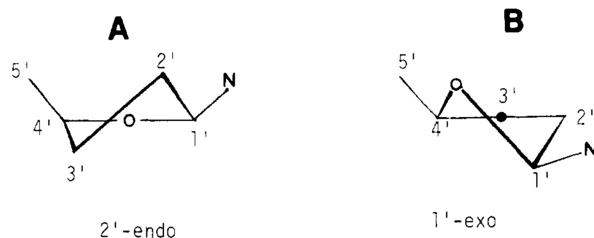
nonprotonated carbon signals are detected in this experiment as shown in Figure 2Cc. We can assign the signals at 155.6, 148.9, and 120.4 ppm to the carbon resonances of C-6, C-4, and C-5, respectively, on the basis of the NMR data in solution. The remaining peaks at 138.6 and 155.6 ppm can thus be designated to C-8 and C-2, respectively (Table I).

All the guanine carbons of guanosine can also be measured by the same approach (Figure 2D). The crystallographic analysis of guanosine showed the presence of two molecules (A and B) in a unit cell.[16] The ribose ring of



molecule A assumes a C-(2′) endo conformation whereas that of molecule B assumes an unusual C(1′) exo conformation. This conformational difference was disclosed by the splittings of the C-2′ (76.7 and 72.9 ppm) and C-3′ (79.2 and 76.7 ppm) signals in the solid-state NMR spectrum of guanosine. Further interpretation of the observed chemical shift change in terms of a specific variation in conformation must await the results from additional studies on the related compounds.

From our preliminary data, it appears that solid-state NMR can be an extremely useful tool to study the conformations of ribose in the solid state since the ^{13}C NMR demands on the proper size and form of crystal is much less stringent. It can at least furnish the X-ray crystallographer a very valuable starting point for the refinement of molecular structure. We are unable at present to specially correlate the solid-state NMR data with the features of base-pairing and base-stacking of nucleosides because of the limited resolution in the region of the base carbon resonances. This is in part ascribed to the residual ^{13}C–^{14}N dipolar interaction.

One of the unique advantages of solid-state NMR is that it enables one to study the molecules that are insoluble or denatured in solution. This is particularly important in studying biological macromolecules and intact tissues. We measured the ^{13}C natural-abundance spectrum of Torula yeast RNA (Figure 4). Compared with the spectrum in solution,[17] it takes less time to acquire natural-abundance carbon signals of RNA in the solid state. But the resolution is relatively too poor to provide much specific information. It may therefore be required to prepare a specific stable isotope-labeled compound by chemical or biochemical methods for obtaining more specific structure information.

Experimental Section

The high-resolution solid-state ^{13}C NMR spectra were all obtained on either a Bruker CXP-100 or a Bruker CXP-200 instrument, both equipped with Z32DR ^{13}C-MASS Supercon magnet probe heads for proton-enhanced magic angle spinning experiments (CP/MAS). Samples were carefully packed in Andrews-type rotors made from boron nitride (body material) and Kel-F (spinner head material). These rotors, constructed in this laboratory, will hold approximately 200 milligrams of material. The spinning speeds ranged from 3.2 to 3.6 KHz which was sufficient to suppress any unwanted spinning side bands found in these types of biomaterials. All chemical shifts are expressed externally referenced to the ^{13}C resonance of Me_4Si. The actual referencing material used was hexamethylbenzene, either periodically mixed with the sample or run separately in the rotor prior to running the sample alone. The high-field peak of solid hexamethylbenzene is assumed to be at 17.6 ppm downfield from Me_4Si. The cross-polarization contact times ranged from 1.25 to 3.0 ms and the recycle times from 1 to 2 s. These were determined experimentally for best sensitivity results for each sample. Each spectra resulted from averaging as little as 10 000 and as much as 60 000 scans, depending upon sample sensitivity. The dipolar-dephased data were obtained by using a 50 μs delay. This particular delay period seems to be optimal for obliterating all methine and methylene carbon resonances in the spectra of these types of compounds.

All nucleosides and the Torula yeast RNA were obtained from Sigma Chemical Co. The RNA was purified according to the procedures previously described.[17]

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Registry No. Cytidine, 65-46-3; uridine, 58-96-8; adenosine, 58-61-7; guanosine, 118-00-3.

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Synthesis and Properties of the Seven Isomeric Phenols of Dibenz[*a*,*h*]anthracene

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The seven possible monohydroxy derivatives of dibenz[*a*,*h*]anthracene (**4a–g**) were synthesized by using the reductive cyclization of *o*-naphthoylnaphthoic acids with hydroiodic acid–red phosphorus. The mass, ^1H NMR, and UV spectral properties are discussed in detail as a means of identifying metabolically formed phenols of dibenz[*a*,*h*]anthracene.

