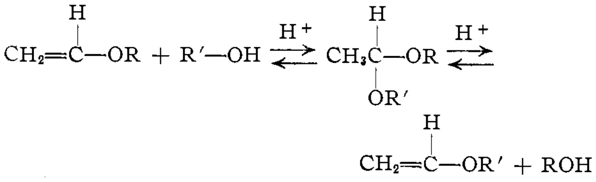


$$CH_2{=}\overset{H}{\overset{|}{C}}{-}OR + R'{-}OH \overset{H^+}{\rightleftarrows} CH_3\overset{H}{\overset{|}{C}}{-}OR \overset{H^+}{\rightleftarrows} CH_2{=}\overset{H}{\overset{|}{C}}{-}OR' + ROH$$
$$\qquad\qquad \underset{OR'}{\underset{|}{}}$$

However, Hill's mechanism appears to be inapplicable to mercuric sulfate-catalyzed interchanges of vinyl ethers with alcohols, for (1) the vinyl ether–alcohol interchange reaction occurs more readily than acetal formation from vinyl ethers and alcohols, and under much milder conditions than acetal cleavage to vinyl ethers and alcohols[4]; (2) mercuric sulfate appears to be a specific catalyst under these conditions, whereas Hill's experiments were acid-catalyzed; (3) I observed no reaction of the acetal of methyl glycolate with vinyl ethyl ether at −20° for 1.5 hours in the presence of mercuric sulfate. If Hill's mechanism were applicable, a mixture of acetals, the acetal of methyl glycolate and the mixed acetal of methyl glycolate and ethanol, should have been isolated.

On the other hand, experimental data thus far obtained may be explained adequately by a reaction course previously offered for other interchange reactions of vinyloxy compounds.[5,6] This reaction course assumes the dissociation of the vinyl ether into an acetylene–mercury complex and an alcohol. On reassociation, a mixture of vinyl ethers would be formed.

Experimental

I. Preparation of Vinyl Ethyl Ether from Vinyl Butyl Ether and Ethanol.—Two moles (200 g.) of vinyl butyl ether (b.p. 92° (750 mm.), $n^{21}D$ 1.3995), 0.5 mole (23 g.) of ethanol (absolute, $n^{21}D$ 1.3602), 0.4 g. of mercuric acetate and 3 drops of concentrated sulfuric acid were added in the above order with good stirring to a flask held at −20°. After standing for 2.5 hours, 10 g. of sodium carbonate was stirred into the reaction solution and the mixture was then distilled. The fractions obtained were as follows: (a) 15 g. (0.21 mole, 42%), b.p. 35–36°, with the infrared spectrum, odor and polymerization character of vinyl ethyl ether; (b) 3 g., b.p. 37–87°; (c) 82 g. (0.82 mole, 41%), b.p. 87–94°, recovered vinyl butyl ether; (d) 5 g., b.p. 138–145°; (e) 119 g., initial b.p. 145°; the distillation was discontinued after 13 g., b.p. 145°, $n^{21.5}D$ 1.3969; fraction e contains a mixture of acetals.

II. Preparation of Vinyl Tetrahydrofurfuryl Ether from Vinyl Ethyl Ether and Tetrahydrofurfuryl Alcohol at −78°. Solution A.—Two grams of mercuric acetate and 0.001 g. of hydroquinone were dissolved in 3 moles (216 g.) of vinyl ethyl ether (b.p. 35°).

Solution B.—Seven-tenths of a gram of concentrated sulfuric acid was dissolved in 1 mole (103 g.) of tetrahydrofurfuryl alcohol (b.p. 79° (17 mm.), $n^{25}D$ 1.4499).

Solution A and B were cooled to −70° and then mixed with agitation. No exotherm was observed. The external temperature was kept at −78° for 2 hours. Six grams of anhydrous sodium acetate was then added with vigorous shaking and the mixture was heated at reduced pressures in a 3-foot fractionating column filled with protruded stainless steel packing. The fractions obtained were as follows: (a) 200 g., b.p. <30° (45 mm.) (recovered vinyl ethyl ether); (b) 96 g., b.p. 63–76° (17–12 mm.); (c) 26 g. hold-up plus residue.

