to light in the presence of riboflavin and $MnCl_2$ is essentially the same as that of pure estrone. The chromatographic data (Fig. 4) on estrone exposed to light in the presence of riboflavin alone show a marked deviation from those expected for estrone. Further work with larger rubber chromatographic columns showed that there are at least three chemically unstable products of irradiated estrone.

Discussion

On the basis of the chemical, spectrophotometric, chromatographic and bioassay data presented in this article, it appears that the estrogens, and more specifically estrone, are oxidatively altered on exposure to light when dissolved in a 95% ethanol solution containing either riboflavin or lumichrome. Under these experimental conditions, the photooxidation of estrone is accompanied by a large loss in biological activity. Manganous ions present in a concentration of 10^{-2} mole per liter almost completely inhibit these photoöxidations.

The finding that estrogens are destroyed by light when in solution with riboflavin or lumichrome is of importance in isolation studies on urinary and blood estrogens, since in these fluids steroids are mixed with appreciable quantities of flavins.

LOS ANGELES, CALIFORNIA

[CONTRIBUTION FROM VENABLE CHEMICAL LABORATORY OF THE UNIVERSITY OF NORTH CAROLINA]

Kinetics of the Catalytic Hydrogenation of Certain Schiff Bases[1]

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The rates of hydrogenation of benzalaniline and twenty-four of its derivatives have been studied. It was found that Hammett's equation does not hold for this reaction, although substituents on the ring do definitely affect the rate of hydrogenation. These effects are discussed.

This work was undertaken to determine quantitatively the effects of various ring substituents on the rate of catalytic hydrogenation of the carbon–nitrogen double bond of various Schiff bases. The Schiff bases used are listed in Table I as compounds 1–24; the secondary amines resulting from their reduction are listed in Table I as compounds 1a–24a. Adams platinum catalyst was chosen for this study because of the reproducibility of results and because its activity remains constant for relatively long periods of time. The hydrogenations were carried out at atmospheric pressure, as this procedure gave convenient reaction rates which could be observed easily and accurately by following the change in volume of hydrogen in a gas buret.

Experimental

Materials.—The Schiff bases used were prepared in one of two ways. **Method A.**—The aldehyde and amine were dissolved in benzene or petroleum ether and the solution refluxed in a round-bottom flask attached to a Dean–Stark trap and reflux condenser until the theoretical amount of water collected in the trap. The solvent was then removed and the Schiff base distilled *in vacuo* or recrystallized from a suitable solvent, usually either ethyl alcohol or petroleum ether.

Method B.—The aldehyde and amine were fused on a steam-bath for about a half hour as described by Law.[2] The product was then purified as in method A.

The Adams platinum catalyst was prepared in the usual manner.[3] Three different batches of the catalyst were prepared, but no appreciable difference in the activity of the three batches could be detected. Ethyl alcohol was used as a solvent for the reductions and tank hydrogen was used directly.

Hydrogenation Procedure.—The hydrogenations were carried out in a 500-ml. erlenmeyer flask which could be connected, by means of a three-way stopcock, to either a water aspirator or a 500-ml. gas measuring buret (filled with water and equipped with a leveling bulb). By means of the same stopcock the measuring buret could be filled with hydrogen from a tank. The solution in the erlenmeyer flask was stirred with a magnetic stirrer and variations in the rate of stirring due to line voltage fluctuations were eliminated by the use of a thordarson automatic voltage regulator.

The anil (0.01 mole) was placed in the erlenmeyer flask with 0.02 g. of prereduced Adams catalyst and 100 ml. of ethyl alcohol. The system was evacuated and then filled with hydrogen. The initial reading of the buret was taken and the magnetic stirrer cut on. The reaction temperature was maintained between 24 and 25° by means of a water-bath. There was no appreciable variation in barometric pressure during any run. Benzalaniline was reduced several times during the course of these experiments to check on reproducibility of results; excellent checks were obtained in every case.

Hydrogenation Products.—After each hydrogenation the platinum catalyst was filtered off and the secondary amine formed by the reduction isolated and identified either as the hydrochloride or the free base (except for benzal-*p*-iodoaniline, which decomposed when the alcohol was removed by distillation). The Schiff bases and their reduction products are listed in Table I along with their physical properties and analytical data for new compounds or a literature reference if the compound is known.

Discussion

In agreement with previous work,[4,5] it was established that the hydrogenations were of zero order with respect to the substrate and directly proportional to the amount of catalyst used. This is shown in Tables II, III and IV.

