(22) The first paper of this series outlines the preparations of the polymer and its application to the synthesis of gastrin tetrapeptide. P. G. Pietta, P. F. Cavallo, G. R. Marshall, and M. Pace, *Gazz. Chim. Ital.*, in press.
(23) This work was the subject of a preliminary communication at the 11th European Peptide Symposium, Vienna, 1971. See P. G. Pietta, P. F. Cavallo, and G. R. Marshall, "Peptides 1971," H. Nesvadba, Ed., North-Holland Publishing Co., Amsterdam, 1972.
(24) V. Erspamer and A. Anastasi, *Experientia*, **18**, 58 (1962).
(25) M. Capka, V. Chvalovsky, K. Kochloefl, and M. Kraus, *Collect. Czech. Chem. Commun.*, **34**, 118 (1969).
(26) G. L. Southard, G. S. Brooke, and J. M. Pettee, *Tetrahedron Lett.*, 3505 (1969).
(27) L. C. Dorman, *Tetrahedron Lett.*, 2319 (1969).
(28) K. Esko, S. Karlsson, and J. Porath, *Acta Chem. Scand.*, **22**, 3342 (1968).
(29) This procedure has also been used successfully in the preparation of benhydrylamine polymer for the synthesis of FSH-LH-RH: P. Rivaille, A. Robinson, M. Kamen, and G. Milhaud, *Helv. Chim. Acta*, **54**, 2772 (1971).
(30) (a) B. F. Gisin and R. B. Merrifield, *J. Amer. Chem. Soc.*, **94**, 3102 (1972); (b) M. C. Khosla, R. R. Smeby, and F. M. Bumpus, *J. Amer. Chem. Soc.*, **94**, 4721 (1972); (c) M. Rothe and J. Mazanek, *Angew. Chem., Int. Ed. Engl.*, **11**, 293 (1972).
(31) While this work was in progress, the syntheses of TRH and analogs on benzhydrylamine supports were reported: (a) J. M. Stewart, M. Knight, A. C. M. Paiva, and T. Paiva in "Progress in Peptide Research," S. Lande, Ed., Gordon and Breach, New York, N. Y., 1972, p 59. (b) J. Rivier, W. Vale, M. Monahan, W. Ling, and R. Burgus, *J. Med. Chem.*, **15**, 479 (1972).
(32) G. Flouret, *J. Med. Chem.*, **13**, 813 (1970).
(33) A. Anastasi, V. Erspamer, and J. M. Cei, *Arch. Biochem. Biophys.*, **108**, 341 (1964).
(34) While this work was in progress, a preliminary communication of the synthesis of substance **P** on the benzhydrylamine support was reported: G. W. Tregear, H. D. Niall, J. T. Potts, Jr., S. E. Leeman, and M. M. Chang, *Nature New Biol.*, **232**, 87 (1971).
(35) V. Erspamer, G. Erspamer, and M. Inselvini, *J. Pharm. Pharmacol.*, **22**, 875 (1970).
(36) T. Nakajima, T. Tanimura, and J. J. Pisano, *Fed. Proc.*, **29**, 282 (1970).
(37) G. L. Callewaert, R. Shipolini, and C. A. Vernon, *FEBS Lett.*, **1**, 111 (1968).
(38) E. Habermann and J. Jentsch, *Hoppe-Seyler's Z. Physiol. Chem.*, **348**, 37 (1967).
(39) (a) L. Yu. Skylarov and I. V. Shaškova, *Zh. Obshch. Khim.*, **39**, 2779 (1969); (b) J. Meienhofer and A. Trzeciak, *Proc. Nat. Acad. Sci. U. S.*, **68**, 1006 (1971); (c) J. D. Glass, I. L. Schwartz, and R. Walter, *J. Amer. Chem. Soc.*, **94**, 6209 (1972).
(40) A. I. Vogel, "Textbook of Practical Organic Chemistry," 3rd ed, Longmans, Green and Co., New York, N. Y., 1964.
(41) J. Scotchler, R. Lozier, and A. B. Robinson, *J. Org. Chem.*, **35**, 3151 (1970).
(42) C. Y. Bowers and A. V. Schally in "Hypophysiotropic Hormones of the Hypothalamus," J. Meites, Ed., Williams and Wilkins, Baltimore, Md., 1970.
(43) S. Shaltiel and M. Fridkin, *Biochemistry*, **9**, 5122 (1970).
(44) L. M. Pourchot and J. J. Johnson, *Org. Prep. Proced.*, **1**, 121 (1969).

