for 1 °C less than other uncertainties. Yao and Emmett[3a] give 13–14 kcal/mol for the energy of activation in the reduction of nitrobenzene. According to that figure, an increase in temperature of 1 °C should produce a rate increase of about 8%. No figures are available for the other substrates used. One suspects that the energy of activation for hydrogenation of benzene may be relatively high.

(14) W. T. Olson, H. F. Hipscher, C. F. Buess, I. A. Goodman, I. Hart, J. M. Lamneck, Jr., and L. C. Gibbons, *J. Am. Chem. Soc.*, **69**, 2451 (1947).

(15) Since the acetophenone reductions were not run near to completion, it was possible and convenient to recover substrate after filtration from catalyst, a number of batches being combined. Control runs were made on all batches, recovered or new, before use.

(16) Commercial acetophenone could also be purified by repeated passages through Raney nickel columns, followed by distillation. This process had no advantage over synthesis. Aside from the complications of handling very large amounts of substrate in solutions, the adsorption is not very efficient. E. B. Maxted [*J. Chem. Soc.*, 624 (1947)] considered thiophene a relatively weak poison which acts mainly through reduction to tetrahydrothiophene. Under nonreducing conditions, the inhibitor competes poorly with the much larger amount of substrate. An attempt at a similar column purification of benzyl methyl ether was unsuccessful.

(17) $C_{i\,1/2}$ is the concentration of poison that lowers the reduction rate to half the standard value.

(18) Darco G-60 was used. In the earlier part of this work, the sample was a special one obtained from the manufacturer (Darco Department, Atlas Powder Co.) and prepared by the method in use when the author first employed this method (ca. 1940). A later sample, here called "New Darco," was the usual commercial grade of the present time.

(19) The method of E. Ott and R. Schröter, *Ber.*, **60**, 624 (1927).

(20) R. Baltzly, *J. Am. Chem. Soc.*, **74**, 4586 (1952).

(21) H. I. Zeliger, *J. Catal.*, **7**, 198 (1967).

(22) Zeliger reported that chloroplatinic acid was reduced by hydrogen and platinum deposited on finely divided carriers *wetted* by the solution. This does not appear to have been investigated previously since it was "known" that hydrogen did not precipitate metal from chloroplatinic acid solutions.

(23) Hussey and co-workers[4a] reported acetic acid to have been unusable in their studies. This may correspond to the greater precision of their operations or the acetic acid modifying the nature of their support (activated alumina).

(24) That such an adsorption of acid exists has been suspected but not demonstrated previously. Cf. ref 20.

(25) Perchloric acid was preferred. The sulfuric acid available gave consistently *lower* rates for about the first 5 min of reductions. It is suspected that traces of nitrous or nitric acid were present which acted initially as poisons but were then reduced to ammonia which would have been nontoxic under the conditions.

(26) Cf. M. Freifelder, "Practical Catalytic Hydrogenation", Wiley-Interscience, New York, N.Y., 1971, p 26. Freifelder appears to be the first to suspect this inhibitory action, which, however, he believed confined to nonaqueous solutions.

(27) Phosphoric and oxalic acids were intermediate between perchloric and hydrochloric. The oxalic acid may have produced some inhibition as its anion.

(28) That a significant amount of $BzOH_2^+$ is present is suggested by the observation that when the charge of benzyl alcohol was added to the solvent containing perchloric acid the temperature of the solution rose about 2 °C. When acid was absent, a fall in temperature of about the same size was noted. These temperature effects were not observed with the benzyl ethers.

(29) W. P. Dunworth and F. F. Nord, *J. Am. Chem. Soc.*, **74**, 1459 (1952).

(30) The rates of 2–2.4 mmol/min per 0.1 mg of Rh give turnover rates of about 2×10^3 mol atom^{-1} min^{-1}: reported for invertase, 4×10^3, carboxylase, 10^3, choline esterase and catalase, ca. 10^6. The figure of 2×10^3 is, of course, based on the number of Rh atoms on the catalyst sample, whereas the enzyme figures are per active site, usually one to a molecule. If one assumes that the metal plaques average five atoms thick and that an adsorbed molecule of cyclohexene obscures the surface of four atoms of Rh, the turnover rate becomes 4×10^4.

(31) Specifically they were asked whether they employed (a) reduction by hydrogen, (b) chemical reduction, or (c) ignition of carrier impregnated with metal salt. (All these methods have been employed in the past for one catalyst or another.) They were also asked what charcoal they use.

Studies on Catalytic Hydrogenation. II. Poisoning by Nucleophiles[1]

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A selected group of nucleophilic inhibitors has been studied in the reduction of different types of substrates and with platinum, palladium, and rhodium on carbon catalysts. Variation of solvent affects the adsorption of inhibitors along the same lines as with substrates. Higher molecular inhibitors, having high intrinsic toxicity through obstructing access to an extended surface, also show diminished adsorption coefficients. Certain irregularities in poisoning tendencies may be due to differing details of hydrogenation of different substrates.

The extensive investigations of catalyst poisoning by Maxted[3] permit a division of poisons into two main classes,[4] those attaching themselves to the catalyst through an unshared electron pair, and a second group of metallic cations—the subject of the third communication of this series.

