are known compounds and had spectral properties in accord with literature data.

The following 2(5*H*)-furanones are new.

5-Methyl-5-(2-methylpropyl)-2(5*H*)-furanone (4c): IR ν(CO) 1765 cm^{-1}; NMR δ ($CDCl_3$); 0.90 (d, 6 H, J = 6.2 Hz, $(CH_3)_2CH$), 1.10 (m, 1 H, $CH(CH_3)_2$), 1.40 (s, 3 H, CH_3), 1.65 (d, 2 H, J = 6.9 Hz, CH_2), 6.00 and 7.35 (2d, 2 H, J = 5.6 Hz, CH=CH), 7.35 (d, 1 H, CH=); MS (m/e) 97 $(M - C_4H_9)^+$. Anal. Calcd for $C_9H_{14}O_2$: C, 70.10; H, 9.15. Found: C, 70.01; H, 9.20.

5-(3-Butenyl)-5-methyl-2(5*H*)-furanone (4e): IR ν(CO) 1755 cm^{-1}; NMR δ ($CDCl_3$) 1.40 (s, 3 H, CH_3), 1.80-2.15 (m, 4 H, CH_2CH_2), 5.00 (m, 2 H, CH_2=), 5.72 (m, 1 H, CH=CH_2), 6.02 and 7.35 (2d, 2 H, J = 5.6 Hz, CH=CH); MS (m/e) 98 $(M - C_4H_6)^+$. Anal. Calcd for $C_9H_{12}O_2$: C, 71.03; H, 7.95. Found: C, 70.75; H, 7.58.

5,5-Heptamethylene-2(5*H*)-furanone (4h): IR ν(CO) 1745 cm^{-1}; NMR δ ($CDCl_3$) 1.30-2.10 (m, 14 H, $(CH_2)_7$), 6.05 and 7.40 (2d, 2 H, J = 5.7 Hz, CH=CH); MS (m/e) 180 $(M)^+$. Anal. Calcd for $C_{11}H_{16}O_2$: C, 73.30; H, 8.95. Found: C, 72.96; H, 9.04.

Acknowledgment. We are indebted to the Natural Sciences and Engineering Research Council and to British Petroleum for support of this research.

Registry No. **1a**, 115-18-4; **1b**, 918-85-4; **1c**, 3732-61-4; **1d**, 6051-52-1; **1e**, 78-70-6; **1f**, 10473-13-9; **1g**, 598-32-3; **1h**, 4798-44-1; **1i**, 4393-06-0; **1j**, 924-41-4; **1k**, 17123-61-4; **1l**, 10473-14-0; **1m**, 922-65-6; **1n**, 107-18-6; **1o**, 513-42-8; **2a**, 3123-97-5; **2b**, 2865-82-9; **2c**, 54796-80-4; **2d**, 21303-80-0; **2e**, 134359-15-2; **2f**, 2981-96-6; **2g**, 108-29-2; **2h**, 105-21-5; **2i**, 1008-76-0; **2j**, 134359-16-3; **2k**, 134359-17-4; *cis*-**2l**, 10150-95-5; *trans*-**2l**, 10150-96-6; **2m**, 29949-29-9; **3a**, 115-19-5; **3b**, 77-75-8; **3c**, 107-54-0; **3d**, 127-66-2; **3e**, 51193-99-8; **3f**, 17356-19-3; **3g**, 78-27-3; **3h**, 55373-76-7; **4a**, 20019-64-1; **4b**, 30336-19-7; **4c**, 110296-01-0; **4d**, 53774-21-3; **4e**, 134359-18-5; **4f**, 5732-90-1; **4g**, 4435-19-2; **4h**, 134359-19-6; $Pd(dba)_2$, 32005-36-0; dpph, 7688-25-7; CH_3CH=CHCOOH, 3724-65-0; $(CH_3)_2C$=CHCOOH, 541-47-9.

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Arylmagnesium Bromide Additions to 1-Tetralone-2-acetic Acid Followed by Catalytic Hydrogenolysis: Stereochemical Consequences[1a]

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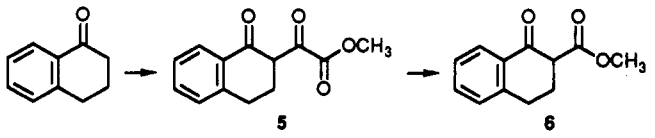
A Stork reaction route (**7** → **1b**) was utilized to synthesize 1-tetralone-2-acetic acid methyl ester (**1a**) from 1-tetralone. Addition of a 2'-(*o*-methoxyphenyl) magnesium bromide to this ketone followed by palladium-catalyzed hydrogenation of the intermediate cis lactones (**2**, verified by X-ray crystal structure determination of **2a**, Figure 1), afforded predominantly a 1,2-cis tetralin (**3**) accompanied by smaller yields of the corresponding 1,2-trans tetralin (**4**). The stereochemical consequences of this reaction sequence was unequivocally established by X-ray crystal structure elucidation of 1,2-cis methyl ester **3b** (Figure 2) and 1,2-trans carboxylic acid **4a** (Figure 3). Stereochemical assignments for the analogous diastereoisomeric sets **3c-f** and **4c-f** were obtained by high-field (400-MHz) ^{1}H and ^{13}C NMR correlations with the crystal structures. The overall reaction pathway illustrates a useful approach to 1,2-cis-alkylated tetralins and certain sterically hindered 1,2-trans-alkylated tetralins.

Some 36 years ago,[1] our interest in elucidating the structures of certain dienone-phenol rearrangement[2] products[3] led us to study the reaction between 1-tetralone-2-acetic acid methyl ester (**1a**) and the Grignard reagent from 2-bromo-4-methylanisole in order to open a route toward substituted benzo[*c*]phenanthrenes. Subsequent saponification, acidification, and hydrogenation (**1a** → **2** → **3** and/or **4**) resulted in a 1,2-cis-substituted tetralin **3** as major product. As summarized in the sequel, elucidation of the stereochemical consequences of this reaction sequence required modern instrumental techniques such as X-ray crystal structure determination and high-field (400-MHz) 2D ^{1}H and ^{13}C NMR, which were then not available. We now describe the successful completion of this early research.[1]

Several synthetic routes were evaluated for obtaining 1-tetralone-2-acetic acid methyl ester (**1a**). The following previously known procedure was employed to obtain the original supply of this ketone. Condensation of 1-tetralone[4a-c] with methyl oxalate, in the presence of freshly prepared sodium methoxide, led to glyoxalate (**5**).[4c] De-



5 **6**

carbonylation of the glyoxalate afforded 1,2,3,4-tetrahydro-2-carbomethoxy-1-oxonaphthalene (**6**).[5] Alkylation of ketone **6** with methyl bromoacetate gave 1,2,3,4-tetrahydro-1-oxo-2-naphthaleneacetic acid (**1b**) following hydrolysis and decarboxylation.[5,6] Yields in the latter pro-

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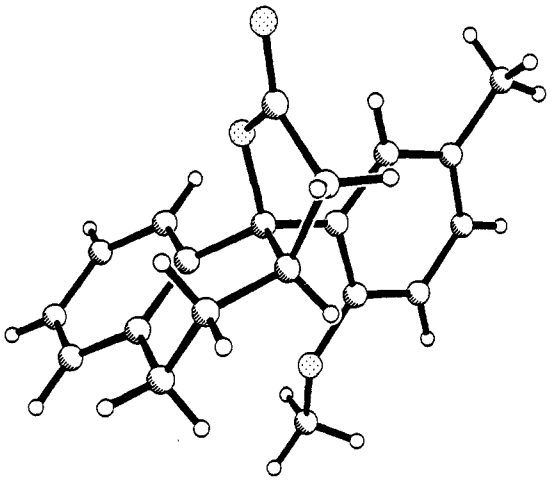
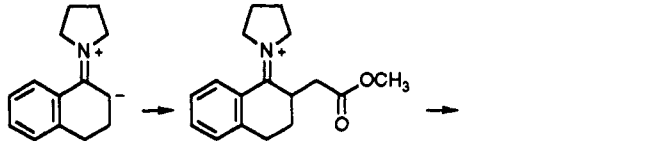


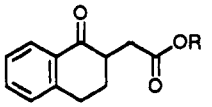
Figure 1. Computer-generated perspective view of lactone **2a**.

cedure proved to be erratic[7] and cannot generally be reproduced.[6] Broad application of this general route has been applied to obtaining a variety of substituted 2-naphthylacetic acids with antiinflammatory, analgesic, and antipyretic activities.[7]

Since the preceding Bachmann route to ketone **6** proved laborious and generally resulted in a low overall yield (<-14%) from 1-tetralone, a more efficient route to this important intermediate was developed. Application of the Stork reaction[8] to alkylation of 1-tetralone pyrrolidine enamine (**7**) with methyl bromoacetate gave the intermediate Schiff base (**8**), which was readily hydrolyzed to ketone **1a**. The overall yield was 42%, and sufficient 1-tetralone was recovered to increase the corrected yield to 89%. The superiority of the Stork reaction route over the previous methods was amplified by eliminating the isolation of intermediates.

