ml. of water. An excess (15.2 ml.) of thioglycolic acid[5] was added and the mixture was heated to 100° with rapid stirring. When the solution became almost clear, it was filtered rapidly while very hot. The filtrate was allowed to cool, and a copious crystalline precipitate formed immediately. The precipitate was filtered off and washed with three portions of 50 ml. of cold water. It was then dried to constant weight at 40° and then in a vacuum desiccator; yield was 18.8 g., 98%; m. p., 158–162°.

Anal. Calcd. for $C_{11}H_{12}O_5NS_2As$; N, 3.71; As, 19.85; neut. eq., 184.5. Found: N, 3.63; As, 19.75; neut. eq., 185.7.

The acid (II) is insoluble in cold water but soluble in water above 90°. It is sparingly soluble in cold ethanol and methanol, and very soluble in these solvents when warm. It is insoluble in warm isopropyl ether. The acid dissociation constant is $pK_a = 4$, which is similar to that of thioglycolic acid. A potentiometric titration of the acid showed that the disodium salt is stoichiometrically formed in solution at *p*H 7–8.

For therapeutic purposes II is used in the form of an aqueous solution prepared by dissolving the acid in sufficient 0.2 *N* sodium hydroxide to yield a solution of *p*H 7. A 2% solution, formed in this way and sterilized by filtration, is stable in sealed amber ampules at room temperature for at least six months. In practice it has been useful to include, for each liter of solution, 72 ml. of *M*/15 Na_2HPO_4 and 48 ml. KH_2PO_4 to maintain the *p*H value. Both unbuffered and buffered solutions have been used successfully for intravenous therapy in dogs.

(5) Attention must be given to the purity of $HSCH_2COOH$. It should be water-white, spec. grav. 1.32, and distilled at 105–109° under 13–16 mm. pressure. The acid used in this Laboratory was purchased according to these specifications from Wallace Laboratories, New Brunswick, New Jersey.

DEPARTMENT OF PARASITOLOGY
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Solid Esters of Cellosolves and Carbitols

BY DAVID C. O'DONNELL AND RICHARD J. CAREY[1,2]

Many derivatives of the alcohol-ethers of the cellosolve and carbitol type have been prepared by various methods,[3] but these have not usually been easily obtained solids of characteristic melting points. We have therefore now prepared nine esters of these alcohol-ethers with 3,4,5-triiodobenzoic acid. The alcohol-ethers were generously supplied by the Carbide and Carbon Chemical Corporation and were simply fractionated except for the methyl and ethyl carbitols which were purified by the method of Seikel.[4] The acid chloride of the 3,4,5-triiodobenzoic acid was prepared by the method of Klemme and Hunter[5] and proved to be quite stable, a sample of it kept in a stoppered vial melting unchanged after two years.

Procedure.—To 1 g. of the acid chloride in a 10-cm. test-tube 0.5 cc. of the alcohol-ether was added and the mixture was heated gently over a micro burner until the evolution of hydrogen chloride ceased. This usually required from three to five minutes. The molten mass was then poured into 20 cc. of a 20% solution of alcohol to which cracked ice had been added. Some of the compounds solidified instantly and those that came down as oils changed to solids in a few minutes without further manipulation. All of the esters can be recrystallized from 95% alcohol, but 50% alcohol is a better recrystallizing solvent for the esters obtained from methyl and butyl carbitols. One recrystallization is frequently enough to give a pure compound, but two may be needed. The esters precipitate in granular form, with the exception of the isopropyl cellosolve derivative which comes down in the form of fine needles. The melting points were taken with Anschutz thermometers, but are not corrected.

TABLE I

ESTERS OF 3,4,5-TRIODOBENZOIC ACID

Cellosolve or carbitol used	M. p., °C.	Yield, %	Formula	Iodine, % Calcd.	Found
Methyl cellosolve	152.0–152.3	54.2	$C_{10}H_9O_5I_3$	68.26	68.47
Cellosolve	127.7–128.2	74.3	$C_{11}H_{11}O_5I_3$	66.58	67.11
Isopropyl cellosolve	79.5– 80.0	47.7	$C_{12}H_{13}O_5I_3$	64.99	65.45
Butyl cellosolve	85.0– 85.5	37.1	$C_{13}H_{15}O_5I_3$	63.46	63.93
Phenyl cellosolve	144.9–145.3	71.7	$C_{15}H_{11}O_5I_3$	61.41	61.60
Benzyl cellosolve	103.5–104.0	65.6	$C_{16}H_{13}O_5I_3$	60.06	60.61
Methyl carbitol	82.0– 82.5	39.7	$C_{12}H_{13}O_6I_3$	63.26	63.25
Ethyl carbitol	75.5– 76.5	42.0	$C_{13}H_{15}O_6I_3$	61.81	62.20
Butyl carbitol	53.8– 54.5	37.1	$C_{15}H_{19}O_6I_3$	59.11	58.99

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(1) Taken for the most part from a thesis submitted by Richard J. Carey in partial fulfilment for the M.S. degree.