Poisons of the first class are acting as nucleophiles and a logical extension of the original concept led to the recognition of bases and of iodide ion as poisons. Weaker nucleophiles such as chloride,[5] bromide, and acetate (or carboxylate ions, generally) have not usually been recognized as inhibitors in default of specific investigation. Two major questions left unanswered by Maxted's work were:

1. To what extent are his generalizations, based mainly on the study of Willstätter platinum and, to a lesser degree, of a supported nickel catalyst, valid for hydrogenation catalysts in general?

2. To what extent are toxicities altered by comparison with different substrates and by changes in solvent?

It seemed worthwhile, therefore, to attempt a study using several metallized charcoals with some variation of substrates and of solvent conditions and a representative group of poisons, though not the very large selection examined by Maxted.

In the preceding communication, the effect of solvent conditions on reaction rate has been considered, and it has been shown that under suitable conditions the rate may be of zero order in respect to hydrogen pressure and substrate concentration: i.e., the adsorption terms approximate the value of 1. Under such conditions, presence of poison should modify the substrate adsorption term (θ_s) so that

$$\theta_s = \frac{\alpha_s C_s}{\alpha_s C_s + \alpha_i C_i} \quad (1)^6$$

and at half-poisoning, $\theta_s = \frac{1}{2}$ and $\alpha_i C_i = \alpha_s C_s$.

Plots of rate against poison concentration according to eq 1 with $C_{i\,1/2}$ as the unit of poison concentration give theoretical poisoning curves such as curve A of Figure 1. The characteristic feature of such a curve is that at $C_i = 2C_{i\,1/2}$ the rate should be one-third of the standard and at $C_i = \frac{1}{2}C_{i\,1/2}$, two-thirds. (Obviously, other simple relationships are also deducible.) On this basis in a poisoning study, one

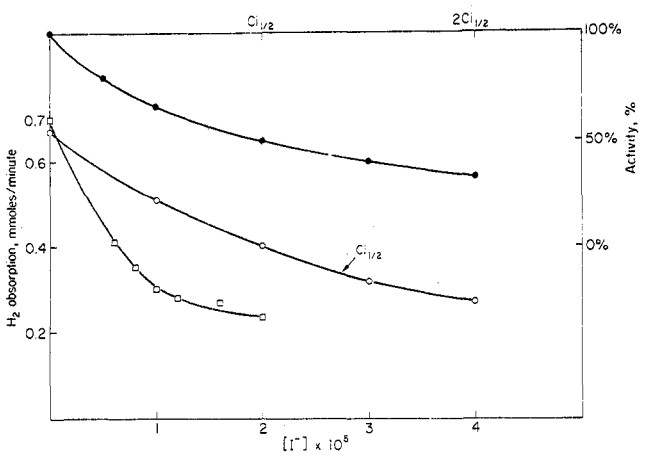

Figure 1. A, ●—●, theoretical poisoning curves; B, ○—○, I^- vs. PhCOMe in 75% MeOH; C, □—□, I^- vs. PhCOMe in 99% MeOH.

can easily discern if eq 1 is being approximated. Three main conditions became apparent that produced major deviations.

1. With quite weak poisons, such as chloride and bromide, increasing concentrations so modify the medium that half-poisoning is not attainable. An example is shown in Figure 2 for the reduction of nitrobenzene in 75% methanol over platinum (and by the data of Table IA of the preceding communication). If HCl is the source of Cl^-, the anion concentration cannot be increased without increasing acidity. The acidity tends to increase the rate, and beyond about 0.6 M the rate increases. If NaCl is the source of chloride, increasing salt concentration also increases the activity, and presumably the adsorption coefficient of the substrate.

2. With very strong poisons, a large part of the inhibitor may be resident on the catalyst, and the real concentration in solution may be much less than the apparent concentration. This situation can be dealt with by cross-over experiments (vide infra). Whether this situation can possibly exist is deducible by consideration of the quantities present. A 1-mg batch of platinum contains approximately 5×10^{-6} g-atom, not all of which are on the surface.[7] When $C_{i\,1/2} = 10^{-4}$, the amount of inhibitor in 50 ml is 5×10^{-6} *mol*—capable of covering all the atoms of metal wherever situated. At such or higher concentrations of inhibitor, the true and apparent C_i values must be very close.

3. There is evidence of competing interaction of inhibitor and substrate. This applies principally to the cationic inhibitors to be taken up in the following communication. Because of anticipation of such interaction, however, it was felt inadvisable to examine some poisoning situations; e.g., the inhibition of the reduction of benzaldehyde by cyanide or butyl mercaptan.

The considerations advanced in the preceding communication as to the effect of solvent changes on the adsorption coefficient of the substrate should apply also to an inhibitor. Thus, an inorganic poison such as the anion of a neutral salt should be more toxic in a less aqueous solvent. This is usually the case: curve B of Figure 1 is a poisoning curve of iodide ion vs. acetophenone in 75% methanol with platinized charcoal. It closely resembles the theoretical curve A. Curve C is for iodide poisoning in 99% methanol and is clearly quite different.[8] Not only is the toxicity of iodide greater in the less aqueous solvent, but the curve appears discontinuous. Crossover experiments showed that at half-poisoning, the iodide was about evenly divided between catalyst and solution and that $C_{i\,1/2}$ was in fact 3×10^{-6} rather than 8×10^{-6}, as suggested by curve C.

