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HYDROGENATION OF HYDROXYL-SUBSTITUTED AROMATIC KETONES AND RELATED COMPOUNDS

J. L. R. WILLIAMS

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Hydrogenation of simple aromatic ketones to the carbinols using copper chromite catalysts is well known. Nightingale and Radford (1) reported that *ortho-* and *para-*hydroxyl-substituted alkylaryl ketones yield not the expected carbinols but the corresponding alkyl derivatives when hydrogenation is carried out at 130–150° and 220–240 atmospheres in the presence of copper chromite. With *meta-* substitution, the carbinols are obtained. Similar results were found by Reynolds, Cathcart and Williams for acetylhydroquinone (2).

During the stepwise hydrogenation of ketones, the following sequence must occur:

In order that isolation of the carbinol be possible, the reaction rate of Step B must be small compared with that of Step A under the particular operating conditions of temperature and pressure. The use of Raney nickel catalysts at high pressures for such systems has been limited since there exists a greater tendency for Reaction B to predominate, leading to hydrogenolysis and also ring hydrogenation (3).

There is, however, a certain amount of overlap between the use of copper chromite and Raney nickel catalysts since simple ketones such as acetophenone can be hydrogenated at high pressures to the carbinols using Raney nickel at relatively low temperatures (60–80°). Triacetylbenzene similarly can be hydrogenated to the triol (4). The use of W-7 and W-6 Raney nickel catalysts (5), which show special activity, also afford the carbinols from several ketones at 25–50 p.s.i.

Recently, Adkins, Burgoyne, and Schneider (6) demonstrated that 2-acetonaphthone could be hydrogenated to 2-naphthylmethylcarbinol at 25° and 4000 p.s.i. during 8 minutes in 94% yield, by using a specially prepared, activated, and pre-reduced copper chromite catalyst designated HJS-2.

The foregoing facts suggested that hydrogenolysis of the carbinol during hydrogenation of hydroxyl-substituted alkylaryl ketones might be prevented if the hydrogenations were carried out at the lowest possible operating temperature, in order that Step A might be favored over Step B. It was, therefore, decided to determine the minimum operating ranges for a number of ketones sensitive to hydrogenolysis. Accordingly, acetylhydroquinone was hydrogenated in the presence of pre-reduced HJS-2 at 70–80° and 3800 to 4000 p.s.i. and found to give 2,5-dihydroxyphenylmethylcarbinol. Pre-reduced Harshaw copper chromite required a temperature of 90° for initiation of the hydrogenation. When

TABLE I
Hydrogenation Conditions and Results

RUN	CATALYST (4 G.)	TEMP. RANGE (°C.)	TIME (MIN.)	COLD DROP (P.S.I.)		PRODUCT		PRODUCT	M.P., °C.	LIT. REF.
				Calc'd	Found	Wt.	%			
ACETYLHYDROQUINONE: 41 g. (0.27 mole)										
1	HJS-2	104–110	20	830 (110°)	780	Ethylhydroquinone				1
		130–150[d]	60	1300	1150	22.1 g.			112	1
2	Harshaw #	90–108	28	650	600	61	81	2,5-Diacetoxyphenylmethylcarbinol acetate		
3	HJS-2	100–106	28	650	680	62	82	2,5-Diacetoxyphenylmethylcarbinol acetate		2
4	Harshaw	105–110	33	650	720	65	86	2,5-Diacetoxyphenylmethylcarbinol acetate		
5	HJS-2 #[a, b]	40–60	45	650	640	65	86	2,5-Diacetoxyphenylmethylcarbinol acetate		
6	HJS-2 #[c]	40–135	105	No hydrogenation; recovered starting material						
p-HYDROXYACETOPHENONE: 34 g. (0.25 mole)										
7	HJS-2 #	60–75	33	600	630	33.5	98.5	*p*-Hydroxyphenylmethylcarbinol	135–136	7
8	HJS-2	100–106	24	600	600	32.2	95.0	*p*-Hydroxyphenylmethylcarbinol	124–129	
9	Harshaw	105–106	33	600	650	30.0	88.5	*p*-Hydroxyphenylmethylcarbinol	129–131	
10	Harshaw #	75–80	70	600	600	33.1	97.0	*p*-Hydroxyphenylmethylcarbinol	127.5–132	
11	HJS-2	105–110	29	(1.0 mole-absorbed)						
		130–135[d]	37	1200	1100	26.7	91	*p*-Ethylphenol	46.5–47	8

