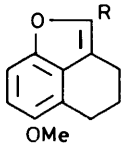
Furan Derivatives. Part 6.[1] On Effect of Ring Size in Synthesis of 4,5-Dihydro-3*H*-naphtho[1,8-*bc*]furans and Their Analogues

Takaaki Horaguchi,* Shigeru Tamura, and Naohiro Hiratsuka
Department of Chemistry, Faculty of Science, Niigata University, Ikarashi, Niigata 950-21, Japan
Tsuneo Suzuki
Nippon Dental University, Niigata, Hamaura-cho, Niigata 950, Japan

Furan derivatives have been synthesized from 7-hydroxy-4-methoxy-2,3-dihydroinden-1-one (**7b**), 8-hydroxy-5-methoxy-1,2,3,4-tetrahydronaphthalen-1-one (**4b**), 4-hydroxy-1-methoxy-6,7,8,9-tetrahydro-5*H*-benzocyclohepten-5-one (**8b**), 6-hydroxy-2a,3-dihydro-2*H*-naphtho[1,8-*bc*]furan-5(4*H*)-one (**9b**), 7-hydroxy-2,3,3a,4-tetrahydronaphtho[1,8-*bc*]pyran-6(5*H*)-one (**10b**), and 7-hydroxy-2,2a,3,4-tetrahydrocyclohepta[*cd*]benzofuran-6(5*H*)-one (**11b**). Hydroxy ketones such as (**4b**), (**8b**), (**10b**), and (**11b**) which have a strong intramolecular hydrogen bond between the hydroxy and the carbonyl groups easily produced the furan derivatives (**1**), (**13**), (**15**), and (**16**). However, the hydroxy ketones (**7b**) and (**9b**) in which the intramolecular hydrogen bond was weak failed to give the furan derivatives (**12**) and (**14**).

Benzofurans may be synthesized by a variety of methods. These include the treatment under reflux with sodium acetate in acetic anhydride[2] of 2-acylphenoxyacetic acids, and heating of esters of the latter with bases such as potassium carbonate[3] or potassium hydroxide.[4] Royer *et al.*[5] applied such methods to the synthesis of naphtho[1,8-*bc*]furans (**1**) and cyclohepta[*cd*]-benzofurans (**2**). Whilst cyclohepta[*cd*]benzofurans (**2a**) and (**2b**) were obtained in fairly good yield by the reaction of 4-hydroxycyclohepten-5-one (**5**) and chloroacetone or 4′-methoxy-2-chloroacetophenone in the presence of potassium carbonate, the yield of naphtho[1,8-*bc*]furans (**1c**) and (**1d**) was poor when 8-hydroxynaphthalen-1-one (**4b**) was treated with chloroacetone or 4′-methoxy-2-chloroacetophenone. Furthermore, whilst intramolecular cyclization of benzofuran-3-ylbutyric acids (**6a**; $n = 3$) and (**6b**; $n = 3$) with polyphosphoric acid was reported[6] to proceed smoothly to give the ketones (**3a**; $n = 3$) and (**3b**; $n = 3$) in good yield, that of benzofuran-3-ylpropionic acid (**6a**; $n = 2$) was difficult. The reason for the difficulty of cyclization is attributed to strain in the molecule of naptho[1,8-*bc*]furan (**3a**; $n = 2$).[7] We recently reported[8] that the reaction of naphthoxyacetic acid (**4c**) with sodium acetate in acetic anhydride gave a 1:1 mixture of naphtho[1,8-*bc*]furan (**1a**) and lactone (**18**). However, compound (**9c**) which had a similar structure to compound (**4c**) afforded only the lactone (**20**), none of the furan (**14c**) being obtained. Thus, it seems that furan and lactone formation are competing reactions. These results led us to investigate the relationship between ring size and facility of furan formation. We are particularly interested in compounds which have five-, six-, or seven-membered rings.



(1)
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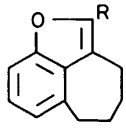
b; R = CO_2H
c; R = Ac
d; R = CO(Ph)OMe



(2)
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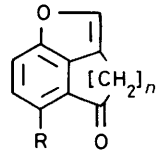

(3)
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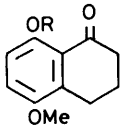

(4)
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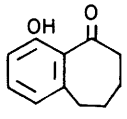
b; R = H
c; R = CH_2CO_2H
d; R = CH_2CO_2Et



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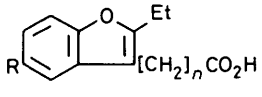

(6)
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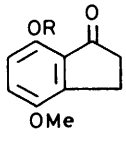
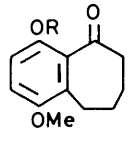
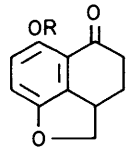
b; R = Me



(7)



(8)



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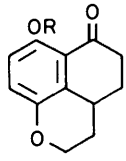

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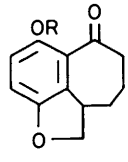


(11)

a; R = Me
b; R = H
c; R = CH_2CO_2H
d; R = CH_2CO_2Et

Results and Discussion

Several acids (**7c**)—(**11c**) and their esters (**7d**)—(**11d**) were prepared, in order to examine the facility of furan-ring formation. The synthetic pathways to the acids (**7c**)—(**11c**) and esters (**7d**)—(**11d**) are described in Experimental section. Initially, the reaction of the acids (**7c**)—(**11c**) with sodium acetate in acetic anhydride was examined; the results are shown in Table 1.