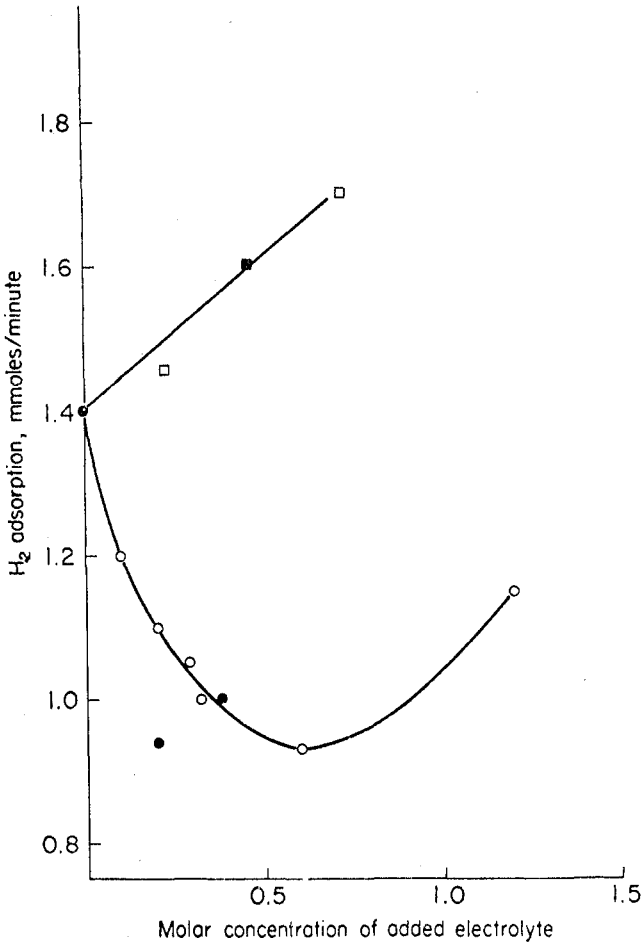

Figure 2. Effect of electrolytes on rate of reduction of $PhNO_2$ in 75% MeOH, 1 mg of Pt as 5% Pt/C: □, H_2SO_4; ■, $HClO_4$; ○, HCl; ●, NaCl.

Choice of Poisons. Butyl mercaptan and dibutyl sulfide were selected from the much larger list studied by Maxted and Evans,[9] in part because of relative ease in handling, in part to investigate a particular point. These authors observed that toxicity in their series of sulfur compounds increased with size (the relative toxicities of these two compounds being 6 and 15 referred to hydrogen sulfide as 1). Their interpretation was that the poison, being bound by the sulfur to one platinum atom, shielded also a number of neighboring atoms. Calculations suggested that dimethyl sulfide could block the surface of nine platinum atoms. In fact, the relative toxicity of dimethyl sulfide to hydrogen sulfide was 9 when corrected for the amounts of the two poisons *on the catalyst*. Based on the amounts of poison in the reduction mixtures, however, the relative toxicity was only 7.1. The dimethyl sulfide was less completely adsorbed.

It would seem that a corollary of Maxted's interpretation would require that the bulkier molecule, while occluding a greater surface area, should be exposed to stronger forces tending to its removal, wherefore it should have a smaller adsorption coefficient. Unfortunately, Maxted and Evans did not examine the distribution of their higher molecular poisons. In the present investigation it was expected that the relative toxicities of dibutyl sulfide and butyl mercaptan in competition with differently absorbed substrates might elucidate this point.

Cyanide and iodide were taken as typical strong poisons and ammonia, acetate, and alkalinity as relatively weak ones. Alkali (indicated as OH^-–OMe^-) is somewhat indefinite under the conditions, the actual concentrations of the

Table I. Half-Poisoning Concentrations. Substrate Nitrobenzene

	C_s in = 0.39					
	Pt/C (1 mg Pt)		Pd/C (0.5 mg Pd)		Rh/C (5 mg Rh)	
Inhibitor	Solvent	$C_{i\,1/2}$	Solvent	$C_{i\,1/2}$	Solvent	$C_{i\,1/2}$
OH^-–OMe^-	99% MeOH	$\sim 7 \times 10^{-2}$	n.i.[e]		Pr[e]	
N_3^-	95% MeOH	$> 8 \times 10^{-3}$	75% MeOH	$\sim 5 \times 10^{-3}$		
I^-	90% MeOH	$\sim 4 \times 10^{-3}$ [a]	90% MeOH	1.8×10^{-6} [b]		
			75% MeOH	1.8×10^{-6} [b]		
CN^-	75% MeOH	4×10^{-5}	75% MeOH	4×10^{-5}		
	65% MeOH	6×10^{-4} [b]	90% MeOH	2×10^{-5}		
Bu_2S	75% MeOH	2×10^{-6} [b,c]	75% MeOH	2×10^{-6} [b]	75% MeOH	10^{-5}
BuSH	75% MeOH	1.7×10^{-6} [d]	75% MeOH	1.2×10^{-6} [b]	75% MeOH	1.5×10^{-5}

[a] Done with Pt/C (Z). [b] Poisoning data in fair agreement with theoretical curves. [c] From crossover experiments. Apparent $C_{i\,1/2} = 2.6 \times 10^{-6}$. [d] From crossover experiments. Apparent $C_{i\,1/2} = 5 \times 10^{-6}$. [e] n.i. = no inhibition; Pr = promotion.