				o-HYDROXYACETOPHENONE: 34 g. (0.25 mole)					
12	Harshaw	135–145	180	1200	1250	29	93	*o*-Ethylphenol		
13	HJS-2	115–125	16	600	650		49	*o*-Acetoxyphenylmethylcarbinol acetate		
14	HJS-2#	50–70	26	600	520	45	51 90	*o*-Ethylphenyl acetate *o*-Acetoxyphenylmethylcarbinol acetate		
				2-HYDROXY-5-METHOXYACETOPHENONE: 41 g. (0.25 mole)					
15	HJS-2#	65–72	17	600	600	33	79	2-Acetoxy-5-methoxyphenylmethylcarbinol acetate	71–74	
				2,5-DIMETHOXYACETOPHENONE: 45 g. (0.25 mole)					
16	HJS-2	100–108	25	600	600	42	93	2,5-Dimethoxyphenylmethylcarbinol		
				RESACETOPHENONE: 30 g. (0.2 mole)					
17	HJS-2#	70–85	85	600	1200	Product not isolated				
				p-HYDROXYBENZALDEHYDE: 30.5 g. (0.25 mole)					
18	Harshaw	105–108	50	600	650	17	56	*p*-Hydroxybenzyl alcohol	112–114	9, 10
19	HJS-2#	55–60	15	600	600	30.2	99	*p*-Hydroxybenzyl alcohol	109–113	

TABLE I—*Concluded*

RUN	CATALYST (4 G.)	TEMP. RANGE (°C.)	TIME (MIN.)	COLD DROP (P.S.I.)		PRODUCT		PRODUCT	M.P., °C.	LIT. REF.
				Calc'd	Found	Wt.	%			
6-METHOXY-2-ACETONAPHTHONE: 50 g. (0.25 mole)										
20	HJS-2#	30–65	10	600	600	49.8	99	6-Methoxy-2-naphthyl methyl carbinol	111–112	
21	Harshaw#	85–100	17	600	650	49.7	99	6-Methoxy-2-naphthyl methylcarbinol	112.5–113.5	
22	Harshaw	105–118	13	600	650	49.5	99	6-Methoxy-2-naphthylmethylcarbinol	114–115	
23	HJS-2	103–109	5	600	690	49.4	99	6-Methoxy-2-naphthylmethylcarbinol	112–113	
24	HJS-2	140–150	60	1200	1350	28.5	61	2-Ethyl-6-methoxynaphthalene	61–62	11
1-METHOXY-2-ACETONAPHTHONE: 40 g. (0.2 mole)										
25	HJS-2#[a]	30–55	20	480	400	39	97.5	1-Methoxy-2-naphthylmethylcarbinol	90–92	
26	Harshaw#	70–87	30	480	420	39.5	98	1-Methoxy-2-naphthylmethylcarbinol	90–93	
27	Harshaw	115–140	28	480	510	36.8	92	1-Methoxy-2-naphthylmethylcarbinol	89–91	
28	HJS-2	104–115 165–200[d]	(Absorbed 1.0 mole) 60	960	1350	24.1		Mixture		
1-HYDROXY-2-ACETONAPHTHONE: 55.8 g. (0.3 mole)										
29	HJS-2#	70–90	40	720	1400	50.8	98	2-Ethyl-1-hydroxynaphthalene	69–70.5	12
30	HJS-2#	30–50	60	720	1280	48	94	2-Ethyl-1-hydroxynaphthalene	69–70	12
4-ACETYL-2',5'-DIHYDROXYBIPHENYL: 57 g. (0.25 mole)										
31	HJS-2#	70–80	20	600	580	53	93	4-(2',5'-dihydroxybiphenylyl)methylcarbinol	146	