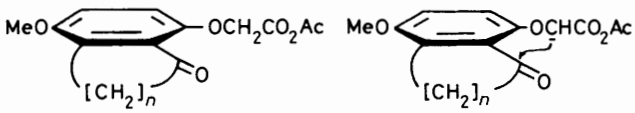
The acid (**7c**) which contains a five-membered cyclic ketone failed to give the furan (**12a**) or the lactone (**17**), only starting material being recovered. In contrast, the acid (**8c**) having a seven-membered cyclic ketone afforded the furan (**13a**) (89%) and the lactone (**19**) (3%). The acid (**4c**), which contains a six-membered cyclic ketone gave the furan (**1a**) (41%) and the

Table 1. Reactions of the carboxylic acids (**4c**) and (**7c**)—(**11c**) with sodium acetate in acetic anhydride[a]

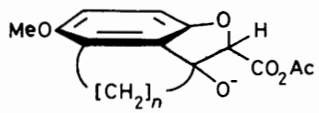
Compd.	Products	Yield (%)
(**7c**)	(**12a**)	0[b]
	(**17**)	0[b]
(**4c**)	(**1a**)	41[c]
	(**18**)	40[c]
(**8c**)	(**13a**)	89[c]
	(**19**)	3[d]
(**9c**)	(**14a**)	0
	(**20**)	82[e]
(**10c**)	(**15a**)	16[c]
	(**21**)	64[f]
(**11c**)	(**16a**)	81[c]
	(**22**)	17[d]

[a] Reactions were carried out at 150 °C for 1 h. [b] T.l.c. analysis did not show production of the furan (**12a**) and the lactone (**17**) from the reaction mixture and the starting material (**7c**) was recovered. [c] Isolated yield. [d] Lactones (**19**) and (**22**) were initially produced, but they were hydrolysed to the corresponding starting materials (**8c**) and (**11c**) during the isolation procedure. [e] The lactone (**20**) easily undergoes hydrolysis and the yield contains the starting material (**9c**) (34%) obtained by hydrolysis of (**20**) during the isolation procedure. [f] The lactone (**21**) easily undergoes hydrolysis and the yield contains the starting material (**10c**) (18%) obtained by hydrolysis of (**21**) during isolation procedure.

lactone (**18**) (42%).[8] Thus, there is an increase in furan yield with increase in the cyclic ketone ring size; production of indenofuran (**12a**) was, however difficult by this method. The most plausible mechanism for furan-ring formation is as follows.[9] The acid (**4c**) is converted into its acid anhydride (**23b**) and a proton on the methylene group in (**23b**) is removed by sodium acetate to give an anion (**24b**). The latter then attacks the carbonyl carbon atom to afford an intermediate (**25b**) which



(**23**) (**24**)



(**25**)

a; $n = 2$
b; $n = 3$
c; $n = 4$

produces the furan (**1a**) by decarboxylation. For furan ring formation it is necessary that the anion (**24b**) attacks the carbonyl carbon atom from above the plane of the carbonyl group. The five-membered cyclic ketone (**7c**) would be an almost fixed and planar molecule, the angle between the planes of the benzene ring and the carbonyl group being small.[10,11] As a result, the anion (**24a**) could not attack the carbonyl carbon atom since the latter could not take up a conformation favourable for furan-ring formation. In contrast, the seven-membered cyclic ketone (**8c**) is very flexible with a large angle between the planes of the benzene ring and the carbonyl group.[10,11] Thus, the carbonyl group of (**24c**) could take up a conformation which was favourable for furan-ring formation and easily undergo attack by the anion. The six-membered cyclic ketone (**4c**) is a rather rigid molecule, the angle between the benzene ring and carbonyl group planes being less[10,11] than that of the seven-membered cyclic ketone (**8c**). Indeed, the rate of furan formation is comparable with that of lactone formation. Thus, it seems that facility in furan-ring formation is explained in terms of the flexibility of the five-, six-, and seven-membered cyclic ketones.

The acid (**9c**) gave only the lactone (**20**),[8] but the analogous acid (**10c**) containing a pyran ring afforded the furan (**15a**) (16%) and the lactone (**21**) (64%). Furthermore, the acid (**11c**) having a furan ring and a seven-membered cyclic ketone gave the furan (**16a**) (81%) and the lactone (**22**) (17%) respectively. The reason that the acid (**9c**) produces only the lactone (**20**) might be attributed to strain in the difuran (**14**), the methylene and the carbonyl groups in the acid (**9c**) being too far apart for furan-ring formation. In contrast, in the acid (**10c**) the methylene and the carbonyl groups are sufficiently close for furan-ring formation to take place. In the case of (**11c**) the carbonyl group could take up a conformation favourable for furan-ring formation, the seven-membered cyclic ketone being sufficiently flexible for this to occur. Accordingly, it is concluded that the seven-membered cyclic ketones (**8c**) and (**11c**) are much more effective for furan-ring formation than the six-membered cyclic ketones (**4c**) and (**10c**).

Although the methylene and carbonyl group separation in (**4c**) and (**7c**)—(**11c**) is difficult to determine directly, it is possible to elucidate roughly by examining the n.m.r. spectra of the hydroxy ketones (**4b**) and (**7b**)—(**11b**). The chemical shifts of the hydrogen-bonded hydroxy groups in those compounds have been measured and are summarized in Table 2.

Chemical shifts have been shown to be a good measure of intramolecular hydrogen-bond strength in compounds analogous to those described here.[12] Strong hydrogen bonding is