Table II. Half-Poisoning Concentrations. Substrate Acetophenone

	Pt/C (10 mg Pt) C_s in = 1.7		Pd/C (5 mg Pd) C_s in = 1.38		Rh/C (5 mg Rh) C_s in = 1.7	
Inhibitor	Solvent	$C_{i\,1/2}$	Solvent	$C_{i\,1/2}$	Solvent	$C_{i\,1/2}$
OH^-–OMe^-	99% MeOH	10^{-4} [a]	90% MeOH	$\sim 10^{-4}$	75% MeOH	6×10^{-3}
Acetate	99% MeOH	10^{-4} [a]			75% MeOH	$\sim 2 \times 10^{-2}$
NH_3	99% MeOH	5×10^{-4} [a]	90% MeOH	7×10^{-4}	75% MeOH	$\sim 10^{-2}$
I^-	99% MeOH	3×10^{-6} [b]	90% MeOH	5×10^{-6} [a]	75% MeOH	4×10^{-5} [a]
	75% MeOH	2.8×10^{-5} [a]				
CN^-	99% MeOH	2×10^{-6} [a]				
	75% MeOH	4×10^{-5} [a]				
Bu_2S	75% MeOH	2.5×10^{-6} [c,e]	90% MeOH	3×10^{-5} [a,e]	75% MeOH	1.6×10^{-5} [a]
BuSH	75% MeOH	3×10^{-6} [d,e]	90% MeOH	1.4×10^{-5} [a,e]	75% MeOH	8×10^{-5} [a]

[a] Poisoning data in fair agreement with theoretical curve. [b] From crossover experiments. Apparent $C_{i\,1/2} = 8 \times 10^{-6}$. [c] From crossover experiments. Apparent value about the same. [d] From crossover experiments. Apparent $C_{i\,1/2} = 8 \times 10^{-6}$. [e] Run in 0.115 M $HClO_4$.

two anions being unknown. Since, however, these other anions and ammonia were to be examined in previously neutralized solution, it was essential to know what effect small amounts of OH^-–OMe^- would have on the rate. Inhibition with chloride and bromide was readily demonstrated, but half-poisoning could seldom be attained. Later, attempts were made in the reduction of benzene and acetophenone on Rh/C where the substrates seemed weakly absorbed. Azide ion was examined in several reductions because of possible inhibition from it when azide is used to introduce the amino group into nucleosides and a noncrystalline intermediate is hydrogenated.[10]

Experimental Section

Materials. The preparation of catalysts and purification of substrates have been discussed in the preceding communication. Standard solutions of NaCl, KI, NaBr, KCN, and NaCN, NaN_3, K and Na acetate, and NH_4Cl were prepared in methanol, usually M/10 in concentration and diluted further when required. Alkali was 1 M NaOH diluted 1:10 in methanol. Dibutyl sulfide (Aldrich) and butyl mercaptan (E.K.) were prepared as M/10 solutions in methanol, which were diluted further as needed. The more dilute solutions of butyl mercaptan were prepared shortly before use.

Methods. The procedure for poisoned reductions was mainly the same as in the kinetic runs described in the previous communication except that when the poison concentration was low (below 10^{-3}), it was necessary to shake in vacuo before admitting hydrogen. This shaking period was 2 or 3 min with very low poison concentrations.[11]

Somewhat greater tolerance of temperature deviations was possible. In exploratory runs when the rate was not close to the critical half-poisoned value, an informative result could be obtained without concern for the temperature. When the rate was in the vicinity of half that of the standard, an approximately constant range covering the consumption of 5–10 mmol of hydrogen (and lasting 5–20 min) was the best that could be expected.[12] The hydrogenation was usually stopped 3–5 min after a significant drop in rate had been observed. As cooling was generally excessive in this period, it was considered normal for the final temperature to be about 1 °C low.

Standards. These are given in the preceding communication. Since it was desired to avoid uncertainty as to the nature of the poison, all these inhibitors except the sulfur compounds were added to neutralized solutions, and poisoning was referred to the *neutral* reduction rate. Two methods were employed with ammonia. The first, used with platinized charcoal, was to add to the catalyst preparation sufficient of a standard solution of ammonia in methanol to neutralize the residual HCl and produce the desired concentration of ammonia. The second procedure, regarded as preferable, was to add NH_4Cl solution to give an M/100 solution and, thereafter, to add M/10 alkali (in methanol) to neutralize the residual HCl and liberate the amount of ammonia desired. With this procedure, the reference standard was the rate in a neutralized solution M/100 in NH_4Cl (generally about 10% lower than the neutral rate).

Under the above conditions, inhibition by ammonia could be differentiated clearly from hydroxide (or alkoxide) poisoning. This was not the case with the stronger base pyrrolidine. Assuming that the dissociation constants known for aqueous solutions were approximately valid in the partly methanolic solutions employed, it could not be determined whether toxicity was due to pyrrolidine base or to hydroxide and alkoxide predictably present.[13]

The sulfur compounds were studied in acid solution, and the poisoned runs referred to acid rates except for the reductions of benzene and acetophenone by Rh/C, which were in neutral solution.

Crossover Experiments. This procedure is a variant of that devised by Maxted and Evans[9c] to determine the distribution of poison between catalyst and solution. The essential difference is due to the physical properties of the catalysts used. Maxted and Evans operated with Willstätter platinum, a relatively dense powder, from which almost all of the solution could be drawn off. While platinized charcoal, the only one of the present catalysts regarded as stable enough for this type of experiment, settles fairly well, clearly not all the solution could be removed.

