C nmr (deuteriochloroform): δ 12.0 (q), 27.0 (t), 28.0 (t), 28.3 (t), 29.9 (t), 56.8 (q), 107.2 (d), 107.2 (d), 114.7 (s), 123.0 (s), 129.5 (s), 149.3 (s), 150.1 (s), 152.4 (s).

*Anal.* Calcd. for $C_{14}H_{16}O_2$: C, 77.75; H, 7.46. Found: C, 77.50; H, 7.57.

2-Ethyl-7-methoxy-3,4,5,6-tetrahydrocyclohepta[*cd*]benzofuran (**7c**).

This compound was obtained as a colorless oil, bp 112° (0.78 Torr); $^1$H nmr (deuteriochloroform): δ 1.25 (t, J = 8 Hz, 3H, $CH_2CH_3$), 1.76-2.06 (m, 4H, $C_4$-$H_2$ and $C_5$-$H_2$), 2.64 (q, J = 8 Hz, 2H, $CH_2CH_3$), 2.60-2.82 (m, 2H, $C_3$-$H_2$ or $C_6$-$H_2$), 2.90-3.10 (m, 2H, $C_3$-$H_2$ or $C_6$-$H_2$), 3.82 (s, 3H, $OCH_3$), 6.76 (d, J = 9 Hz, 1H, $C_8$-H or $C_9$-H), 7.16 (d, J = 9 Hz, 1H, $C_8$-H or $C_9$-H); $^{13}$C nmr (deuteriochloroform): δ 12.4 (q), 20.1 (t), 26.9 (t), 28.1 (t), 28.4 (t), 29.9 (t), 56.9 (q), 107.4 (d), 107.4 (d), 113.8 (s), 123.2 (s), 129.6 (s), 149.4 (s), 152.5 (s), 155.2 (s).

*Anal.* Calcd. for $C_{15}H_{18}O_2$: C, 78.23; H, 7.88. Found: C, 78.02; H, 7.68.

2-Isopropyl-7-methoxy-3,4,5,6-tetrahydrocyclohepta[*cd*]benzofuran (**7d**).

This compound was obtained as a colorless oil, bp 108° (0.8 Torr); $^1$H nmr (deuteriochloroform): δ 1.28 (d, J = 7 Hz, 6H, $(CH_3)_2CH$), 1.68-2.08 (m, 4H, $C_4$-$H_2$ and $C_5$-$H_2$), 2.50-2.80 (m, 2H, $C_3$-$H_2$ or $C_6$-$H_2$), 2.86-3.29 (m, 3H, $(CH_3)_2CH$ and $C_3$-$H_2$ or $C_6$-$H_2$), 3.79 (s, 3H, $OCH_3$), 6.73 (d, J = 9 Hz, 1H, $C_8$-H or $C_9$-H), 7.16 (d, J = 9 Hz, 1H, $C_8$-H or $C_9$-H); $^{13}$C nmr (deuteriochloroform): δ 20.8 (q), 26.6 (d), 26.8 (t), 28.1 (t), 28.4 (t), 29.9 (t), 56.9 (q), 107.4 (d), 107.5 (d), 112.7 (s), 123.3 (s), 129.6 (s), 149.3 (s), 152.4 (s), 158.2 (s).

*Anal.* Calcd. for $C_{16}H_{20}O_2$: C, 78.65; H, 8.25. Found: C, 78.42; H, 8.32.

7-Methoxy-2-phenyl-3,4,5,6-tetrahydrocyclohepta[*cd*]benzofuran (**7e**).

This compound was obtained as colorless prisms from methanol, mp 108-109°; $^1$H nmr (deuteriochloroform): δ 1.72-2.14 (m, 4H, $C_4$-$H_2$ and $C_5$-$H_2$), 2.90-3.18 (m, 4H, $C_3$-$H_2$ and $C_6$-$H_2$), 3.81 (s, 3H, $OCH_3$), 6.82 (d, J = 9 Hz, 1H, $C_8$-H or $C_9$-H), 7.20-7.48 (m, 4H, Ph-$H_3$ and $C_8$-H or $C_9$-H), 7.69-7.80 (m, 2H, Ph-$H_2$); $^{13}$C nmr (deuteriochloroform): δ 28.0 (t), 29.1 (t), 29.8 (t), 56.8 (q), 107.8 (d), 108.8 (d), 117.0 (s), 124.0 (s), 127.0 (d), 127.6 (d), 128.4 (d), 129.9 (s), 131.8 (s), 149.5 (s), 150.1 (s), 152.7 (s).

*Anal.* Calcd. for $C_{19}H_{18}O_2$: C, 81.98; H, 6.52. Found: C, 81.80; H, 6.69.

Lactone **8b**.

This compound was obtained as colorless plates from benzene-hexane, mp 88.5-89°; ir (potassium bromide): 1770 $cm^{-1}$ ($C$-$CO_2$-$C$); $^1$H nmr (deuteriochloroform): δ 1.55 (d, J = 6 Hz, 3H, $CH_3$), 1.88-2.38 (m, 5H, $CH_2CH_2CH_2$), 3.12-3.34 (m, 1H, Ph-CH), 3.78 (s, 3H, $OCH_3$), 5.24 (q, J = 7 Hz, 1H, $CH_3CH$), 6.10 (t, J = 8 Hz, 1H, C=CH), 6.72 (d, J = 9 Hz, 1H, Ph-H), 6.84 (d, J = 9 Hz, 1H, Ph-H); $^{13}$C nmr (deuteriochloroform): δ 16.9 (q), 22.9 (t), 23.7 (t), 32.6 (t), 56.8 (q), 70.7 (d), 113.9 (d), 116.3 (d), 119.6 (d), 121.4 (s), 130.6 (s), 145.4 (s), 149.1 (s), 152.0 (s), 168.9 (s).