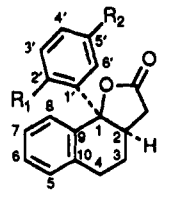


7 **8**

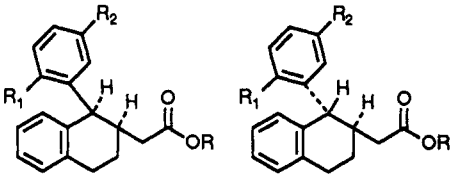


1a, R = CH_3
b, R = H

Reaction of 1,2,3,4-tetrahydro-1-oxo-2-naphthaleneacetic acid methyl ester (**1a**) with the Grignard reagent from 2-bromo-4-methylanisole, followed by saponification of the hydrolyzed product and acidification, gave one diastereoisomer of 1-hydroxy-1-(2′-methoxy-5′-methylphenyl)-1,2,3,4-tetrahydro-2-naphthaleneacetic acid lactone (**2a**).



2a, $R_1 = OCH_3$, $R_2 = CH_3$
b, $R_1 = R_2 = H$
c, $R_1 = OCH_3 = R_2 = H$



3 **4**

a, R = H, $R_1 = OCH_3$ $R_2 = CH_3$
b, R = CH_3, $R_1 = OCH_3$, $R_2 = CH_3$
c, R = $R_1 = R_2 = H$
d, R = CH_3, $R_1 = R_2 = H$
e, R = $R_2 = H$, $R_1 = OCH_3$
f, R = CH_3, $R_1 = OCH_3$, $R_2 = H$

The infrared spectrum of the product showed the characteristic γ-lactone carbonyl band at 5.65 μM. The stereochemical configuration of the lactone ring **2a** was subsequently established as cis by X-ray crystallographic structure determination (Figure 1). Several attempts to vary the reaction time and temperature of this inverse Grignard reaction resulted in an optimum yield of only 25% due to competitive reaction with the ester.

Catalytic hydrogenation of benzhydryl lactone **2a** over palladium–charcoal produced a mixture of the two diastereoisomeric 1-(2′-methoxy-5′-methylphenyl)-1,2,3,4-tetrahydro-2-naphthaleneacetic acids (**3a**, **4a**). The diastereoisomers were separated in poor yield by fractional crystallization, but more efficiently by chromatographic separation of the methyl esters **3b** and **4b**. The acids **3a** and **4a** and esters **3b** and **4b** possessed identical chromophoric systems as evidenced by their ultraviolet spectra, and the major component exhibited the higher melting point. Pronounced differences in their solution infrared spectra ruled out the possibility of polymorphism. Further evidence in favor of diastereoisomerism was obtained when the isomeric acids gave two different methyl esters, and each ester could be saponified to yield the corresponding original acid.

Dannenberg and Laufer[9a] found that the catalytic hydrogenation of 1-hydroxy-1-phenyl-1,2,3,4-tetrahydro-2-naphthaleneacetic acid lactone (**2b**) with palladium(II) oxide gave only one of the two possible diastereoisomeric acids, which we subsequently determined to be **3c**. Apparently, the key transition-state intermediate, unhindered by a bulky substituent in the 2′ position, gave exclusively one diastereoisomer. In the case of lactone **2a** the steric and/or electronic effects of the 2′-methoxy group appear to affect product formation and give rise to the two isomers found experimentally. Before such effects could be attributed to the 2′-methoxy group, it seemed advisable to reexamine the unhindered lactone **2b** and at least one other lactone, **2c**, with a 2′-methoxy group.

Catalytic hydrogenation over palladium–charcoal of the unsubstituted **2b** prepared from ketone **1a** and phenylmagnesium bromide gave a carboxylic acid **3c** that was converted to its methyl ester using diazomethane. Careful

(6) Compare: Dannenberg, H.; Laufer, S. *Chem. Ber.* **1954**, *87*, 733. Johnson, G. D.; Lindsey, W. B.; Jones, B. R. *J. Am. Chem. Soc.* **1956**, *78*, 461.

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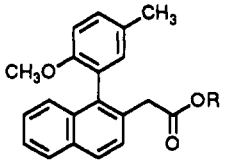
Table I. 400- (^{1}H) and 100- (^{13}C) MHz NMR Assignments for Lactones 2a–c in Deuteriochloroform

	lactone					
	2a		2b		2c	
	^{13}C	^{1}H	^{13}C	^{1}H	^{13}C	^{1}H
			Position			
1	86.3 s		87.9 s		86.5 s	
2	40.0 d	3.07	44.0 d	2.83	40.1 d	3.10 dddd (12.7, 8.0, 6.1, 1.5)
3a	27.5 t	1.59	24.9 t	1.78	27.7 t	1.63 ddd (13.2, 7.5, 3.7)
b		2.00		2.03		2.01 ddd (13.2, 12.7, 3.7)
4a	28.3 t	2.95	26.9 t	2.93	28.5 t	2.95 ddd (15.6, 12.6, 3.9)
b		2.80				2.82 ddd (15.6, 7.5, 3.7)
5	129.3 d	7.0	127.6 d	7.10	126.2 d	7.02
6	127.3 d	7.12	126.1 d	7.16	127.5 d	7.14
7	127.3 d	7.10	126.1 d	7.16	127.5 d	7.12
8	128.9 d	7.02	131.6 d	7.06	129.0 d	7.04
9	137.5 s		137.6 s		137.6 s	
10	136.0 s		136.8 s		136.1 s	
1′	132.7 s		145.7 s		133.0 s	
2′	153.1 s		128.9 d	7.21	155.3 s	
3′	112.8 d	6.68	129.0 d	7.32	112.7 d	6.79
4′	125.7 d	7.05	128.1 d	7.24	129.3 d	7.27
5′	129.7 s				120.6 d	6.99
6′	126.0 d	7.41			125.4 d	7.59 ddd (8.0, 2.2)
ArMe	20.6 q	2.32 s				
ArOMe	55.4 q	3.32 s			55.4 q	3.40 s
			Lactone			
>C=O	176.5 s		176.5 s		176.6 s	
—CH_2—	35.6 t	2.19	34.2 t	2.37	35.8 t	2.21 dd (17.2, 1.5)
		2.71		2.73		2.70 dd (17.2, 8.0)

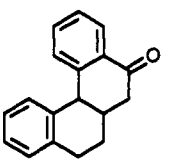
chromatography of the ester on alumina gave a series of fractions with similar melting points. The infrared spectra of three fractions from separated points along the chromatogram were found to be identical. Further, saponification of a series of fractions from the top and a second series from the bottom portion of the chromatogram gave identical acids. Mixture melting point and infrared comparison showed that the carboxylic acid samples were identical, thereby indicating the presence of only one diastereoisomer and confirming Dannenberg and Laufer's[9a] results. Assignment of the cis stereochemistry, i.e., structure **3c**, to the exclusive product of hydrogenolysis of lactone **2b** was based on structural and stereochemical facts summarized in the sequel and the ^{1}H NMR analysis (smaller coupling constant, J = 5.4 Hz for hydrogen attached to C_1, see Table I). Here it is important to emphasize that formation of cis tetralin **3c** requires attachment of hydrogen *exclusively* from the α-face of the tetrahydronaphthalene ring system (*inversion* at C_1 of 2b). In general, hydrogenation of benzyl alcohol derivatives over palladium catalysts has been found[9b] to occur with *inversion* of configuration. Thus, hydrogenolysis of lactone **2b** might well be expected to afford cis carboxylic acid **3c**. However, a priori prediction of the major product's configuration in hydrogenolysis of an asymmetric center is often difficult. The rate and stereochemical outcome of the hydrogenolysis reaction appears to depend on steric factors and a number of other variables, including the amount and type of catalyst, solvent, pH, temperature, and nature of the leaving group(s).[9b]

Reaction of ketone **1a** with (*o*-methoxyphenyl)magnesium bromide led to the lactone of 1-hydroxy-1-(2′-methoxyphenyl)-1,2,3,4-tetrahydro-2-naphthaleneacetic acid (**2c**). The lactone was hydrogenated to a mixture that, as is the case of the more highly substituted acids **3a** and **4a**, was found to be composed of two diastereoisomers (**3d** and **4d**). Separation of the isomeric acids and corresponding methyl esters was accomplished as previously noted (**3a**, **4a**). From these results it was apparent that the 2′-methoxy group had a decided influence on the diastereoisomeric ratio resulting from the lactone **2** catalytic hydrogenation step. Separation of the diastereomers provided a higher melting isomer in major amount and a minor, lower melting isomer. Examination of the *minor* component by 2D ^{1}H NMR techniques (see below) revealed a larger coupling constant for the hydrogen at C_1 (J = 7.8 Hz, Table II), indicating a trans configuration from attack of the hydrogen-catalyst complex from the β-face. Consequently, structures **3e** and **4e** were assigned to the major and minor components, respectively. At a time (1954) when NMR was not yet available, we had eliminated the possibility of skeletal rearrangement for the isomers already in hand employing methyl ester **3b** as follows.

