addition of water. The R_f value was 0.20 to 0.23 in 25% butanone-hexane. The material slowly gave a magenta spot when sprayed with DMACA reagent.

The total yield was 395 mg. (40%) (m.p. 138-39° C.) Anal. Calcd. for $C_{26}H_{31}NO_{11}$: C, 58.53; H, 5.86; N, 2.63. Found: C, 58.19; H, 5.83; N, 2.87.

Methyl-1-(β-D-glucopyranosyl-3-indoleacetate (V). To an ice-cold solution of 250 mg. of ethyl-1-(β-tetra-*O*-acetylglucopyranosyl)-3-indoleacetate in 25 ml. of methanol was added 3.2 ml. of 0.04*N* $Ba(OCH_3)_2$ solution. The solution was allowed to stand for 24 hours at 5° C. Approximately 100 mg. of damp IR Amberlite resin was added and the mixture stirred for 1 hour and filtered. After evaporation and readdition of methanol, the product crystallized on standing at −5° C. for 1 to 2 days. The R_f was 0.15 in $HCCl_3$–ETOAc–HCO_2H(5:4:1 v./v.). A slowly developing magenta spot appeared when the material was treated with DMACA reagent. The yield was 110 mg. (67%) {m.p. 163–64°, $[\alpha]_D^{25} = -8.3°$ C. (c = 1.0, CH_3OH)}. Absorption spectra indicated $\lambda_{\max(\mu)}^{\mathrm{KBr}}$ 2.75 to 3.20 (OH), 5.83 (ester C=O), 8.10 to 8.55 $(\mathrm{R{-}O{-}\overset{\overset{O}{\|}}{C}{-}})$; $\lambda_{\max(m\mu)}^{\mathrm{ethanol}}$ (95%) 272, 279, and 290. Anal. Calcd. for $C_{17}H_{21}NO_7$: C, 58.11; H, 6.03; N, 3.99. Found: C, 57.73; H, 6.17; N, 3.96.

Saponification of the methyl ester with barium hydroxide gave an amorphous precipitate which could be separated from the starting material with preparative thin-layer chromatography, but resisted crystallization.

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Hydrogenation of Acetophenone Oxime and Its O-Acylated Derivatives

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The O-acetyl and O-benzoyl derivatives of acetophenone oxime give faster rates of hydrogenation and higher primary amine yields than the oxime itself in the presence of palladium and rhodium catalyst. Secondary amine formation was also examined and a technique for determining the possible intermediacy of Schiff bases in the hydrogenation of the oximes is proposed.

IN CONNECTION with the investigation of factors involved in the formation of primary and secondary amines in the hydrogenation of oximes, the reduction of acetophenone oxime and its *O*-acetyl and *O*-benzoyl derivatives was studied using palladium and rhodium catalysts.

EXPERIMENTAL

Acetophenone oxime was recrystallized from ethanol before use. The *O*-acetyl (*1*) and *O*-benzoyl (*3*) derivatives of acetophenone oxime and the Schiff base II, *N*-methylbenzylidene-α-methylbenzylamine (*4*), were prepared by known procedures. The solvents were analytical reagent grade.

The palladium and rhodium catalysts were commercial preparations manufactured by Engelhard Industries, Newark, N. J., of 5% reduced metal on carbon of high surface area (Norit).

The hydrogenations were carried out in a Parr low pressure hydrogenation apparatus at room temperature at an initial pressure of 50 p.s.i. In a typical run, 0.1 mole of the oxime or its derivative in 75 ml. of solvent was charged together with 5 grams of catalyst. After an essentially quantitative uptake of 0.2 mole of hydrogen, the catalyst was filtered off. Concentrated hydrochloric acid (16 ml.) was added to the filtrate and the solution evaporated to dryness. The amine hydrochlorides that formed were washed with ether, dried, and weighed. The salts were then treated with a 10% sodium hydroxide solution and the free amines extracted with ether. The ether layer was washed once with water and subjected to gas chromatographic analysis. The chromatography was carried out with an Aerograph Autoprep, Model A-700, using a 10-foot 30% Carbowax 20M on 60/80 Chromosorb W column at 220°. To this ether layer was again added concentrated hydrochloric acid (16 ml.) and the mixture evaporated to dryness to yield approximately the same weight of amine hydrochlorides as originally isolated. These hydrochlorides when converted again to the free amines with base gave the same ratios of primary to secondary amine and of *d,l*- to *meso*-secondary amine, indicating that no losses were encountered in our original workup procedure.