Four typical hydrogenation curves are shown in Fig. 1. These show that a plot of ml. of hydrogen used *versus* time results in a straight line,

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[1] Taken in part from the dissertation of John A. Montgomery submitted in June, 1951, in partial fulfillment of the requirements for the Ph.D. degree.

[2] H. D. Law, *J. Chem. Soc.*, **101**, 158 (1916).

[3] R. Adams, V. Voorhees and R. L. Shriner, "Organic Syntheses," 2nd Ed., Coll. Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1940, p. 463.

[4] L. Herandez and F. F. Nord, *J. Colloid Sci.*, **3**, 363 (1948).

[5] H. A. Smith and co-workers, THIS JOURNAL, **67**, 272, 276, 279 (1945); **71**, 81, 413, 415 (1949).

TABLE I

COMPOUNDS HYDROGENATED (1–24) AND THEIR PRODUCTS (1a–24a)

No.	Compound	Method of prepn.	n^{25}_{D}	d^{25}_{25}	B.p., °C. (mm.)	M.p., °C.	Nitrogen, % Calcd.	Nitrogen, % Found
1	Benzal-*o*-chloroaniline[a]	A	....	...	168 (5)	.....	...	...
1a	N-(*o*-Chlorophenyl)-benzylamine		....	...	....	39–40	6.42	6.38
2	*p*-Benzalaminobenzoic acid[b]	A	....	...	....	190–191	...	...
2a	*p*-Benzylaminobenzoic acid[c]		....	...	....	165–166	...	...
3	*p*-Dimethylaminobenzalaniline[d]	A	....	...	....	100–102	...	...
3a	N-(*p*-Dimethylaminophenyl)-benzylamine		....	...	....	72–73[e]	12.39	12.19
4	Benzalaniline[f]	A	....	...	....	52	...	...
4a	N-Phenylbenzylamine[h]		....	...	....	214–216[g]	...	...
5	Benzal-*p*-nitroaniline[i]	A	....	...	....	117–119	...	...
5a	N-Benzyl-*p*-phenylenediamine[j]		....	...	....	30	...	...
6	Ethyl *p*-benzalaminobenzoate[k,l]	A	....	...	205–206 (5)	42.5	...	...
7	Benzal-*p*-bromoaniline[m]	A	....	...	....	66	...	...
7a	N-(*p*-Bromophenyl)-benzylamine[n]		....	...	....	51–52	...	...
8	*m*-Benzalaminobenzoic acid	A	....	...	....	131–132[o]	6.22	6.41
8a	*m*-Benzylaminobenzoic acid[c]		....	...	....	101–103	...	...
9	*p*-Chlorobenzalaniline[p]	B	....	...	....	64–65	...	...
9a	N-(*p*-Chlorobenzyl)-phenylamine[p]		....	...	....	210–211[g]	...	...
10	*p*-Chlorobenzal-*p*-chloroaniline[m]	B	....	...	....	110–111	...	...
10a	N-(*p*-Chlorophenyl)-*p*-chlorobenzylamine		....	...	....	65–66	5.56	5.58
11	*p*-Methylbenzalaniline[p]	B	1.6394	1.046	320 (747)	.....	...	...
11a	N-Phenyl-*p*-methylbenzylamine[p]		....	...	....	187–189[g]	...	...
12	Benzal-*p*-toluidine[p]	B	....	...	150–151 (4)	29–30	...	...
12a	N-Benzyl-*p*-methylphenylamine[p]		....	...	....	177–179[g]	...	...
13	*p*-Methylbenzal-*p*-toluidine[p]	B	....	...	....	91–93	...	...
13a	N-(*p*-Tolyl)-*p*-methylbenzylamine[p]		....	...	....	162–164[g]	...	...
14	Benzal-*m*-toluidine[p]	B	1.6353	1.040	317 (747)	.....	...	...
14a	N-Benzyl-*m*-methylphenylamine[p]		....	...	....	195–197[g]	...	...
15	Benzal-*p*-fluoroaniline	B	....	...	....	56.8	7.04	6.98
15a	N-(*p*-Fluorophenyl)-benzylamine		....	...	....	32–33	6.97	7.00
16	Benzal-*p*-anisidine[k]	B	....	...	162–163 (3)	70–71	...	...
16a	N-Benzyl-*p*-anisidine[q]		....	...	154 (2)	50–51	...	...
17	*p*-Methoxybenzalaniline[r]	B	....	...	167–168 (4)	64	...	...
17a	N-Phenyl-*p*-methoxybenzylamine[s]		....	...	154–155 (2)	48–49	...	...
18	Benzal-*o*-toluidine[p]	B	1.6310	1.036	122 (3)	.....	...	...
18a	N-(*o*-Tolyl)-benzylamine[p]		1.6078	1.027	122–124 (2)	.....	...	...
19	Benzal-*p*-iodoaniline[t]	B	....	...	....	82–84	...	...
19a	[u]							
20	*m*-Chlorobenzalaniline[p]	B	1.6510	1.172	141–143 (3)	.....	...	...
20a	N-Phenyl-*m*-chlorobenzylamine[p]		1.5893	1.137	144–145 (2)	.....	...	...
21	Benzal-(*m*-trifluoromethyl)-aniline	B	....	...	113–114 (2)	66–68	5.62	5.76
21a	*m*-Benzylaminobenzotrifluoride		1.5408	1.229	118–119 (2)	.....	5.58	5.55
22	Benzal-(*p*-acetyl)-aniline[v]	B	....	...	....	95–97	...	...
22a	*p*-Benzylaminoacetophenone		....	...	....	89–90	6.22	6.29
23	Benzal-(*p*-trifluoromethyl)-aniline	B	....	...	136–138 (5)	63–65	5.62	5.73
23a	*p*-Benzylaminobenzotrifluoride		....	...	....	53.4	5.58	5.54
24	Benzal-*p*-chloroaniline[m]	B	....	...	....	62–63	...	...
24a	N-(Benzyl)-*p*-chlorophenylamine[w]		....	...	....	46–48	...	...