Sulfur dehydrogenation of 1-(2′-methoxy-5′-methylphenyl)-1,2,3,4-tetrahydro-2-naphthaleneacetic acid methyl ester (**3b**) furnished the fully aromatic 1-(2′-methoxy-5′-methylphenyl)-2-naphthaleneacetic acid methyl ester (**9a**).



9a, R = CH_3
b, R = H



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Saponification gave the corresponding acid **9b**. Unexpectedly, acetic acid **9b** failed to cyclize with anhydrous hydrogen fluoride, phosphorus pentachloride–stannic chloride, or acetic anhydride–zinc chloride under the usual reaction conditions.[10] On the other hand, cyclization of the higher melting (209–211 °C) predominant diastereoisomer **3a** of the corresponding tetralin-2-acetic acid with phosphorus pentachloride–stannic chloride afforded a 64% yield of isomeric ketones of unknown constitution. Reaction of diastereoisomer **3e** with anhydrous hydrogen fluoride gave a 75% yield of neutral ketonic products that

(10) Interaction between the 2′ methoxy group and the 8 position of the naphthalene ring should make aromatization, with its planar structural requirement, more difficult.

Table II. ^1H (400-MHz) and ^{13}C (100-MHz) NMR Assignments for a Selection of Tetralin-2-acetic acid Derivatives in Deuteriochloroform Solution

	tetralin derivative							
	3b		**3c**		**4a**		**4e**	
	^{13}C	^1H	^{13}C	^1H	^{13}C	^1H	^{13}C	^1H
				Position				
1	39.3 d	4.83 d (5.3)	48.0 d	4.26 d (5.4)	43.9 d	4.83 d (8.6)	43.9 d	4.25 d (7.8)
2	34.8 d	2.61 m	34.9 d	2.57 m	37.7 d	2.45 m	37.5 d	2.45 m
3a	23.7 t	1.75 m	23.4 t	1.79 m	27.3 t	2.08 m	26.9 t	2.05 m
b		1.61 m		1.69 m		1.62 m		1.60 m
4a	28.8 t	3.01 m	28.6 t	2.99 m	28.5 t	2.96 ddd (15.8, 10.4, 5.4)	28.2 t	2.94 m
b		2.95 m		2.95 m		2.87 ddd (15.8, 11.7, 5.0)		2.84 m
5	128.7 d	7.15 dd (6.8, 1.0)	127.0 d	7.16 dd (7.5, 1.7)	128.4 d	6.79 br d (7.7)	130.4 d	6.81 d
6	125.8 d	7.11 dd	126.8 d	7.11	125.7 d	6.98	125.6 d	7.05
7	125.7 d	7.02	126.5 d	7.02	125.5 d	6.98	125.7 d	7.06
8	130.7 d	6.87 dd (7.6, 1.0)	131.3 d	6.90 br d (7.8)	130.9 d	6.71 d (8.3)	128.5 d	6.88 d
9	139.9 s		139.6 s		139.2 s		138.9 s	
10	136.7 s		136.8 s		136.7 s		136.7 s	
1′	131.3 s		143.2 s		133.4 s		133.8 s	
2′	155.1 s		128.5 d	7.21 dd (6.7, 1.4)	155.7 s		157.6 s	
3′	109.8 d	6.75 d (8.2)	130.9 d	7.18	110.7 d	7.05 br d (7.4)	110.6 d	6.68 br d (7.8)
4′	127.5 d	6.94 dd (8.2, 2.0)	129.4 d	6.96 dd (6.6, 1.4)	127.9 d	7.10 dd (7.4, 1.3)	127.5 d	7.14
5′	129.1 s				129.9 s		120.7 d	6.96
6′	132.7 d	6.37 d (2.0)			130.0 d	6.66 d (2.0)	130.0 d	7.16
7′a	37.3 t	2.42 dd	38.0 t	2.28 dd (16.2, 7.1)	38.5 t	2.42 dd (16.4, 3.8)	38.5 t	2.39 dd (16.6, 4.6)
b		1.83 dd		1.93 dd (16.2, 7.9)		2.23 dd (16.4, 10.4)		2.23 dd (16.6, 5.8)
8′	173.7 s		179.6 s		178.3 s		178.3 s	
				Atom				
$ARCH_3$	20.7 q	2.21 s			20.6 q	2.17 s		
$ArOCH_3$	55.3 q	3.79 s			55.7 q	3.75 q	55.5 q	3.76 s
$-CO_2CH_3$	51.3 q	3.65 s						
$-CO_2H$				11.4 s		11.5 s		11.4 s

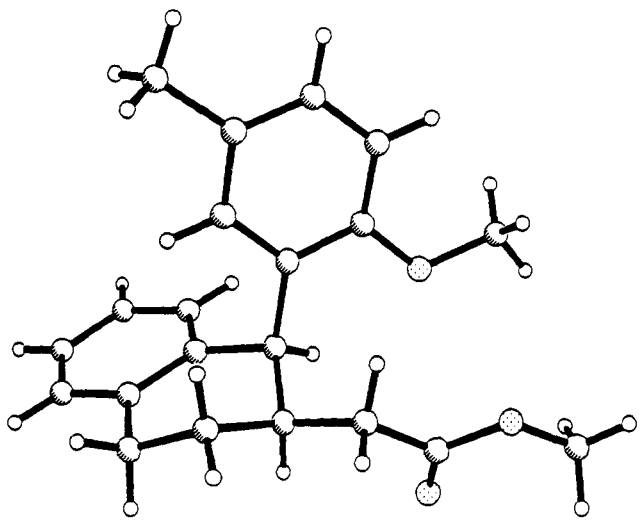

Figure 2. Computer-generated representation of cis methyl ester **3b**.

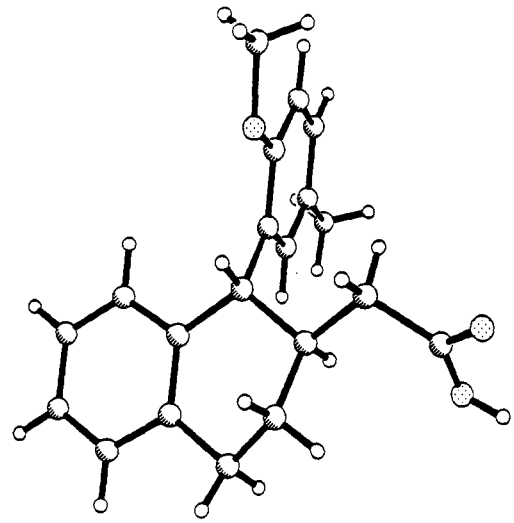

Figure 3. Computer-generated structure of trans carboxylic acid **4a**.

again did not contain the expected counterpart of ketone **10**. Interestingly, Dannenberg and Laufer[11] prepared the expected ketone **10** from tetralin-2-acetic acid **3c** by the phosphorus pentachloride–stannic chloride method and obtained a presumed homogeneous product. In retrospect, these results with the substituted carboxylic acids **3a** and **3e** (where the 2′-methoxyphenyl ring is orientated, for steric reasons, perpendicular to the tetralin ring) are thereby readily explained (cf. Figure 2 and 3). The derived ketone mixtures probably result from intermolecular condensation reactions.

