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The Catalytic Hydrogenation of Arylphosphonic Acids[1]

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A number of arylphosphonic acids and one diarylphosphinic acid were reduced to the corresponding cyclohexyl derivatives by means of a rhodium catalyst and hydrogen at 60 lb. pressure. Halogen substituents are cleaved from the aromatic ring under these reaction conditions. The catalyst is poisoned by hydrogen bromide or hydrogen iodide. Phenylphosphinic acid, benzenearsonic acid and triphenylbismuth could not be hydrogenated.

A recent advertisement has described the use of rhodium on alumina as a catalyst for the reduction of aromatic rings.[2] Since we had available a number of aromatic phosphonic and phosphinic acids, the preparation of which has been described in recent communications[3] from this Laboratory, it seemed of interest to attempt the reduction of some of these compounds to the corresponding cyclohexyl derivatives and to compare their therapeutic activity with that of the corresponding aromatic compounds.[4]

Although rhodium has been used as a catalyst for the reduction of a wide variety of functional groups,[5] a survey of the chemical literature revealed no information concerning its applicability to the hydrogenation of aromatic rings.[6] Using the rhodium-on-alumina catalyst we have reduced arylphosphonic and diarylphosphinic acids to the corresponding cyclohexyl compounds in a variety of solvents which include alcohol, water, dilute aqueous ammonia and dilute hydrochloric acid.

The compounds prepared, together with their analyses, yields, and m.p.'s, are listed in Table I. Although cyclohexylphosphonic acid[7] and dicyclohexylphosphinic acid[7d] have been described previously, none of the methods employed in these earlier preparations is as convenient as the hydrogenation of the readily available aromatic compounds. The disubstituted cyclohexane derivatives in Table I are new compounds. No attempt was made to determine whether they are *cis*- or *trans*-isomers. However, they probably possess the former configuration, since the catalytic hydrogenation of aromatic compounds over noble metal catalysts usually occurs by *cis* addition of hydrogen.[8]

Halogen-substituted phosphonic acids could not be reduced to the corresponding cyclohexyl derivatives by this procedure. Thus, when *p*-bromophenylphosphonic acid was dissolved in alcohol and shaken with the rhodium catalyst and hydrogen, less than 10% of the theoretical amount of hydrogen was absorbed, even at 50°. Further investigation showed that hydrogen bromide had been formed and that this acid has a pronounced inhibitory effect on the catalyst. For example, the catalytic hydrogenation of phenylphosphonic acid with the rhodium catalyst is almost completely prevented by the addition of a small amount of aqueous hydrobromic acid. This inhibition is in marked contrast to the results of Brown, Durand and Marvel[9] who found that hydrogen bromide increases the effectiveness of Adams platinum oxide catalyst.

Hydrogen iodide similarly poisons the rhodium catalyst. When *o*-iodophenylphosphonic acid was subjected to hydrogenation over the catalyst, less than one mole of hydrogen per mole of phosphonic acid was absorbed. Analysis of the reaction mixture showed that about 6% of the iodine had been cleaved from the ring.

The hydrogenation of *m*-chlorophenylphosphonic acid over rhodium-on-alumina gave hydrogen chloride and cyclohexylphosphonic acid. However, the reaction does not seem to offer a satisfactory scheme for removing chlorine without reducing the ring. Thus, when the reduction was interrupted after the absorption of one mole of hydrogen per mole of *m*-chlorophenylphosphonic acid, we found that only 0.29 mole of hydrogen chloride had been formed. Apparently, the rate of reduction of the aromatic nucleus is comparable to the rate of removal of chlorine.[10]

The rhodium catalyst can also remove fluorine from the ring. When *o*-fluorophenylphosphonic acid was reduced in the usual way, almost four moles of hydrogen per mole of phosphonic acid was absorbed rapidly. Hydrogen fluoride was demonstrated qualitatively, and pure cyclohexylphosphonic acid was isolated from the reaction mixture.

In addition to arylphosphonic and diarylphos-

(1) The organophosphorus nomenclature used in this paper is that proposed by the Organic Division's Advisory Committee on the Nomenclature of Organic Phosphorus Compounds; *cf. Chem. Eng. News*, **30**, 4515 (1952).

(2) Engelhard Industries News-Letter, January, 1950.