[a] Hydrogenation took place slowly even at room temperature.
[b] Methanol solvent.
[c] Dioxane solvent.
[d] Continuation of run at higher temperature.
[e] B.p. 62–92°/0.5 mm.
Designates pre-reduced catalyst.

both HJS-2 and Harshaw catalysts were not pre-reduced, hydrogenation did not occur until a temperature of approximately 105° was reached. In all four cases, only one mole of hydrogen was absorbed per mole of carbonyl. For isolation purposes, the hydrogenation products were acetylated and distilled since 2,5-dihydroxyphenylmethylcarbinol has not been crystallized and cannot be readily distilled (2). Table I summarizes the conditions and results. Figure 1 shows pressure-*versus*-temperature curves for four typical runs and indicates the temperature at which hydrogenation was initiated under the various conditions.

Hydrogenolysis of the carbinol was carried out in one experiment. A standard run was carried out, with the first mole of hydrogen being absorbed at 105–110° as shown in Figure 2. At 110–130°, the second mole of hydrogen was absorbed to give ethylhydroquinone.

Hydrogenation of *p*-hydroxyacetophenone to *p*-hydroxyphenylmethylcarbinol was carried out under conditions similar to those for acetylhydroquinone, as indicated in Table I. In all runs, relatively pure *p*-hydroxyphenylmethylcarbinol was produced when the temperature of hydrogenation was below 110°. Above 130°, a 92% yield of *p*-ethylphenol was obtained, in agreement with the work of Nightingale and Radford (1).

Hydrogenations of 6-methoxy-2-acetonaphthone using HJS-2 and Harshaw copper chromites were carried out as for acetylhydroquinone. The results are summarized in Table I and are shown in Figure 3. At temperatures below 118°, the product was 6-methoxy-2-naphthylmethylcarbinol, whereas, 2-ethyl-6-methoxynaphthalene was the product at 140–150°.

A series of hydrogenations of 1-methoxy-2-acetonaphthone gave results similar to those above for 6-methoxy-2-acetonaphthone. The product, 1-methoxy-2-

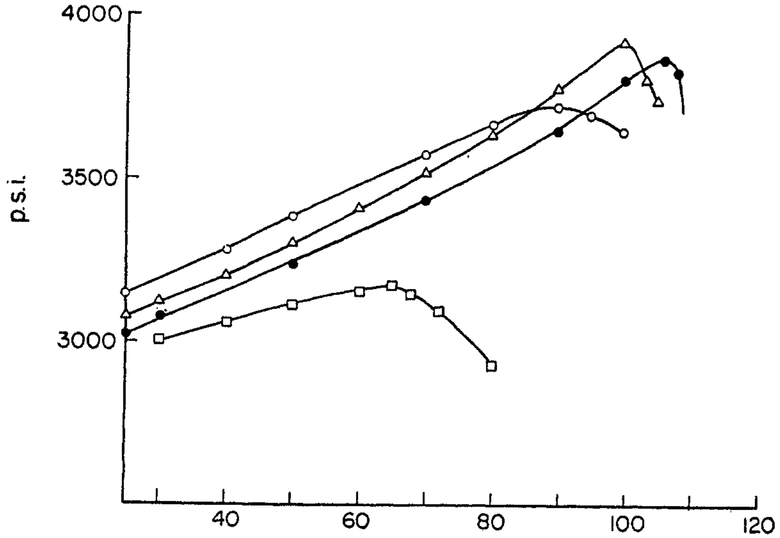

FIG. 1. ACETYLHYDROQUINONE (41 g., 0.27 mole; ethanol to make 150 ml.; catalyst, 4 g.; ○, Harshaw, pre-reduced; ●, Harshaw; □ HJS-2, pre-reduced; △, HJS-2.

