Anal. Calcd. for $C_{20}H_{18}N_2O_{12}$: N, 5.86; O, 10.03. mol. wt., 478.4. Found: N, 5.96; O, 10.42; mol. wt., 480 (cryoscopic in dioxane).

This derivative was too explosive for carbon and hydrogen analyses. An infrared spectrum of a mull in Nujol showed a strong band at 1765–1760 cm.$^{-1}$ due to the perester groups, and two bands at 850 and 870 cm.$^{-1}$, due to the —O—O— groups, and no bands in the hydroperoxy region.

Acknowledgment.—The authors wish to thank Dr. S. M. Nagy for all the combustion analyses, Dr. P. H. Niklaus for the n.m.r. spectra, Miss Jessie C. J. Ho for technical assistance, and the Lucidol Division of Wallace and Tiernan, Inc., and Research Corporation for financial support of this investigation.

Selective Semihydrogenation of Tertiary Ethynylcarbinols in the Presence of Base

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An improved method for the semihydrogenation of tertiary ethynylcarbinols has been developed. Low pressure hydrogenations in the presence of bases such as potassium hydroxide, sodium hydroxide, sodium methoxide, and alkali metals using palladium, platinum, or rhodium catalysts on carriers such as charcoal, barium carbonate, calcium carbonate, or barium sulfate yield vinylcarbinols in good yield (77–92%) and purity (95–97%). A catalyst to base weight ratio of 1:1 to 1:2 is employed. In the absence of base, vinylcarbinols of lower purity (82–88%), contaminated with the corresponding ethynyl and saturated carbinols are obtained. Unprotected hydrogenations also show no tendency to halt selectively. The catalyst system of palladium on barium carbonate in the presence of powdered potassium hydroxide was found to be the most useful studied.

The partial hydrogenation of tertiary ethynylcarbinols has been discussed by Johnson[1] and K. N. Campbell.[2] Palladium[3] and Raney nickel catalysts[4,5] have been used frequently in this operation and were claimed to be selective for the semihydrogenation of the triple bond. This selective action involves not only the specific hydrogenation of the acetylenic to vinylcarbinol but also the halting of further hydrogenation after all the acetylenic has been converted to ethylenic derivative. The unsaturated carbinol should be absent or present in a very small amount. Raphael[6] has pointed out that in recent years palladium has come to be regarded as the most useful catalyst for semihydrogenation. However, the development of the Lindlar catalyst[7] (palladium on calcium carbonate inactivated with lead acetate and quinoline) demonstrated that palladium without a suitable inhibitor does not always show selective action. Recently Hennion and co-workers[8] claimed a selective technique for the semihydrogenation of tertiary ethynyl carbinols using very small amounts of palladium on barium carbonate catalyst.

Attempts in this laboratory to prepare tertiary vinylcarbinols in 95% or better purity by the Lindlar or the Hennion method were unsuccessful. The resulting product was always contaminated with varying amounts of unreduced acetylenic and an equal amount of saturated carbinol. The longer the chain length of the starting material the less selective the hydrogenation became showing also no tendency to stop selectively at the end of the first stage ($-C\equiv C= \rightarrow -CH=CH-$) of hydrogenation.

While investigating[9] the hydrogenation and hydrogenolysis of tertiary 1,4-acetylenic glycols, it was observed that small amounts of alkali metal base eliminated hydrogenolysis, and also inhibited the more rapid rate of hydrogenation of the first stage, although complete cessation of hydrogenation was not observed. While hydrogenolysis was found to be an insignificant side reaction for the tertiary ethynyl and vinyl carbinols, the above results indicated that increased amounts of base might also function as an inhibitor for the more rapid first stage of carbinol hydrogenation, and show selectivity for producing pure tertiary vinylcarbinols. Also, the known instability of the tertiary ethynylcarbinols to base at higher temperatures might be useful in the preparation of pure vinylcarbinols by cleaving unchanged ethynylcarbinols into acetylene and lower boiling ketone.

The systematic use of potassium hydroxide or sodium hydroxide with a variety of tertiary acetylenic carbinols was found to give distilled vinylcarbinols of 95–97% minimum purity in good yield (77–92%). Hydrogenation under the same

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(9) R. J. Tedeschi, *ibid.*, **27**, 2398 (1962); U.S. Patent 2,992,278 (July 11, 1961).