Accordingly, two identical batches of catalyst were prepared. To the first (A) methanol was added to give 50 ml of the desired composition. The solution was mixed and allowed to stand overnight stoppered. To the second batch of catalyst (B) was added solvent,

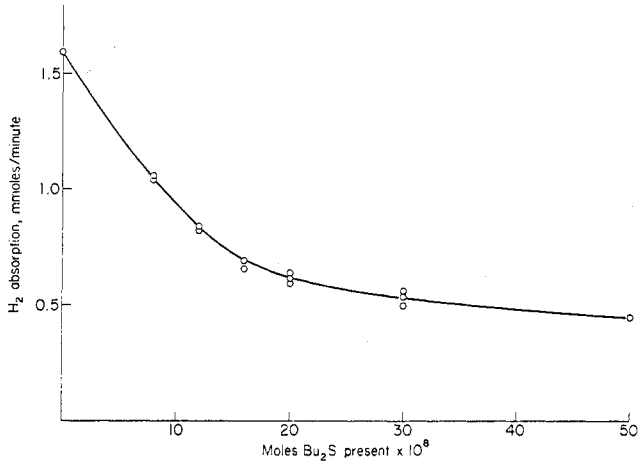

Figure 3. Poisoning curve: Bu_2S vs. $PhNO_2$ in 75% MeOH, 0.46 M $HClO_4$, 1 mg of Pt as Pt/C (5%).

substrate, and a quantity of poison sufficient to produce a known degree of inhibition, conveniently with about one-third of standard activity. (With reference to a previously determined poisoning curve such as that shown in Figure 3.) The mixture, now with a volume of 50 ml, was placed on the reducing apparatus, evacuated, and shaken for 5 min. It was then allowed to settle overnight in vacuo. In the morning, 40 ml of the supernatant of bottle A was removed and discarded. Forty milliliters of the supernatant of bottle B was transferred to A plus one-fifth of the standard charge of substrate (and of $HClO_4$ if used). To bottle B was added $\frac{4}{5}$ of the standard charge of substrate (and acid) plus solvent to 50 ml. The two batches were then reduced and the rates determined. By reference to the poisoning curve, it was then possible to determine how much poison was in each reduction mixture. The sum of these quantities should equal the amount initially placed in B (a deviation of ±10% was considered acceptable). The container A had, during reduction, $\frac{4}{5}$ of the poison present in solution. Container B held $\frac{1}{5}$ of the poison in solution plus that adsorbed on the catalyst. The distribution, of course, applied to the poisoning level of B as originally equilibrated. From this, assuming the validity of the theoretical curve, the half-poisoning concentration was deduced.

It is, of course, obvious that this operation must be futile unless a considerable proportion of the poison is present in both solutions. It is, therefore, of no use with weak poisons (if, for example, one should wish to learn if an apparent inhibitor is really being adsorbed).

Results and Discussion

Tables I–IV show the half-poisoning concentrations obtained. The azide data are given as tentative. This inhibitor was relatively weak, and there was some question as to its stability under the conditions.[14]

In nitrobenzene reductions with Pt/C, iodide behaved rather irregularly. Speculations are possible as to reversible involvement in the reduction process whereby part of the poison could have a different valence state temporarily. All that can be said on this definitely is that at the end of one such reduction, the iodide introduced could be quantitatively recovered as silver iodide.

Cyanide seemed to be stable in the presence of platinum but to be vulnerable to the larger amount (5 mg) of palladium used in acetophenone reductions. With the rhodium catalysts all inhibition was gone after 2 min of hydrogenation.[15]

With the sulfur compounds, especially dibutyl sulfide, there was a tendency with the lower concentrations of poison for the rate to *increase* after about 10 min. This is interpretable as due to rupture of the R–S bond to liberate a compound of lower toxicity.[16] In such cases the level rate *before* the increase was regarded as valid.

The difficulties encountered in cyclohexene reductions with the enormously active rhodium catalyst have been mentioned in the previous communication. The data in the last column of Table III are tentative, except for the case of NH_3 poisoning, since obtained on substrate giving inferior ($\frac{2}{3}$–$\frac{3}{4}$ of standard) control values. They are probably correct within a factor of 2.

Only a few poisoning data are given here for the Pd/C reductions of benzaldehyde, benzyl alcohol, and benzyl methyl ether. With the benzyl compounds, the neutral rate was not usefully above zero. With benzaldehyde, most of these poisons could be expected to react with the substrate.

Table III. Half-Poisoning Concentrations. Substrate Cyclohexene[d]

Inhibitor	Pt/C (1 mg Pt) 3% catalyst	Pd/C (0.5 mg Pd) 3% catalyst	Rh/C (0.1 mg Rh) 1% catalyst
$O\bar{H}$–$O\bar{M}e$	5×10^{-5} [a]	Pr	Pr
Acetate	8×10^{-5}	$4\text{-}5 \times 10^{-2}$	(3×10^{-3}) [b]
NH_3	10^{-3}	1.2×10^{-3}	1.5×10^{-3}
N_3^-		$\sim 6 \times 10^{-3}$	
I^-		1.5×10^{-4} [a]	(1.6×10^{-6}) [b]
CN^-	8×10^{-7}	8×10^{-5}	
Bu_2S	7×10^{-7} [a,c]	3×10^{-6} [c]	(6.4×10^{-7}) [b,c]
BuSH	4×10^{-6} [a,c]	3.2×10^{-6} [c]	(1.6×10^{-6}) [b,c]

[a] Poisoning data in fair agreement with theoretical curves. [b] Tentative values obtained with relatively poor substrate. [c] 0.023 M $HCl\ O_4$ present. [d] 90% MeOH, C_s in = 0.6.