---

# Reactions Catalyzed by $Co_2(CO)_8$. Selective Deuterium Incorporation into Some Polycyclic Hydrocarbons

Thomas A. Weil

*Department of Chemistry, University of Chicago, Chicago, Illinois 60637*

Sidney Friedman* and Irving Wender

*Pittsburgh Energy Research Center, U. S. Bureau of Mines, Pittsburgh, Pennsylvania 15213*

*Received March 15, 1973*

Anthracene and anthraquinone can be converted to 9,9,10,10-tetradeuterio-9,10-dihydroanthracene in the presence of excess $D_2$ (or $D_2O$), CO, and catalytic amounts of $Co_2(CO)_8$. Pyrene also undergoes reduction and H–D exchange at the 4 and 5 positions; phenanthrene fails to react. When 1-octene is treated with CO and $Co_2(CO)_8$ in the presence of the tetradeuteriodihydroanthracene, as a deuterium source, $C_9$ aldehydes, randomly substituted with deuterium, result.

Both heterogeneous and homogeneous metal catalytic systems effect random hydrogen–deuterium exchange between water (or $D_2O$) and alkylbenzenes, benzene, and polycyclic aromatics.[1-7] Garnett and coworkers have extensively studied the homogeneous aqueous system for H–D exchange based on $PtCl_4^{2-}$.[2-7] Recently, a homogeneously catalyzed exchange between deuterium gas and an aromatic compound has been reported.[8]

We wish to report that $Co_2(CO)_8$ will catalyze selective hydrogen–deuterium addition and exchange involving anthracene (or 9,10-dihydroanthracene) and anthraquinone with either deuterium gas or $D_2O$. To our knowledge, this is the first example of an exchange catalyst that has high selectivity for specific hydrogens and that can use either $D_2$ or $D_2O$ as its isotope source.

When anthracene is treated with synthesis gas and catalytic amounts of $Co_2(CO)_8$,[9] quantitative yields of 9,10-dihydroanthracene are obtained.[10] The reduction has now been done using $D_2$ or $D_2O$, CO, and $Co_2(CO)_8$. We find, accompanying the reduction of anthracene, exchange at the 9 and 10 positions takes place, resulting in formation of 9,9,10,10-tetradeuterio-9,10-dihydroanthracene (I). The same product is formed when anthraquinone is treated with $D_2$ or $D_2O$ in the presence of CO and $Co_2(CO)_8$. This reaction, using successive equilibrations, offers a synthetic route to I. By chemical, rather than catalytic, dehydrogenation of I, it should be possible to prepare anthracene isotopically labeled on the 9 and 10 carbon atoms (V).

## Experimental Section

Mass spectral analysis was done on a Consolidated Electrodynamics Corp. Model 110-B high-resolution instrument.[11] The inlet system was operated at 160°[12] and $10^{-6}$ Torr. It has been shown that deuteration does not change the sensitivity of the component in the mass spectrometer.[13] The data therefore are shown as a per cent of total ionization, which assumes equal sensitivities for all components.

Nmr spectra were run on a Varian A-60 spectrometer with chemical shifts reported in parts per million from TMS (δ).

**Reduction–Exchange of Anthracene Using $Co_2(CO)_8$, and $D_2$.** To a 200-ml rocking autoclave were added 0.2 g of $Co_2(CO)_8$, 2 g of anthracene, and 30 ml of benzene. The system was flushed several times with CO and pressured with a mixture of $D_2$ (98 atom %) and CO (see Table I). Upon completion of the reaction, the mixture was refluxed in air for 8 hr to decompose the $Co_2(CO)_8$ and filtered, and the solvent was removed. The product was recrystallized from ethanol.

**Reduction–Exchange of Anthracene Using $Co_2(CO)_8$ and $D_2O$.** To a 200-ml rocking autoclave were added 0.2 g of $Co_2(CO)_8$, 2 g of anthracene, 30 ml of dioxane, and 5 ml of $D_2O$. The system was flushed several times with CO and pressured to 3000 psi with CO. The work-up of the reaction product was the same as above.