[a] O. Fisher and P. Neber, *Ber.*, **45**, 1094 (1912).
[b] W. Manchot and J. R. Furlong, *ibid.*, **42**, 4389 (1909).
[c] G. Lockemann and H. Rein, *ibid.*, **80**, 485 (1947).
[d] F. Sachs and W. Lewin, *ibid.*, **35**, 3573 (1902).
[e] L. Zechmeister and J. Truka, *ibid.*, **63**, 2883 (1930), report a melting point of 62°.
[f] L. A. Bigelow and H. Eatouger in H. Gilman, Ed., "Organic Syntheses," 2nd Ed., Coll. Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1944, p. 80.
[g] Melting point of the amine hydrochloride.
[h] S. M. McElvain, "The Characterization of Organic Compounds," The Macmillan Co., New York, N. Y., 1945, p. 211.
[i] W. v. Miller, J. Plöchl and G. Rohde, *Ber.*, **25**, 2053 (1892).
[j] R. Medola and J. H. Coste, *J. Chem. Soc.*, **55**, 591 (1889).
[k] G. Reddelien and H. Danilof, *Ber.*, **54**, 3132 (1921).
[l] Reduction of Compound 6 did not take place under these conditions.
[m] A. Hantzsch and O. Schwab, *Ber.*, **34**, 822 (1901).
[n] W. S. Emerson and C. H. Shunk, THIS JOURNAL, **63**, 2485 (1941).
[o] A. Hantzsch and F. Knalft, *Ber.*, **24**, 3518 (1891), report a melting point of 119°.
[p] See reference 2.
[q] E. Frolich and E. Wedekind, *Ber.*, **40**, 1010 (1907).
[r] H. Schiff, *Ann.*, **150**, 195 (1869).
[s] O. J. Steingart, *ibid.*, **241**, 337 (1887).
[t] F. B. Dains, O. O. Malleis and J. T. Meyers, THIS JOURNAL, **35**, 974 (1913).
[u] The reduced compound decomposed during removal of the alcohol in the isolation process.
[v] M. Scholtz and L. Huber, *Ber.*, **37**, 392 (1904).
[w] R. E. Davies, H. T. Openshaw, F. S. Spring, R. H. Stanley and A. R. Todd, *J. Chem. Soc.*, 295 (1948).

the slope of which is equal to the specific reaction rate (in ml. per minute). The volume of hydrogen per unit of time was corrected to standard conditions and the reaction rates then calculated in moles per second. Tabulation of the rate constants thus obtained is given in Table V.

