Anal. Calcd. for $C_{14}H_{16}O_3I_2$: I, 52.30. Found: I, 52.50.

(19) α-(Δ¹-Cyclohexenyl)-3,5-diiodo-4-hydroxycinnamic acid: a mixture of 17.9 g. (0.1 mole) of anhydrous potassium cyclohexylidineacetate,[8] 37.4 g. (0.1 mole) of 3,5-diiodo-4-hydroxybenzaldehyde and 100 cc. of acetic anhydride was heated for twenty-five to thirty hours at 105 to 110°. After decomposing the excess anhydride with water, the reaction mixture was poured on ice. The crude substituted cinnamic acid was taken up in 5% sodium carbonate solution, the solution filtered and the filtrate acidified with sulfur dioxide, yield 12.5 g. (25%), m. p. 201–203°; recrystallized from benzene–petroleum ether for analysis, m. p. 203–204°.

Anal. Calcd. for $C_{15}H_{14}O_3I_2$: C, 36.28; H, 2.84. Found: C, 36.39; H, 3.12.

Acknowledgment.—The authors wish to express their appreciation to Dr. Richard Tislow and Mrs. Annette La Belle for the pharmacological data reported herein.

Summary

Three series of aliphatic acids having the 3,5-diiodo-4-hydroxyphenyl radical have been synthesized for pharmacological study as cholecystographic agents. Preliminary toxicity data and cholecystographic properties of the compounds are discussed.

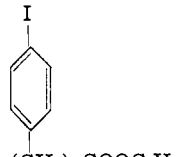
BLOOMFIELD, N. J. RECEIVED OCTOBER 8, 1949

[CONTRIBUTION FROM THE CHEMICAL RESEARCH DIVISION OF SCHERING CORPORATION]

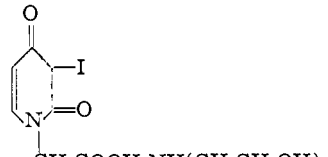
X-Ray Diagnostics. III. Iodinated Alkoxyaryl Aliphatic Acids and Ethyl Esters[1]

BY DOMENICK PAPA, ERWIN SCHWENK AND ERWIN KLINGSBERG[2]

Halogenated vegetable oils[2] have been used clinically for many years for visualization of body cavities such as spinal cord, urethra, seminal vesicles, uterine cavity and tubes, fistulas and sinuses. In recent years, radiopaque substances of greater opacity and increased safety have been developed. The latter substances, in contrast to the halogenated vegetable oils, are iodinated compounds in which the iodine atoms are firmly bound to aromatic or heterocylic ring systems. Two compounds of this type are shown in formulas I and II; the former is used clinically for



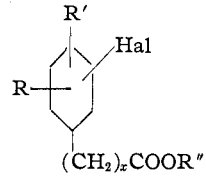
I



II

myelography,[3] the latter for hysterosalpingography.[4]

In continuation of studies[5] on the correlation of structure and pharmacological action of X-ray diagnostic agents, we prepared a series of iodinated alkoxyaryl aliphatic acids (III) (Table I) and esters (IV) (Table II) of the following general formula, wherein R is hydrogen, a methyl or methoxy group, R′ is a methoxy or ethoxy group



(III) R″ = H; (IV) R″ = C_2H_5
Hal = Br or I

and x is an integer from 1 to 10. The acids (III) were secured readily by the iodination of the previously described alkoxyaryl aliphatic acids[6] (V), whereas the esters (IV) were secured from III by esterification or by direct iodination of the esters of V.

Four iodination procedures were studied in this investigation, namely, mercuric acetate and iodine, iodine chloride, silver acetate and iodine, and iodine plus the anhydrous silver salt of the acids V. After several exploratory experiments, the mercuric acetate–iodine procedure was abandoned because the by-product, mercuric iodide, being soluble in the usual organic solvents, had to be removed with hydrogen sulfide, an unsatisfactory and time consuming procedure. Furthermore, in several instances, the iodinated acids or esters were found to contain mercury, notwithstanding repeated treatment of the crude iodinated products with hydrogen sulfide. Iodination with iodine chloride[7] proceeded smoothly and good yields were obtained in the majority of cases.

The iodination procedures utilizing silver ace-

(1) This is part of a paper presented before the Division of Organic Chemistry at the Chicago Meeting of the American Chemical Society, April, 1948.

(2) Lipidol, iodized poppy seed oil, and Iodochloral, iodinated and chlorinated peanut oil are representative of these types of substances. Recently, Olsson and Ekman (*Acta Radiologica*, **31**, 33 (1949)) have described the use of emulsified brominated sesame oil in rats for liver visualization.

(3) Strain, Plati and Warren, U. S. Patent 2,348,231, May 9, 1944; THIS JOURNAL, **64**, 1436 (1942); Steinhausen, *et al.*, *Radiology*, **43**, 230 (1944).