Hydroxy derivatives of polycyclic aromatic hydrocarbons (PAH) were the first observed metabolites of this class of chemical carcinogens.[1] Phenols of PAH can be metabolically formed either by direct hydroxylation or by no-

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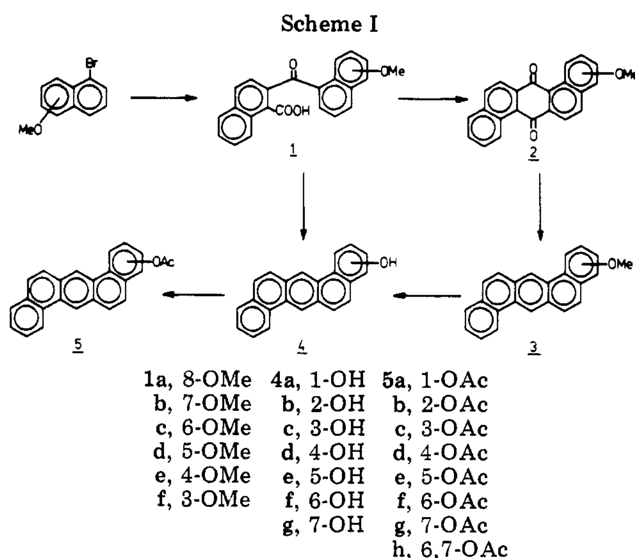
Scheme I



nenzymic rearrangement of the primarily formed arene oxides.[2,3] The position of the hydroxy group consequently provides insight into the regiospecificity of the oxidative attack by the monooxygenase system. Phenols of PAH can also be further metabolized to compounds of higher biological activity that covalently bind to cellular macromolecules[4] and could be ultimate carcinogens of PAH.

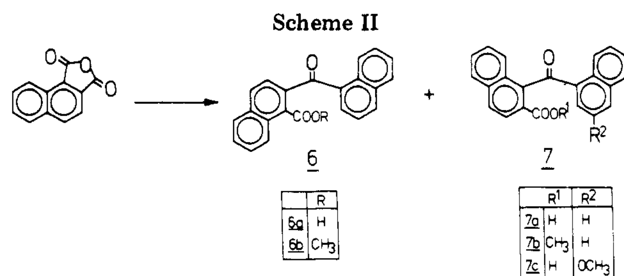
For the investigation of phenol formation and phenol metabolism of a PAH, therefore, the complete series of all possible phenols of this PAH are needed as reference compounds. All twelve phenols of benzo[*a*]pyrene[5] and the six phenols of benzo[*e*]pyrene[6] as well as most of the twelve phenols of benz[*a*]anthracene[7] have been synthesized. For investigations concerning the metabolism and biological activity of dibenz[*a*,*h*]anthracene (DBA), we needed all seven possible monohydroxy derivatives of this PAH.

Attempts to prepare these phenols started in 1931 when 7-hydroxy-DBA was synthesized by Cook[8] and were completed in 1980 when Lee and Harvey[9] prepared 3-hydroxy-DBA. Although all seven phenols were then synthetically available the complexity and/or the low yield of most syntheses did not allow a convenient preparation of larger quantities of the seven DBA phenols. Our goal was, therefore, to develop a generally applicable high-yield method for the synthesis of all DBA phenols.

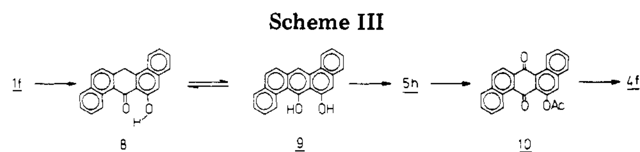
Results and Discussion

Synthesis. The synthetic pathway to the DBA phenols (Scheme I) starts with the addition of the Grignard reagent from 1-bromomethoxynaphthalene to 1,2-naphthalic anhydride resulting in the formation of the methoxy keto acid **1**. In the classic synthesis by La Budde and Heidelberger[10]

Scheme II



Scheme III



1 is cyclized to the 7,14-quinone **2**, which is reduced to the methoxy-DBA **3** and cleaved to form the DBA phenol **4**. The last three steps afford very low yields, making this approach not feasible for the preparation of larger quantities of the DBA phenols. Our observation that *o*-naphthoylnaphthoic acids can be easily transformed to dibenzanthracenes by reductive cyclization with hydroidic acid–red phosphorus,[11] however, circumvented the problem and allowed the convenient, high-yield converson of **1** directly to **4**. To facilitate purification the air-sensitive phenols were transformed to their acetates **5**.

The reaction sequence was checked by using 1-bromonaphthalene (Scheme II) in order to establish the optimal reaction conditions for the formation of the keto acids and for their reductive cyclization. Upon addition of 1-bromomagnesium naphthalene to 1,2-naphthalic anhydride, either of its two carbonyl functions could be attacked by the Grignard reagent, leading to a mixture of keto acids **6a** and **7a**. From 3-methylphthalic anhydride[12] and other ortho-substituted phthalic anhydrides it is known that Grignard reagents add preferentially to the sterically less hindered carbonyl function at C-1, which would correspond to C-2 in 1,2-naphthalic anhydride.