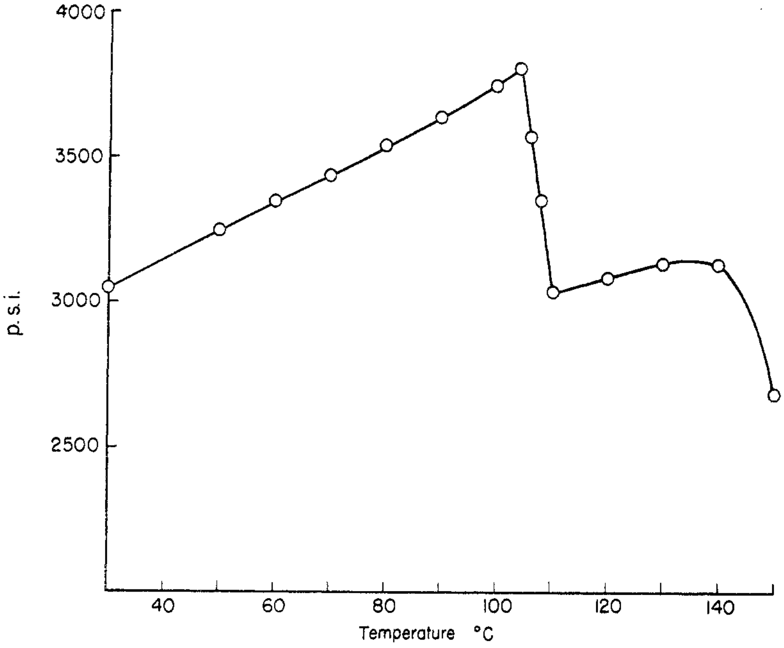

FIG. 2. ACETYLHYDROQUINONE (41 g., 0.27 mole); HJS-2, 4 g.; ethanol to make 150 ml.

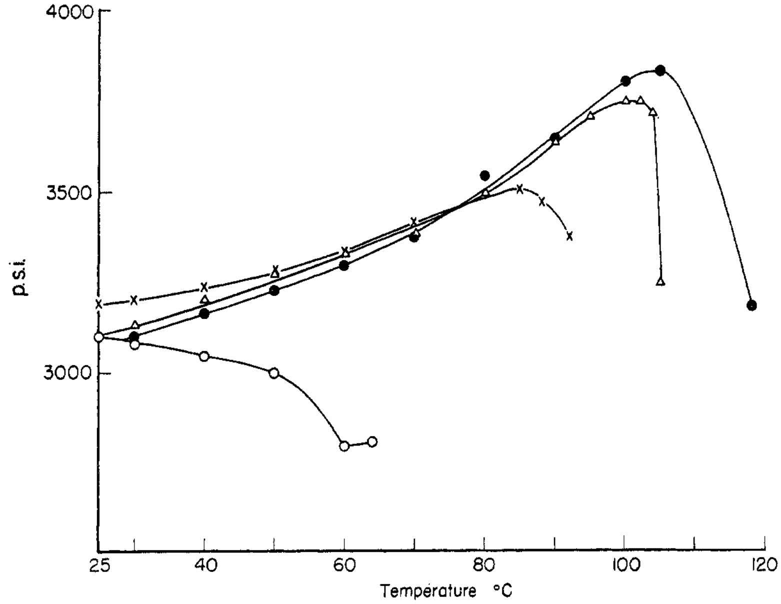

FIG. 3. 6-METHOXY-2-ACETONAPHTHONE (50 g., 0.25 mole); ethanol to make 150 ml.; catalyst, 4 g.; ○, HJS-2, pre-reduced; ×, Harshaw, pre-reduced; ●, Harshaw; △, HJS-2.

naphthylmethylcarbinol, was obtained in pure form by recrystallization and chromatographic adsorption on alumina. By these separation techniques, it was shown that pre-reduction definitely leads to smaller amounts of side products during the reduction of the ketone to the carbinol. These side products are believed to be both the ethyl and ring-hydrogenated derivatives, since the ease of ring hydrogenation is evident from the results of experimental run No. 28. Results are shown in Table I.

Hydrogenation of 1-hydroxy-2-acetonaphthone at 70–80° and 3200 p.s.i. with pre-reduced HJS-2 catalyst failed to prevent hydrogenolysis of the carbinol, as evidenced by the absorption of two molecular equivalents of hydrogen and the formation of 2-ethyl-1-naphthol in 98% yield. No improvement was indicated by operating at 50–60° and 3900 p.s.i.