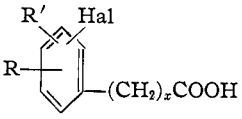
(4) Schnider, U. S. Patent 2,212,187, August 20, 1940; Norment, *Am. J. Obst. and Gynec.*, **49**, 253 (1945); Montgomery and Lang, *ibid.*, **51**, 702 (1946).

(5) For previous investigations on X-ray diagnostic agents reported from this Laboratory, see Schwenk and Papa, U. S. Patent 2,436,270, Feb. 17, 1948; Papa, *Arch. Biochem.*, **23**, 163 (1949); Papa, Schwenk, Breiger and Peterson, THIS JOURNAL, 2619 (1950); Papa, *ibid.*, in press.

(6) Papa, Schwenk and Hankin, *ibid.*, **69**, 3018 (1947).

(7) Iodination with iodine chloride has been employed by Pratt, Hoppe and Archer (*J. Org. Chem.*, **13**, 576 (1948)) for the preparation of compounds 4 and 7 in Table I.

TABLE I

HALOGENATED ACIDS OF FORMULA 

No.	R	R'	Hal	x	Method	Yield,[a] %		M. p., °C.	Recryst. solvent	Formula	Analyses, % Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found
1	H	4-OCH_3	3-I	1	I; III	82	85	128–129	C_2H_5OH-H_2O	$C_9H_9O_3I$[b]	37.01	37.32	3.11	3.07
2	H	5-OCH_3	2-Br	2	I; II	82	88	83–84	C_6H_6-P. E.[c]	$C_{10}H_{11}O_3Br$[d]	*i*			
3	H	5-OCH_3	2-I	2	I; II	84	90	109–110	$CHCl_3$-P. E.	$C_{10}H_{11}O_3I$	*k*			
4	H	4-OCH_3	3-I	3	I; III	86	78	106–107[e]	C_6H_6OH	$C_{11}H_{13}O_3I$[f]	41.27	41.21	4.09	4.34
5	H	4-OC_2H_5	3-I	3	I; III	80	83	74–74.5	C_2H_5OH	$C_{12}H_{15}O_3I$	43.18	43.27	4.52	4.87
6	3-OCH_3	4-OCH_3	I[g]	3	I; III	81	74	168–168.5	C_2H_5OH-H_2O	$C_{12}H_{15}O_4I$	41.14	41.26	4.32	4.75
7	H	4-OCH_3	3-I	4	I; II	80	84	146–148[h]	C_2H_5OH-H_2O	$C_{12}H_{15}O_3I$	43.18	43.48	4.52	4.55
8	H	4-OCH_3	3-I	5	I; III	84	86	85.5–86.5	C_2H_5OH	$C_{13}H_{17}O_3I$	44.84	45.04	4.92	4.99
9	H	4-OCH_3	3-I	9	I		76	52–52.5	C_6H_6-P. E.[c]	$C_{17}H_{25}O_3I$[j]	50.45	50.62	6.23	6.08

[a] The yields are calculated on the basis of recrystallized products. [b] *Anal.* Calcd. I, 43.5. Found: I, 43.6. [c] P. E. is petroleum ether, b. p. 35–60°. [d] The configuration of the brominated acid was established by alkaline permanganate oxidation to the known 2-bromo-5-methoxybenzoic acid, m. p. 159.5–160.5°; literature 161–162°, Bauer and Vogel, *J. prakt. Chem.*, [2] **88**, 330 (1913); Pschorr, *Ann.*, **391**, 29 (1912). [e] Literature m. p. 105–107°: ref. 7. [f] *Anal.* Calcd. I, 39.6. Found: I, 39.3. [g] The position of the iodine atom was not established; it is very likely that the compound is the 6-iodo derivative. [h] Literature m. p. 146–148°; ref. 7. [i] Secured from the ester (Table II, no. 9) by alkali saponification. *Anal.* Calcd. I, 31.4. Found: I, 31.5. [j] Calcd. for $C_{10}H_{11}O_3Br$: Br, 30.75; neut. equiv., 259.1. Found: Br, 30.41; neut. equiv., 260. [k] Calcd. for $C_{10}H_{11}O_3I$: I, 41.3; neut. equiv., 306.1. Found: I, 41.4; neut. equiv., 307.2.

tate or the silver salt of the aryl-aliphatic acid[8] were studied in detail in view of the mild reaction conditions and simplicity and ease of isolating the iodinated products. Iodination with silver acetate is carried out in acetic acid at room temperature essentially as described for mercuric acetate, except that the by-product silver iodide is quantitatively removed from the reaction mixture by filtration. The filtrate is then diluted with water and the iodinated acid or ester isolated by ether extraction and purified by distillation and/or recrystallization.

In general, the iodination of the acids and esters, wherein x equals 1 to 5, inclusive, proceeded rapidly, whereas the higher homologous acids and esters (x = 9 to 10) reacted somewhat slower. At no time during the iodination was any large excess of iodine and/or silver acetate present.