Table IV. Miscellaneous Poisoning Data

Catalyst	Substrate	Solvent	Inhibitor	$C_{i\,1/2}$
Rh/C (E)[a]	Benzene	85% MeOH	Cl^-	$\sim 2 \times 10^{-2}$
	(C_s in = 2.0)		Br^- [b]	8×10^{-3}
Rh/C (E)[a]	(C_s in = 2.0)		I^- [b]	5×10^{-5}
Rh/C (E)[a]	(C_s in = 2.0)		$O\bar{H}$–$O\bar{M}e$	8×10^{-3}
Rh/C (E)[a]	(C_s in = 2.0)		NH_3 [b]	5.5×10^{-3}
Rh/C (E)[a]	(C_s in = 2.0)		Bu_2S [b]	1.5×10^{-5}
Rh/C (E)[a]	(C_s in = 2.0)		BuSH	10^{-4}
Rh/C (E)[a]	Acetophenone	75% MeOH	Cl^-	$>2 \times 10^{-2}$
	(C_s in = 1.7)	75% MeOH	Br^-	10^{-2}
Pd/C	Ph CHO	90% MeOH	I^- [b]	10^{-5}
	(C_s in = 2.08)	(Neutral)		
Pd/C	(C_s in = 2.08)	(0.23 M $HClO_4$)	Bu_2S [b]	3×10^{-5}
	Ph CH_2 OH	90% MeOH		
	(C_s in = 1.95)	0.23 M $HClO_4$	Bu_2S [b]	1.2×10^{-5}
	(C_s in = 1.95)	0.23 M $HClO_4$	BuSH [b]	2.4×10^{-5}
	Ph CH_2 OMe	75% HAc	Bu_2S [b]	2.5×10^{-5}
	(C_s in = 1.58)	0.23 M $HClO_4$	BuSH	3.5×10^{-5}

[a] All rhodium reductions done in neutral solution. [b] Poisoning data in fair agreement with theoretical curve.

Table V. Analysis of Crossover Experiments

Substrate	Inhibitor	C_s in/$C_{i\,1/2} = \alpha_i/\alpha_s$	Activity at equilibration level, %	Inhibitor on catalyst, mol	M[a]/i
$PhNO_2$	Bu_2S	2×10^5	33	10^{-7}	50
(75% MeOH)	BuSH	2.3×10^5	40	2×10^{-7}	25
(75% MeOH)	Cd^{2+}	6.6×10^4	25	2×10^{-7}	25
PhCOMe					
(75% MeOH)	Bu_2S	6.7×10^5	33	1.5×10^7	330
(75% MeOH)	BuSH	5.7×10^5	33	5.5×10^7	90
(75% MeOH)	Cd^{2+}	1.1×10^5	33	4×10^7	125
(99% MeOH)	I^-	5.7×10^5	33	2.8×10^7	200

[a] g-atoms of Pt in catalyst/mol of inhibitor adsorbed.

General Aspects. Inspection of Tables I–IV shows two major classes of inhibitors: strong poisons—cyanide, iodide, and the sulfur compounds—and weak inhibitors—ammonia, azide, acetate, and alkali. The half-poisoning concentrations of the strong poisons are low, and it is probably not justified to attempt fine analysis except for the crossover experiments.

The half-poisoning concentrations of the weak poisons cannot be seriously in error because of extensive adsorption. Consideration of these and of a few of the situations with stronger poisons reveals certain anomalies (conditions in which an inhibitor, certainly adsorbed because of the result with one substrate, has no effect or very much less effect in the reduction of another substrate by the same catalyst). Particularly marked is the behavior of alkali in the reduction of nitrobenzene on all three metals and in the reduction of cyclohexene over Pd and Rh. The reductions of acetophenone on all three metals and of cyclohexene on Pt are clearly inhibited; also, the behavior of the iodide in the platinum-catalyzed reduction of nitrobenzene. It seems possible that these anomalies are related to the existence of alternative reduction schemes (differing in fine detail) for some of which the initial adsorption and first attachment of hydrogen may not be uniquely rate determining. Nitrobenzene is almost certainly reduced stepwise. Reduction of olefins at low hydrogen pressure has frequently been observed to be accompanied by bond migration and occasionally aromatization.[17] Thus, residence of substrate on the catalyst surface is of finite though small duration and interference by other adsorbed substances may at times affect the overall rate.

It had been anticipated that inorganic poisons would be less potent in more aqueous solutions. This is borne out by comparisons of the $C_{i\,1/2}$ data for cyanide poisoning against nitrobenzene and acetophenone and for iodide poisoning against acetophenone with platinum. With the weaker poisons variation of solvent was not always attempted. The choice of high methanol percentages in the platinum reductions generally came from inability to obtain half-poisoning in more aqueous solutions.