Table I. Hydrogenation of Acetophenone Oxime and Its Derivatives

Compound	Catalyst	Solvent	Time, Min.	VPC Analysis				Yield of Primary Amine, %[a]
				Amine Composition, %		Secondary Amine Composition, %		
				Primary	Secondary	*d,l*	*meso*	
Oxime	Pd	MeOH	10	54	46	59	41	48
O-Benzoate	Pd	MeOH	9	74	26	88	12	63
O-Acetate	Pd	MeOH	8	83	17	80	20	66
Oxime	Pd	MeOH + 1 equiv. AcOH	14	78	22	60	40	66
	Pd	AcOH	20	88	12	46	54	50
	Pd	THF	22	91	9	66	34	82
	Rh	MeOH	115	84	16	71	29	55
O-Benzoate	Rh	MeOH	53	96	4	83	17	59
O-Acetate	Rh	MeOH	29	100	0	0	0	62
Schiff base II	Pd	THF				85	15	

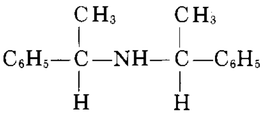
[a] Calculated from VPC analysis and weight of isolated amine hydrochlorides.

DISCUSSION

Rylander (*2*) has reported the hydrogenation of cyclohexanone oxime in several solvent systems in the presence of platinum metal catalysts. The data in Table I on the hydrogenation of acetophenone oxime indicate that the effect of catalyst cannot be reliably predicted from one oxime to the other. Whereas Rylander (*2*) found palladium to be far less active than rhodium in the hydrogenation of cyclohexanone oxime, in the case of acetophenone oxime the rate of reduction with palladium was much faster than with rhodium. Both cyclohexanone oxime and acetophenone oxime are reduced more slowly in acetic acid than in methanol.

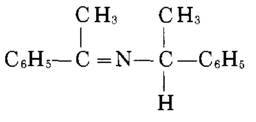
Of particular interest was the comparative behavior on hydrogenation of the oxime and its *O*-acylated derivatives. Rosenmund (*5*) indicated that he had obtained improved yields of primary amine by hydrogenating benzaldehyde and benzophenone oxime acetates. Table I shows that the *O*-acetyl and *O*-benzoyl derivatives of acetophenone oxime give not only better over-all yields of primary amine but also faster rates of reduction than the oxime itself, using either palladium or rhodium. The distinct advantage of the oxime derivatives is their enhanced reactivity. In addition, the oxime acetate gives consistently better results than the benzoate. This trend was also observed by us with cyclohexanone oxime, which was not reduced at all under the experimental conditions using palladium while the *O*-acetyl and *O*-benzoyl cyclohexanone oxime hydrogenated very rapidly. Here again the acetate had the advantage over the benzoate. The improved primary amine yields with the derivatives can be explained in part by the formation of the acid, either acetic or benzoic, which ties up the amine and prevents it from further reaction. Evidence for this hypothesis was obtained by carrying out the hydrogenation of the oxime in the presence of an equimolar amount of acetic acid. The yield was similar to that of the derivatives.

A potentially useful mechanistic aspect of this work on the formation of secondary amines derives from the fact that the secondary amine obtained from the hydrogenation of acetophenone oxime—namely, α,α'-dimethyldibenzylamine (I)—can exist in a *d,l*- and *meso*-form and that these two isomers can be analyzed for very easily by vapor phase chromatography (VPC).



$$\mathrm{C_6H_5}-\overset{\mathrm{CH_3}}{\underset{\mathrm{H}}{\mathrm{C}}}-\mathrm{NH}-\overset{\mathrm{CH_3}}{\underset{\mathrm{H}}{\mathrm{C}}}-\mathrm{C_6H_5}$$

I



$$\mathrm{C_6H_5}-\overset{\mathrm{CH_3}}{\mathrm{C}}=\mathrm{N}-\overset{\mathrm{CH_3}}{\underset{\mathrm{H}}{\mathrm{C}}}-\mathrm{C_6H_5}$$

II

The ratios of the *d,l*- and *meso*-secondary amine I obtained in the various hydrogenations are compiled in Table I. For comparison, I was also prepared by the method of Overberger (*4*), which involves hydrogenation of the Schiff base II. The hydrogenation of II in THF using palladium gave 85% of *d,l*-amine I and 15% *meso*-amine I. Overberger (*4*) claims 88% stereospecificity toward the *d,l*-amine in this reduction and offers a plausible explanation for the predominance of one isomer. From Table I one observes that hydrogenation of the oxime in THF gives a ratio of 66 to 34 *d,l* to *meso*. These results indicate that in the hydrogenation of acetophenone oxime the Schiff base II may not be an intermediate in the formation of the secondary amine (I).

The reduction of the oxime derivatives, on the other hand, gives ratios of *d,l*- to *meso*-I which are closer to those obtained from II. Based on these data it is not possible to draw any conclusions on the intermediacy of the Schiff base II in the case of the derivatives.

CONCLUSIONS

To obtain a clearer picture of the mechanism, it would be of interest to hydrogenate oximes of unsymmetrical ketones (since only these would give *d,l*- and *meso*-secondary amines) under conditions which would lead to substantial secondary amine formation and compare with the hydrogenation of the corresponding Schiff bases under similar reaction conditions. If significantly different ratios of *d,l*- to *meso*-secondary amines are obtained from the oxime and the Schiff base, it might be possible to rule out the Schiff base as a key intermediate in the formation of the secondary amines.

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