Addition of 1-bromomagnesium naphthalene to 1,2-naphthalic anhydride led indeed to a mixture of **6a** and **7a**, and their ratio was influenced by reaction conditions. While under the originally described conditions[10,13] (Et_2O, benzene, reflux) a mixture of 82% **6a** and 18% **7a** was obtained, a change in the conditions described by Braun[14] (THF, TMEDA, −70 °C) led to a mixture that contained just 4% **7a** besides the desired **6a**. The ratio of **6a**/**7a** could not be determined directly but was quantitated by GLC of the methyl esters **6b** and **7b**. In cases of the methoxy keto acids **1a–f**, the presence of the undesired isomer could be determined simply by ^{1}H NMR spectroscopic comparison of the intensities of the methoxy signals of both isomers. Again the temperature of the Grignard reaction was the important factor influencing regioselectivity; e.g., a mixture of 74% **1f** and 26% **7c** was obtained at +50 °C, while lowering of the temperature to −70 °C resulted in a mixture of 95% **1f** and 5% **7c**. Besides providing higher regioselectivity, the low reaction temperature led also to higher yields of keto acids. The yields of 75–82% obtained at −70 °C contrast favorably with the yields of 19–56% obtained when the Grignard reagent was

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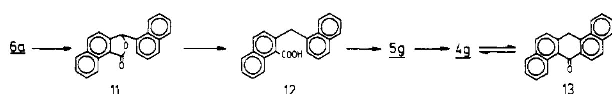
Table I. Ultraviolet Absorption Data for the Phenols of Dibenz[a,h]anthracene

compd	position of substituent	abs max (logarithms of mol ext coeff),[a] nm (log ϵ_{max})							
4a	1	281 (4.86)	292 (5.12)	312 (4.41)	325 (4.54)	334 (4.44)	349 (4.36)	378 (3.76)	399 (3.86)
4b	2	275[b]	292 (4.89)	298 (4.89)	323 (4.28)	339 (4.10)	356 (4.06)	378 (3.30)	400 (3.24)
4c	3	278 (4.58)	291 (4.81)	303 (5.06)	322 (4.33)	338 (4.17)	352 (3.78)	376 (2.98)	397 (2.92)
4d	4	282 (4.78)	292 (5.00)	300[b]	329 (4.31)	335 (4.33)	351 (4.26)	379 (3.68)	400 (3.74)
4e	5	272 (4.66)	294 (4.93)	301 (4.93)	321 (4.28)	338 (4.25)	355 (4.27)	387 (3.40)	409 (3.43)
4f	6	277[b]	296 (4.81)	303[b]	321 (4.17)	341[b]	358 (3.86)	378[b]	400 (3.08)
4g	7	280 (4.65)	291 (4.94)	302 (5.08)	321 (4.04)	345 (4.04)	362 (4.01)	382 (3.76)	404 (3.78)

[a] Spectra were taken in ethanol at concentrations of 6.8×10^{-6} and 6.8×10^{-5} mol·L^{-1}, respectively. [b] Exact extinction coefficient cannot be given because of absorption shoulder.

Scheme IV



added to the 1,2-naphthalic anhydride in boiling benzene.[10,13]

Reductive cyclization of keto acids **1a–e** with hydroiodic acid–red phosphorus in boiling glacial acetic acid under the conditions described[11] afforded smoothly the phenols **4a–e**, which were acetylated and purified by column chromatography and recrystallization to give the acetates **5a–e** in 62–71% overall yield from the keto acids **1a–e**.[15] If phenols were needed, the acetates were cleanly cleaved by NaOMe-catalyzed methanolysis to give the DBA phenols **4a–e** in 85–95% yield. These results demonstrate the broad usefulness of reductive cyclization of keto acids with hydroiodic acid–red phosphorus.[11]

Reductive cyclization and acetylation of **1f** under the same conditions as described above yielded not the desired 6-acetoxy-DBA **5f** but a diacetate identified as 6,7-diacetoxy-DBA **5h**. This surprising result can be explained by the proposed reaction mechanism[11] of the reductive cyclization with hydroiodic acid–red phosphorus. According to this mechanism **1f** is transformed to **8** (Scheme III), which is stabilized by internal hydrogen bonding, and therefore, resists further reduction to **4f**. Since **8** probably takes part in an anthrone–anthrol equilibrium, acetylation of **8** and/or the mixture of **8** and **9** leads to the diacetate **5h**. An attempt to remove the 7-acetoxy group in **5h** with HI–AcOH, as described for the reduction of 7-acetoxybenz[a]anthracene to benz[a]anthracene[16] failed. However, when **5h** was first transformed to the quinone **10**, reduction with HI–AcOH to 6-hydroxy-DBA **4f** could be achieved.

For the synthesis of 7-hydroxy-DBA **4g** (Scheme IV) the keto acid **6a** was transformed to the lactone **11**, with hydroiodic acid–red phosphorus.[11] Reductive cleavage to the (naphthylmethyl)naphthoic acid **12** was achieved with zinc–acetic acid–hydrochloric acid,[13] while other methods described in the literature for this transformation proved marginally or not successful.[17–19] Acid **12** can be cleanly cyclized to 7-acetoxy-DBA **5g** by zinc chloride in acetic acid–acetic anhydride under the conditions described for the preparation of 7-acetoxy benz[a]anthracene.[20]

Cleavage of 7-acetoxy-DBA **5g** by NaOMe-catalyzed methanolysis afforded 7-hydroxy-DBA **4g**. It is known that phenols such as **4g** can take part in an anthrol–anthrone equilibrium.[21] However, no benzylic protons at C-14 (proof of the anthrone structure **13**) were detected by ^{1}H NMR in acetone or Me_2SO. The IR spectrum of a KBr pellet of **4g** showed no C=O stretching absorption band in the region of 1870–1540 cm^{-1} which would indicate the presence of the keto tautomer **13**. The UV spectrum of **4g** (Table I) showed a close similarity to the UV spectra of the other DBA phenols. All spectral evidence, therefore, leads to the conclusion that 7-hydroxy-DBA exists mainly in the phenolic form.