The further hypothesis offered earlier as to the binding forces of higher molecular sulfur compounds is also well borne out. Against the strongly adsorbed nitrobenzene it is evident that butyl mercaptan is a better competitor than dibutyl sulfide though inherently less toxic. (The *inherent* toxicities of Maxted based on adsorbed quantities are in good agreement with those calculated from the crossover experiments.[18]) All of the substrates of the present work are probably better adsorbed than that of Maxted and Evans, who started with molar solutions of crotonic acid in glacial acetic acid. If Maxted was generally operating below the C_s lim of his substrate, the toxicities he would have observed should have been generally higher than in the present work, and a greater proportion of his poisons should have been on the catalysts. This seems to have been the case for the instances investigated.

Table V shows a further analysis of the crossover results, in which are included data on cadmium poisoning from the succeeding communication.[19] The last two columns give the amounts of poison *on* the catalyst corresponding to the poisoning level of the equilibrated solutions and the ratio of total platinum atoms to moles (or atoms) of adsorbed poison.[20]

Beyond the expected evidence that nitrobenzene competes more successfully with inhibitors than acetophenone, a curious relationship emerges: *A much larger fraction of the catalyst surface has to be occupied by inhibitor to suppress the reduction of nitrobenzene comparably.* There appear to be two simple interpretations of this, not necessarily mutually exclusive.

1. Reduction of acetophenone requires complete planar adsorption, whereas with nitrobenzene, approach of the oxygen atoms to the surface suffices for primary attachment.

2. The more strongly adsorbed substrate may be able to nudge aside single particles of inhibitor.

If the first interpretation is valid, experiments of this sort could provide means of studying the mode of attachment of other substrates.

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Registry No.—Cl^-, 16887-00-6; Br^-, 24959-67-9; I^-, 20461-54-5; MeO^-, 3315-60-4; HO^-, 14280-30-9; Cd^{2+}, 22537-48-0; N_3^-, 14343-69-2; CN^-, 57-12-5; NH_3, 7664-41-7; Bu_2S, 544-40-1; BuSH, 109-79-5; rhodium, 7440-16-6; palladium, 7440-05-3; platinum, 7440-06-4; acetate, 71-50-1; cyclohexene, 110-83-8; acetophenone, 98-86-2; benzene, 71-43-2; nitrobenzene, 98-95-3.

References and Notes

(1) Part I: R. Baltzly, *J. Org. Chem.*, preceding paper in this issue.
(2) The author wishes to express his gratitude to the Wellcome Research Laboratories and to the Public Health Service Grant CA-08748 from the National Cancer Institute for partial financial support of this investigation.
(3) For a review, cf. R. Baltzly, *Ann. N.Y. Acad. Sci.*, **145**, 31–45 (1967).
(4) This omits substances the toxicity of which may be due to reduction to a primary poison. For example, a sulfoxide may be a poison *per se* but is almost certainly reduced to a sulfide. A number of such poisons were examined by V. Horner, H. Reuter and E. Herrmann, *Justus Liebigs Ann. Chem.*, **660**, 1 (1962). Except when the ostensible poison is more potent than its presumptive reduction product (e.g., Mexted's mercaptans and dialkyl sulfides which are more toxic than hydrogen sulfide), it is not a simple matter to identify the true inhibitor in such cases.
(5) Cf. ref 26 of part I of this series.
(6) The α symbols are adsorption coefficients of substrate and inhibitor; the C symbols are concentrations corresponding. The relationship between this equation and that used by Maxted is discussed in ref 3. $C_{i\,1/2}$ is the concentration of poison that produces a rate half that of the unpoisoned standard.
(7) E. B. Maxted and S. Akhtar [*J. Chem. Soc.*, 1995 (1960)] showed that on metal oxide supports catalytic metals were in patches. A more gen-

eral argument is that the metal layer on a charcoal such as Darco cannot be continuous since a monatomic layer covering the reported surface of this charcoal would require more metal (30% of the weight of the carrier) than corresponds to high efficiency. Further, since too high a carrier–metal ratio results in *less* active catalysts, it must be possible for the metal to be spread too thin. It, therefore, seems likely that active surfaces are supported by several layers of underlying metal.

(8) Curve C resembles some of those shown in the earlier Maxted papers, in which he proposed the existence of two types of active sites. An alternative interpretation is offered in ref 2, p 38.

(9) (a) E. B. Maxted and H. C. Evans, *J. Chem. Soc.*, 1004 (1937); (b) *ibid.*, 455 (1937); (c) *ibid.*, 2071 (1938).

(10) In various instances (e.g., G. B. Elion, private communication), protective benzyl groups elsewhere in the molecule were removed poorly by the Pd/C hydrogenation employed to convert N_3 to $NH_2 + N_2$. The author is of the opinion that poisoning through sulfur analogues present in commercial benzyl chloride is probably responsible. The shape of nucleosides, with ring systems at a sharp angle to each other, also presents a possibility for self-poisoning, should the nitrogen-containing heterocycle be adsorbed preferentially.

(11) In low concentration the poison does not attain the catalyst surface immediately. Without such a period of equilibration, the reduction data resemble those often observed in preparative reductions with poison present: the initial rate is almost normal and diminishes after 1 or 2 min to a low or zero level.