TABLE I
TERTIARY VINYLCARBINOLS $RR'C(OH)CH=CH_2$
(1.0 Mole starting material)

R	R'	t, °C.	Time, min.	Catalyst, g.	KOH, g.	Purity $CH=CH_2$ -01	Impurities $C\equiv CH$ -01	RR'CO	Yield
CH_3	CH_3	27–30	44	Pd-C 0.30	0	90.3	2.1	0	87.4
CH_3	CH_3	27–30	58	Pd-C 0.30	0.30	94.6	0	0	76.5
CH_3	CH_3	27–30	56	Pd-$BaCO_3$ 0.15	0	92.2	0.88	0	86.7
CH_3	CH_3	27–30	75	Pd-$BaCO_3$ 0.15	0.30	96.5	0	0	80.1
CH_3	C_2H_5	27–30	59	Pd-C 0.15	0	88.3	4.4	0	87.0
CH_3	C_2H_5	27–30	102	Pd-C 0.15	0.30	96.6	0	0.15	79.0
CH_3	C_2H_5	27–30	70	Pd-$BaSO_4$ 0.15	0	89.0	4.2	0.39	83.0
CH_3	C_2H_5	27–30	55	Pd-$BaCO_3$ 0.15	0	94.6	0.63	0	87.5
CH_3	i-C_4H_9	27–30	74	Pd-C 0.15	0	86.3	6.5	0	89.3
CH_3	i-C_4H_9	27–30	89	Pd-C 0.15	0.30	95.3	0	1.5	88.3
CH_3	i-C_4H_9	25–45	50	Pd-$BaCO_3$ 0.15	0	87.1	3.83	0	91.7
CH_3	i-C_4H_9	25–45	150	Pd-$BaCO_3$ 0.15	0.30	96.1	0	0.22	84.5
CH_3	i-C_4H_9	25–45	190	Pd-$BaSO_4$ 0.15	0.30	96.7	0.26	3.1	82.8
CH_3	C_6H_{13}	35–45	40	Pd-C 1.0	0	85.4	3.5	0	89.7
CH_3	C_6H_{13}	35–45	34	Pd-C 1.0	1.0	95.1	0	1.3	92.3
CH_3	C_6H_{13}	27–30	90	Pd-$BaCO_3$ 0.15	0	85.4	6.2	0	95.8
CH_3	C_6H_{13}	27–30	102	Pd-$BaCO_3$ 0.15	0.30	95.5	0	0	85.2
$(CH_2)_5$		35–45	30	Pd-C 1.0	0.05	83.0	2.5	0	78.0
$(CH_2)_5$		38–40	74	Pd-C 1.0	1.0	97.8	0	1.8	85.0
$(CH_2)_5$		27–30	117	Pd-C 0.15	0.30	97.3	0	0	83.5
$(CH_2)_5$		27–30	82	Pd-$BaCO_3$ 0.15	0	82.4	7.8	0	97.5
$(CH_2)_5$		27–30	109	Pd-$BaCO_3$ 0.15	0.30	95.7	0	1.1	85.0
$(CH_2)_5$		27–30	150	Pd-C 0.15	NaOH 0.30	95.6	0	0.57	81.5
CH_3	C_6H_5	30–35	90	Pd-$BaCO_3$ 0.15	0.30	95.0	0	0.05	83.8

TABLE II
PHYSICAL CONSTANTS

Compound	Purity, %	B.p., °C.	Mm. Hg	$n^{20}D$
3-Methyl-1-buten-3-ol	96.5	97–98	750	1.4164
3-Methyl-1-penten-3-ol	96.6	115–116	750	1.4287
3,5-Dimethyl-1-hexen-3-ol	96.1	145–146	750	1.4341
3-Methyl-1-nonen-3-ol	95.5	84–84.5	10	
		124–125	49	1.4419
1-Vinyl cyclohexan-1-ol	97.3	171–172	750	
		96–97	48	1.4771
3-Phenyl-1-buten-3-ol	95.0	101–102	11	1.5340

conditions in the absence of base gave average purities of only 82–89%. Sodium hydroxide inhibited the reaction rate considerably more than potassium hydroxide and the latter is consequently preferred for semihydrogenation. A catalyst to base weight ratio of 1:1 to 1:2, using 0.15–0.30 g. of palladium (5%) catalyst per mole of starting material, was found satisfactory in all cases studied. Small amounts of base (ratio 20:1, 1-vinylcyclohexan-1-ol) were ineffective, while larger amounts of catalyst (0.30–1.0 g.) when used with the specified catalyst to base ratio still gave excellent results (Table I) even though the hydrogenation rate was considerably faster.