Spectral and Chromatographic Properties. Mass spectra and ^{1}H NMR spectra of the DBA phenols and their acetates as well as UV spectra of the phenols were recorded and compared to find ways to distinguish between the individual isomers. Only the successful resolution of this problem will then allow positive identification of metabolically formed phenols of DBA. This task has not yet been accomplished.[22,23]

Mass spectra of phenol acetates show the molecular ion at m/e 336, which eliminates the neutral molecule ketene to give the phenol at m/e 294. The next fragmentation step consists in loss of 29 mass units, typical for phenols,[24] which leads to a fragment ion at m/e 265. The only prominent peaks in the mass spectra of the phenols are the molecular ion and the fragment ion M − 29. The intensities of all other singly charged ions account for less than 10% of the total. The mass spectra of the isomeric phenol acetates and phenols of DBA are too similar to provide a means for distinguishing between isomers. The relatively high intensity of the fragment ion at m/e 265 in the cases of the 5- and 6-isomers seems, however, to be

(15) Cyclization of the crude keto acids **1** is expected to result in 4–5% of dibenz[a,j]anthracene derivatives as impurity in the DBA phenols **4**. Since dibenz[a,j]anthracene and its derivatives are much more soluble in organic solvents than the isomeric DBA and its corresponding derivatives (Platt, K. L.; Frank, H., unpublished results), recrystallization removes the derivatives of dibenz[a,j]anthracene that remain in the mother liquor. GLC analysis of the purified phenol acetates **5a–g** as well as HPLC analysis of the phenols **4a–g** confirmed the absence of the corresponding dibenz[a,j]anthracene isomers and hence the high purity of the DBA derivatives.

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typical for the K-region[25,26] phenols of DBA.

The ^{1}H NMR spectra of DBA[27] and its phenol acetates and phenols are characterized by the position of the bay-region[28,29] hydrogens H_1, H_7, H_8, and H_{14}, which appear at the lowest field due to their repulsive van der Waals interaction[29,30] and edge deshielding by the aromatic ring in the bay position.[31] Introduction of acetoxy or hydroxyl groups into DBA is generally recognized in the 60-MHz ^{1}H NMR spectra by the signal of the ortho hydrogen in the same ring, which is shifted upfield from the edge of the aromatic region. Signals of hydrogens at the peri position to a hydroxyl group appear between the edge of the aromatic region and the bay region protons as a result of their characteristic downfield shifts.[31] A further significant downfield shift is observed in the 1- and 7-substituted DBA for the bay region hydrogens H_{14} and H_8, respectively. In the case of the phenol acetates this shift is about 0.4 ppm, whereas in the case of the phenols it increases to about 1.1 ppm. These results are consistent with ^{1}H NMR investigations of the isomeric phenols of other polycyclic aromatic hydrocarbons.[5-7] The spectral properties of the DBA phenol acetates and phenols as determined by ^{1}H NMR spectrometry can, therefore, be used to distinguish between isomers; this is especially true in the case of the phenols, where the spectral differences are even more pronounced than in the case of the phenol acetates.

For the identification of DBA phenols that are metabolically formed the applicability of ^{1}H NMR spectrometry is usually limited due to the small amount of metabolites available. Therefore, UV spectra of the phenol acetates and phenols of DBA were recorded. While the UV spectra of the individual isomeric phenol acetates are indistinguishable from the UV spectrum of the parent hydrocarbon, the UV spectra of the phenols (Table I) show distinct differences among the isomers. These differences are not so much based on the positions of the absorption maxima, which are indeed very similar with all phenols, but on the typical shape of the UV spectra of different isomers. It seems, therefore, possible to identify metabolically formed phenols of DBA by their UV spectra provided the phenolic metabolites can be completely separated by chromatography.

Reversed-phase HPLC separation of the seven synthetic phenols resulted in two unresolved peaks, with the 2- and 3-phenols contained in the first peak and the 1-, 4-, 5-, 6-, and 7-phenols in the second.[32] From this observation and the chromatographic results obtained with the phenols of anthracene,[33] phenanthrene,[33] benz[*a*]anthracene,[5] 5-methylchrysene,[34] and benzo[*a*]pyrene,[5] we conclude that the isomers in which the hydroxyl group correspond to the β position in naphthalene generally elute from a reversed-phase column first. Complete separation of the DBA-phenols could be achieved[32] by optimizing the selectivity of the mobile phase[35] with THF as the modifier.[36]

Biological Studies. Phenols of DBA have been found to be principal metabolites of this carcinogenic aromatic hydrocarbon formed in vitro[22,23] as well as in vivo.[1] Our metabiolic studies indicate that the 2- and the 4-phenol of DBA are the main microsomal metabolites formed in rat liver.[32] We are presently investigating the biological activity of the seven isomeric phenols of DBA. Mutagenicity tests with use of different strains of histidine-dependent *Salmonella typhimurium* showed that all phenols of DBA were mutagenic after activation with the postmitochondrial fraction of rat liver.[32] The mutagenic potency, however, differed among isomers with the 5-OH DBA being comparable in its biological activity to *trans*-3,4-dihydroxy-3,4-dihydro-DBA, one of the proposed proximate mutagenic and carcinogenic metabolites of DBA.[37] The 1-, 2-, and 3-phenols showed mutagenicities similar to that of DBA itself. The other phenols were less active.