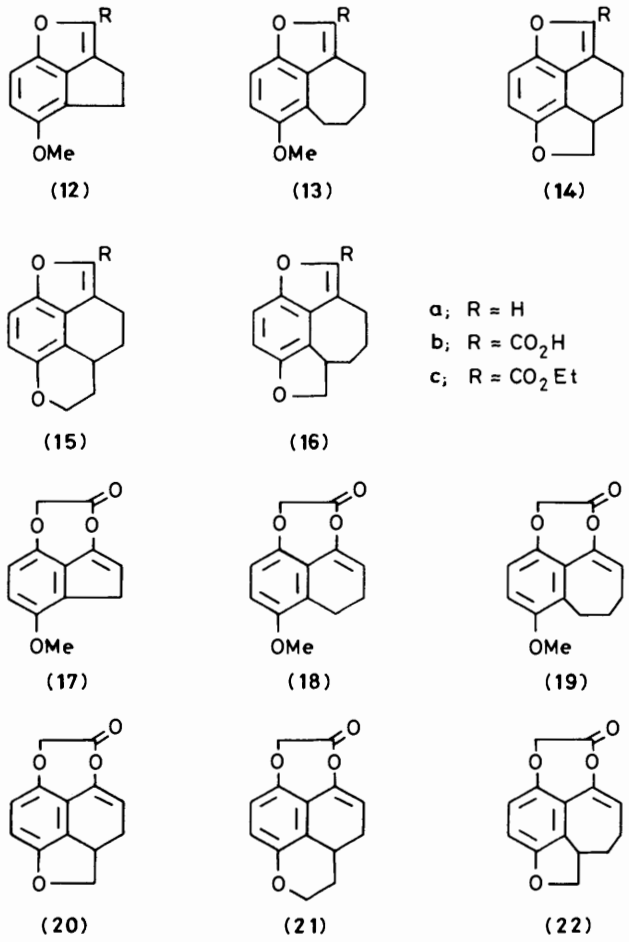


Table 2. ^{1}H N.m.r. chemical shifts of the hydrogen-bonded hydroxy group in the hydroxy ketones (**4b**) and (**7b**)—(**11b**)

Compd.	Chemical shift (δ)[a]
(**7b**)	8.39
(**4b**)	11.63
(**8b**)	11.29
(**9b**)	9.67
(**10b**)	11.75
(**11b**)	11.22

[a] Spectra were taken in a 0.4 mol l^{-1} solution of carbon tetrachloride at room temperature. The chemical shifts are constant at concentrations down to 0.025 mol l^{-1}.

Table 3. ^{13}C n.m.r chemical shifts of the carbonyl group in hydroxy ketones (**4b**) and (**7b**)—(**11b**) and their methyl ethers (**4a**) and (**7a**)—(**11a**)

Compd.	Chemical shift (δ)[a]	Δδ
(**7a**)	200.0	7.7
(**7b**)	207.7	
(**4a**)	193.5	9.7
(**4b**)	203.2	
(**8a**)	203.0	5.0
(**8b**)	208.0	
(**9a**)	191.0	8.9
(**9b**)	199.9	
(**10a**)	192.5	9.6
(**10b**)	202.1	
(**11a**)	199.0	6.0
(**11b**)	205.0	

[a] Spectra were taken in a 0.4 mol l^{-1} solution of carbon tetrachloride at room temperature. The concentration was used for comparison with chemical shifts of the hydrogen-bonded hydroxy group in ^{1}H n.m.r. spectra.

characterized by lowfield signals compared with those for weak hydrogen bonding where the shift is to highfield. For the three hydroxy ketones (**4b**), (**7b**), and (**8b**), the hydroxy group signal in the five-membered ketone (**7b**) appears at much higher field (δ 8.39) than those (δ 11.63 and 11.29) for the six- and seven-membered hydroxy ketones (**4b**) and (**8b**). Similarly, in the three hydroxy ketones (**9b**), (**10b**), and (**11b**) the chemical shift of the hydroxy group in (**9b**) is at higher field (δ 9.67) than those (δ 11.75 and 11.22) for the other hydroxy ketones (**10b**) and (**11b**). These results suggest that the hydroxy and the carbonyl groups in the hydroxy ketones (**7b**) and (**9b**) are well separated, so making furan-ring formation difficult.

The ^{13}C n.m.r. spectra of the hydroxy ketones (**7b**)—(**11b**) and their methyl ethers (**7a**)—(**11a**) have also been determined. The chemical shifts of the carbonyl groups in those compounds are shown in Table 3.

A carbonyl signal usually shifts to lower magnetic field with increasing strength of the intramolecular hydrogen bond.[13] Methylation of the hydroxy group and consequent disappearance of the intramolecular hydrogen bonding of the hydroxy ketones (**7b**)—(**11b**) shifts the carbonyl signal to higher magnetic field. Thus the differences (Δδ) in the carbonyl group chemical shifts for the hydroxy ketones (**7b**)—(**11b**) and their methyl ethers (**7a**)—(**11a**) might be a good measure of intramolecular hydrogen bond strength.[13] The difference between the hydroxy ketone (**7b**) and its methyl ether (**7a**) is smaller than that between (**4b**) and (**4a**) or between (**10b**) and (**10a**), thus showing the weakness of the intramolecular hydrogen bond in the hydroxy ketone (**7b**). For the hydroxy ketone (**8b**) and its ether (**8a**), the difference is much smaller than that between (**4b**) and (**4a**). This is attributed to flexibility of the seven-membered ketone (**8a**) in which the carbonyl group is only partially conjugated with the benzene ring because the dihedral angle between the planes of the benzene ring and the carbonyl group is large.[10] However, the angle in hydroxy ketone (**8b**) will be small owing to the intramolecular hydrogen bond. A similar explanation might be applicable to the chemical-shift difference between the hydroxy ketone (**11b**) and its methyl ether (**11a**). The difference in chemical shifts of the carbonyl group in (**9b**) and (**9a**) is not as small as expected. Farmer *et al.*[10] have previously examined the strength of the intramolecular hydrogen bond in the hydroxy ketones (**4b**), (**7b**), and (**8b**) by i.r. and u.v. spectrometry, and our results using n.m.r. spectrometry are in accordance with their conclusions.

Table 4. Reactions of the esters (**4d**) and (**7d**)—(**11d**) with potassium hydroxide in dioxane[a]

Compd.	Products	Yield (%)
(**7d**)	(**12a**)	0[b]
	(**12b**)	0[b]
(**4d**)	(**1a**)	71[c]
	(**1b**)	22[c]
(**8d**)	(**13a**)	90[c]
	(**13b**)	4[c]
(**9d**)	(**14a**)	0[d]
	(**14b**)	0[d]
(**10d**)	(**15a**)	20[e]
	(**15c**)	14[e]
(**11d**)	(**16a**)	70[c]
	(**16c**)	12[f]

[a] The reactions were carried out at 100 °C for 1 h. [b] The ester (**7d**) was saponified to its acid (**7c**) during the reaction. [c] Isolated yield. [d] The starting ester (**9d**) did not react and was recovered. [e] 49% Of the starting ester (**10d**) was saponified to its acid (**10c**) during the reaction, therefore, the yield was low. [f] Acid (**16b**) was initially produced but was isolated as its ethyl ester (**16c**) because 10% of the starting ester (**11d**) was saponified to its acid (**11c**) during the reaction.