The alternate role of base namely the base-catalyzed cleavage of unconverted tertiary ethynyl carbinols quantitatively into ketone and acetylene, is a minor reaction, since essentially no ethynylcarbinol remains at the end of the first stage. Heating the vinyl carbinols after hydrogenation at 100–110° for one to two hours, after solvent removal, ensures complete removal of any possible residual ethynylcarbinol impurity. The following experimental results substantiate the directive action of base in the hydrogenation.

The semihydrogenation of 3-methyl-1-pentyn-3-ol in the absence of potassium hydroxide at 27–30° gave a distilled vinylcarbinol of only 88.3% purity containing 4.2% unchanged acetylenic diol. Hydrogenation in the presence of potassium hydroxide followed by cleavage at 100–110° results in an ethynyl-free product of 96.6% purity. When potassium hydroxide is omitted from the hydrogenation, but employed for base cleavage, the purity of acetylenic-free vinylcarbinol is 91.0%.

The role of base becomes more important with increasing chain length of the acetylenic carbinol. Hydrogenations of 3,5-dimethyl-1-hexyn-3-ol, 3-methyl-1-nonyn-3-ol, and 1-ethynylcyclohexan-1-ol in the absence of base gave distilled purities of only 87.1, 83.3, and 82.4%, respectively. The same hydrogenations conducted with potassium hydroxide present gave purities of 96.1, 95.5, and 97.3%, respectively. The unselective nature of the hydrogenation in the absence of base with increasing chain length is again evident by the increase in the amount of unchanged ethynylcarbinol (3.8, 6.2, 7.8%, respectively). In the presence of base the ethynyl carbinol content after hydrogenation and before base cleavage is 0.1 to 0.3% maximum.

The completely selective hydrogenation of 3-methyl-1-butyn-3-ol could not be accomplished with either sodium or potassium hydroxides, using palladium or platinum catalysts. The hydrogenation repeatedly proceeded beyond the end of the first stage, although good purities (>90%) could be obtained by manually halting the hydrogenation at the end of stage. However, the combination of rhodium (5%) on charcoal used with sodium methoxide in 1:1 ratio was found to semihydrogenate methyl butynol selectively and to give an ethynyl impurity of less than 0.1% before cleavage. In the absence of methoxide no selectivity was noted. The rhodium–methoxide catalyst system has not been studied as yet with other acetylenic carbinols.

Potassium metal when used with palladium-on-charcoal catalyst in 1:2 ratio showed selectivity when tested with 3-methyl-1-pentyn-3-ol. The rate of this hydrogenation was about one third that observed normally with potassium hydroxide under identical conditions. The potassium dissolved in the reaction mixture of acetylenic carbinol and hexane before hydrogenation probably as a mixture of the corresponding tertiary alkoxide and potassium acetylide derivatives of methylpentynol. The marked difference in hydrogenation rate compared to potassium hydroxide is indicative of different species being present during both reductions.

Present evidence indicates that the alkali metal hydroxides may exert their selectivity in semihydrogenations via 1:1 mole complexes of acetylenic carbinol and alkali hydroxide. A rapid, quantitative reaction[10] between finely divided potassium hydroxide and 3-methyl-1-butyn-3-ol is observed in dry, inert solvents to yield a 1:1 mole adduct. The resulting, white, stable solid when used as a substitute for potassium hydroxide in a concentration equivalent to the potassium hydroxide normally employed in the semihydrogenation shows the same selectivity towards methylpentynol and ethynylcyclohexanol.

Hydrogenations carried out with palladium on a charcoal carrier did not stop selectively at the end of the first stage although a marked change in rate was observed, using base to catalyst ratios of 1:2. However, halting the hydrogenation manually followed by base cleavage at elevated temperature gave purities of 95–97% in good yield (77–92%). Other carriers with palladium, as well as rhodium and platinum on charcoal, using the same catalyst to base ratio, resulted in hydrogenations which halted selectively at the end of the first stage. The inhibitory effect of base was much more pronounced with the less active catalysts such as palladium on barium carbonate, calcium carbonate, and barium sulfate, during the initial stages of the reduction. In several cases (3,5-dimethyl-1-hexyn-3-ol, 2-methyl-1-nonyn-3-ol, and 1-ethynylcyclohexan-1-ol) preliminary warming to 40–45° for five to ten minutes was necessary to activate the reaction. Once the hydrogenation had started, however, the temperature could be lowered to the preferred range of 27–30°. The lower ethynylcarbinols (methylbutynol and methyl pentynol) are best hydrogenated at 20–30°.