Fraction b was washed three times with fourfold volumes of water; the washed organic layer weighed 29 g. It was dried with a mixture of anhydrous sodium sulfate and sodium carbonate for 5 days at 0°. Fifteen grams of the product was distilled in a spinning band column of approximately 30 theoretical plates efficiency. (b_1) 1.6 g., b.p. 68–77° (40–42 mm.); (b_2) 11.1 g., b.p. 77–77.8° (42 mm.), $n^{25}D$ 1.4468; C, 65.82; H, 9.25. The infrared spectrum was identical with the spectrum of samples of the vinyl ether prepared by other methods. No absorption band characteristic of hydroxyl groups was present at 3.0 μ, and new absorption bands characteristic of vinyloxy groups were present at 6.1 μ (v.s.), 7.6 μ (v.s.), 10.45 μ (v.s.), 14.3 μ (w). (Properties of the vinyl ether of tetrahydrofurfuryl alcohol are: b.p. 80–81 (45 mm.), $n^{20}D$ 1.4480; C, 65.63; H, 9.38);[6] (b_3) 1.5 g. hold-up and residue, straw-colored liquid.

Thus, approximately 0.17 mole (17% conversion) of the vinyl ether was formed and less than 2% acetal could be isolated. Over 75% of the tetrahydrofurfuryl alcohol was recovered from the aqueous extracts by salting out with potassium carbonate and distillation.

III. Preparation of Vinyl Tetrahydrofurfuryl Ether from Vinyl Ethyl Ether and Tetrahydrofurfuryl Alcohol at 20°.—One mole (103 g.) of tetrahydrofurfuryl alcohol, 4 moles (288 g.) of vinyl ethyl ether, 0.86 g. of mercuric acetate, 0.3 g. of sulfuric acid and 0.001 g. of hydroquinone were mixed and reacted as in I for 3.5 hours at −20°. There was obtained the vinyl ether of tetrahydrofurfuryl alcohol in 9% conversion and tetrahydrofurfuryl alcohol was recovered to an extent of 66%. The remaining material was a mixture of acetals.

IV. Reaction of Vinyl Ethyl Ether and Tetrahydrofurfuryl Alcohol at −78° with Sulfuric Acid as Catalyst.—This reaction was carried out as in II but with no mercuric acetate addition. After 2 hours at −78°, less than 2% vinyl ether of tetrahydrofurfuryl alcohol was isolated, approximately 30% of the tetrahydrofurfuryl alcohol was recovered, and the remaining product was composed of a mixture of acetals.

V. Attempted Reaction of Vinyl Ethyl Ether and Tetrahydrofurfuryl Alcohol at −78° with Mercuric Acetate as Catalyst.—This reaction was carried out as in II but with no sulfuric acid addition. After 2 hours at −78°, the vinyl ethyl ether and tetrahydrofurfuryl alcohol were recovered almost quantitatively (99%).

ELECTROCHEMICALS DEPARTMENT
E. I. DU PONT DE NEMOURS & CO., INC.
NIAGARA FALLS, NEW YORK

---

[4] Acetal cleavage at 270–400° occurs over palladium-on-asbestos (K. Bauer, U. S. Patent 1,931,858), over thoria (M. Cabanac, *Compt. rend.*, **190**, 881 (1930)), and over silver-on-asbestos (D. D. Coffman, G. H. Kalb and A. B. Ness, *J. Org. Chem.*, **13**, 223 (1948)). Pyrolysis of unsymmetrical acetals over strong acid catalysts at 140–150° is described by N. F. Shostakovskii, B. I. Mikhant'ev and N. N. Ovihinnikova (*Izvest. Akad. Nauk, S.S.S.R. Otdel Khim Nauk*, 1099 (1952); see *C. A.*, **48**, 1242^c (1954)).