Experimental Section

General Methods. Hydroiodic acid (57%) stabilized with hypophosphoric acid was supplied by Riedel-deHaen, Seelze, FRG. Mass spectra were obtained with a Varian CH7A mass spectrometer at 70 eV. ^{1}H NMR spectra were measured on a Varian EM 360 spectrometer at 60 MHz with tetramethylsilane as the internal standard. UV spectra were taken in ethanol and recorded on a Beckman 25 spectrophotometer. Melting points were determined in open capillary tubes and are uncorrected. All new compounds gave satisfactory microanalyses for C and H (within ±0.3%).

2-(8-Methoxy-1-naphthoyl)-1-naphthoic Acid (1a). Magnesium turnings (608 mg, 25 mmol), iodine (20 mg), and dry THF (40 mL) were refluxed under argon. A solution (9 mL) of 1-bromo-8-methoxynaphthalene[38] (5.0 g, 21 mmol) in dry THF (32 mL) was added, the reaction was started by the addition of methyl iodide (80 μL), and then the remainder of the above solution was added over 20 min. After two more hours at reflux and subsequent cooling to room temperature, TMEDA (8 mL) was added. The resulting yellowish solution was added within 2 h at −70 °C to a fine suspension of 1,2-naphthalic anhydride[40] (4.2 g, 21 mmol) in dry THF (120 mL). Stirring was continued overnight at room temperature. Water (30 mL) was added to the slightly turbid solution, and most of the solvent was removed in vacuo. The resulting oil was distributed between Et_2O (500 mL) and 7% KOH solution (800 mL). Acidification of the alkaline phase with concentrated HCl led to **1a** as an off-white solid (6.2 g, 85%). Recrystallization (acetone–hexane) afforded **1a** as a white powder: mp 196–198 °C; NMR (Me_2SO-d_6/D_2O) δ 3.48 (s, 3, methoxy), 6.69–8.17 (m, 12, Ar H).

Recrystallization of **1a** as well as of the other methoxy keto acids resulted in considerable loss and was only used to obtain analytical pure samples.

The following naphthoylnaphthoic acids were prepared essentially as described for **1a**:

2-(7-Methoxy-1-naphthoyl)-1-naphthoic acid (1b) from 1-bromo-7-methoxynaphthalene[10] in 75% yield; mp 204–206 °C; NMR (Me_2SO-d_6/D_2O) δ 3.79 (s, 3, methoxy), 7.05–8.63 (m, 12, Ar H).

2-(6-Methoxy-1-naphthoyl)-1-naphthoic acid (1c) from

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1-bromo-6-methoxynaphthalene[41] in 75% yield; mp 226–228 °C (lit.[10] mp 228–229 °C); NMR (Me_2SO-d_6/D_2O) δ 3.90 (s, 3, methoxy), 7.06–8.68 (m, 12, Ar H).

2-(5-Methoxy-1-naphthoyl)-1-naphthoic acid (1d) from 1-bromo-5-methoxynaphthalene[42] in 77% yield; mp 212–215 °C (lit.[10] mp 213–215 °C); NMR (Me_2SO-d_6/D_2O) δ 3.96 (s, 3, methoxy), 6.78–8.52 (m, 12, Ar H).

2-(4-Methoxy-1-naphthoyl)-1-naphthoic acid (1e) from 1-bromo-4-methoxynaphthalene[43] in 79% yield: mp 238–239 °C; NMR (Me_2SO-d_6/D_2O) δ 3.98 (s, 3, methoxy), 6.63–8.98 (m, 12, Ar H).

2-(3-Methoxy-1-naphthoyl)-1-naphthoic acid (1f) from 1-bromo-3-methoxynaphthalene[17] in 82% yield; mp 202–203 °C; NMR (Me_2SO-d_6/D_2O) δ 3.84 (s, 3, methoxy), 7.05–8.77 (m, 12, Ar H).

2-(1-Naphthoyl)-1-naphthoic acid (6a) from 1-bromonaphthalene in 82% yield; mp 179–180 °C (lit.[13] mp 184 °C).

1-Hydroxydibenz[a,h]anthracene (4a). Phenol acetate **5a** (336 mg, 1 mmol) was dissolved in a mixture of dry THF (30 mL) and dry MeOH (20 mL). NaOMe (50 mg) was added, and the resulting clear solution was stirred at 60 °C under argon for 20 min. Glacial acetic acid (200 μL) and water (60 mL) were then added. Removal of most of the organic solvent in vacuo resulted in the precipitation of **4a**, which was isolated by filtration as a white powder: 250 mg (85%); mp 277–278 °C (lit.[44] mp 269–270 °C); NMR (acetone-d_6/D_2O) δ 7.29–7.46 (m, 1, H_2), 7.51–8.20 (m, 9, Ar H), 9.02–9.17 (m, 1, H_8), 9.32 (s, 1, H_7), 10.40 (s, 1, H_{14}); UV, see Table I; MS, *m/e* 294 (100, M^+), 265 (43).