The ethynylcarbinols studied were found to be stable to base cleavage at temperatures of 25–40° for a two-hour period. These conditions correspond approximately to those employed in typical hydrogenations. However, at temperatures of 100–110°, a minimum of 8% acetylenic impurity can be quantitatively cleaved to acetylene and ketone in one to two hours. The corresponding vinylcarbinols were found to be completely stable at elevated temperatures in the presence of 5% of their weight of potassium hydroxide. At reflux, 3-methyl-1-buten-3-ol (98°) and 3-methyl-1-nonen-3-ol (180°) after three hours were unchanged in purity. Consequently, even the higher boiling vinylcarbinols can be distilled safely in the presence of base at temperatures above 150° at atmospheric pressure if desired.

Experimental

General Hydrogenation Procedure.—(Standard Parr Shaker apparatus[11] 1.0 m. H_2 equivalent to 85 p.s.i. drop at 30–55 p.s.i.). The following reactor charge was used: 1.0 mole of tertiary acetylenic carbinol (98–100% purity), 100 cc. of *n*-hexane or petroleum ether (20–40°, 0.15 g. of palladium (5%) on charcoal, $BaCO_3$, $CaCO_3$, or $BaSO_4$, 0.30 g. of powdered 90–100% KOH.

The powdered potassium hydroxide was dissolved in the ethynylcarbinol at 30–40° with stirring in the course of several minutes. The resulting solution was transferred with solvent rinses to a jacketed copper stainless steel hydrogenation vessel,[12] equipped with a thermometer well, into which was placed a stainless steel Weston dial thermometer. The reaction temperature was adjusted to 25–30° and maintained in this range during the hydrogenation.

The hydrogenation was exothermic and occasional cooling was necessary. The theoretical pressure drop of 85 p.s.i. was reached after repressurizing the apparatus four times, in approximately 1.5–2 hr. and the hydrogenaton was halted at this point when palladium–charcoal catalyst was used. The reaction rate at different pressure drops was fairly constant except for the last 5 p.s.i. drop. Base significantly decreases the over-all reduction time (Table I) compared to results in its absence. When the other carriers were used the hydrogenation rate became noticeably slow at a pressure drop of 80 p.s.i. and halted at a total pressure drop of 85–87 p.s.i. The ethynyl content at this point was very low (0–0.3%). In the case of 3-methyl-1-butyn-3-ol it was preferable to use petroleum ether (b.p. 20–40°) as solvent to facilitate later isolation of product.

The hydrogenation mixture, including catalyst, was transferred with hexane rinses to a distilling flask and solvent distilled over to a pot temperature of 100–110°. The reaction mixture was held at 100–110° for 1–2 hr. to decompose completely any unconverted acetylenic carbinol.

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[10] R. J. Tedeschi and M. F. Wilson, Air Reduction Co.; the preparation of these complexes and evidence for their structures will be presented in a later paper.

[11] Parr Instrument Co., Inc., Moline, Ill., Serial No. 1145, max. rating 60 p.s.i.

[12] Specially fabricated metal hydrogenation vessel of 575-ml. capacity. Inner wall of stainless steel, outer wall of copper. Cooling water or steam can be circulated between the side walls. Copper to stainless steel contact at bottom of vessel allows efficient electrical heating if desired. Narrow thermometer well adapted for thermocouple or Weston dial thermometer.

The reaction mixture was then filtered from catalyst and fractionated through a 25-plate electrically heated column packed with "monel helipak." The desired vinylcarbinol was collected over a 1–2 degree range. All carbinols studied could actually be distilled at atmospheric pressure but for the higher boiling members of the series (3-methyl-1-nonen-3-ol and vinylcyclohexanol) vacuum distillation at 50–60 mm. is preferable.

Analytical Methods.[13] **A. Ethynylcarbinol Impurity.**[14]—Ethynylcarbinol or vinylcarbinol suspected of containing —C≡CH impurity was treated with a concentrated silver nitrate solution followed by standard base titration of the liberated nitric acid.

B. Vinylcarbinol.[15]—The vinylcarbinol was treated with excess bromine in methanol saturated with sodium bromide at room temperature. Bromination was complete in 3–5 min. Addition of potassium iodide followed by titration of the liberated iodine with standard sodium thiosulfate determines the bromine consumed. Ethynylcarbinols are completely unreactive under these conditions.