### Table I
### Hydrogen-Deuterium Exchange Products

| Substrate, g | Anthracene, 2.0 | Anthracene, 2.0 | Anthracene, 2.0 | Anthracene, 2.0 | Anthracene, 2.0 | Anthracene, 2.0 | 9,10-Dihydroanthracene, 2.0 | Phenanthrene, 2.0 | 9,10-Dihydrophenanthrene, 1.0 | Anthraquinone, 10 | Pyrene, 2.3 |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Solvent, 30 ml | Benzene | Benzene | Benzene | Dioxane (5 ml) $D_2O$ | Dioxane | Benzene | Benzene | Benzene | Benzene | Benzene (250 ml) | Benzene |
| Reaction temp, °C | 200 | 160 | 200 | 175 | 175 | 135 | 160 | 160 | 180 | 250 | 175 |
| Time at reaction temp, hr | 5 | 13 | 11.2 | 6 | 6 | 6 | 6 | 5 | 6 | 6 | 6 |
| Starting gas[a] compn, psi | 500 $D_2$<br>700 CO | 1000 $D_2$<br>1000 CO | 1300 $D_2$<br>1350 CO | 3000 CO | 1400 $D_2$<br>1400 CO | 1200 $D_2$<br>1200 CO | 900 $D_2$<br>1100 CO | 600 $D_2$<br>800 CO | 800 $D_2$<br>1200 CO | 800 $D_2$<br>1100 CO | 500 $D_2$<br>700 CO |
| Mass spectral analysis, % | | | | | | | | | | | |
| m/e 178 | 1.0 | 0.7 | | 2.3 | 0.1 | 1.1 | 3.8 | 96.7 | 3.0 | | m/e 202 39.0 |
| 179 | 0.5 | 1.6 | 0.3 | 0.6 | 0.6 | 5.1 | 5.6 | 0.1 | 1.4 | 0.4 | 203 31.0 |
| 180 | 2.4 | 4.4 | 1.6 | 2.2 | 2.3 | 14.1 | 25.0 | 1.4 | 93.7 | 4.2 | 204 20.0 |
| 181 | 3.3 | 13.3 | 1.0 | 1.0 | 3.5 | 28.1 | 19.9 | | 0.9 | 1.0 | 205 5.0 |
| 182 | 12.9 | 26.7 | 4.3 | 6.6 | 19.2 | 37.5 | 23.6 | 1.0 | 1.0 | 7.5 | 206 3.0 |
| 183 | 29.0 | 35.6 | 21.5 | 28.5 | 36.5 | 12.2 | 16.6 | 0.4 | | 19.8 | 207 1.3 |
| 184 | 50.9 | 17.7 | 71.3 | 57.4 | 37.8 | 1.7 | 5.5 | 0.4 | | 66.0 | 208 0.3 |
| % of isotopic equilibrium[b] | 84 | 64 | 93 | 88 | 79 | 40 | 39 | | | | |

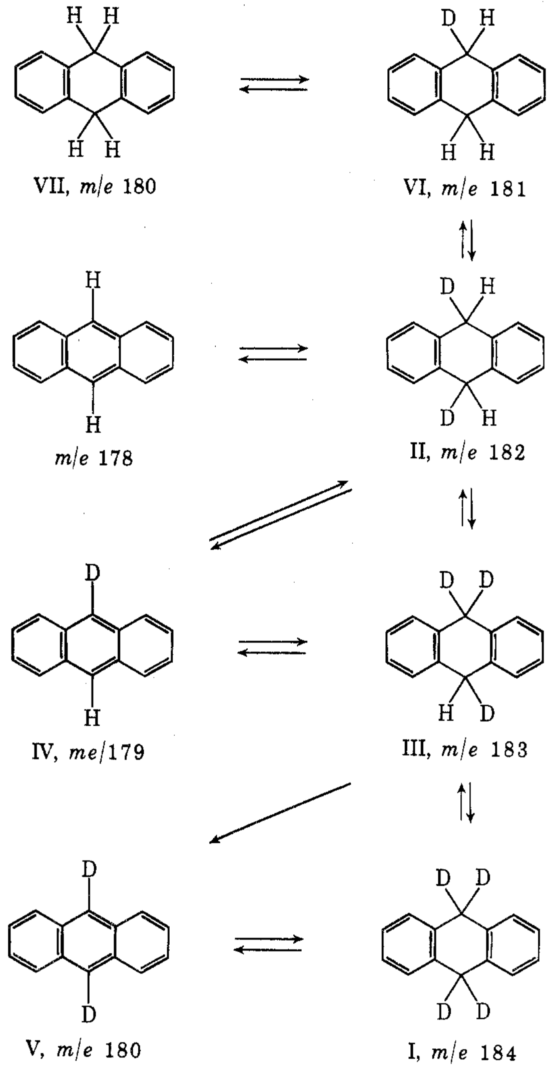
[a] CO necessary to keep $Co_2(CO)_8$ from decomposing. [b] Equilibrium concentration of deuterium was between 93 and 97% for all experiments, depending on deuterium source and available protons from substrate.