[5] R. L. Adelman, *J. Org. Chem.*, **14**, 1057 (1949).

[6] R. L. Adelman, THIS JOURNAL, **75**, 2678 (1953).

Some Reactions with N-Bromosuccinimide

BY MOHAMED ZAKI BARAKAT, MOHAMED FATHY ABD EL-WAHAB AND MOHAMED MAHMOUD EL-SADR

RECEIVED MAY 17, 1954

N-Bromosuccinimide (NBS) has been used as a brominating agent[1] for a wide variety of organic compounds and as an oxidizing agent for the conversion of primary and secondary aliphatic alcohols to the corresponding aldehydes and ketones; in many cases its action is highly selective.[2,3] N-Chlorosuccinimide[4] has been shown to react with the aromatic secondary alcohol, benzhydrol, to give the corresponding ketone. α-Aminoacids[5] (alanine) and aliphatic dicarboxylic acids[6] (oxalic acid) are degraded in aqueous solution at room temperature by NBS.

---

[1] C. Djerassi, *Chem. Revs.*, **43**, 271 (1948).

[2] L. F. Fieser and S. Rajagopalan, THIS JOURNAL, **71**, 3935 (1949); **71**, 3938 (1949).

[3] M. Z. Barakat and G. M. Mousa, *J. Pharm. Pharmacol.*, **4**, 115 (1952).

[4] Hebbelynck and R. H. Martin, *Experientia*, **5**, 69 (1949).

[5] A. Schönberg, R. Moubasher and M. Z. Barakat, *J. Chem. Soc.*, 2504 (1951).

[6] M. Z. Barakat, *J. Pharm. and Pharmacol.*, **4**, 582 (1952).

We have studied the reaction of NBS with keto-alcohols, secondary and tertiary aromatic alcohols, and hydroquinone. With the exception of the tertiary alcohol, triphenylcarbinol, which did not react, the hydroxy compounds were oxidized to the corresponding carbonyl compounds. Benzoin and anisoin yielded the α-diketones, benzil and anisil; benzhydrol, fluorenyl alcohol and xanthydrol were oxidized to the respective monoketones; and hydroquinone yielded *p*-benzoquinone. These reactions and the following were accompanied by the evolution of hydrogen bromide and the formation of succinimide.

Diphenylmethane reacts with NBS in carbon tetrachloride to yield diphenylmethyl bromide[7]; we obtained benzhydryl ether when the reaction was run in aqueous solution.

NBS reacted readily with benzophenone hydrazone, fluorenone hydrazone and benzilmonohydrazone to yield the corresponding *sym*-diarylketazines in almost quantitative yield.

Staudinger[8] oxidized hydrazones with mercuric oxide to the diaryldiazomethanes, which lose nitrogen with the formation of the corresponding *sym*-diarylketazines. Diphenyldiazomethane is not an intermediate in our synthesis of *sym*-diphenylketazine from NBS and benzophenone hydrazone, for when the reaction was run in ether or in benzene in an atmosphere of carbon dioxide at room temperature, no violet color was observed.

Hydrazine hydrate reacted vigorously with NBS to give nitrogen, hydrogen bromide and succinimide; phenylhydrazine reacted to give these substances and hydrazobenzene.

NBS reacted instantaneously at room temperature with formic acid in aqueous solution to yield carbon dioxide, hydrogen bromide and succinimide, while acetic acid did not react under the same conditions. This behavior of acetic acid was to be expected in view of its use as a solvent for NBS[9] and for N-bromoacetamide which is considerably more reactive than NBS.[10]

Experimental

The procedures differed according to whether carbon tetrachloride or water was used as the solvent. Succinimide and hydrogen bromide were products of all the reactions in these two solvents; the former was recrystallized from benzene and identified by its melting point and mixed melting point with an authentic sample; the latter was detected with 10% silver nitrate solution acidified with nitric acid.