Finally, the reaction of the esters (**7d**)—(**11d**) with potassium hydroxide[1] has been carried out in dioxane. The results are shown in Table 4.

The ester (**4d**) gave the furan (**1a**) and furancarboxylic acid (**1b**) in good yield.[1] Similarly, the esters (**8d**) and (**11d**) readily afforded the corresponding furans (**13a**) and (**16a**) and the furancarboxylic acids (**13b**) and (**16b**) respectively. However, the ester (**10d**) produced the furan (**15a**) and the furancarboxylic acid (**15b**) in low yield as a result of the starting ester (**10d**) being partially saponified to its acid (**10c**) during the reaction. This suggests that furan-ring formation in (**10d**) is more difficult than in (**4d**). In contrast, the ester (**7d**) failed to give the corresponding furans (**12a**) and (**14a**) and furancarboxylic acids (**12b**) and (**14b**) even when strong base, which is effective for furan-ring formation, was used. These results are compatible with the results using sodium acetate in acetic anhydride. Synthesis of the furans (**12a**) and (**14a**) by the usual methods is difficult because of strain in the molecules.

Experimental

M.p.s are uncorrected. Column chromatography was performed on silica gel (Wakogel C-200). Unless otherwise stated anhydrous sodium sulphate was employed as the drying agent. I.r. spectra were determined on a Hitachi EPI-G grating i.r. spectrophotometer. N.m.r. spectra (^{1}H and ^{13}H n.m.r.) were determined at 90 MHz on a JEOL JNM-FX 90Q FT NMR spectrometer, using tetramethylsilane as the internal standard. Ether refers to diethyl ether.

7-*Hydroxy*-2,3,3a,4,-*tetrahydronaphtho*[1,8-bc]*pyran*-6-5(H)-*one* (**10b**).—Powdered aluminium chloride (5.00 g, 37.5 mmol)[14] was added to (**10a**) (5.00 g, 22.9 mmol: prepared from 6-methoxybenzopyran-4-one[15]) in nitrobenzene (80 ml) and the mixture was heated with stirring at 70 °C for 8 h. The mixture was poured into ice–hydrochloric acid and extracted with benzene. The extracts were washed, dried, and evaporated. After removal of the nitrobenzene by distillation under reduced pressure, the resulting oil was chromatographed and eluted with benzene to give (**10b**) (4.0 g, 86%), as yellow needles, m.p. 91.5—92.5 °C (from light petroleum) (Found: C, 70.45; H, 6.05. $C_{12}H_{12}O_3$ requires C, 70.6; H, 5.9%); $\nu_{max.}$(KBr) 1 630 cm^{-1} (CO); δ_H($CDCl_3$) 1.53—2.27 (4 H, m, 3-H_2 and 4-H_2), 2.59—2.76 (2 H, m, 5-H_2), 2.84—3.10 (1 H, m, 3a-H), 3.94—4.48 (2 H, m, 2-H_2), 6.71 (1 H, d, *J* 9 Hz, 8-H), 6.95 (1 H, d, *J* 9 Hz, 9-H), and 12.01 (1 H, s, OH); δ_C($CDCl_3$) 28.6(t), 29.6(t), 32.5(d), 38.6(t), 65.7(t), 115.0(s), 116.6(d), 125.8(d), 126.5(s), 145.1(s) 156.8(s), and 204.2(s).

6-*Oxo*-2,3,3a,4,5,6-*hexahydronaphtho*[1,8-bc]*pyran*-7-*yloxyacetic Acid* (**10c**).—A mixture of (**10b**) (1.0 g, 4.98 mmol), ethyl bromoacetate (4.0 g, 24.0 mmol), potassium phosphate (4.0 g, 9.24 mmol), and dioxane (20 ml) was refluxed for 20 h. After removal of the potassium phosphate by filtration the dioxane was evaporated. To the resulting oil was added aqueous potassium hydroxide (3M; 30 ml) and the mixture was refluxed for 10 min. The alkaline solution was acidified with 6M-hydrochloric acid and the resulting precipitates were extracted with hot benzene. The combined extracts were washed, dried, and evaporated to give (**10c**) (1.0 g, 78%), as colourless needles, m.p. 158—159 °C (from benzene–hexane) (Found: C, 63.9; H, 5.4. $C_{14}H_{14}O_5$ requires C, 64.1; H, 5.4%); $\nu_{max.}$(KBr) 1 785, 1 760 (CO_2H), and 1 655 cm^{-1} (CO); δ_H($CDCl_3$) 1.69—2.42 (4 H, m, 3-H_2 and 4-H_2), 2.62—2.83 (2 H, m, 5-H), 2.86—3.10 (1 H, m, 3a-H), 3.99—4.51 (2 H, m, 2-H_2), 4.66 (2 H, d, *J* 1 Hz, OCH_2CO_2), 6.79 (1 H, dd, *J* 1 and 9 Hz, 8-H), 7.03 (1 H, d, *J* 9 Hz, 9-H), and 10.24 (1 H, br s, CO_2H); δ_C($CDCl_3$) 28.4(t), 29.3(t), 32.8(d), 39.9(t), 65.9(t), 68.6(t), 115.9(d), 120.9(s), 123.7(d), 130.2(s), 148.7(s), 152.1(s), 169.8(s), and 199.8(s).