(3) See for example (a) G. O. Doak and L. D. Freedman, THIS JOURNAL, **73**, 5658 (1951); (b) *ibid.*, **74**, 753 (1952); **75**, 683 (1953); (c) L. D. Freedman, H. Tauber, G. O. Doak and H. J. Magnuson, *ibid.*, **75**, 1379 (1953); (d) L. D. Freedman and G. O. Doak, *ibid.*, **77**, 173 (1955).

(4) Some of the results obtained with the aromatic compounds have already been reported; *cf.* J. D. Thayer, H. J. Magnuson and M. S. Gravatt, *Antibiotics and Chemotherapy*, **3**, 256 (1953).

(5) (a) L. Hernandez and F. F. Nord, *Experientia*, **3**, 489 (1947); *J. Colloid Sci.*, **3**, 363 (1949); (b) O. Beeck in "Advances in Catalysis," Vol. 2, Academic Press, Inc., New York, N. Y., 1950, p. 151; (c) W. P. Dunworth and F. F. Nord, THIS JOURNAL, **74**, 1457 (1952); (d) *ibid.*, **74**, 1459 (1952); (e) G. W. Watt, A. Broodo, W. A. Jenkins and S. G. Parker, *ibid.*, **76**, 5989 (1954).

(6) L. C. Burman in a personal communication has stated that rhodium-on-alumina is substantially superior to platinum for the hydrogenation of benzene, alkylbenzenes, phenols and heterocyclic compounds; *cf.* ref. 2.

(7) (a) J. O. Clayton and W. L. Jensen, THIS JOURNAL, **70**, 3880 (1948); (b) P. Lesfauries and P. Rumpf, *Bull. soc. chim., France*, 542 (1950); (c) R. Graf, *Chem. Ber.*, **85**, 9 (1952); (d) A. R. Stiles, F. F. Rust and W. E. Vaughan, THIS JOURNAL, **74**, 3282 (1952); (e) P. Fay and H. P. Lankelma, *ibid.*, **74**, 4933 (1952); (f) T. C. Myers, S. Preis and E. V. Jensen, *ibid.*, **76**, 4172 (1954).

(8) R. P. Linstead, W. E. Doering, S. B. Davis, P. Levine and R. R. Whetstone, *ibid.*, **64**, 1985 (1942).

(9) J. H. Brown, H. W. Durand and C. S. Marvel, *ibid.*, **58**, 1594 (1936).

(10) Dunworth and Nord, ref. 5d, found that rhodium-on-charcoal can catalyze the dehalogenation of *p*-chloronitrobenzene. They did not report any evidence of hydrogenation of the ring.

TABLE I

Compound	Yield, %	M.p.,[a] °C.	Recryst. from[b]	Empirical formula	Phosphorus, %[c] Calcd.	Found	Neut. equiv.[d] Calcd.[e]	Found
Cyclohexylphosphonic acid	86	166–167[f]	A	$C_6H_{13}O_3P$	18.87	18.71	164.1	165.6
4-Aminocyclohexylphosphonic acid[g,h]	87	>300		$C_6H_{14}NO_3P$	17.29	17.00	[i]	
4-Methylcyclohexylphosphonic acid	81	107–110	A	$C_7H_{15}O_3P$	17.39	17.31	178.2	180.2
2-Ethylcyclohexylphosphonic acid	80	135–138	B	$C_8H_{17}O_3P$	16.12	15.79	192.2	194.3
4-Ethylcyclohexylphosphonic acid	75	103–106	C	$C_8H_{17}O_3P$	16.12	15.95	192.2	190.6
Dicyclohexylphosphinic acid[j]	82	145–146.5[k]	D	$C_{12}H_{23}O_2P$	13.45	13.07	230.3	232.6