Carbon Tetrachloride as Solvent.—NBS (0.01 mole) was added to 0.01 mole of the reactant dissolved in 50–60 ml. of carbon tetrachloride and the mixture refluxed on a water-bath, Completion of the reaction was indicated by (a) the disappearance of the insoluble NBS on the bottom of the vessel with the simultaneous appearance of crystals floating on top, (b) the absence of bromine (starch–iodide test), and (c) in the case of the secondary aromatic alcohols, the disappearance of a yellow or orange color. The reaction mixture was filtered and succinimide isolated from the solid in about 85% yield.

The filtrate was worked up in a manner suitable for the isolation of the product either by concentration to a small volume (benzoin, anisoin, and phenylhydrazine) or by removal of the solvent by distillation *in vacuo* (secondary aromatic alcohols and hydrazones). The product was recrystallized from the appropriate solvent and identified by its melting point and mixed melting point with an authentic sample. In the case of the sym-diarylketazines and hydrazobenzene, nitrogen was detected by a sodium fusion test.

These reactions are summarized in Table I.

TABLE I

Compound	Reaction time, hr.	Yield, %	Product
Benzoin	1.5	95	Benzil
Anisoin	0.5	82	Anisil
Benzhydrol	0.5	55–60	Benzophenone
Fluorenyl alcohol	0.5	89	Fluorenone
Xanthydrol	3	92	Xanthone
Triphenylcarbinol	3	93	Triphenylcarbinol[a]
Benzophenone-hydrazone	2.5	90	*sym*-Diphenylketazine[b]
Fluorenone hydrazone	1.5	81	*sym*-Difluorenylketazine[b]
Benzil monohydrazone	2.5	85	*sym*-Benzoylphenylketazine[b]
Phenylhydrazine	3	87	Hydrazobenzene[b]

[a] NBS isolated. [b] N_2 evolved during the reaction.

Water as Solvent. Hydroquinone and Diphenylmethane.—Hydroquinone (1.10 g., 1 mole) dissolved in hot water (10 ml.) was added gradually with shaking to a solution of NBS (1 mole) in 40 ml. of water at 80°. As the reaction mixture cooled, yellow crystals were deposited which were filtered after the mixture had stood for an hour. They were recrystallized from benzine (b.p. 80–100°) to give *p*-benzoquinone (m.p. 115–116°, yield 0.6 g.) which was identified by a mixed melting point determination with an authentic sample and by the formation of quinhydrone with an equimolecular weight of hydroquinone in aqueous solution.

NBS (1 mole) and diphenylmethane (1.68 g., 1 mole) in 40 ml. of water were heated for half an hour on an electric plate. The reactants went into solution with the evolution of hydrogen bromide and the separation of a yellow oil, which became colorless when the reaction was complete. On cooling, the oil solidified and was filtered. The solid was recrystallized from alcohol to give colorless crystals (m.p. 109–110°, yield 1.4 g.) which were proved to be benzhydryl ether by a mixed melting point determination with an authentic sample.

Succinimide (0.8 g.) was obtained from the filtrate in both cases.

Hydrazine Hydrate.—NBS (1.42 g., 2 moles) was added to 95% hydrazine hydrate (0.134 g., 1 mole) in water (20 ml.). The reaction proceeded vigorously at room temperature with the evolution of nitrogen. When the reaction mixture was heated, hydrogen bromide was detected in the vapor. After nitrogen ceased to be evolved, the yellow reaction mixture was distilled *in vacuo* and succinimide (0.6 g.) obtained from the solid residue.

Formic Acid.—NBS (1 mole) was added gradually with shaking to formic acid (0.46 g., 1 mole) dissolved in 20 ml. of water. The reaction proceeded instantaneously at room temperature. The gases evolved were identified as hydrogen bromide and carbon dioxide. Succinimide (0.7 g.) was obtained from the reaction mixture which had been concentrated to about 5 ml.

Acetic acid and NBS did not react under these conditions.