The following phenols were prepared as described for **4a**:

2-Hydroxydibenz[a,h]anthracene (4b) from **5b** in 93% yield as a white powder: mp 281–282 °C; NMR (acetone-d_6/D_2O) δ 7.31 (d, 1, H_3), 7.66–8.21 (m, 8, Ar H), 8.42 (br s, 1, H_1), 8.99–9.14 (m, 1, H_8), 9.21 (s, 1, H_7), 9.34 (s, 1, H_{14}); UV, see Table I; MS, *m/e* 294 (100, M^+), 265 (48).

3-Hydroxydibenz[a,h]anthracene (4c) from **5c** in 95% yield as a white powder: mp 288–289 °C (lit.[9] mp 288–290 °C); NMR (acetone-d_6/D_2O) δ 7.22–7.46 (m, 1, H_2), 7.62–8.18 (m, 8, Ar H), 8.79–9.08 (m, 2, $H_{1,8}$), 9.21 (s, 1, H_7), 9.30 (s, 1, H_{14}); UV see Table I; MS, *m/e* 294 (100, M^+), 265 (24).

4-Hydroxydibenz[a,h]anthracene (4d) from **5d** in 91% yield as a white powder: mp 305–307 °C; NMR (acetone-d_6/D_2O) δ 7.22 (d, 1, H_3), 8.59 (d, 1, H_5), 7.52–8.42 (m, 7, Ar H), 9.02–9.22 (m, 2, $H_{1,8}$), 9.36 (br s, 2, $H_{7,14}$); UV, see Table I; MS, *m/e* 294 (100, M^+), 265 (45).

5-Hydroxydibenz[a,h]anthracene (4e) from **5e** in 89% yield as an off-white powder: mp 263–264 °C; NMR (acetone-d_6/D_2O) δ 7.41 (s, 1, H_6), 7.67–8.19 (m, 7, Ar H), 8.44–8.59 (m, 1, H_4), 8.96–9.12 (m, 2, $H_{1,8}$), 9.18 (s, 1, H_7), 9.27 (s, 1, H_{14}); UV, see Table I; MS, *m/e* 294 (100, M^+), 265 (80).

6-Hydroxydibenz[a,h]anthracene (4f) from **5f** in 85% yield as an off-white powder: mp 258–259 °C; NMR (acetone-d_6/D_2O) δ 7.18 (s, 1, H_5), 7.56–8.27 (m, 8, Ar H), 8.90–9.16 (m, 2, $H_{1,8}$), 9.35 (s, 1, H_{14}), 9.75 (s, 1, H_7); UV, see Table I; MS *m/e* 294 (100, M^+), 265 (64).

7-Hydroxydibenz[a,h]anthracene (4g) from **5g** in 91% yield as an off-white powder: mp 254–256 °C; NMR (acetone-d_6/D_2O) δ 7.46–8.02 (m, 9, Ar H), 8.40 (d, 1, H_6), 8.74–8.98 (m, 1, H_1), 8.89 (s, 1, H_{14}), 9.80–10.02 (m, 1, H_8); UV, see Table I; MS, *m/e* 294 (100, M^+), 265 (36).

1-Acetoxydibenz[a,h]anthracene (5a). A mixture of **1a** (1.1 g, 3.1 mmol), red phosphorus (1.1 g, 34 mmol), and 57% hydroiodic acid (10 mL) in glacial acetic acid (100 mL) was stirred in an atmosphere of argon under reflux for 64 h. The red suspension was poured into ice water (400 mL), and the precipitate was isolated by filtration, washed with 5% $Na_2S_2O_3$ solution, and dried. The resulting red powder containing **4a** was added to a mixture of acetic anhydride (15 mL) and pyridine (20 mL) at 5 °C and stirred under argon at room temperature for 16 h. The red suspension was poured into ice water (200 mL), made acidic with concentrated HCl, and stirred for 2 h. The precipitate was isolated by filtration and dried. Extraction (CH_2Cl_2) of the resulting powder in a Soxhlet apparatus gave crude **5a**, which was purified by chromatography on silica gel with $CHCl_3$–petroleum ether (4:1) and recrystallization from EtOH–benzene yielding **5a** as a white crystalline powder: 645 mg (62%); mp 203–205 °C; NMR (CD_2Cl_2) δ 2.63 (s, 3, acetate), 7.25–7.50 (m, 1, H_2), 7.56–8.03 (m, 9, Ar H), 8.71–8.93 (m, 1, H_8), 9.10 (s, 1, H_7), 9.60 (s, 1, H_{14}); MS, *m/e* 336 (37, M^+), 294 (100), 265 (45).

The following phenol acetates were prepared as described for **5a**:

2-Acetoxydibenz[a,h]anthracene (5b) from **1b** in 67% yield as a white crystalline powder: mp 225–226 °C; NMR (CD_2Cl_2) δ 2.41 (s, 3, acetate), 7.39 (dd, 1, H_3), 7.53–8.03 (m, 8, Ar H), 8.55 (d, 1, H_1), 8.82–8.98 (m, 1, H_8), 9.06 (s, 1, H_7), 9.18 (s, 1, H_{14}); MS, *m/e* 336 (35, M^+), 294 (100), 265 (35).