Ethyl 6-*Oxo*-2,3,3a,4,5,6-*hexahydronaphtho*[1,8-bc]*pyran*-7-*yloxyacetate* (**10d**).—Concentrated sulphuric acid (four drops) was added to a solution of (**10c**) (1.0 g, 3.82 mmol) in ethanol (30 ml), and the mixture was refluxed for 3 h, poured into water, and extracted with ether. The extracts were washed with aqueous 1M-potassium carbonate and with water, dried, and evaporated to give (**10d**) (0.9 g, 81%), as colourless prisms, m.p. 80.5—81.5 °C (from hexane) (Found: C, 66.0; H, 6.4. $C_{16}H_{18}O_5$ requires C, 66.2; H, 6.25%); $\nu_{max.}$(KBr) 1 755 (CO_2Et) and 1 685 cm^{-1} (CO); δ_H($CDCl_3$) 1.29 (3 H, t, *J* 7 Hz, CH_2CH_3), 1.50—2.39 (4 H, m, 3-H_2 and 4-H_2), 2.54—2.76 (2 H, m, 5-H_2), 2.83—3.09 (1 H, m, 3a-H), 3.98—4.49 (2 H, m, 2-H_2), 4.26 (2 H, q, *J* 7 Hz, CH_2Me), 4.63 (2 H, d, *J* 1 Hz, OCH_2CO_2), 6.79 (1 H, dd, *J* 1 and 9 Hz, 8-H), and 6.94 (1 H, d, *J* 9 Hz, 9-H); δ_C($CDCl_3$) 14.1(q), 28.8(t), 29.5(t), 32.8(d), 40.0(t), 61.0(t), 65.7(t), 68.3(t), 117.1(d), 121.9(d), 122.8(s), 129.7(s), 148.3(s), 152.5(s), 169.0(s), and 196.1(s).

7-*Hydroxy*-4-*methoxy*-2,3-*dihydroinden*-1-*one* (**7b**).—Compound (**7b**) (51%) was prepared from (**7a**)[16] in a manner similar to the synthesis of (**10b**); it formed colourless needles, m.p. 121—122 °C (from methanol) (Found: C, 67.3; H, 5.8. $C_{10}H_{10}O_3$ requires C, 67.4; H, 5.7%); $\nu_{max.}$(KBr) 1 680 cm^{-1} (CO); δ_H($CDCl_3$) 2.62—2.76 (2 H, m, 3-H_2), 2.96—3.09 (2 H, m, 2-H), 3.83 (3 H, s, Me), 6.71 (1 H, d, *J* 9 Hz, 6-H), 6.99 (1 H, d, *J* 9 Hz, 5-H), and 8.53 (1 H, s, OH); δ_C($CDCl_3$) 27.6(t), 40.7(t), 60.9(q), 118.6(d), 124.0(d), 128.1(s), 147.2(s), 154.5(s), 155.6(s), and 214.8(s).

4-*Methoxy*-1-*oxo*-2,3-*dihydroinden*-7-*yloxyacetic Acid* (**7c**).—Compound (**7c**) (62%) was prepared from (**7b**) in a manner similar to the synthesis of (**10c**); it formed colourless needles, m.p. 165—167.5 °C (from acetone) (Found: C, 56.8; H, 5.8. $C_{12}H_{12}O_5 \cdot H_2O$ requires C, 56.7; H, 5.6%); $\nu_{max.}$(KBr) 1 750 (CO_2H) and 1 695 cm^{-1} (CO).

Ethyl 4-*Methoxy*-1-*oxo*-2,3-*dihydroinden*-7-*yloxyacetate* (**7d**).—Compound (**7d**) (89%) was prepared from (**7c**) in a manner similar to the synthesis of (**10d**); it formed colourless prisms, m.p. 78—79.5 °C (from ether–hexane) (Found: C, 63.6; H, 6.2. $C_{10}H_{10}O_3$ requires C, 63.6; H, 6.1%); $\nu_{max.}$(KBr) 1 760 ($CO_2C_2H_5$) and 1 710 cm^{-1} (CO); δ_H($CDCl_3$) 1.28 (3 H, t, *J* 7 Hz, CH_2Me), 2.61—2.74 (2 H, m, 3-H_2), 2.93—3.07 (2 H, m, 2-H_2), 3.85 (3 H, s, OMe), 4.25 (2 H, q, *J* 7 Hz, CH_2Me), 4.74 (2 H, s, OCH_2CO_2), 6.68 (1 H, d, *J* 9 Hz, 6-H), and 6.95 (1 H, d, *J* 9 Hz, 5-H); δ_C($CDCl_3$) 14.2(q), 22.3(t), 36.7(t), 55.9(q), 61.2(t), 67.1(t), 113.4(d), 116.3(d), 127.3(s), 145.9(s), 149.7(s), 151.7(s), 168.9(s), and 204.2(s).

4-*Hydroxy*-1-*methoxy*-6,7,8,9-*tetrahydro*-5H-*benzocyclohepten*-5-*one* (**8b**).—Compound (**8b**) (82%) was prepared from (**8a**)[17] in a manner similar to the synthesis of (**10b**); it formed yellow needles, m.p. 29.2—30.0 °C (from methanol) (Found: C, 69.9; H, 6.9. $C_{12}H_{14}O_3$ requires C, 69.9; H, 6.8%); $\nu_{max.}$(KBr) 1 630 cm^{-1} (CO); δ_H($CDCl_3$) 1.73—1.87 (4 H, m, 7-H_2 and 8-H_2), 2.74—2.93 (2 H, m, 9-H_2), 2.97—3.07 (2 H, m, 6-H_2), 3.79 (3 H, s, OMe), 6.79 (1 H, d, *J* 9 Hz, 3-H), 7.06 (1 H, d, *J* 9 Hz, 2-H), and 11.56 (1 H, s, OH); δ_C($CDCl_3$) 21.0(t), 23.5(t), 24.4(t), 41.8(t), 57.2(q), 115.8(d), 120.2(d), 121.6(s), 132.6(s), 149.6(s), 156.1(s), and 209.9(s).

Ethyl 1-*Methoxy*-5-*oxo*-6,7,8,9-*tetrahydro*-5H-*benzocyclohepten*-4-*yloxyacetate* (**8d**).—Compound (**8d**) (38%) was prepared from (**8b**) without hydrolysis in a manner similar to the synthesis of (**10c**); it formed colourless prisms, m.p. 51—52 °C (from ethanol) (Found: C, 65.7; H, 7.0. $C_{16}H_{20}O_5$ requires C, 65.7; H, 6.9%); $\nu_{max.}$(KBr) 1 750 (CO_2Et) and 1 690 cm^{-1} (CO); δ_H($CDCl_3$) 1.27 (3 H, t, *J* 7 Hz, CH_2Me), 1.73—1.83 (4 H, m, 7-H_2 and 8-H_2), 2.57—2.87 (4 H, m, 6-H_2 and 9-H_2), 3.78 (3 H, s, OMe), 4.22 (2 H, q, *J* 7 Hz, CH_2Me), 5.60 (2 H, s, OCH_2CO_2), 6.74 (1 H, d, *J* 9 Hz, 3-H), and 6.86 (1 H, d, *J* 9 Hz, 2-H); δ_C($CDCl_3$) 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), 127.6(s), 133.1(s), 148.3(s), 151.5(s), 169.1(s), and 206.6(s).