*Anal.* Calcd. for $C_{15}H_{16}O_4$: C, 69.21; H, 6.20. Found: C, 69.01; H, 6.34.

Lactone **8c**.

This compound was obtained as colorless prisms from benzene-hexane, mp 77-78°; ir (potassium bromide): 1775 $cm^{-1}$ ($C$-$CO_2$-$C$); $^1$H nmr (deuteriochloroform); δ 1.07 (t, J = 7 Hz, 3H, $CH_3CH_2$), 1.70-2.40 (m, 5H, $CH_2CH_2CH_2$), 3.04-3.32 (m, 1H, Ph-CH), 3.79 (s, 3H, $OCH_3$), 4.93 (t, J = 7 Hz, 1H, $CHCO_2$), 6.10 (t, J = 7 Hz, 1H, C=CH), 6.82 (s, 2H, Ph-$H_2$); $^{13}$C nmr (deuteriochloroform): δ 9.4 (q), 22.9 (t), 23.7 (t), 24.4 (t), 32.6 (t), 56.6 (q), 75.7 (d), 113.6 (d), 116.1 (d), 119.5 (d), 121.5 (s), 130.5 (s), 145.3 (s), 149.2 (s),

151.9 (s), 168.5 (s).

*Anal.* Calcd. for $C_{16}H_{18}O_4$: C, 70.05; H, 6.61. Found: C, 69.85; H, 6.77.

Lactone **8d**.

This compound was obtained as colorless plates from benzene-hexane, mp 80-89°; ir (potassium bromide): 1780 $cm^{-1}$ (C-$CO_2$-C); $^1H$ nmr (deuteriochloroform): δ 1.05 (d, J = 6 Hz, 3H, C$H_3$CH), 1.13 (d, J = 6 Hz, 3H, C$H_3$CH), 1.68-2.58 (m, 5H, $CH_2CH_2CH_2$), 2.96-3.24 (m, 1H, Ph-CH), 3.78 (s, 3H, $OCH_3$), 4.62 (d, J = 8 Hz, 1H, $OCHCO_2$), 6.08 (t, J = 7 Hz, 1H, C=CH), 6.82 (s, 2H, Ph-$H_2$); $^{13}C$ nmr (deuteriochloroform): δ 17.5 (q), 18.7 (q), 22.9 (t), 23.7 (t), 29.7 (d), 32.6 (t), 56.6 (q), 79.8 (d), 113.6 (d), 116.1 (d), 119.0 (d), 121.9 (s), 130.6 (s), 145.4 (s), 149.3 (s), 152.0 (s), 167.9 (s).

*Anal.* Calcd. for $C_{17}H_{20}O_4$: C, 70.81; H, 6.99. Found: C, 70.61; H, 6.79.

Ethyl 7-Methoxy-3,4,5,6-tetrahydrocyclohepta[*cd*]benzofuran-2-carboxylate (**7g**).

This compound was obtained as colorless needles from benzene-hexane, mp 76-77°; ir (potassium bromide): 1710 $cm^{-1}$ ($CO_2C_2H_5$); $^1H$ nmr (deuteriochloroform): δ 1.42 (t, J = 7 Hz, 3H, $CH_2CH_3$), 1.80-2.10 (m, 4H, $C_4$-$H_2$ and $C_5$-$H_2$), 2.90-3.14 (m, 2H, $C_3$-$H_2$ or $C_6$-$H_2$), 3.14-3.36 (m, 2H, $C_3$-$H_2$ or $C_6$-$H_2$), 3.84 (s, 3H, $OCH_3$), 4.42 (q, J = 7 Hz, 2H, $CH_2CH_3$), 7.01 (d, J = 9 Hz, 1H, $C_8$-H or $C_9$-H), 7.33 (d, J = 9 Hz, 1H, $C_8$-H or $C_9$-H); $^{13}C$ nmr (deuteriochloroform): δ 14.4 (q), 27.3 (t), 27.8 (t), 28.5 (t), 29.9 (t), 56.9 (q), 60.9 (t), 109.1 (d), 112.5 (d), 125.8 (s), 128.3 (s), 131.3 (s), 140.4 (s), 150.1 (s), 152.8 (s), 160.5 (s).

*Anal.* Calcd. for $C_{16}H_{18}O_4$: C, 70.05; H, 6.61. Found: C, 70.33; H, 6.82.

7-Methoxy-3,4,5,6-tetrahydrocyclohepta[*cd*]benzofuran-2-carboxylic Acid (**7f**).

This compound was obtained as colorless needles from acetone, mp 235-236°; ir (potassium bromide): 1680 $cm^{-1}$ ($CO_2H$).

*Anal.* Calcd. for $C_{14}H_{14}O_4$: C, 68.28; H, 5.73. Found: C, 68.56; H, 5.90.

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