Reaction of Benzophenone Hydrazone in Ether and Benzene.—When NBS (1 mole) was gradually added to benzophenone hydrazone (1.96 g., 1 mole) dissolved in 200 ml. of dry ether, bubbles of nitrogen appeared. At the end of the reaction, the ether was distilled and the solid residue extracted with boiling water (100 ml.) and filtered while hot. The solid was recrystallized from alcohol to give *sym*-diphenylketazine in about 90% yield. The filtrate was concentrated to about 25 ml. and allowed to cool. Colorless crystals deposited which were shown to be succinic acid (0.7 g.) by melting point, mixed melting point, a positive acidity test, and a negative sodium fusion test for nitrogen.

This experiment was repeated in benzene at room tem-

---

(7) Buu-Hoi, *Ann.*, **556**, 1 (1944).

(8) H. Staudinger and O. Kupfer, *Ber.*, **44**, 2197 (1911).

(9) H. J. Dauben and L. L. McCoy, Abstracts of the Am. Chem. Soc., Meeting, March, 1949, p. 3L.

(10) E. Schmidt, W. v. Knilling and A. Ascherl, *Ber.*, **59B**, 1280 (1926).

perature in an atmosphere of carbon dioxide, but no violet color of diphenyldiazomethane was observed.

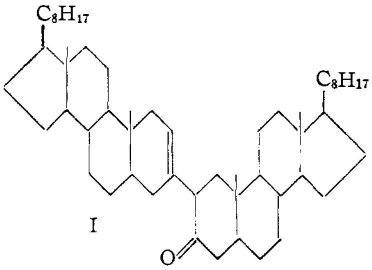
BIOCHEMISTRY DEPARTMENT
FACULTY OF MEDICINE ABBASSIA
IBRAHIM PASHA EL-KEBIR UNIVERSITY
CAIRO, EGYPT

A New Steroid Coupling Product from Cholesterol

BY ELIAS J. COREY AND RICHARD L. YOUNG

RECEIVED OCTOBER 28, 1954

The catalytic hydrogenation of cholestanone over platinum in di-*n*-butyl ether containing a small amount of concentrated aqueous hydrobromic acid affords epicholestanol as the major product together with a small amount of cholestanol.[2,3] We have found, however, that if the hydrogenation is carried out in anhydrous medium using an acetic acid solution of hydrogen bromide instead of a concentrated aqueous solution a new substance, $C_{54}H_{90}O$, is formed in *ca.* 40% yield. Furthermore, the same substance can be obtained in the absence of hydrogen and platinum simply by heating cholestanone in dibutyl ether–acetic acid–hydrogen bromide solution. The new compound is an unsaturated, non-conjugated ketone as is indicated by the infrared spectrum (carbonyl absorption at 1710 cm.$^{-1}$), formation of a yellow 2,4-dinitrophenylhydrazone, yellow coloration with tetranitromethane and lack of high-intensity absorption in the ultraviolet. Only one structure (I) seems to accommodate these facts and to be consistent with the conditions of the transformation. The attachment of the cholestene moiety to C_2 follows from the preferred direction of enolization of cholestanone and the position of the double bond follows from the greater stability of Δ^2- over Δ^3-cholestene. The more stable α-orientation of the cholestene substituent seems probable because the compound is not isomerized even by long treatment with strong acid.



I

Although the coupling product reacts rapidly with bromine in carbon tetrachloride to form an unstable, bromine-containing material (presumably a dibromide), all attempts to reduce either the double bond or the carbonyl group catalytically were unsuccessful.

Experimental

Aldol Coupling of Cholestanone.—A solution of 5 g. of cholestanone in 125 ml. of di-*n*-butyl ether containing 15 ml. of 3.3% hydrogen bromide in acetic acid was heated to 60° for four hours. The catalyst was removed by filtration and the filtrate was washed with 10% aqueous sodium hydroxide, then with water, and evaporated under reduced pressure. Recrystallization of the residual solid from methylene chloride–acetone afforded 2.28 g. of crude product, m.p. *ca.* 175°. Further recrystallization furnished 2.0 g. of pure material as a colorless, granular solid, m.p. 209–211°, $[\alpha]_D$ +40.9° (*c* 2.3, chloroform).