1-*Methoxy*-5-*oxo*-6,7,8,9-*tetrahydro*-5H-*benzocyclohepten*-4-*yloxyacetic Acid* (**8c**).—Compound (**8c**) (71%) was obtained by hydrolysis of (**8d**) with a 3M-sodium hydroxide solution; it formed colourless needles, m.p. 119.5—120.5 °C (from acetone–benzene) (Found: C, 63.6; H, 6.0. $C_{14}H_{16}O_5$ requires C, 63.6; H, 6.1%); $\nu_{max.}$(KBr) 1 730 (CO_2H) and 1 690 cm^{-1} (CO).

Ethyl 5-*Oxo*-2a,3,4,5-*tetrahydro*-2H-*naphtho*[1,8-bc]*furan*-6-*yloxyacetate* (**9d**).—The compound (**9d**) (89%) was prepared from (**9b**)[8] without hydrolysis in a manner similar to the synthesis of (**10c**); it formed colourless prisms, m.p. 80—81 °C (from ethanol) (Found: C, 65.0; H, 5.7. $C_{15}H_{16}O_5$ requires C, 65.2; H, 5.8%); $\nu_{max.}$(KBr) 1 760 (CO_2Et) and 1 675 cm^{-1} (CO); δ_H($CDCl_3$) 1.29 (3 H, t, *J* 7 Hz, CH_2Me), 1.79—2.75 (4 H, m, 3-H_2 and 4-H_2), 3.45—3.86 (1 H, m, 2a-H), 4.11 (1 H, dd, *J* 9 and 11 Hz, 2-H), 4.25 (2 H, q, *J* 7 Hz, CH_2Me), 4.66 (2 H, s, OCH_2CO_2), 4.85 (1 H, t, *J* 9 Hz, 2-H), 6.69 (1 H, d, *J* 9 Hz, 7-H), and 6.87 (1 H, d, *J* 9 Hz, 8-H); δ_C($CDCl_3$) 14.1(q), 27.8(t), 39.3(d), 39.8(t), 61.0(t), 68.1(t), 78.7(t), 114.5(d), 116.2(d), 120.2(s), 139.2(s), 151.2(s), 153.5(s), 168.9(s), and 194.4(s).

7-Hydroxy-6-oxo-2,2a,3,4-tetrahydrocyclohepta[cd]*benzofuran-6(5H)-one* (**11b**).—Compound (**11b**) (73%) was prepared from (**11a**) (obtained from 5-methoxybenzofuran-3-ylpropionic acid[18]) in a manner similar to the synthesis of (**10b**); it formed yellow needles, m.p. 60.5—61.5 °C (from hexane) (Found: C, 70.6; H, 6.0. $C_{12}H_{12}O_3$ requires C, 70.6; H, 5.9%); $\nu_{max.}$(KBr) 1 640 cm^{-1} (CO); $\delta_H(CDCl_3)$ 1.72—2.12 (4 H, m, 3-H_2 and 4-H_2), 2.73—2.93 (2 H, m, 5-H_2), 3.60—4.13 (1 H, m, 2a-H), 4.10 (1 H, t, *J* 8 Hz, 2-H), 4.79 (1 H, dd, *J* 8 and 9 Hz, 2-H), 6.71 (1 H, dd *J* 1 and 9 Hz, 8-H), 6.92 (1 H, d, *J* 8 Hz, 9-H), and 11.49 (1 H, s, OH); $\delta_C(CDCl_3)$ 21.0(t), 30.0(t), 42.0(d), 42.3(t), 79.9(t), 116.7(d), 117.1(d), 117.3(s), 131.9(s), 152.4(s), 156.3(s), and 206.8(s).

6-Oxo-2,2a,3,4,5,6-hexahydrocyclohepta[cd]*benzofuran-7-yloxyacetic Acid* (**11c**).—Compound (**11c**) (70%) was prepared from (**11b**) in a manner similar to the synthesis of (**10c**); it formed colourless needles, m.p. 111.5—113 °C (from benzene–hexane) (Found: C, 63.9; H, 5.4. $C_{14}H_{14}O_5$ requires C, 64.1; H, 5.4%); $\nu_{max.}$(KBr) 1 780, 1760 (CO_2H), and 1 665 cm^{-1} (CO); $\delta_H(CDCl_3)$ 1.61—2.25 (4 H, m, 3-H_2 and 4-H_2), 2.79—2.92 (2 H, m, 5-H_2), 3.56—3.92 (1 H, m, 2a-H), 4.13 (1 H, dd, *J* 9 and 10 Hz, 2-H), 4.68 (2 H, s, OCH_2CO_2), 4.71 (1 H, t, *J* 9 Hz, 2-H), 6.78 (1 H, d, *J* 9 Hz, 8-H), 6.89 (1 H, d, *J* 9 Hz, 9-H), and 9.81 (1 H, br s, OH); $\delta_C(CDCl_3)$ 23.8(t), 30.4(t), 43.2(d), 44.4(t), 68.9(t), 77.3(t), 113.8(d), 116.2(d), 126.2(s), 132.0(s), 150.0(s), 155.4(s), 170.6(s), and 204.5(s).