With evidence mounting that complete structural elucidation of the tetralin ring isomer sets (**3** and **4**) would provide results of stereochemical utility for further synthesis of cis and trans 1,2-dialkylated tetralins, both isomers **3b** and **4a** were selected for X-ray crystal structure determination. Crystallographic quality crystals of methyl ester **3b** were obtained from heptane, and a direct methods solution of the crystal structure problem revealed the 1,2-cis tetralin **3b** orientation shown in Figure 2 for the major product of the Grignard → hydrogenation sequence. Recrystallization of the lower melting minor component, carboxylic acid **4a**, from glacial acetic acid provided excellent crystals, and analogous X-ray crystal analysis afforded an unequivocal structure (Figure 3) for the 1,2-trans tetralin **4a**.

The nature of the hydrogenolysis products of the lactones **2a–c** suggests that steric factors contributed to the divergence in reaction course from exclusive cis product formation with an unsubstituted phenyl in lactone **2b** to partial trans product for the two lactones **2a** and **2c** containing a methoxy group at the 2′-phenyl position. Ex-

(11) Dannenberg, H.; Laufer, S. *Chem. Ber.* **1954**, *87*, 733.

amination of the crystal structure of lactone **2a** (Figure 1) indicates that if steric factors were operative the 2'-methoxy group would tend to *disfavor* formation of the cis product due to shielding effects on the α-face, assuming that the most favored orientation of the lactone corresponds to the crystal structure. Since this might not be so with the heterogenous mixture of catalyst complex and lactone in solution, a better perception of the solution structures was obtained by NMR experiments. In addition, complete ^{13}C and ^{1}H chemical shift assignments were deduced for several key intermediates and products from the synthetic procedures.

Complete ^{1}H NMR assignments for the aromatic resonances were complicated by extensive overlap of signals. However, by first making ^{13}C assignments it was possible to use the heteronuclear ^{13}C–^{1}H correlation experiment (HETCOR) to aid in ^{1}H assignments. The ^{13}C assignments for aromatic positions 5–8 was facilitated by previous work done on tetraline systems.[12,13] By use of NOE experiments, it was found that tetralin hydrogen H-8 was shifted upfield from that in tetralins previously reported. The upfield shift was explained by the H-8 hydrogen being forced into the shielding portion of the phenyl ring at position 1 of the tetralin system. Such an observation supports the assumption that the X-ray structures of these tetralin derivatives, where the phenyl ring at position 1 was found perpendicular to the aromatic tetralin ring, closely approximates the favored conformation of the lactones in solution.

The spin systems of the aromatic tetralin protons at positions 5–8 were easily isolated from other aromatic hydrogen resonances by use of the COSY experiment. Once the spin system was identified, the ^{1}H assignments were aided by NOE studies. To differentiate between protons 5 and 8, the aliphatic protons at position 4 were irradiated to observe an NOE to the aromatic proton at position 5. The aromatic ring ^{13}C and ^{1}H assignments at position 1 were simplified once the ^{13}C and ^{1}H resonances for positions 5–8 of the tetralin ring were assigned. Again, the NOE experiment was used to irradiate substituents on the ring (methyl and methoxy) to aid in ^{1}H assignments. Comparison of the ^{13}C spectra of the lactones, the tetralin-2-acetic acids, and methyl esters aided in arriving at the ^{13}C assignment at position 1. With the lactones, the aliphatic region of the APT spectrum exhibited a singlet at about 85 ppm that was absent in the corresponding spectra of the tetralin-2-acetic acids and esters. Conversely, a doublet was observed in the APT spectra of the latter tetralins that was absent in the respective lactone spectra.

Differentiating the aromatic methoxy from the ester methyl was simplified by comparison between ester **3b** and carboxylic acid **4a**. In the ^{1}H spectrum of carboxylic acid **4a**, a singlet that integrated for 3 protons was observed at 3.75 ppm. By use of the heteronuclear ^{13}C–^{1}H correlation experiment, this methoxy signal was observed at 55.7 ppm in the ^{13}C spectrum. With methyl ester **3b**, analogous two singlets, each integrating for three protons (at 3.79 and 3.65) ppm, were observed in the ^{1}H spectrum. By comparing the two methoxy signals to the single methyl signal observed for acid **4a**, the 3.65 ppm signal was assigned to the methyl ester.

Use of the heteronuclear ^{13}C–^{1}H correlation experiment also aided in assignment of the ^{13}C resonances. The methylene α to the carbonyl was was easily recognized in each of the compounds studied. Both of these protons showed large (~16 Hz) geminal groupings typical of being adjacent to an sp^2 center with smaller couplings (3–10 Hz) due to the H-2 proton. The other aliphatic protons were easily assigned by the use of the COSY experiment. Good correlation between the configuration and the vicinal $H\text{-}C_1\text{–}C_2\text{-}H$ coupling constant for hydrogenation protucts 3 and 4 was noted. With cis ester **3b**, a smaller coupling constant was observed for the hydrogen on C_1 (5.3 Hz, equatorial–axial) vs the trans (diaxial) product **4a** (8.6 Hz). The preceding NMR assignments should greatly assist in defining the stereochemistry of analogous reaction products.

Verification of the structures assigned to lactone **2a** (cis), 1,2-cis tetralin **3b**, and 1,2-trans tetralin **4a** by X-ray crystallographic analyses confirms the unexpected stereochemical course of this superficially straightforward reaction sequence. In turn, the overall synthetic procedure now provides a stereochemically established and useful route to certain 1,2-cis alkylated tetralins. Reference to the crystal structures and NMR assignments reported here should allow ready assignments of structures to analogous tetralin derivatives.

Experimental Section[14]

2-Bromo-4-methylanisole. Procedure A. A mixture of 2-bromo-4-methylphenol[15] (156 g, 0.84 mol, prepared in 84% yield from 2-bromo-4-methylaniline,[16] in turn obtained from *p*-methylacetanilide in a 73% yield) and 340 mL of water was treated with 33.6 g of sodium hydroxide (0.84 mol). The resulting solution was cooled before adding dimethyl sulfate (102 g, 0.84 mol). The mixture was heated at reflux for 2 h, cooled, and extracted with ether. Removal of solvent from the dried ethereal extracts left a dark oil that was distilled through a 12-in. Vigreux column. The main fraction of pale yellow oil weighed 132 g (79%) and boiled at 156–160 °C (100 nm). The reported boiling point is 126–127 °C (25 mm).[17]

(12) Adamczyk, M.; Watt, D. S.; Netzel, D. A. *J. Org. Chem.* **1984**, *49*, 4226.

(13) Morin, F. G.; Horton, W. J.; Grant, D. M.; Dalling, D. K.; Pugmire, R. J. *J. Am. Chem. Soc.* **1983**, *105*, 3992.

(14) All solvents were redistilled, and ether refers to diethyl ether. Solvent extracts of aqueous solutions were dried over anhydrous sodium sulfate. Ethyl acetate washed alumina (Activity II) was employed for column chromatography. Melting points were taken in open Kimble glass capillaries and are uncorrected. The boiling points are also uncorrected. The infrared spectra were determined with a Baird Associates Double Beam Infrared Spectrophotometer using a cell thickness of 0.1 mm (chloroform solution). Ultraviolet absorption spectra were measured in 95% ethanol solution with Beckman Model DU spectrophotometer connected to a Warren Spectrocord. The microanalyses were performed by Geller Laboratories, Hackensack, NJ, Microanalytical Laboratory of the Max-Planck Institute, Mulheim, Germany, Spang Microanalytical Laboratory, Plymouth, MI, and the Microanalytical Laboratory of Wayne State University. NMR spectra were obtained using a Bruker Am-400 narrow bore spectrometer, operating at 400.13 and 100.62 MHz for ^{1}H and ^{13}C, respectively. Processing and acquisition of data was assisted by use of an Aspect 3000 computer and pulse programmer. All spectra was obtained in deuteriochloroform, with chemical shifts referenced to TMS (0.00 ppm) for ^{1}H experiments, and deuteriochloroform (77.0 ppm) for ^{13}C experiments. The 90° pulse lengths for ^{1}H and ^{3}C were 10 and 7.5 μs, with a line broadening of 0.0 and 3.0 Hz applied, respectively. The ^{1}H–^{1}H COSY and ^{1}H–^{13}C heteronuclear shift correlated spectra were acquired with quadrature detection in the f_2 dimension, sine bell multiplication in f_1 and f_2, and zero-filling in f_1. ^{1}H–^{13}C heteronuclear shift correlated spectra was obtained according to the Bax[33] pulse sequence, with Δ0.5 s, Δ_1 3.3 ms, Δ_2 17 ms, size 4*K*, 128 transients, and 256 increments. ^{1}H–^{1}H COSY was obtained with the standard COSY pulse sequence with phase cycling[34] Δ0.5-s acquisition time, size 2*K*, 16 transients, and 256 increments. ^{1}H–[^{1}H] NOE was obtained using a block size of 16*K*, sweep width of 4800 Hz, 800 transients for each on and off resonance, recovery delay 4.0 s, with decoupling time of 0.5 s used. Mass spectral analyses were performed at Midwest Center for Mass Spectrometry, University of Nebraska, Lincoln, NE, Department of Chemistry. X-ray data collections were accomplished with an Enraf-Nonius CAD4 diffractometer.