3-Acetoxydibenz[a,h]anthracene (5c) from **1c** in 63% yield as a white crystalline powder: mp 249 °C (lit.[9] mp 247–248 °C); NMR (CD_2Cl_2) δ 2.37 (s, 3, acetate), 7.48 (dd, 1, H_2), 7.63–8.12 (m, 8, Ar H), 8.83–9.00 (m, 2, $H_{1,8}$), 9.15 (br s, 2, $H_{7,14}$); MS, *m/e* 336 (26, M^+), 294 (100), 265 (28).

4-Acetoxydibenz[a,h]anthracene (5d) from **1d** in 71% yield as a white crystalline powder: mp 268–270 °C; NMR (CD_2Cl_2) δ 2.50 (s, 3, acetate), 7.39 (dd, 1, H_3), 7.60–8.13 (m, 8, Ar H), 8.74–8.98 (m, 2, $H_{1,8}$), 9.20 (s, 2, $H_{7,14}$); MS, *m/e* 336 (38, M^+), 294 (100), 265 (53).

5-Acetoxydibenz[a,h]anthracene (5e) from **1e** in 64% yield as a white crystalline powder: mp 219–220 °C (lit.[10] mp 215–220 °C); NMR (CD_2Cl_2) δ 2.50 (s, 3, acetate), 7.37–7.97 (m, 9, Ar H), 8.60–8.87 (m, 2, $H_{1,8}$), 8.98 (s, 2, $H_{7,14}$); MS, *m/e* 336 (23, M^+), 294 (100), 265 (66).

6,7-Diacetoxydibenz[a,h]anthracene (5h) from **1f** in 82% yield as a white crystalline powder: mp 248–250 °C; NMR (CD_2Cl_2) δ 2.44 (s, 3, acetate), 2.49 (s, 3, acetate) 7.41 (s, 1, H_5), 7.43–7.90 (m, 8, Ar H), 8.58–8.80 (m, 1, H_1), 9.00 (s, 1, H_{14}), 9.15–9.37 (m, 1, H_8); MS, *m/e* 394 (33, M^+), 352 (36), 310 (100), 281 (41), 252 (44).

6-Acetoxydibenz[a,h]anthracene (5f). A mixture of **10** (1.1 g, 3.0 mmol), 57% hydroiodic acid (5 mL), and glacial acetic acid (50 mL) was stirred in an atmosphere of argon under reflux for 16 h. The dark solution was poured into a 1% sodium bisulfite solution (300 mL), and the precipitate was isolated by filtration, yielding crude **4f**. Acetylation and purification as described for **5a** omitting the extraction step afforded **5f** as a white crystalline powder: 697 mg (69 %); mp 214–215 °C; NMR (CD_2Cl_2) δ 2.62 (s, 3, acetate), 7.43–7.93 (m, 9, Ar H), 8.62–8.86 (m, 2, $H_{1,8}$), 9.08 (s, 1, H_{14}), 9.17 (s, 1, H_7); MS, *m/e* 336 (40, M^+), 294 (100), 265 (75).

7-Acetoxydibenz[a,h]anthracene (5g). A mixture of **12** (1.6 g, 5.1 mmol), zinc chloride (100 mg), acetic anhydride (10 mL), and acetic acid (30 mL) was kept under reflux for 3 h and then poured onto ice (200 g). The resulting suspension was stirred for 2 h at room temperature. Filtration led to crude **5g**, which yielded after recrystallization (EtOH–benzene) **5g** as a white crystalline powder: 1.4 g (81%); mp 234–235 °C (lit.[8] mp 235 °C); NMR (CD_2Cl_2) δ 2.66 (s, 3, acetate), 7.51–8.03 (m, 10, Ar H), 8.68–8.94 (m, 1, H_1), 9.06 (s, 1, H_{14}), 9.07–9.30 (m, 1, H_8); MS, *m/e* 336 (20, M^+), 294 (100), 265 (40).

6-Acetoxydibenz[a,h]anthra-7,14-quinone (10). A suspension of **5h** (1.2 g, 3.0 mmol) and sodium dichromate (1.6 g, 5.4 mmol) in glacial acetic acid (100 mL) was stirred at 100 °C for 2 h. The resulting dark red solution was poured into ice water (200 mL). The precipitate was isolated, dried, and recrystallized from $CHCl_3$–hexane yeilding **10** as a yellow crystalline solid: 900 mg (81%); mp 177–178 °C; NMR ($CDCl_3$) δ 2.52 (s, 3, acetyl), 7.40–7.97 (m, 7, Ar H), 8.13 (s, 2, $H_{12,13}$), 8.92–9.21 (m, 1, H_1), 9.25–9.60 (m, 1, H_8).

2-(1-Naphthylmethyl)-1-naphthoic Acid (12). A mixture of **11**[11] (1.3 g, 4.2 mmol), amalgamated zinc turnings[45] (50 g), toluene (10 mL), glacial acetic acid (40 mL), and concentrated HCl (50 mL) was vigorously stirred under reflux. Two portions of concentrated HCl (2 × 50 mL) were added after 12 and 24 h. Twelve hours after the last addition the organic phase was separated and the aqueous phase extracted with benzene (2 × 50 mL).

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The combined organic phases were extracted with 7% NaOH solution (3 × 100 mL). Acidification of the alkaline phase with concentrated HCl yielded **12** as a white powder: 864 mg (66%); mp 191–193 °C.