Anal. Calcd. for $C_{54}H_{90}O$: C, 85.63; H, 12.24; mol. wt., 757.26. Found: C, 85.51; H, 12.27; mol. wt., 706 (ebullioscopic, benzene).

The same product was obtained when the reaction mixture was shaken with hydrogen and pre-reduced platinum catalyst; identified by m.p., mixture m.p. and infrared spectra.

The 2,4-dinitrophenylhydrazone was prepared in the usual way and recrystallized from methylene chloride–acetone, m.p. 150° dec. The same dinitrophenylhydrazone was made from samples of I formed by condensation in the presence or absence of hydrogen–platinum.

Anal. Calcd. for $C_{60}H_{94}O_4N_4$: C, 76.87; H, 10.32; N, 5.97. Found: C, 77.14; H, 10.46; N, 6.05.

DEPARTMENT OF CHEMISTRY
UNIVERSITY OF ILLINOIS
URBANA, ILLINOIS

---

(1) From the B.S. thesis of R. L. Young.

(2) G. Vavon and B. Jakubowicz, *Bull. soc. chim. France*, [4] **53**, 583 (1933).

(3) L. Ruzicka, H. Brungger, E. Eichenberger and J. Meyers, *Helv. Chim. Acta*, **17**, 1407 (1934).

2,5-Di-*t*-butyl-4-methoxyphenol and 2,6-Di-*t*-butyl-4-methoxyphenol

BY CLINTON D. COOK, RICHARD G. INSKEEP, ARTHUR S. ROSENBERG AND EARL C. CURTIS, JR.

RECEIVED JULY 21, 1954

During a study[1] of the thermal decomposition of bis-(1,3,5-tri-*t*-butyl-2,5-cyclohexadiene-4-one) peroxide[2] a product believed to be 2,6-di-*t*-butylbenzoquinone was isolated. Bickel and Kooyman[3] have reported this compound from the reaction of 2,4,6-tri-*t*-butylphenol with oxygen initiated by 2,2′-azoisobutylnitrile. However, they cite no structural evidence. To prove the identity of our product, it was reduced to the corresponding hydroquinone and alkylated with methyl sulfate to give 2,6-di-*t*-butyl-4-methoxyphenol. This product has been reported by Sears and Kitchen[4] as a result of the alkylation of 4-methoxyphenol with isobutylene by the method of Stillson, Sawyer and Hunt.[5] In our hands the products prepared by these two methods were not identical.[6] Further investigation showed that the major product formed on isobutylene alkylation—under conditions closely approximating those cited by Stillson, *et al.*, for the preparation of 2,4,6-tri-*t*-butylphenol—is 2,5-di-*t*-butyl-4-methoxyphenol. Our evidence is as follows: The infrared spectrum of the product formed from the di-*t*-butylhydroquinone shows a marked absorption for the hydroxyl group at 3659 cm.$^{-1}$ but only slight indications of hydrogen bonding in the region from 3300 to 3500 cm.$^{-1}$ (see Fig. 1, A). This product was insoluble in Claisen solution. These facts are consistent with a 2,6-orientation of the *t*-butyl groups. (For comparison with a com-

---

(1) C. D. Cook and R. C. Woodworth, unpublished work.

(2) C. D. Cook and R. C. Woodworth, THIS JOURNAL, **75**, 6242 (1953).

(3) A. F. Bickel and E. C. Kooyman, *J. Chem. Soc.*, 3211 (1953).

(4) W. C. Sears and L. J. Kitchen, THIS JOURNAL, **71**, 4110 (1949).

(5) G. H. Stillson, D. W. Sawyer and C. K. Hunt, *ibid.*, **67**, 303 (1945).

(6) In a personal communication, Dr. Kitchen reports that this reaction is unusually sensitive to conditions and that, under his conditions, the 2,6-isomer predominates. He plans to report this work in a forthcoming publication.