(15) Ungnade, H. E.; Orwoll, E. F. *Org. Synth.* **1943**, *23*, 11.

(16) Johnson, J. R.; Sandborn, L. T. *Organic Syntheses*, 2nd ed.; John Wiley and Sons: New York, 1981; Collect. Vol. I, p 111.

(17) Ungnade, H. E.; Orwoll, E. F. *J. Am. Chem. Soc.* **1943**, *65*, 1736.

Procedure B. In this case, the direct bromination of *p*-methylanisole, as described by Dubinin,[18] was found to be satisfactory. The colorless product boiled at 140–142 °C (53 mm) and was obtained in 80% yield. Dubinin reported a boiling point of 126–130 °C (25 mm).

1-Tetralone. The basic decomposition of the peroxide obtained from the air oxidation of tetralin yields a mixture of the corresponding ketone and alcohol along with unreacted tetralin.[19] Fractionation of this mixture through a 30-cm packed column, as described, yielded unreacted tetralin and two fractions boiling at 97–99 °C (2 mm) and 103–108 °C (2 mm). The infrared spectra indicate that both fractions are composed of almost equal mixtures of alcohol and ketone. The established procedure indicates the pure 1-tetralone, boiling at 105–107 °C (2 mm), should have been obtained.

The ketone was obtained essentially free of alcohol by the following method of purification.[20] The ketone–alcohol mixture (292 g) in 380 mL of glacial acetic acid was stirred and treated with 108 g of chromic oxide in 380 mL of 80% acetic acid at such a rate that the temperature did not rise above 50 °C. Stirring was continued for 20 h before the mixture was diluted with 2 L of water and extracted with benzene. Before removal of the solvent, the combined extract was shaken with 5% sodium bicarbonate and then with water. Distillation of the residue through a 6-in. Vigreux column gave a single colorless fraction; weight 219 g, bp 99–102 °C (2 mm).

1,2,3,4-Tetrahydro-1-oxo-2-naphthaleneacetic Acid Methyl Ester (1a). Procedure A. Methyl 1,2,3,4-Tetrahydro-1-oxo-2-naphthaleneglyoxalate[21] (5) was obtained in 83% yield from 1-tetralone and methyl oxalate.[21] Decarbonylation of the glyoxalate with powdered glass in a Claisen flask, followed by distillation directly from the powdered glass, gave a 65% yield of colorless **1,2,3,4-tetrahydro-2-carbomethoxy-1-oxonaphthalene (6).** The product boiled at 135–140 °C (2 mm) and gave a deep violet blue color with ethanolic ferric chloride solution. Buchta[4] reports a bp of 176–177 °C (13 mm).

1,2,3,4-Tetrahydro-1-oxo-2-naphthaleneacetic acid (1b) was prepared in 32% yield from 1,2,3,4-tetrahydro-2-carbomethoxy-1-oxonaphthalene and methyl bromoacetate, as described by Bachmann.[5] The crude product melted at 104–105 °C with sintering from 90 °C (lit.[5] mp 106–108 °C). The sample obtained in this case was almost colorless, while in other attempts, the crude acid was a deep brown soild or oil. The crude acid was readily purified by conversion to its methyl ester and then fractionally distilled as described below. The yield could be increased to 50% by extending the period of acid hydrolysis to 4.5 h.

A solution of the acid (13.5 g) in methanol was treated with an excess of diazomethane. After 30 min at ice-bath temperature the solvents were removed and the residue distilled through a 4-in. Vigreux column. The viscous colorless product weighed 9.3 g (63%) and boiled at 140–141 °C (0.5 mm). The ester slowly crystallized upon standing.

For larger scale methylation the following procedure proved useful. A solution of 1,2,3,4-tetrahydro-1-oxo-2-naphthaleneacetic acid (**1b**, 32 g, 0.16 mol) in benzene (60 mL), methanol (15 g, 0.45 mol), and 5 mL of concentrated sulfuric acid was heated to reflux for 24 h. After being cooled, the reaction mixture was diluted with water and extracted with benzene. The combined benzene extract was washed successively with 1 N sodium hydroxide and water. Removal of solvent left a residue that was distilled through a 4-in. Vigreux column; weight 27 g (79%), bp 140–145 °C (0.7 mm). The colorless viscous oil crystallized upon standing over a period of several hours and melted at 55–57 °C following recrystallization from hexane (lit.[5] mp 55–56.5 °C).

Procedure B. The reagents used in this preferred synthesis of ester **1a** were purified and dried out by the following methods. Pyrrolidine was dried over potassium hydroxide and distilled. The 1-tetralone was dried by azeotropic distillation with benzene. Reagent-grade absolute methanol containing less than 0.1% water was satisfactory. Benzene and methyl bromoacetate were also purified by distillation.

Pyrrolidine (60 g, 0.84 mol) was added to a solution of 1-tetralone (111 g, 0.76 mol) in 300 mL of benzene contained in a 1-L flask equipped with a water separator. The solution was then heated to reflux for 48 h before the benzene was removed, first under atmospheric pressure and then in vacuo. The theoretical volume (13.7 mL) of water was collected over the 48-h period. The dark red enamine that remained after removal of solvent was dissolved in 400 mL of absolute methanol. Next, 113 g of methyl bromoacetate (0.76 mole) was added.[7] Before the methanol was removed and the residue diluted with excess water, the resulting solution was heated at reflux for 65 h. The aqueous mixture was warmed on the steam bath for 30 min. After being cooled, the mixture was extracted with benzene and the benzene extract thoroughly washed with water. The residue obtained, by removal of solvent from the benzene extract, was distilled under reduced pressure through a 6-in. Vigreux column. The fraction boiling at 130–138 °C (0.1 mm) weighed 71 g (42%) and contained the main fraction, which boiled at 135–138 °C (0.1 mm). A forerun of 1-tetralone boiling at 93–94 °C (0.7 mm) weighed 58 g. The yield corrected for recovered starting material amounted to 89%. Crystallization of the product from a previous run from hexane gave a colorless analytical sample, mp 54–56 °C.

Anal. Calcd for $C_{13}H_{14}O_3$: C, 71.54; H, 6.47. Found: C, 71.50; H, 6.57.

The yield was 32% in one experiment in which absolute ethanol was substituted for absolute methanol in the alkylation step. In this case, the reflux period was decreased to 24 h. Enough 1-tetralone was recovered to afford a corrected yield of 71%.

Lactone of 1-Hydroxy-1-(2′-methoxy-5′-methylphenyl)-1,2,3,4-tetrahydro-2-naphthaleneacetic Acid (2a). A solution of 2-bromo-4-methyl anisole (42.8 g, 0.224 mol) in 300 mL of dry ether was shaken with phosphorus pentoxide before slowly being added to 6.05 g of magnesium (0.25 mol) under nitrogen. The magnesium had previously been activated with a few milliliters of the halide solution containing methyl iodide and a few crystals of iodine. The reaction was essentially complete after 3 h at reflux. The Grignard solution was added under nitrogen to a cooled (ice–salt) and stirred solution[22] of 1,2,3,4-tetrahydro-1-oxo-2-naphthaleneacetic acid methyl ester (**1a**, 37 g, 0.16 mol) in 600 mL of dry ether. The dropwise addition took 45 min. The mixture of ethereal solution and precipitated yellow complex was stirred 1 h longer at ice–salt bath temperature and for 2 h at room temperature. Before extraction with ether, the mixture was cooled and treated with ice and 100 mL of 6 N sulfuric acid. Removal of solvent from the ethereal extract left a red oil that was dissolved in 500 mL of methanol. After 100 mL of 2 N sodium hydroxide was added, the solution was heated at reflux for 2 h. The methanol was removed and 200 mL of water added. The dark green aqueous solution was extracted with ether, and 60 mL of 6 N sulfuric acid was added. The resulting red oil was extracted with benzene. Removal of solvent from the dry (sodium sulfate) benzene extracts left an oil that was dissolved in ca. twice its volume of ether. The mixture[23] of lactone and 1,2,3,4-tetrahydro-1-oxo-2-naphthaleneacetic acid (**1b**), which crystallized upon cooling the ethereal solution overnight, weighed 23 g. Another 2.3 g of acid **1b**, melting at 90–95 °C, was obtained by diluting the mother liquors with hexane and allowing crystallization to take place. The crude product was dissolved in benzene and washed with 1 N sodium hydroxide[24] and water. Before the solvent was removed, trituration of the residual oil with hexane yielded 12.5 g (25%) of the pale orange crystalline lactone, mp 174–176 °C.[25] Crystallization from ether afforded a colorless analytical sample of lactone **2a**, mp 174.5–176 °C, λ_{max} 5.65 μm.