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Registry No. **1a**, 83710-47-8; **1b**, 83710-48-9; **1c**, 83710-49-0; **1d**, 83710-50-3; **1e**, 77321-43-8; **1f**, 83710-51-4; **4a**, 4615-77-4; **4b**, 72007-85-3; **4c**, 1421-80-3; **4d**, 1421-81-4; **4e**, 4002-76-0; **4f**, 83710-52-5; **4g**, 63041-68-9; **5a**, 83710-53-6; **5b**, 83710-54-7; **5c**, 72378-87-1; **5d**, 83710-55-8; **5e**, 83710-56-9; **5f**, 83710-58-1; **5g**, 63077-06-5; **5h**, 83710-57-0; **6a**, 77321-41-6; **6b**, 83710-63-8; **7a**, 7702-48-9; **7b**, 41774-30-5; **7c**, 83710-64-9; **10**, 83710-59-2; **11**, 73540-67-7; **12**, 77321-47-2; 1-bromo-8-methoxynaphthalene, 83710-60-5; 1-bromo-7-methoxynaphthalene, 83710-61-6; 1-bromo-6-methoxynaphthalene, 83710-62-7; 1-bromo-5-methoxynaphthalene, 74924-95-1; 1-bromo-4-methoxynaphthalene, 5467-58-3; 1-bromo-3-methoxynaphthalene, 5111-34-2; 1-bromonaphthalene, 90-11-9; 1,2-naphthalic anhydride, 5343-99-7; 1-amino-8-bromonaphthalene, 62456-34-2.

Supplementary Material Available: UV spectra of the phenols **4a–g** (7 pages). Ordering information is given on any current masthead page.

Rearrangements of Oxocyclopropanecarboxylate Esters to Vinyl Ethers. Disparate Behavior of Transition-Metal Catalysts

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Diverse transition-metal compounds catalyze the conversion of 2-alkoxycyclopropanecarboxylate esters to derivative vinyl ethers in high yield under mild conditions. With $[Rh(CO)_2Cl]_2$, $PtCl_2{\cdot}2PhCN$, or $[Ru(CO)_3Cl_2]_2$, structural rearrangement occurs with concurrent epimerization of the reactant cyclopropane compound, and identical isomeric mixtures of vinyl ethers are formed from either of the two stereoisomeric cyclopropane reactants. Rhodium(II) acetate catalyzed reactions occur at higher temperatures than those required with $[Rh(CO)_2Cl]_2$, epimerization of the (*Z*)-cyclopropane isomer, but not the *E* isomer, is observed, and individual stereoisomeric cyclopropane reactants produce different isomeric mixtures of vinyl ether products. The characteristics of copper bronze and copper(I) chloride catalyzed reactions are generally similar to those of $Rh_2(OAc)_4$, except with ethyl 2-methoxy-2-vinylcyclopropanecarboxylate, which undergoes rearrangement to the isomeric ethyl 3-methoxycyclopentenecarboxylates in the presence of these copper catalysts. Participation by the carbethoxy group in rhodium(I)-, platinum(II)-, and ruthenium(II)-catalyzed reactions is indicated in results from comparative reactions with nitrile and sulfone derivatives, and the mechanistic involvement of a six-membered ring metallocycle is suggested. In rhodium(II)- and copper-catalyzed reactions, metallocyclobutane intermediates are proposed to account for their contrasting results. Catalytic rearrangement of (allyloxy)cyclopropanecarboxylate esters affords 3-allyl-4-oxoalkanoate esters in good yield by a synthetic coupling of the oxocyclopropane–vinyl ether and Claisen rearrangement transformations.

Activation by vicinal carbonyl substituents for ring-opening reactions of oxocyclopropanes has only recently become apparent in thermal[1,2] and Lewis acid promoted transformations.[3,4] β-Alkoxycyclopropanecarbonyl compounds, which are conveniently accessible from vinyl ethers and diazocarbonyl compounds,[5] have been termed "donor–acceptor cyclopropanes" in recognition of the electronic influence of their constituent substituents in ring-opening reactions. We have recently reported that β-alkoxycyclopropanecarboxylate esters undergo structural rearrangement to vinyl ethers under relatively mild conditions in the presence of a wide variety of transition-metal catalysts.[6] Rhodium(I), platinum(II), and ruthenium(II) compounds, which have known activity for structural rearrangements of small-ring hydrocarbons,[7–14] are the most effective catalysts for the conversion of oxocyclopropanes to vinyl ethers; however, copper and rhodium(II) compounds also catalyze this ring-opening transformation.

The facility with which vicinally substituted alkoxycyclopropanecarboxylates are converted to vinyl ethers contrasts with the known inhibition of cyclopropane ring opening by carboalkoxy substituents.[8] The combination of alkoxy and carboalkoxy substituents provides a synergism for cyclopropane ring opening by electrophilic reagents that intimates a specific participating role for these substituents in catalytic structural rearrangements. We now report the scope and limitations of the oxocyclopropane–vinyl ether transformation, examples of methodology for its synthetic utilization, and mechanistic details of this catalytic conversion that suggest a relationship between the oxocyclopropane–vinyl ether rearrangement and the apparent allyl CH insertion by carboalkoxycarbenoid species in catalytic cyclopropanation reactions with vinyl ethers[15] as well as with catalytic cis → trans isomerization of disubstituted cyclopropanes.[12,16a]

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