(12) As mentioned in the previous communication, a true C_s lim cannot exist in the presence of serious concentrations of inhibitor. However, deviations from constancy do not become notable during the first 10–20% of reaction.

(13) E. B. Maxted and M. S. Biggs, *J. Chem. Soc.*, 3844 (1957), reported on the toxicity of ammonia, butylamine, cyclohexylamine, and dicyclohexylamine in the reduction of cyclohexene over platinum. To avoid inhibition by solvent anions, they employed cyclohexane as solvent. This, in turn, raises questions as to the influence of the solvent on the activity of the poisons. (All were considerably more toxic than in the present study, but there was about a twofold variation among the first three with dicyclohexylamine much less toxic. Maxted suggested that this might be a case of hindrance, ignoring solubility effects.) In the present study it had been planned to examine ammonia, pyrrolidine, piperidine, and morpholine, whose activities should not vary much because of solubility. This plan was abandoned when it was found impossible to deal with the stronger bases under comparable conditions.

(14) Regarding N_3^- as a nucleophile, its adsorbed condition has some resemblance to hydrazoic acid.

(15) Rhodium has been especially recommended for the reduction of nitriles. Cf. M. Freifelder, *J. Am. Chem. Soc.*, **82**, 3286 (1960).

(16) While this phenomenon does not appear to have been observed previously with noble metals, preparative dethiation with Raney nickel is, of course, a familiar process.

(17) E.g., the occurrence of β-naphthol as a by-product in the reduction of octalone. Cf. R. L. Augustine, D. C. Migliorini, R. F. Fusante, C. S. Sudano, and M. J. Sisbarro, *J. Org. Chem.*, **34**, 1075 (1969).

(18) Maxted's ratio was 2.5:1 relating to the reduction of crotonic acid. From Table V we see that 2×10^{-7} mol of BuSH permitted 40% activity vs. nitrobenzene, whereas 10^{-7} of Bu_2S permitted 33%. Against acetophenone at 33% activity, the ratio is 3.7:1.

(19) R. Baltzly, *J. Org. Chem.*, following paper in this issue.

(20) Maxted preferred not to work with supported catalysts since he feared that adsorption of poison on the carrier would complicate the situation unduly. Consideration of the data of this table in light of the fact that in the acetophenone reductions ten times as much carrier was used as well as ten times as much metal shows that adsorption on the carrier cannot be significant. Comparing lines 1 and 4 of Table V (Bu_2S poisoning), if the carrier per se in the former case held 10% of the adsorbed poison, the carrier per se in the latter case should have held two-thirds. This seems unlikely.

Studies on Catalytic Hydrogenation. III. Poisoning and Promotion by Cations[1]

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The toxicities of zinc, cadmium, and manganese as bivalent cations earlier reported as equipotent poisons toward platinum have been examined with platinum, palladium, and rhodium on carbon and against a variety of substrates. Zinc and manganese are essentially nontoxic toward palladium and rhodium and, in fact, act as promoters in the palladium-catalyzed hydrogenolysis of benzyl alcohol. The observed promotion and certain variations in toxicity from substrate to substrate are interpreted as due to complex formation between cation and substrate and preferential adsorption of the complex in certain situations.

Maxted and Marsden[3,4] investigated the toxic action of a number of metallic cations in the reduction of crotonic acid in alcohol by Willstätter platinum. It was desired to reexamine a representative group of these against metallized charcoals, and zinc, cadmium, and manganese were selected for study. Of the 12 metallic elements identified by Maxted and Marsden as toxic, these have certain advantages. They are unlikely to be reduced to the metals under the conditions (as are Cu^{2+}, Ag^+, and Hg^{2+} or perhaps Pb^{2+} and Sn^{2+}). They were among the most toxic agents of this type, and their solutions are stable (whereas Fe^{2+} tends to pass to Fe^{3+}). It was anticipated that by using substrates having varying adsorption tendencies, further variation in the toxicities might be revealed, taking into account the arguments of the preceding communications of this series as to reaction kinetics and toxicity.

Since the variation in behavior far exceeded anticipation, it may be in point to outline the chronological course of this investigation. At the start of the program platinized charcoal was studied and the necessary conditions and techniques were worked out with it, using nitrobenzene and acetophenone as substrates. Toxicity studies were interspersed with standard runs as was convenient. The troublesome substrate, cyclohexene, was taken up later after which palladized charcoal was examined and finally (though somewhat incompletely) rhodium on charcoal.

The first data on cationic poisons that became available were, therefore, those of the left half of Table II followed by those of the first section of Table III. While poisoning by nucleophiles (the subject of the preceding communication) showed few unanticipated peculiarities of major importance, the nitrobenzene reductions exhibited far greater variation between Maxted's equitoxic ions than had been felt to be possible. The data with cyclohexene, when obtained, did, however, display the sort of behavior anticipated.

When the study of palladized charcoal was begun, there was special interest in the hydrogenation of benzyl alcohol (taken as an example of debenzylation for which this catalyst is especially preferred). When poisoning by zinc was studied, it was found that increasing concentrations of zinc ion had at first little effect on the reduction rate, but eventually produced a clear *increase* in rate. The prospect then presented itself that some or all of the anomalous results might be the result of concurrent poisoning and promotion.

Major interest in promotion arose from the work of Carothers and Adams[5] and of Faillebin.[6] Carothers and Adams studied promotion in the reduction of aldehydes by Adams'