The bromination values represent minimum purities since gas chromatographic analyses of several samples of methyl butynol and methylpentynol from potassium hydroxide runs showed total impurities of less than 1%.

C. Ketone Impurity.[16]—The vinylcarbinol was treated with excess hydroxylamine hydrochloride solution in methanol solution for several hours at room temperature followed by titration of the liberated acid. Less active ketones such as acetophenone require refluxing for several hours.

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[13] The services of L. Molinini and the Air Reduction Co. Analytical Department are gratefully acknowledged.

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[15] N. D. Cheronis and J. B. Entrikin, "Semi Micro Qualitative Analysis," Thomas Y. Crowell Co., New York, N. Y., 1947, p. 471.

[16] Staff of Hopkins and Williams Research Laboratory, "Organic Reagents for Analysis," Chemical Publishing Co., Brooklyn, N. Y., 1946, p. 60.

The Action of Lithium Aluminum Hydride and of Grignard Reagents on Some Heterocyclic β-Ketoamides. Synthesis of 1-Aldehydes and 1-Ketones[1] of Phenothiazine, Phenoxazine, and Carbazole

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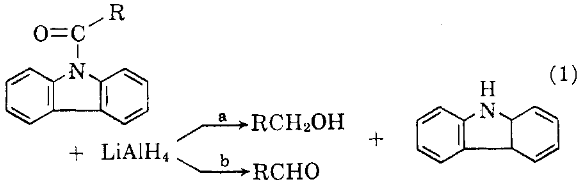
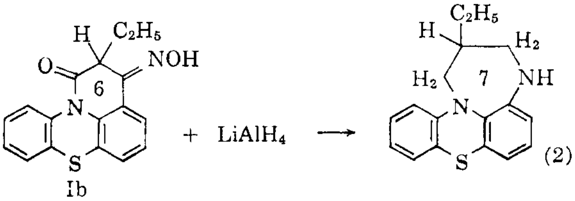
Condensation products of diethyl monoalkylmalonates with phenothiazine, carbazole, and phenoxazine, such as Ig and Il, can be converted by bromination and displacement of bromine by secondary amines, to the C,C-disubstituted "alkylmalonyl heterocycles"[6] *e.g.*, Ia and Ic–Ie. These and one example of a C,C-dialkyl analog (If) are reduced, by lithium aluminum hydride, to the hydroxycarbinolamines (of which IIb and IIc were isolated and characterized). These yield the retro-aldol products phenothiazine-1-aldehyde, phenoxazine-1-aldehyde, and carbazole-1-aldehyde, on decomposition of the hydride reduction mixture. Analogously, 1-acetylcarbazole was made by action of methylmagnesium iodide on Id to give IV, and a separate base-catalyzed retro-aldol reaction of IV. Some aspects of the significance of these results to the mechanisms of such reductions are briefly discussed.

Lithium aluminum hydride and related reducing agents are used so frequently in synthetic and structure determination problems in organic chemistry that any unusual reactions produced by these substances are of special interest. It is well known that treatment of amides derived from amines such as certain aromatic amines[2] and ethylene imine[3] with lithium aluminum hydride can lead to the aldehydes corresponding to replacement of the amine fragment by one hydrogen (equation 1, path b). In general, inverse addition of barely equivalent amounts of the hydride at temperatures below ambient is recommended to prevent further reduction either to the tertiary amine corresponding to loss of oxygen, or to the alcohol corresponding to loss of amine from the amine.[4] For example, N-benzoylcarbazole is reported[5] to give benzyl alcohol when treated with lithium aluminum hydride (equation 1, path a).



We had previously reported[1] the reduction with rearrangement of the oxime Ib by lithium aluminum hydride, with conversion of the carbonyl attached to the phenothiazine nitrogen to a CH_2 group (equation 2). This occurred at least to a


Ib

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[1] Paper II on tetracyclic phenothiazines and related compounds. Paper I is M. Harfenist and E. Magnien, *J. Am. Chem. Soc.*, **80**, 6080 (1958).

[2] *Cf.* N. G. Gaylord, "Reductions with Complex Metal Hydrides," Interscience Publishers, Inc., New York, N. Y., 1956, pp. 544 *et. seq.* and W. Ried and F. J. Königstein, *Angew. Chem.*, **70**, 165 (1958).

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[5] A. Mustafa, *et al.*, *J. Am. Chem. Soc.*, **76**, 5447 (1954).