**Conversion of Anthraquinone to Deuterated Dihydroanthracenes.** To a 500-ml stainless steel rocking autoclave were added 10 g of anthraquinone, 0.5 g of $Co_2(CO)_8$, and 250 ml of benzene. The system was flushed with CO and pressured with 800 psi of $D_2$ ($D_2O$ may also be used as the deuterium source) and 1100 psi of CO. Upon completion of the reaction, the mixture was refluxed for 8 hr to decompose the $Co_2(CO)_8$ and filtered, and the $D_2O$ was removed. The resulting solution was evaporated to dryness and the product was recrystallized from ethanol.

## Results and Discussion

When anthracene is treated with $Co_2(CO)_8$, CO, and $D_2$ in benzene or with $Co_2(CO)_8$, CO, and $D_2O$ in dioxane, selective reduction and exchange at the 9 and 10 positions occur (as shown by vpc, uv, and nmr analysis), giving varying amounts of compounds I-VII (Scheme I; not all possible equilibria are shown). Table I shows the conditions under which the reactions were run and the various hydroaromatic products formed as determined by mass spectral analysis. The reaction goes in either benzene or dioxane solvent and in dioxane either $D_2$ or $D_2O$ can be used as the isotope source, both giving good yields of I-III.

Scheme I
The Reductive Hydrogen-Deuterium Exchange of Anthracene Showing Some of the Possible Equilibrium Reactions



In each experiment shown in Table I, the product distribution makes it clear that anthracene is readily reduced to II (m/e 182) followed by H-D exchange to give III and I. The exchange may be directly on II to give III and then I, or it may involve successive dehydrogenation-hydrogenation, such as II → IV → III. Very little unreduced anthracene is observed by either uv or vpc; the small peaks in the mass spectra at *m/e* 178–180 are believed due largely to dehydrogenation of I–III in the mass spectrometer[12] and not exchange of the protons on anthracene to form IV and V. Some of the 180 peak is due to VII formed by back-equilibration with $H_2$.

The distribution of products I–III as a function of temperature and time is further indication that reduction is faster than exchange and that an equilibrium amount of I is formed only after considerable time at higher temperature.

The selective nature of the reduction–exchange reaction can be evaluated from the mass spectral data. No significant peaks in the mass spectra, above *m/e* 184 (I), have been observed. If exchange of ring protons 1–8 did occur, incorporation of more than four deuterium atoms would be expected and peaks above *m/e* 184 would be observed. The specific selectivity for positions 9 and 10 in anthracene is further substantiated by the nmr spectra. The nmr spectra of 9,10-dihydroanthracene has sharp singlets at 3.87 and 7.18 ppm, corresponding to the 9,10 protons and protons 1–8, respectively. The nmr spectra of the mixtures of deuterated products were run and compared with the spectrum of pure 9,10-dihydroanthracene (using solutions of equal weight concentration). The peak at 7.2 ppm is a sharp singlet of nearly equal intensity in each sample. The peak at 3.8 ppm, however, is broadened and considerably reduced in intensity in the deuterated samples; the broadening is due to H–D coupling. The fact that no loss in intensity is observed in the peaks at 7.2 ppm for the deuterated samples further demonstrates the lack of exchange of protons 1–8.

In order to test the hypothesis that reduction is the faster of the two reactions and that exchange occurs predominantly in the dihydro species, II, the exchange reaction was carried out using 9,10-dihydroanthracene as the starting substrate. Exchange of the 9 and 10 protons does occur, resulting in a distribution of deuterated products (Table I). Equilibration is slower when starting with the dihydro compound, since all four protons must exchange.