Anal. Calcd for $C_{20}H_{20}O_3$: C, 77.90; H, 6.54. Found: C, 77.62; H, 6.78.

Acidification of the basic extracts gave 10 g of acid **1b**, mp 90–95

(18) Dubinin, B. M. *C. R. Acad. Sci. URSS* **1935**, *8*, 263.
(19) Thompson, R. B. *Org. Synth.* **1940**, *20*, 94.
(20) A similar mixture was separated through the oxime: Turner, D. L. *Bull. Soc. Chim. Fr.* **1949**, 439.
(21) Bowden, E. *Org. Synth.* **1930**, *10*, 70.
(22) Solution of the methyl ester can be facilitated by melting (steam bath) the crystalline ester, allowing it to cool, and then adding ether.
(23) In several experiments, the lactone was obtained almost pure at this point and the acid could be recovered as a second crop.
(24) The emulsion that may form during the base extraction is easily broken by adding chloroform.
(25) This method of separation (applied to the freshly acidified red oil) showed that the lactone was not present immediately following acidification and slowly forms upon standing.

°C. The crude yield of lactone, corrected for the amount of acid **1b** recovered, amounted to 39.5%. The crude (red colored) acid **1b** was dissolved in *N*-butyl ether and treated with decolorizing charcoal. After being filtered and cooled, the colorless acid was collected. Repeated recrystallization from ether–hexane gave a pure sample, mp 105–107 °C (lit.[5] mp 106–108 °C).

Anal. Calcd for $C_{12}H_{12}O_3$: C, 70.57; H, 5.92. Found: C, 70.40; H, 6.14.

X-ray Crystal Structure Determination: Lactone from 1,2-*cis*-1-Hydroxy-1-(2′-methoxy-5′-methylphenyl)-1,2,3,4-tetrahydro-2-naphthaleneacetic Acid (2a). Recrystallization of the lactone from heptane–acetone provided colorless prisms suitable for X-ray crystallography. One quadrant of data on a crystal of dimensions ≈ 0.10 × 0.20 × 0.50 mm was collected to a maximum of 2θ = 150° on an Enraf-Nonius CAD-4 diffractometer at 26 ● 1 °C. Crystal data: lactone, $C_{20}H_{20}O_3$, monoclinic, space group $P2_1/n$, with a = 14.576 (5) Å, b = 7.435 (4) Å, c = 15.937 (4) Å, β = 109.438 (21)°, V = 1627.7 (5) Å^3, ρ_o = 1.247 g cm^{-3}, ρ_c = 1.258 g cm^{-3} for Z = 4. The $\omega/2\theta$ scan technique was used with graphite monochromated Cu Kα radiation (λ 1.5418 Å). After Lorentz and polarization corrections, merging of equivalent reflections, and rejection of systematic absences, 2798 reflections ($F_o > 3\sigma(F_o)$) were used in the structure determination. An empirical absorption correction was made using the ψ scan technique.[26] Direct methods were used in the structure determination. All non-hydrogen atom coordinates were revealed in the initial runs from SHELXS-86.[27] Refinement was performed with SHELXTL-PLUS.[28] The hydrogen atom coordinates were calculated at optimum positions and allowed to ride during final stages of refinement. Full-matrix least-squares anisotropic refinement on all non-hydrogen atoms and isotropic temperature factors (U = 0.06) for hydrogens yielded standard crystallographic residuals of R = 0.052, R_w = 0.049. A computer-generated drawing of the lactone is shown in Figure 1.

1-(2′-Methoxy-5′-methylphenyl)-1,2,3,4-tetrahydro-2-naphthaleneacetic Acid (3a and 4a). A solution of the lactone from 1-hydroxy-1-(2′-methoxy-5′-methylphenyl)-1,2,3,4-tetrahydro-2-naphthaleneacetic acid (12 g, 0.039 mol) in 240 mL of warm glacial acetic acid was added to 1.6 g of prehydrogenated 10% palladium–charcoal catalyst in 200 mL of warm glacial acetic acid. The mixture was then stirred and hydrogenated at 65–68 °C for 5 h (or 3 h for 1–3 g of lactone) under a slightly positive hydrogen pressure. The theoretical volume of hydrogen was absorbed during this period. After the catalyst was collected, ca. half of the solvent was removed and the remaining solution cooled. The colorless crystalline product was collected, weight 7.1 g, (58.6%), mp 195–203 °C (purer samples of this isomer were obtained from larger volumes of reaction solvent). Several recrystallizations from glacial acetic acid afforded an analytical sample of the cis isomer **3a**, mp 209–211.5 °C. λ_{max} (log ϵ) 279 (3.51) and 246 (2.73) mμm; λ_{max} 3.38, 3.48 (broad bands), and 5.84 μm.

Anal. Calcd for $C_{20}H_{22}O_3$: C, 77.39; H, 7.14. Found: C, 77.64; H, 7.06.

The remaining solvent was removed from the hydrogenation product, and the crystalline residue was recrystallized from methyl ethyl ketone, weight 2.1 g, (17.3%), mp 159–169 °C. Partial evaporation of the mother liquors, followed by cooling, gave 0.6 g of the trans isomer **4a** as crystals melting at 171–172 °C: HREIMS 310.1572 (M$^+$) for $C_{20}H_{22}O_3$ (calcd 310.1569); λ_{max} (log ϵ) 279 (3.42), and 246 (2.67) mμm; λ_{max} 3.35, 3.45 (broad bands), and 5.81 μm. The NMR data have been recorded in Table I.

Anal. Calcd for $C_{20}H_{22}O_3$: C, 77.39; H, 7.14. Found: C, 77.66; H, 7.19.

Repeated recrystallization from methyl ethyl ketone of the crop melting at 159–169 °C raised the melting point to 160–170 °C. The remaining mother liquors were separated by chromatography as described in the following procedure (B).

1-(2′-Methoxy-5′-methylphenyl)-1,2,3,4-tetrahydro-2-naphthaleneacetic Acid Methyl Ester (3b). Procedure A. The higher melting diastereoisomer of 1-(2′-methoxy-5′-methylphenyl)-1,2,3,4-tetrahydro-2-naphthaleneacetic acid (0.85 g), mp 208–210 °C, was dissolved in tetrahydrofuran and methylated with diazomethane. Removal of solvents left an oily residue that crystallized from hexane as coral-shaped crystals, weight 0.75 g, mp 90–94 °C. Four recrystallizations from hexane gave a pure sample **3b**, mp 101.5–103.5 °C: λ_{max} (log ϵ) 282 (3.60), and 248 (2.78) mμm; λ_{max} 5.75 μm. A slightly higher melting sample of this isomer was obtained by chromatographic purification, mp 105–106.5 °C: HREIMS 324.1723 (M$^+$) for $C_{21}H_{24}O_3$ (calcd 324.1726). The NMR data have been recorded in Table I.

Anal. Calcd for $C_{21}H_{24}O_3$: C, 77.75; H, 7.46. Found: C, 77.45; H, 7.69.

In an analogous manner, a sample of the lower melting diastereoisomer was methylated and crystallized from hexane. An analytical sample of **4b** was obtained as colorless hemispheres, mp 82–83 °C: λ_{max} (log ϵ) 279 (3.58), and 246 (2.83) μm; λ_{max} 5.75 μm.

Anal. Calcd for $C_{21}H_{24}O_3$: C, 77.75; H, 7.46. Found: C, 77.54; H, 7.60.

The pronounced difference in the crystalline appearance of the isomers also made possible a manual separation of the two isomers from a mixture.

Procedure B. The combined mother liquor residues (3.9 g), obtained after separating the isomeric acids by fractional crystallization, as described previously, were dissolved in tetrahydrofuran and methylated with diazomethane. Removal of solvents left a residue that was dissolved in hexane and chromatographed on 120 g of alumina. After removal of solvent from each 150-mL fraction, the resulting oil was dissolved in hexane and allowed to crystallize. The lower melting isomer crystallized as smooth colorless hemispheres and the higher melting one as colorless needle clusters. The weight of recovered isomeric esters amounted to 3.34 g. Fractions 5 and 6 (1.15 g eluted with 2:1 hexane–benzene) gave purest specimens of the 1,2-trans isomer melting at 81.5–83 °C. Pure samples of the 1,2-cis isomer melting from 102–104 to 105–106.5 °C (0.66 g) were obtained from fractions 13–23 (2:1 → 1:1 hexane–benzene).