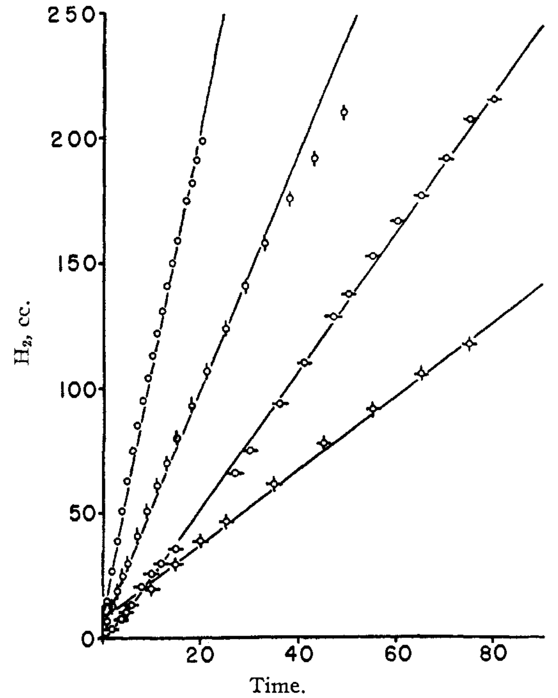

Fig. 1.—Typical hydrogenation curves: O, *p,p'*-dichlorobenzalaniline; ϕ, benzal-*p*-anisidine; -O-, benzal-*o*-chloroaniline; -ϕ-, benzalaniline.

TABLE II

EFFECT OF CONCENTRATION OF BENZALANILINE ON THE RATE OF HYDROGENATION

Concn. benzalaniline, g./100 ml.	*k*, ml./min., 0.02 g. PtO_2
0.45	1.29
0.90	1.20
1.81	1.33
2.50	1.42
3.20	1.40

TABLE III

EFFECT OF CONCENTRATION OF *p*-CHLOROBENZAL-*p*-CHLOROANILINE ON THE RATE OF HYDROGENATION

Concn. *p*-Chlorobenzal-*p*-chloroaniline, g./100 ml.	*k*, ml./min., 0.02 g. PtO_2
1	10.0
2	9.9
2.5	10.0
3	10.2

TABLE IV

EFFECT OF THE AMOUNT OF CATALYST ON THE HYDROGENATION OF *p*-CHLOROBENZAL-*p*-CHLOROANILINE

Amount of catalyst	*k*, ml./min.
0.01	5.3
.02	10.1
.03	15.0

TABLE V

RATE CONSTANTS FOR THE HYDROGENATION OF SOME SCHIFF BASES

Compound	*k* × 10^6, moles/sec. 0.02 g. PtO_2
p-Chlorobenzal-*p*-chloroaniline	9.5
Benzal-*p*-iodoaniline	4.4
p-Methoxybenzalaniline	4.2
Benzal-*p*-bromoaniline	3.7
p-Chlorobenzalaniline	3.6
Benzal-*p*-chloroaniline	3.5
p-Dimethylaminobenzalaniline	3.4
Benzal-*p*-anisidine	3.4
p-Methylbenzal-*p*-toluidine	3.3
Benzal-*p*-toluidine	3.2
p-Methylbenzalaniline	2.8
m-Benzalaminobenzoic acid	2.6
Benzal-*m*-toluidine	2.4
p-Benzalaminobenzoic acid	2.3
Benzal-*o*-chloroaniline	1.9
m-Chlorobenzalaniline	1.8
Benzal-*p*-fluoroaniline	1.7
m-Benzalaminobenzotrifluoride	1.6
p-Benzalaminobenzotrifluoride	1.5
Benzal-*o*-toluidine	1.4
Benzalaniline	0.95
p-Benzalaminoacetophenone	0.70

An attempt was made to fit the above data to Hammett's[6] equation ($\log K - \log K^0 = \rho\sigma$), but the calculated values of rho for the reaction varied widely. This is an indication that other factors outweigh the effect of the electron shifts caused by the introduction of a polar group into the benzene rings. The following observations about the effect of the various substituent groups on the reaction rate should be noted, however.

The effect is of the same magnitude whether the substituent is attached to the benzal or the aniline ring. The effect of halogens in the para position is in the order: I > Br > Cl > > F, all increasing the reduction rate over that of benzalaniline. Chlorine in either the *m*- or the *o*-position has about the same effect—it increases the rate but much less than it does in the *p*-position. In general an electron releasing group in the *p*-position increases the rate more than an electron attracting group in this position. An electron releasing group is much more effective in the *p*-position than in the *m*-position, whereas an electron attracting group has only slightly more effect in the *m*- than in the *p*-position.

Only three groups (acetyl, carbethoxy and cyano—all electron attracting groups) were found to decrease the rate, and two of those—the carbethoxy and the cyano groups—slowed the hydrogenation down to such an extent that a reliable rate could not be obtained. The effect of the nitro group could not be determined since it was reduced at a rate comparable to that of the carbon–nitrogen double bond.

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(6) L. P. Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1940, p. 186.