Ethyl 6-Oxo-2,2a,3,4,5,6-hexahydrocyclohepta[cd]*benzofuran-7-yloxyacetate* (**11d**).—Compound (**11d**) (90%) was prepared from (**11c**) in a manner similar to the synthesis of (**10d**); it formed colourless needles, m.p. 47—48.5 °C (from hexane) (Found: C, 66.0; H, 6.2. $C_{16}H_{18}O_5$ requires C, 66.2; H, 6.25%); $\nu_{max.}$(KBr) 1 765 (CO_2Et) and 1 690 cm^{-1} (CO); $\delta_H(CDCl_3)$ 1.28 (3 H, t, *J* 7 Hz, CH_2*Me*), 1.50—2.31 (4 H, m, 3-H_2, and 4-H_2), 2.81 (2 H, t, *J* 6 Hz, 5-H_2), 3.46—3.86 (1 H, m, 2a-H), 4.09 (1 H, dd, *J* 8 and 9 Hz, 2-H), 4.23 (2 H, q, *J* 7 Hz, CH_2*Me*), 4.61 (2 H, d, *J* 1 Hz, OCH_2CO_2), 4.76 (1 H, dd, *J* 8 and 9 Hz, 2-H), and 6.75 (2 H, s, 8-H and 9-H); $\delta_C(CDCl_3)$ 14.1(q), 25.4(t), 31.4(t), 43.8(d), 45.2(t), 61.0(t), 69.2(t), 77.2(t), 111.8(d), 116.9(d), 129.4(s), 129.5(s), 149.5(s), 155.0(s), 169.1(s), and 202.1(s).

Reaction of (**4c**) *with Sodium Acetate in Acetic Anhydride.*—A mixture of (**4c**) (1.00 g, 4.00 mmol), acetic anhydride (15 ml), and sodium acetate (4.6 g, 56.1 mmol) was refluxed at 150 °C for 1 h. The mixture was poured into ice–water (200 ml), stirred for 5 min to decompose excess of acetic anhydride, and extracted with ether. The extracts were washed with aqueous 1M-potassium carbonate (30 ml × 3) and then with water, dried, and evaporated. The resulting oil was chromatographed and eluted with benzene. The first fraction gave (**1a**) (0.31 g, 41%) and the second fraction afforded the lactone (**18**) (0.40 g, 40%).[8]

Reaction of (**8c**) *with Sodium Acetate in Acetic Anhydride.*—The reaction was carried out in a manner similar to the reaction of (**4c**). 7-Methoxy-3,4,5,6-tetrahydrocyclohepta[*cd*]benzofuran (**13a**) (89%) and lactone (**19**) (3%) were produced, but the latter was hydrolysed to the starting material (**8c**) during chromatography. Compound (**13a**), colourless crystals after distillation, m.p. 25—26 °C (Found: C, 77.0; H, 7.0. $C_{13}H_{14}O_2$ requires C, 77.2; H, 7.0%); $\delta_H(CDCl_3)$ 1.70—2.18 (4 H, m, 4-H_2 and 5-H_2), 2.70—3.10 (4 H, m, 3-H_2 and 6-H_2), 3.85 (3 H, s, OMe), 6.86 (1 H, d, *J* 9 Hz, 8-H), 7.24 (1 H, dt, *J* 9 and 1 Hz, 9-H), and 7.35 (1 H, t, *J* 1 Hz, 2-H); $\delta_C(CDCl_3)$ 26.4(t), 28.0(t), 28.6(t), 29.7(t), 56.5(q), 108.1(d), 108.5(d), 120.8(s), 123.8(s), 128.3(s), 141.3(d), 151.0(s), and 152.5(s).

Reaction of (**10c**) *with Sodium Acetate in Acetic Anhydride.*—The reaction was carried out in a manner similar to the reaction of (**4c**). 4,4a,5,6-Tetrahydro-3*H*-furo[2′,3′,4′:4,5]naphtho[1,8-*bc*]pyran (**15a**) (16%) was obtained as colourless needles, m.p. 88.5—89.5 °C (from hexane) (Found: C, 77.7; H, 6.1. $C_{13}H_{12}O_2$ requires C, 78.0; H, 6.0%); $\delta_H(CDCl_3)$ 1.07—2.33 (4 H, m, 4-H_2 and 5-H_2), 2.43—3.11 (3 H, m, 3-H_2 and 4a-H), 4.03—4.51 (2 H, m, 6-H_2), 6.64 (1 H, d, *J* 9 Hz, 8-H), 7.08 (1 H, dd, *J* 1 and 9 Hz, 9-H), and 7.22 (1 H, d, *J* 2 Hz, 2-H); $\delta_C(CDCl_3)$ 20.3(t), 28.6(t), 30.5(t), 30.9(d), 67.3(t), 109.5(d), 112.2(d), 115.3(s), 116.6(s), 127.4(s), 138.8(d), 147.5(s), and 147.8(s). 2,3,3a,4-Tetrahydro-1,6,9-trioxacyclohepta[*cd*]phenalene-7(8*H*)-one (**21**) (64%) was obtained as colourless needles, m.p. 164—164.5 °C (from benzene–hexane) (Found: C, 68.7; H, 5.1. $C_{14}H_{12}O_4$ requires C, 68.85; H, 4.95%); $\nu_{max.}$(KBr) 1 770 cm^{-1} (lactone); $\delta_H(CDCl_3)$ 1.66—2.56 (4 H, m, 3-H_2 and 4-H_2), 2.68—3.11 (1 H, m, 3a-H), 3.89—4.47 (2 H, m, 2-H_2), 4.56 (1 H, d, *J* 14 Hz, 8-H), 4.78 (1 H, d, *J* 14 Hz, 8-H), 5.88 (1 H, dd, *J* 3 and 7 Hz, 5-H), 6.67 (1 H, d, *J* 9 Hz, 10-H or 11-H), and 6.78 (1 H, d, *J* 9 Hz, 11-H or 10-H); δ_C 28.4(t), 28.5(t), 31.2(d), 65.8(t), 69.6(t), 113.8(d), 117.4(s), 118.5(d), 118.7(d), 122.3(s), 145.3(s), 148.6(s), 149.1(s), and 167.0(s).