Hydrogenation of *o*-hydroxyacetophenone at 135–145° and 4000 p.s.i. gave a 96% yield of *o*-ethylphenol when ordinary copper chromite (Harshaw) was used. When pre-reduced HJS-2 catalyst was used at 55–65° and 3400 p.s.i., approximately one mole of hydrogen was absorbed per mole of ketone with the formation of *o*-hydroxyphenylmethylcarbinol which was converted to *o*-acetoxyphenylmethylcarbinol acetate, isolated in 90% yield. Hydrogenation of *o*-hydroxyacetophenone at 118–126° and 3800 p.s.i. followed by acetylation, gave 49% *o*-acetoxyphenylmethylcarbinol acetate, the remainder being *o*-ethylphenyl acetate.

2-Hydroxy-5-methoxyacetophenone was hydrogenated smoothly to 2-hydroxy-5-methoxyphenylmethylcarbinol in 79% yield when pre-reduced HJS-2 catalyst was used at 65–72° and 3100 p.s.i. 2,5-Dimethoxyacetophenone was hydrogenated to 2,5-dimethoxyphenylmethylcarbinol in 92% yield when HJS-2 catalyst was used without pre-reduction at 103–108° and 3850 p.s.i. Similar results have been reported for *p*-methoxyacetophenone with ordinary copper chromite (1).

On using the optimum conditions described for acetylhydroquinone, 4-acetyl-2′,5′-dihydroxybiphenyl was hydrogenated to 4-(2′,5′-dihydroxybiphenylyl)-methylcarbinol at 70–80° and 3400 p.s.i. in the presence of pre-reduced HJS-2.

Hydrogenation of *p*-hydroxybenzaldehyde to *p*-hydroxybenzyl alcohol in 60% yield was accomplished using Harshaw copper chromite at 105–108° without pre-reduction. The remainder of the material was *p*-cresol. Pre-reduced HJS-2 catalyst at 55–65° gave a nearly quantitative yield of *p*-hydroxybenzyl alcohol.

Hydrogenation of resacetophenone at 55–60° and 3200 p.s.i. with pre-reduced HJS-2 as catalyst resulted in hydrogen absorption corresponding to two molecular equivalents; however, the product was not isolated.

EXPERIMENTAL

Hydrogenations. The hydrogenations were carried out in rocking-type, 300-ml. void, stainless-steel reactors with HJS-2 copper chromite (6) or Harshaw copper chromite, Cu-X-649-57-P, and with sufficient ethanol to give a volume of 150 ml. Reaction conditions and other data are given in Table I.

The isolation of products was carried out by standard means and is not described except in the case of new compounds or where special handling was necessary.

TABLE II

CARBINOLS AND ACETATES

COMPOUND	B.P., °C.	MM.	M.P., °C.	ANALYSES				n_D^{25}
				Calc'd		Found		
				C	H	C	H	
4-(2′,5′-Dihydroxybiphenylyl)methylcarbinol			146	73.0	6.1	72.6	6.1	
4-(2′,5′-Diacetoxybiphenylyl)methylcarbinol acetate			68	67.3	5.6	67.1	5.2	
o-Acetoxyphenylmethylcarbinol acetate	98.5	0.75						1.4950
2,5-Dimethoxyphenylmethylcarbinol	92.5	0.3		66.4	7.7	65.8	7.8	1.5350
2,5-Dimethoxyphenylmethylcarbinol acetate	105	0.4		64.4	6.6	64.6	7.1	1.5100
2-Hydroxy-5-methoxyphenylmethylcarbinol			73–74	64.3	7.2	64.4	7.4	
2-Acetoxy-5-methoxyphenylmethylcarbinol acetate	112–113	0.3		62.0	6.4	62.4	5.9	1.5015
6-Methoxy-2-naphthylmethylcarbinol	113.5–114.5			77.2	6.9	77.5	7.1	
6-Methoxy-2-naphthylmethylcarbinol acetate			53–54	73.8	6.8	73.8	6.7	
1-Methoxy-2-naphthylmethylcarbinol			92–93	77.2	7.0	77.4	7.3	
1-Methoxy-2-naphthylmethylcarbinol acetate	111–112	0.35		73.8	6.8	74.1	6.7	