(2) Present address: Compo Shoe Machinery Corporation, Boston, Mass.

(3) Mason and Manning, THIS JOURNAL, **62**, 1635–1640, 3136–3139 (1940).

(4) Seikel, *Ind. Eng. Chem., Anal. Ed.*, **13**, 388–389 (1941).

(5) Klemme and Hunter, *J. Org. Chem.*, **5**, 508–511 (1940).

Catalytic Acetylation of Steroid Compounds

BY BRADLEY WHITMAN AND ERWIN SCHWENK

Based on the work of Conant and Bramann,[1] we have found that acetylations may be carried out rapidly at room temperature if a trace of anhydrous perchloric acid is used to catalyze the reaction.

Procedure.—One gram of the substance to be acetylated is added to a mixture of 10 cc. of glacial acetic acid and 3 cc. of acetic anhydride. The mixture is cooled to 18° and 0.1 cc. of 5 *N* anhydrous perchloric acid added. The temperature is kept below 35° with external cooling. After standing for thirty minutes, the reaction mixture is cooled to 18° and sufficient ice added to destroy the excess acetic anhydride. The reaction mixture is worked up by pouring into water and filtering the precipitate.

This procedure has been used successfully on a great variety of bile acids and their derivatives. The yields are excellent and the physical constants are in agreement with those in the literature. When the diphenyl carbinols encountered in the Barbier–Wieland[2] degradation of the side-chain of 3,12-dihydroxycholanic and similar acids are acetylated by this method, the 3,12-diacetoxydiphenylethylenes are obtained; water splitting takes place even under the mild conditions of this reaction.

In the course of this work, three cases of polymorphism were encountered. 3(α)-12(β)-Diacetoxy-*nor*-cholanic acid and 3(α)-12(β)-diacetoxy-*bis-nor*-cholanic acid may be obtained in high melting forms by recrystallization from ether–petroleum ether and in low melting forms by salting out the ammonium salts and regenerating the free acids.

(1) Conant and Bramann, THIS JOURNAL, **50**, 2305 (1928).

(2) (a) Barbier and Locquin, *Compt. rend.*, **156**, 1433 (1933); (b) Wieland, Schlichting and Jacobi, *Z. physiol. Chem.*, **161**, 80 (1926).

In each case the mixture of the two forms melted at the melting point of the higher melting form.

3(α)-12(β)-Diacetoxy-*ter-nor*-diphenylethylene prepared by this method had a melting point of 127–129°, while the reported melting point was 158–160°.[3] The high negative rotation (−138° in chloroform) left no doubt that it was the desired substance.

3(α)-12(β)-Diacetoxy-*nor*-cholanic acid,[4] high melting form, 209–210°; low melting form, 164–66°.

Anal. Calcd. for $C_{27}H_{42}O_6$: C, 70.1; H, 9.2. Found: high melting form, C, 69.9; H, 9.4; low melting form, C, 69.6; H, 9.5.

3(α)-12(β)-diacetoxy-*bis-nor*-cholanic acid, high melting form, 167.8°; low melting form, 99.5–100°.

Anal. Calcd. for $C_{26}H_{40}O_6$: C, 69.6; H, 9.0. Found: high melting form, C, 69.4; H, 9.2; low melting form, C, 69.2; H, 8.9.

Two new compounds were prepared, the above 3(α)-12(β)-diacetoxy-*bis-nor*-cholanic acid and ethyl 3(α)-acetoxy-12-ketocholanate (m. p. 123–124°).

Anal. Calcd. for $C_{28}H_{44}O_5$: C, 73.0; H, 9.6. Found: C, 73.0; H, 9.9.

(3) Hoehn and Mason, THIS JOURNAL, **60**, 1493 (1938).

(4) Brink, Clark and Wallis, *J. Biol. Chem.*, **162**, 701 (1946), found a melting point of 205–6°.