Reaction of (**11c**) *with Sodium Acetate in Acetic Anhydride.*—The reaction was carried out in a manner similar to the reaction of (**4c**). 7,8,9,9a-Tetrahydro-1*H*-2,5-dioxacyclohepta[*jkl*]-*as*-indacene (**16a**) (81%) and lactone (**22**) (17%) were produced, but the lactone (**22**) was hydrolysed to the starting material (**11c**) during chromatography. Compound (**16a**), colourless needles, m.p. 97.5—98.5 °C (from benzene–hexane) (Found: C, 77.85; H, 6.1. $C_{13}H_{12}O_2$ requires C, 78.0; H, 6.0%); $\delta_H(CDCl_3)$ 1.45—1.93 (2 H, m, 8-H_2), 2.12—3.25 (4 H, m, 7-H_2 and 9-H_2), 3.38—3.76 (1 H, m, 9a-H), 4.06 (1 H, d, *J* 8 and 13 Hz, 10-H), 4.72 (1 H, t, *J* 8 Hz, 10-H), 6.71 (1 H, d, *J* 9 Hz, 3-H), 7.13 (1 H, dd, *J* 1 and 9 Hz, 4-H), and 7.34 (1 H, d, *J* 1 Hz, 6-H); $\delta_C(CDCl_3)$ 25.3(t), 27.1(t), 30.4(t), 46.0(d), 78.0(t), 105.5(d), 108.9(d), 118.9(s), 123.4(s), 124.9(s), 141.5(d), 150.6(s), and 154.7(s).

Reaction of (**4d**) *with Potassium Hydroxide in Dioxane.*—Powdered potassium hydroxide (0.50 g, 9.00 mmol) was added to (**4d**) (0.50 g, 1.80 mmol) in anhydrous dioxane (10 ml) and the mixture was refluxed for 1 h. The mixture was diluted with water (10 ml) and then poured into 2M-hydrochloric acid (100 ml). After 15 min the solution was extracted with ether, and the combined extracts were washed with 1M-aqueous potassium carbonate (3 × 30 ml) and water, dried, and evaporated. The resulting oil was chromatographed and eluted with benzene to give the furan (**1a**) (0.24 g, 71%). The alkaline solution was acidified with 6M-hydrochloric acid (80 ml) and the resulting precipitates were extracted with ether. The combined extracts were washed with water, dried, and evaporated to give the furancarboxylic acid (**1b**) (0.09 g, 22%).[1]

Reaction of (**8d**) *with Potassium Hydroxide in Dioxane.*—The reaction was carried out in a manner similar to the reaction of (**4d**). The furan (**13a**) (90%) and 7-methoxy-3,4,5,6-tetrahydrocyclohepta[*cd*]benzofuran-2-carboxylic acid (**13b**) (4%) were produced. Compound (**13b**), colourless prisms, m.p. 235—236 °C (from acetone) (Found: C, 68.4; H, 6.0. $C_{14}H_{14}O_4$ requires C, 68.3; H, 5.7%); $\nu_{max.}$(KBr) 1 680 cm^{-1} (CO_2H).

Reaction of (**10d**) *with Potassium Hydroxide in Dioxane.*—The reaction was carried out in a manner similar to the reaction of (**4d**). The furan (**15a**) (20%) and ethyl 4,4a,5,6-tetrahydro-3*H*-furo[2′,3′,4′:4,5]naphtho[1,8-*bc*]pyran-2-carboxylate (**15c**) (14%) were produced. Compound (**15c**), colourless needles, m.p. 168—169 °C (from hexane) (Found: C, 70.7; H, 6.0 $C_{16}H_{16}O_4$ requires C, 70.6; H, 5.9%); $\nu_{max.}$(KBr) 1 725 and 1 710 cm^{-1} (CO_2Et); $\delta_H(CDCl_3)$ 1.42 (3 H, t, *J* 7 Hz, CH_2*Me*), 1.34—2.44 (4 H, m, 4-H_2 and 5-H_2), 2.66—3.47 (3 H, m, 3-H_2 and 4a-H), 4.07—4.61 (2 H, m, 6-H_2), 4.41 (2 H, q, *J* 7 Hz, CH_2Me), 6.82 (1 H, d, *J* 9 Hz, 8-H), and 7.18 (1 H, dd, *J* 1 and 9 Hz, 9-H);

$\delta_C(CDCl_3)$ 14.4(q), 22.2(t), 28.3(t), 30.5(d), 30.6(t), 60.9(t), 67.4(t), 110.5(d), 116.5(s), 116.6(d), 126.5(s), 127.2(s), 139.7(s), 147.6(s), 148.3(s), and 160.2(s).

Reaction of (**11d**) *with Potassium Hydroxide in Dioxane.*—The reaction was carried out in a similar manner to the reaction of (**4d**). The furan (**16a**) (70%) and ethyl 6a,7,8,9-tetrahydro-6*H*-2,5-dioxacyclohepta[*jkl*]-*as*-indacene-1-carboxylate (**16c**) (12%) were produced. Compound (**16c**), colourless needles, m.p. 121—122 °C (from hexane) (Found: C, 70.4; H, 6.1. $C_{16}H_{16}O_4$ requires C, 70.6; H, 5.9%); $\nu_{max.}$(KBr) 1 715 cm^{-1} (CO_2Et); $\delta_H(CDCl_3)$ 1.43 (3 H, t, *J* 7 Hz, CH_2Me), 1.38—2.99 (5 H, m, 6a-H, 7-H_2, and 8-H_2), 3.54—3.81 (2 H, m, 9-H_2), 4.07 (1 H, dd, *J* 8 and 13 Hz, 6-H), 4.42 (2 H, q, *J* 7 Hz, CH_2CH_3), 4.75 (1 H, t, *J* 8 Hz, 6-H), 6.87 (1 H, d, *J* 9 Hz, 4-H), and 7.23 (1 H, dd, *J* 1 and 9 Hz, 3-H); $\delta_C(CDCl_3)$ 14.4(q), 26.8(t), 27.6(t), 30.1(t), 46.3(d), 61.0(t), 78.2(t), 109.9(d), 110.1(d), 125.0(s), 126.0(s), 128.7(s), 141.2(s), 150.0(s), and 160.3(s).

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