Fractions 9 and 10 (1.15 g) were combined and dissolved in a mixture of ethanol (20 mL) and 2 N sodium hydroxide (4 mL). After 2 h at reflux, the solvent was removed. The residue was diluted with water followed by acidification and chloroform extraction. Removal of solvent from the organic extract gave the crystalline 1,2-trans acid **4a**, mp 172–174 °C. One recrystallization from methyl ethyl ketone raised the melting point to 173–174.5 °C; weight 0.73 g.

Fractions 17–24 (0.58 g) were combined and saponified as described for fractions 9 and 10. The recovered crystalline 1,2-cis acid **3a** melted at 209–211 °C (0.4 g). The mixture melting points of these isomeric acids and the corresponding ones, obtained by fractional crystallization, were undepressed.

X-ray Crystal Structure Determinations for 1,2-Cis Methyl Ester 3b and 1,2-Trans Carboxylic Acid (4a). The following crystal summary was recorded for 1,2-cis methyl ester **3b**: $C_{21}H_{24}O_3$, monoclinic, space group $P2_1/n$, with a = 6.233 (1) Å, b = 11.658 (1) Å, c = 24.265 (2) Å, β = 90.252 (8)°, V = 1763.3 (5) Å^3, ρ_o = 1.212 g cm^{-3}, ρ_c = 1.222 g cm^{-3} for Z = 4. One quadrant of data on a crystal of dimensions ca. 0.20 × 0.25 × 0.20 mm was collected to a maximum of 2θ = 150 °C on an Enraf-Nonius CAD-4 diffractometer at 26 ● 1 °C. The $\omega/2\theta$ scan technique was used with graphite monochromated Cu Kα radiation (λ 1.5418 Å). After Lorentz and polarization corrections, merging of equivalent reflections, and rejection of systematic absences, 2417 reflections ($F_o > 3\sigma(F_o)$) were used in the structure determination. No absorption corrections were made. Direct methods were used in the structure determination. All non-hydrogen atom coordinates were revealed in the initial solution from both SHELXS-86[27] and MULTAN-80.[29] Refinement was performed with CRYSTALS.[30] The

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(27) Sheldrick, G. M. *SHELXS-86, A Program for Solution of Crystal Structure from Diffraction Data*; Institut fur Anorganische Chemie der Universitat Gottingen, Gottingen, FRG, 1986.

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hydrogen atom coordinates were calculated at optimum positions. Full-matrix least-squares anisotropic refinement on all non-hydrogen atoms, with hydrogen atom coordinates and isotropic temperature factors (U = 0.06) fixed in the final cycle yielded standard crystallographic residuals of R = 0.064, R_w = 0.079. A computer generated drawing of methyl ester **3b** is shown in Figure 2.

Recrystallization of the minor, 1,2-trans carboxylic acid, isomer **4a** from glacial acetic acid gave colorless crystals, mp 173–174.5 °C, suitable for X-ray crystallography. Crystal data: compound **4a**, $C_{20}H_{22}O_3$, triclinic, space group $P\bar{1}$, with a = 6.747 (1) Å, b = 9.702 (1) Å, c = 13.211 (2) Å, α = 89.814 (12)°, β = 81.726 (12)°, γ = 81.452 (11)°, V = 846.1 (5) Å^3, ρ_o = 1.190 g cm^{-3}, ρ_c = 1.218 g cm^{-3} for Z = 2. One hemisphere of reflections on a crystal of dimensions ca. 0.35 × 0.40 × 0.20 mm was collected to a maximum of 2θ = 150° at 26 ± 1 °C. An empirical absorption correction on the data was made utilizing a ψ scan technique.[26] A total of 2754 reflections ($F_o > 3\sigma(F_o)$) were used for structure determination and refinement. Direct methods solution with MULTAN and refinement in a manner analogous to that described for the major, 1,2-cis methyl ester isomer **3b** resulted in residuals of R = 0.074 and R_w = 0.077, respectively. A computer-generated drawing depicting the 1,2-trans isomer **4a** appears in Figure 3.

1-(2′-Methoxy-5′-methylphenyl)-2-naphthaleneacetic Acid Methyl Ester (9a). The higher melting cis isomer of 1-(2′-methoxy-5′-methylphenyl)-1,2,3,4-tetrahydro-2-naphthaleneacetic acid (**3a**, 2.0 g, 0.0065 mol) was converted to the methyl ester as described above. The ester was intimately mixed with sulfur (0.44 g, 0.014 mol) in a test tube equipped with an outlet tube leading to a solution of zinc chloride. The tube was placed in a metal bath at 200 °C and this temperature raised to 260 °C over a 10-min period. Liberation of hydrogen sulfide began at ca. 240 °C. After 20 min at 260–265 °C, the liberation of hydrogen sulfide subsided. The dark, foul-smelling residue was partially soluble in 3:1 hexane–benzene, and the resulting solution was chromatographed on 60 g of alumina. The remaining residue was shaken with each new solvent mixture until it was completely added to the alumina in 1:2 hexane–benzene. Each fraction was eluted with 75 mL of solvent and obtained as an oil following removal of solvent.

Fractions 9–18 (1:1 to 1:2 hexane–benzene) crystallized from hexane, and the light straw colored product weighed 0.62 g (30%). Recrystallization from hexane gave pure colorless crystals of methyl ester **9a**, mp 70–72 °C: λ_{max} (log ϵ) 227 and 283 (5.23 and 4.28) μm; λ_{min} 252 μm (2.85); λ_{max} 5.70 μm.

Anal. Calcd for $C_{21}H_{20}O_3$: C, 79.73; H, 6.29. Found: C, 78.70; H, 6.45.

1-(2′-Methoxy-5′-methylphenyl)-2-naphthaleneacetic Acid (9b). Methyl ester **9a** (0.59 g) was heated for 2 h in a refluxing mixture of ethanol (25 mL) and 2 N sodium hydroxide (4 mL). After removal of solvent, the residue was diluted to 150 mL with water and acidified by the slow addition of 6 N sulfuric acid. The colorless powdery precipitate was collected and dried, weight 0.51 g, mp 60–70 °C. The acid crystallized over a long period at ice-chest temperatures as colorless needles from heptane, mp 133–135.5 °C. However, recrystallization was easily accomplished, and a pure sample of methyl ester **9b** melted at 134–135.5 °C: λ_{max} (log ϵ) 227 and 283 (4.48 and 3.61) μm; λ_{min} 250 (2.18) μm; λ_{max} 3.20, 3.39 (broad bands) and 5.80 μm.

Anal. Calcd for $C_{20}H_{18}O_3$: C, 78.41; H, 5.92. Found: C, 78.22; H, 6.19.

Lactone of 1-Hydroxy-1-phenyl-1,2,3,4-tetrahydro-2-naphthaleneacetic Acid (2b). The following procedure is a modification of one described by Dannenberg and Laufer.[9] A 25% yield was reported as the best of several runs. The Grignard solution, prepared from bromobenzene (10.1 g, 0.064 mol) and magnesium (1.54 g, 0.064 mol) in dry ether (40 mL), was added under nitrogen over a 30-min period to cooled (ice–salt) and stirred solution of ester **1a** (10.0 g, 0.0459 mol) in 100 mL of dry ether. The remainder of the procedure was carried out as described for preparing the lactone **2a**. In this case, some crystalline material formed following acid hydrolysis of the Grignard reaction mixture and was readily collected by adding a chloroform extraction step to the procedure. The crude, pale gray, crystalline lactone weighed 2.03 g (17%) and melted at 176–178 °C (lit.[9] mp 180–181 °C). Recrystallization from chloroform–ether did not change the melting point. The tan crystals of recovered 1,2,3,4-tetrahydro-1-oxo-2-naphthaleneacetic acid weighed 2.15 g and melted at 90–95 °C. The yield of lactone, corrected for recovered starting material, amounted to 22%. For the NMR summary refer to Table I.