SCHERING CORPORATION
BLOOMFIELD, NEW JERSEY RECEIVED MARCH 9, 1946

The Catalytic Reduction of α-Nitrostilbenes to α, β-Diphenylethylamines

BY WARREN D. MCPHEE, ERNST S. ERICKSON, JR.,[1] AND U. JOSEPH SALVADOR

In a recent publication[2] from these Laboratories it was reported that the methods of the literature did not afford practicable procedures for the catalytic reduction of α-nitrostilbenes to α,β-diphenylethylamines.

$$Ar—CH=\underset{\displaystyle NO_2}{\underset{|}{C}}—C_6H_5 \longrightarrow Ar—CH_2—\underset{\displaystyle NH_2}{\underset{|}{CH}}—C_6H_5$$

Subsequent to our previous work we have found that α-nitrostilbenes may be conveniently reduced in methanol in the presence of a readily prepared palladium-on-charcoal catalyst. The amines are easily isolated as their hydrochlorides in a state of purity. In one instance, α-nitro-4′-methoxystilbene gave rise to a small amount of the corresponding oxime when the hydrogen uptake was less than theoretical.

The diphenylethylamine hydrochlorides described herein are being studied pharmacologically by Dr. T. J. Becker and his associates in these Laboratories.

Experimental[3]

Substituted α-nitrostilbenes were prepared by condensing a substituted benzaldehyde with an equivalent of phenylnitromethane in the presence of methanolic methylamine, either at room temperature (22°) or in the refrigerator (3°). Analytical samples were recrystallized from alcohol.

The following experiment is typical: **α-nitro-2′-methoxystilbene** was prepared by shaking 6.85 g. (0.05 mole) of phenylnitromethane, 6.80 g. (0.05 mole) of *o*-methoxybenzaldehyde and 2.5 cc. of methanolic methylamine (10 g. of methylamine in 70 cc. of methanol) until solution occurred. The solution was placed in the refrigerator for fifteen hours. The resultant bright yellow crystals were admixed with ether to dissolve the oily impurities, filtered and dried in the air. This material (10.8 g.) was pure enough for reduction, melting at 113–115°. Recrystallization from alcohol gave yellow needles of m. p. 117.5–119°. The same reaction carried out at room temperature gave approximately the same yield of material of equal purity.

Substituted α,β-diphenylethylamine hydrochlorides were prepared by the following general method: 10 g. of the substituted nitrostilbene was dissolved in 150 cc. of boiling methanol. One gram of Darco G-60 and 0.2 g. of palladium chloride were added and the hot mixture was hydrogenated immediately at 55° and 50–60 lb. initial pressure. Reductions were generally complete in one to three hours. The catalyst was then removed by filtration and 10 cc. of saturated ethereal hydrogen chloride was added to the cooled filtrate. The resulting solution was evaporated to dryness *in vacuo* and white crystals formed immediately. These were washed with acetone and recrystallized.

TABLE I

SUBSTITUTED α-NITROSTILBENES, $Ar—CH=C(NO_2)—C_6H_5$

Substituent	Reaction temp., °C.	Yield, %	M. p., °C.	N, % Calcd.	N, % Found
2′-Methoxy	3	85	117.5–119	5.49	5.75
2′-Benzyloxy	3	74	131–132	4.23	4.56
4′-Methoxy	22	64	152–153[a]		
4′-Benzyloxy	22	61	113–114.5	4.23	4.74
3′-Methoxy-4′-benzyloxy	22	49	132–132.5	3.88	3.83

[a] Knoevenagel and Walter [*Ber.*, **37**, 4502 (1904)] report m. p. 151.

TABLE II

SUBSTITUTED α,β-DIPHENYLETHYLAMINE HYDROCHLORIDES, $Ar—CH_2—CH(NH_2)—C_6H_5·HCl$

Substituted β-phenyl	Reduction time, hr.	Yield, %	M. p., °C.	Recryst. solvent	N, % Calcd.	N, % Found
2-Methoxy	16	52	249–250.5	Dil. HCl	5.31	5.36
2-Hydroxy	3	86	223–224.5	Dil. HCl	5.61	5.54
4-Methoxy[a,b]	3	67	212–213	MeOH-EtOAc		
4-Hydroxy[a]	3	75	255–256	MeOH-EtOAc		
3-Methoxy-4-hydroxy[a]	1	87	220–221	MeOH-EtOAc		

[a] Ref. 1. [b] Phenyl *p*-methoxybenzyl ketoxime, m. p. 130–131°, was isolated in small amount. *Anal.* Calcd. for $C_{15}H_{15}NO_2$: N, 5.82. Found: N, 5.92. Buck and Ide [THIS JOURNAL, 53, 1536 (1931)] report m. p. 133°.

STERLING-WINTHROP RESEARCH INSTITUTE
RENSSELAER, NEW YORK RECEIVED APRIL 11, 1946

(1) At present, Lieutenant (j.g.), U. S. N. R.

(2) McPhee and Erickson, THIS JOURNAL, **68**, 624 (1946).

(3) Microanalyses by the Misses Alice Rainey and Patricia Curran.