Preparation of acetates. The acetates were prepared by heating the carbinols with 50% excess acetic anhydride on a steam-bath for 16–18 hours in the presence of a trace of pyridine. The acetates were then isolated by distillation. Their properties and analytical data are shown in Table II.

o-Hydroxyacetophenone. Halogen-free *o*-hydroxyacetophenone was prepared by refluxing with Raney nickel followed by distillation.

o-Acetoxyphenylmethylcarbinol acetate. Run 13. The reaction mixture from this run was filtered, and the alcohol was evaporated at the water-pump with a 35°-water bath. The last traces of alcohol were removed with a high-vacuum pump. To the residue there was added 100 ml. of acetic anhydride and 1 ml. of pyridine. The reaction mixture was allowed to stand at room temperature overnight and was evaporated to about 75 ml. at the water-pump. The residue was heated at 60° with 50 ml. of acetic anhydride for 5 hours and distilled through a 12-in. Vigreux-type column. Fractions: (a) 4 g., b.p. 56–59° (0.5 mm.), n_D^{25} 1.4962; (b) 10 g., b.p. 59–88° (0.5 mm.), n_D^{25} 1.4916; (c) 24 g., b.p. 91.5° (0.4 mm.), n_D^{25} 1.4950. Fraction c represents a 49% yield of *o*-acetoxyphenylmethylcarbinol acetate.

Run 14. Acetylation and distillation as for Run 13 gave 45 g. (90% yield) of *o*-acetoxyphenylmethylcarbinol acetate, b.p. 98.5° (0.75 mm.), n_D^{25} 1.4950.

p-Hydroxybenzyl alcohol. Run 18. The catalyst was filtered, and the ethanol was evaporated at the water-pump with a 25–35° water-bath. The residual alcohol was removed with a high-vacuum pump (0.3 mm.). The oil crystallized on standing several days to yield 29 g. of white solid, m.p. 107–114°. Recrystallization from a mixture of 250 ml. of benzene and 50 ml. of acetone gave 17 g. (56% yield) of *p*-hydroxybenzyl alcohol, m.p. 112–114°.

Run 19. The yield of crude material, m.p. 109–113°, was 30.2 g. A small sample was recrystallized from water, m.p. 115–116°. Auwers and Daecke (9) reported m.p. 124°; Sugimoto (10), however, reported m.p. 112°.

6-Methoxy-2-naphthylmethylcarbinol. A 20-inch, 19-mm. I.D. column was prepared from activated alumina (Alcoa Company, Grade F-20). Pre-treatment was carried out by using 250 ml. of acetone, followed by 250 ml. of hexane-benzene 1:1. A solution of 1.0 g. of 6-methoxy-2-naphthylmethylcarbinol, m.p. 95–103°, dissolved in 125 ml. of benzene and 125 ml. of hexane was passed through the adsorption column. The column was then washed with 200 ml. of benzene. Elution with 250 ml. of methanol yielded 1.0 g. of the carbinol, m.p. 113–114°.

1-Methoxy-2-naphthylmethylcarbinol. Runs 25–28. One gram of the solid from Run 25 was recrystallized from 25 ml. of hexane to yield material melting at 92–93°. The crude products from Runs 25, 26, and 27 weighing 38.0, 39.5, and 36.5 g. were each recrystallized from 1000 ml. of hexane to yield (a) 35.5 g., m.p. 90–92°; (b) 31.0 g., m.p. 87.5–89°; (c) 31.5 g., m.p. 85–89°, respectively. The corresponding mother liquors were evaporated to 100 ml. to yield, on cooling, (d) 2.2 g., m.p. 93–94°; (e) 1.8 g., m.p. 86–92°; (f) 2.1 g., m.p. 86–90°. The mother liquors, on evaporation to dryness, gave the following materials: (g) 0.3 g., solid; (h) 0.55 g., oil-solid; (i) 1.45 g., oil.