***cis*-1-Phenyl-1,2,3,4-tetrahydro-2-naphthaleneacetic Acid Methyl Ester (3d).** Lactone **2b** (1.5 g, 0.0057 mol) in 40 mL of warm glacial acetic acid was added to a warm suspension of prehydrogenated 10% palladium–charcoal catalyst (0.23 g) in 40 mL of glacial acetic acid. The mixture was stirred at 65–68 °C for 3 h under a slightly positive hydrogen pressure. The catalyst was collected and solvent removed in vacuo. A solution of the residue in tetrahydrofuran was treated with diazomethane. The methyl ester (1.2 g, 75.5%) was dissolved in 19:1 hexane–benzene and chromatographed in 36 g of alumina. Elution with 160 mL of the original solvent gave only a trace of product. The column was eluted with 40-mL portions of 9:1 hexane–benzene. Product from the first 19 fractions (0.85 g) crystallized from hexane as colorless needles and all melted between 52 and 60 °C. A pure sample of ester **3d** from fraction 7 melted at 58–59.5 °C, λ_{max} 5.75 μm. The infrared spectra of three widely separated fractions (3, 10, and 17) were found to be identical.

Anal. Calcd for $C_{19}H_{20}O_2$: C, 81.40; H, 7.19. Found: C, 81.19; H, 7.42.

Fractions of 4–6 and 8 (0.24 g) were saponified to ***cis*-1-phenyl-1,2,3,4-tetrahydro-2-naphthaleneacetic acid (3c)** as described in the preparation of acid **3a**. Recrystallization from glacial acetic acid gave a solvate melting at 90–135 °C. The long colorless needles melted at 134–136 °C (lit.[9,31] mp 140–140.5 °C and 138–139 °C) after drying in vacuo at 100 °C. Fractions 13–16 (0.08 g) were saponified in a similar manner, and recrystallization of the acid from glacial acetic acid gave a solvate melting at 75–110 °C. After being dried in vacuo at 100 °C, the long colorless needles melted at 135–137.5 °C. A mixture melting point of the dry acids was not depressed. Table II contains an NMR analysis for carboxylic acid **3c**.

Lactone of 1-Hydroxy-1-(2′-methoxyphenyl)-1,2,3,4-tetrahydro-2-naphthaleneacetic Acid (2c). *o*-Bromoanisole was prepared in 72% yield by treating *o*-bromophenol with dimethyl sulfate as described by Holmberg,[32] bp 84–86 °C (8 mm). The reported boiling point is 98–100 °C (8 mm). The Grignard solution, prepared from magnesium (1.54 g, 0.064 mol) and *o*-bromoanisole (12 g, 0.064 mol) in 40 mL of dry ether, was added (rapid stirring) under nitrogen over a 15-min period to a cooled (ice–salt) solution of ketone **1a** (10 g, 0.0459 mol). The procedure was completed employing the method described for preparing lactone **2a**. Here a colorless compound crystallized from the refluxing saponification reaction mixture. After one recrystallization from chloroform–ether, it melted as 230–235 °C and weighed 0.5 g. Since the infrared spectrum of this material did not contain a carbonyl or hydroxyl band, it was not further investigated. The lactone crystallized almost at once from the ethereal (or when necessary from ether–hexane) solution of reaction products; weight 3.03 g (23%), mp 198–201 °C. Two recrystallizations from chloroform–ether afforded pure colorless crystals, mp 199–201.5 °C: λ_{max} 5.60 (br) μm. For the NMR summary see Table I.

Anal. Calcd for $C_{19}H_{18}O_3$: C, 77.53; H, 6.16. Found: C, 77.46; H, 6.21.

A second crop from the ethereal solution of reaction products yielded 2.45 g of recovered reddish brown acid **1b**, mp 90–95 °C. The yield of lactone amounted to 32% after correction for the recovered 1-tetralone-2-acetic acid.

1-(2′-Methoxyphenyl)-1,2,3,4-tetrahydro-2-naphthaleneacetic Acid (3e and 4e). Lactone **2c** (2.0 g, 0.00679 mol) in 70 mL of warm glacial acetic acid was added to a warm suspension of prehydrogenated 10% palladium–charcoal catalyst (0.27 g) in

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40 mL of glacial acetic acid. The mixture was then warmed to 65–68 °C and stirred for 5 h under a slightly positive pressure of hydrogen. After the catalyst was collected, the solution was allowed to stand at room temperature overnight. The colorless crystalline product (0.38 g, 19%) was collected and found to melt at 225–228 °C. An analytical sample of the cis carboxylic acid **3e** recrystallized from glacial acetic acid melted at 225–226 °C: λ_{max} 3.41 (br) and 5.89 μm.

Anal. Calcd for $C_{19}H_{20}O_3$: C, 77.00; H, 6.80. Found: C, 77.05; H, 6.86.

Removal of ca. 70 mL of solvent from the mother liquors gave 0.83 g (41%) of product melting at 222–225 °C (sintering from 210 °C). The remaining solvent was removed from the mother liquors and the resulting residue converted to its methyl esters as described in the following procedure. Isolation of the second diastereoisomeric acid is also described in the methylation procedure.

1-(2′-Methoxyphenyl)-1,2,3,4-tetrahydro-2-naphthaleneacetic Acid Methyl Ester (3f and 4f). The mother liquor residue, obtained following preferential crystallization of acid **3e**, was dissolved in tetrahydrofuran and treated with diazomethane. Removal of solvents left an oil (1 g) that was dissolved in 2:1 hexane–benzene and chromatographed on 30 g of alumina. The column was eluted with 22 30-mL portions of 2:1 hexane–benzene. Fractions 5–17 (0.84 g) were crystallized from hexane. The colorless needle clusters from fractions 5–8 (0.38 g, 18%) melted over a 1–3 °C range between 60 and 68 °C. An analytical sample of cis ester **3f** from fraction 5 recrystallized from pentene and melted at 64.5–66 °C, λ_{max} 5.73 μm.

Anal. Calcd for $C_{20}H_{22}O_3$: C, 77.39; H, 7.14. Found: C, 77.37; H, 7.33.

Fractions 5–8 were saponified as described for preparation of carboxylic acid **3a**, and the product was recrystallized from acetic acid–water. The first crop of crystals melted at 209–217 °C. Three more recrystallizations from glacial acetic acid–water raised the melting point to 226–228 °C. This diastereoisomer was identical with the isomer (**3e**, 1,2-cis) described above. Identity was established by mixture melting point comparison. A second crop of crystals (0.06 g, 3%) from the original glacial acetic acid–water solution melted at 113–116 °C. Recrystallization from acetone–hexane gave a pure sample of the lower melting (1,2-trans) diastereoisomer of **1-(2′-methoxyphenyl)-1,2,3,4-tetrahydro-2-naphthaleneacetic acid (4e)** as colorless parallelograms, mp 122–123 °C, λ_{max} 3.41 (br) and 5.84 μm.

Anal. Calcd for $C_{19}H_{20}O_3$: C, 77.00; H, 6.80. Found: C, 76.58; H, 6.88.

The colorless crystals from fractions 15–17 (0.07 g) melted over wide ranges between 90 and 112 °C. The crystalline material from fractions 9–14 was composed of approximately equal amounts of both isomers. Fractions 15–22 (0.17 g) were saponified as described in the preceding experiment, and the resulting acid weighed 0.05 g (2%). A pure sample of this diastereoisomer (**4e**, 1,2-trans) was converted to its methyl ester with diazomethane. The resulting colorless oil (methyl ester **4f**) crystallized from pentane, mp 112–114 °C, λ_{max} 5.73 μm.

Anal. Calcd for $C_{20}H_{22}O_3$: C, 77.39; H, 7.14. Found: C, 77.78; H, 7.23.

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Registry No. **1a**, 135107-75-4; **1b**, 135107-74-3; **2a**, 135107-76-5; **2b**, 135107-84-5; **2c**, 135107-83-4; **3a**, 135107-77-6; **3b**, 135107-79-8; **3c**, 135107-82-3; **3d**, 135107-85-6; **3e**, 135107-87-8; **3f**, 135107-88-9; **4a**, 135107-78-7; **4b**, 135107-80-1; **4e**, 135107-86-7; **4f**, 135107-89-0; **5**, 135107-73-2; **6**, 125117-36-4; **9a**, 135107-81-2; **9b**, 135144-17-1; 2-bromo-4-methylanisole, 22002-45-5; 2-bromo-4-methylphenol, 6627-55-0; *p*-methylanisole, 104-93-8; 1-tetralone, 529-34-0; methyl oxalate, 553-90-2; pyrrolidine, 123-75-1; *o*-bromoanisole, 578-57-4; bromobenzene, 108-86-1.

Supplementary Material Available: Tables of atomic coordinates, bond lengths and angles, anisotropic displacement coefficients, and thermal parameters for the lactone of **2a** and **3a** and **4a** (19 pages). Ordering information is given on any current masthead page.