[a] Melting points were taken as previously described; *cf.* ref. 3a. [b] A, 3 *N* hydrochloric acid; B, hexane–ether; C, hexane; D, aqueous alcohol. [c] Phosphorus was determined by the procedure of B. C. Stanley, S. H. Vannier, L. D. Freedman and G. O. Doak, *Anal. Chem.*, in press. [d] The indicator used for the phosphonic acids was methyl purple (from Fleisher Chemical Company); the indicator used for dicyclohexylphosphinic acid was phenolphthalein. [e] Calculated for one equivalent of ionizable hydrogen per mole of compound. [f] Previously reported m.p.'s range from 160–161° to 167–168°; *cf.* ref. 7. [g] This compound can be prepared from phosphanilic acid (as described in the Experimental section) or from *p*-nitrophenylphosphonic acid. The reduction of nitro groups with the aid of rhodium has been reported previously; *cf.* ref. 5a, d and e. [h] Calcd.: N, 7.82. Found: N, 7.78. [i] This compound, like other amino-substituted phosphonic acids, presumably exists as a zwitterion; *cf.* H. H. Jaffé, L. D. Freedman and G. O. Doak, THIS JOURNAL, **75**, 2209 (1953). The neutral equivalent, therefore, cannot be determined by titration with alkali to the methyl purple endpoint (*p*H 5.4.). [j] Prepared by dissolving 0.02 mole of diphenylphosphinic acid in 150 ml. of absolute alcohol and reducing at 48° with 3.0 g. of rhodium on alumina. [k] M.p. 140–141.5°, ref. 7d.

phinic acids, the reduction of several other compounds has been attempted. No hydrogen was absorbed when an alcoholic solution of phenylphosphinic acid was shaken with hydrogen and rhodium-on-alumina. This result is not surprising since compounds containing phosphorus-hydrogen bonds are known to be powerful poisons of noble metal catalysts.[11] The reduction of benzenearsonic acid to the corresponding cyclohexyl derivative could not be accomplished with the aid of the rhodium catalyst although a small amount of hydrogen was absorbed. It is probable that the arsono ($-AsO_3H_2$) group was partially reduced to a trivalent form which in turn poisoned the catalyst.[12] We have found also that rhodium-on-alumina is ineffective for the hydrogenation of triphenylbismuth. This result might have been anticipated from the work of Maxted[13] who reported that inorganic compounds of trivalent bismuth are toxic to platinum catalysts.

Experimental

Materials.—All of the arylphosphonic and diarylphosphinic acids used in this investigation were prepared in this Laboratory and have been described previously.[3] Phenylphosphinic acid was kindly furnished us by the Victor Chemical Works. The catalyst, 5% rhodium-on-alumina, was lot #2363 from Baker and Company, Inc., Newark, N. J. The solvents and other chemicals were reagent grade and were not further purified.

The Hydrogenation of Aromatic Compounds.—In each experiment 0.02 mole of aromatic compound and 3.0 g. of fresh catalyst were used. Except for 4-aminocyclohexylphosphonic acid, the conditions were similar to those described below for cyclohexylphosphonic acid.

Cyclohexylphosphonic Acid.—Phenylphosphonic acid (3.16 g.) was dissolved in 100 ml. of 95% ethyl alcohol and reduced at room temperature with 3.0 g. of rhodium-on-alumina and hydrogen at an initial gage pressure of 60 lb. A Parr low-pressure catalytic hydrogenation apparatus was employed. In about one hour the reduction was complete; *i.e.*, 3.0 moles of hydrogen per mole of phosphonic acid had been absorbed. The catalyst was then removed by filtration, and the filtrate was evaporated to dryness on a boiling water-bath. The residue, which consisted of crude cyclohexylphosphonic acid, was purified by recrystallization.

4-Aminocyclohexylphosphonic Acid.—Phosphanilic acid (3.46 g.) was dissolved in 50 ml. of 0.47 *N* aqueous ammonia and hydrogenated at about 40° under conditions similar to those described above for phenylphosphonic acid. After the catalyst was removed, the filtrate was acidified with 50 ml. of 0.50 *N* hydrochloric acid. The resulting solution was then concentrated *in vacuo* to about 20 ml. About 100 ml. of absolute alcohol was added, and the mixture was cooled in the deep-freeze at −25°. The crystals obtained were washed with absolute alcohol and finally dried *in vacuo* at 137° to remove solvent of crystallization.

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(11) E. B. Maxted and R. W. D. Morrish, *J. Chem. Soc.*, 252 (1940).

(12) Maxted and Morrish, ref. 11, found that arsenate, which is not a poison *per se*, is reduced to arsine in the presence of catalytically activated hydrogen.

(13) E. B. Maxted, in "Advances in Catalysis," Vol. III, Academic Press, Inc., New York, N. Y., 1951, p. 129.