Chromatography of fraction c. A chromatography tube was prepared as follows: In a 12-inch, 18-mm. I.D. Pyrex tube there was placed 150 g. of activated alumina (Alcoa Company, Grade F-20). The alumina was pre-treated with 250 ml. of acetone followed by 250 ml. of hexane. A solution of 0.5 g. of Fraction C in 25 ml. of benzene and 500 ml. of hexane was then passed through the column. The tube was washed with 200 ml. of benzene which contained no solids. Elution with 250 ml. of methanol and evaporation under reduced pressure yielded 0.41 g. of material, m.p. 92–93°. Recrystallization from hexane failed to raise the melting point.

SUMMARY

Hydrogenation of hydroxyl-substituted acetophenones to the corresponding carbinols has been found possible when one hydroxyl group occupies a position *ortho* or *para* to the carbonyl group. When hydroxyl groups occupy *both* an *ortho*- and the *para*-position, hydrogenolysis of the carbinol occurs. If, however, the two hydroxyls occupy an *ortho*- and a *meta*-position, the carbinols can be isolated.

The following compounds have been hydrogenated to the corresponding carbinols: acetylhydroquinone, *p*-hydroxyacetophenone, *o*-hydroxyacetophenone, 2-hydroxy-5-methoxyacetophenone, 2,5-dimethoxyacetophenone, *p*-hydroxybenzaldehyde, 4-acetyl-2′,5′-dihydroxybiphenyl, 6-methoxy-2-acetonaphthone, and 1-methoxy-2-acetonaphthone. Hydrogenolysis of the carbinols occurred in the case of 1-hydroxy-2-acetonaphthone and resacetophenone.

A comparison of HJS-2 copper chromite catalyst and a commercial copper chromite catalyst has been made by both the standard hydrogenation technique and by that employing pre-reduction of the catalyst. Following are the initiation temperatures found for standard use of the catalysts and for pre-reduced catalysts when acetylhydroquinone is hydrogenated at 3000–4000 p.s.i.: Harshaw copper chromite, 105°; Harshaw copper chromite pre-reduced, 90°; HJS-2 copper chromite, 105°; and HJS-2 copper chromite pre-reduced, 25°. Hydrogenolysis of 2,5-dihydroxyphenylmethylcarbinol did not occur until a temperature range of 115–130° was reached. Similar results were obtained with 6-methoxy-2-acetonaphthone, 1-methoxy-2-acetonaphthone, and *p*-hydroxyacetophenone.

ROCHESTER 4, NEW YORK

REFERENCES

(1) Nightingale and Radford, *J. Org. Chem.*, **14**, 1089 (1949).
(2) Reynolds, Cathcart, and Williams, *J. Org. Chem.*, **18**, 1709 (1953).
(3) Ungnade and McLaren, *J. Am. Chem. Soc.*, **66**, 118 (1944).
(4) Unpublished work by the author, University of Wisconsin.
(5) Adkins and Billica, *J. Am. Chem. Soc.*, **70**, 695 (1948).
(6) Adkins, Burgoyne, and Schneider, *J. Am. Chem. Soc.*, **72**, 2626 (1950).
(7) Alderman and Hanford (E. I. du Pont de Nemours and Co., Inc.), U. S. Patent 2,276,138 (1942); *Chem. Abstr.*, **36**, 4732 (1942).
(8) Clemmensen, *Ber.*, **47**, 51 (1914).
(9) Auwers and Daecke, *Ber.*, **32**, 3373 (1899).
(10) Sugimoto, *Repts. Imp. Ind. Research Inst. Osaka (Japan)*, **10**, No. 10 (1929); *Chem. Abstr.*, **24**, 837 (1930).
(11) Elsevier's *Encyclopedia of Org. Chem., Series III. "Carboisocyclic Condensed Compounds,"* Vol. **12B**, Elsevier Publishing Co., Inc., New York, 1950, p. 1403.
(12) Ref. 11, p. 1398.