When anthraquinone is treated with $D_2$ in benzene or $D_2O$ in dioxane, in the presence of $Co_2(CO)_8$ and CO, it is readily converted to the deuterated dihydroanthracenes, I–III. A product from an anthraquinone reduction containing 66% I and 20% III was treated for 5 hr, in benzene, with CO and an equimolar amount of 1-octene in the presence of $Co_2(CO)_8$ at 160° to determine if dihydroanthracene would act as a hydrogen source in the oxo reaction. The olefin was readily converted to the $C_9$ aldehydes and the dihydroanthracenes were converted to a mixture of 50% anthracene, 40% 9-deuterioanthracene, and 10% 9,10-dideuterioanthracene.

Mass spectral analysis of the aldehydes indicates considerable deuterium substitution throughout the molecule, thus accounting for the low deuterium content of the anthracene. Deuterium substitution in the aldehyde probably results from isomerization of the olefin, involving exchange with $DCo(CO)_4$, followed by hydroformylation.

Phenanthrene, which is relatively inert to $Co_2(CO)_8$-catalyzed hydrogenation,[10,14] 9,10-dihydrophenanthrene, and diphenylmethane were also used as substrates for the reduction–exchange. No reaction occurred with diphenylmethane and little, if any, reaction occurred with phenanthrene and 9,10-dihydrophenanthrene (Table I). The reduction of pyrene at the 4 and 5 position has been reported,[10] and we have found that exchange at these positions does occur. No tetrahydropyrene is formed and no exchange other than at the 4 and 5 positions is observed. Exchange seems to occur only at positions which undergo reduction, and where some sort of activation is present, *i.e.*, an aromatic ring $\alpha$ to the point of exchange, in both reduced and unreduced compounds.

**Acknowledgments.** The authors are grateful to the National Research Council for a research fellowship to one of us (Thomas A. Weil). We also wish to thank Miss Janet Shultz for help with the mass spectra and Mr. Sol J. Metlin for assistance with the autoclaves.

**Registry No.** Anthracene, 120-12-7; 9,10-dihydroanthracene, 613-31-0; phenanthrene, 85-01-8; 9,10-dihydrophenanthrene, 776-35-2; anthraquinone, 84-65-1; pyrene, 129-00-0; $Co_2(CO)_8$, 10210-68-1.

## References and Notes

(1) T. I. Taylor, "Catalysis," Vol. V, P. H. Emmett, Ed., Reinhold, New York, N. Y., 1957.
(2) J. L. Garnett and W. A. Sollich-Baumgartner, *Advan. Catal.*, **16**, 95 (1966).
(3) R. J. Hodges and J. L. Garnett, *J. Phys. Chem.*, **72**, 1673 (1968).
(4) R. J. Hodges and J. L. Garnett, *J. Catal.*, **13**, 83 (1969).
(5) R. J. Hodges and J. Garnett, *J. Phys. Chem.*, **73**, 1525 (1969).
(6) J. L. Garnett, *Catal. Rev.*, **5**, 229 (1971).
(7) K. P. Davis and J. L. Garnett, *J. Phys. Chem.*, **75**, 1175 (1971).
(8) E. K. Barefield, G. W. Parshall, and F. N. Tebbe, *J. Amer. Chem. Soc.*, **92**, 5234 (1970).
(9) This reduction has also been reported to give 25% 9,10-dihydroanthracene using stoichiometric amounts of cobalt hydrocarbonyl at 25° and 1 atm of CO: F. D. Taylor and M. Orchin, *J. Org. Chem.*, **37**, 3913 (1972).
(10) S. Friedman, S. Metlin, A. Svedi, and I. Wender, *J. Org. Chem.*, **24**, 1287 (1959).
(11) Reference to a company name or product name is made to facilitate understanding and does not imply endorsement by the U. S. Bureau of Mines.
(12) J. L. Shultz, *Spectrosc. Lett.*, **1**, 345 (1968).
(13) J. H. Beyman, "Mass Spectrometry and Its Application to Organic Chemistry," Elsevier, Amsterdam, 1960.
(14) I. Wender, R. Levine, and M. Orchin, *J. Amer. Chem. Soc.*, **72**, 4375 (1950).