Halogenation of the anhydrous silver salts was carried out in carbon tetrachloride at room temperature, the halogen being added preferably in solution. The halogenations proceeded rapidly; and, after filtering off the silver halide, the solvent was removed and the halogenated product distilled or recrystallized.

Pharmacology.—Several of the iodinated esters (Table II) were examined as myelographic agents by injecting them intrathecally in rabbits and dogs in amounts of 1 and 2 cc., respectively. Compounds 2, 6 and 7 were unsatisfactory, because of the relatively high intraperitoneal toxicity, LD/50 = 2–3 mg./kg., and local irritation which they caused. Compounds 8, 9, 10 and 11 gave visualization of the spinal canal comparable to that of compound I and showed very favorable intraperitoneal toxicities, especially compound 11, I. P. LD/50 greater than 24 mg./kg. in rats. In a limited clinical study, compound 11 was very well tolerated and gave sharp and uniform visualization of the human spinal canal.

The halogenated acids (Table I) were examined as cholecystographic agents. None were found satisfactory when compared with Iodoalphionic acid [α-phenyl-β-(3,5-diiodo-4-hydroxyphenyl)-propionic acid] as standard.

Experimental

All melting points are corrected. The halogen analyses were carried out by the Raney alloy reduction method.[9] The following compounds used as intermediates in this investigation were obtained as described[6]: γ-(*p*-methoxyphenyl)-, γ-(*p*-ethoxyphenyl)-, γ-(3,4-dimethoxyphenyl)-, and γ-(2-methyl-4-methoxyphenyl)-butyric acids; ω-(*p*-methoxyphenyl)-valeric, caproic and capric acids; and ω-(*p*-ethoxyphenyl)- and ω-(2,5-dimethylphenyl)-capric acids. Ethyl-ω-(*p*-methoxyphenyl)-undecylic acid was secured from anisole and ethyl undecylenate.[10] The corresponding ethoxy compound was obtained by a similar procedure from phenetole; yield 64%, b. p. 186–188° (1 mm.).

Anal. Calcd. for $C_{21}H_{34}O_3$: C, 75.40; H, 10.24. Found: C, 75.65; H, 10.35.

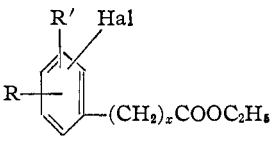
Esterification Procedure.—The ethyl esters described in Table II were prepared as follows: to 0.1 mole of the iodinated acid in 75 cc. of commercial absolute ethyl alcohol, there was added in small portions 10 cc. of acetyl chloride. The flask containing the resulting mixture was stoppered loosely and allowed to stand overnight. The iodinated esters were worked up in the known manner and purified by fractionation, using a Vigreux column. The distillations of iodinated esters, nos. 8–12, were made in all glass apparatus, because, at the distillation tempera-

(8) In the course of studies on the synthesis of *m*-methoxyaralkyl halides by the Hunsdiecker (*Ber.*, **75**, 291 (1942); U. S. Patent 2,176,181, October 17, 1939)) degradation of metallic salts of *m*-methoxyaralkyl carboxylic acids, it was observed that nuclear halogenation occurred exclusively; and, in no case, was any aralkyl halide obtained. A preliminary report of studies of the Hunsdiecker procedure with unsubstituted aralkyl carboxylic acids has been presented.[1] Exploratory experiments with the latter acids gave only poor yields of the aralkyl halides along with varying amounts of nuclear halogenated products. This reaction is being investigated further.

(9) Schwenk, Papa and Ginsberg, *Ind. Eng. Chem., Anal. Ed.*, **15**, 576 (1943).

(10) Fourneau and Baranger, *Bull. soc. chim.*, [4] **49**, 1161 (1931).

TABLE II

HALOGENATED ESTERS OF FORMULA 

No.	R	R′	Hal	x	Method	Yield,[a] %	B. p., °C.	Mm.	Formula	Analyses, % Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found
1	H	4-OCH_3	3-I	1	III[b]	89	132–134	0.5	$C_{11}H_{13}O_3I$	41.27	41.36	4.09	4.38
2	H	4-OCH_3	3-I	3	III[b]	76	174–175	2	$C_{13}H_{17}O_3I$	44.84	45.56	4.92	4.92
3	H	4-OC_2H_5	3-I	3	III[b]	86	180–184	3	$C_{14}H_{19}O_3I$	46.42	46.49	5.29	5.47
4	3-OCH_3	4-OCH_3	I[c]	3	III[b]	80	198–202[d]	6	$C_{14}H_{19}O_4I$	44.46	5.06	44.64	5.22
5	2-CH_3[e]	4-OCH_3	5-I	3	I	74	160–164	1	$C_{14}H_{19}O_3I$[f]	46.39	46.89	5.41	5.81
6	H	4-OCH_3	3-I	4	III	77	185	3	$C_{14}H_{19}O_3I$	46.42	46.70	5.29	5.59
7	H	4-OCH_3	3-I	5	I, III[b]	88, 79	190–192	0.5	$C_{15}H_{21}O_3I$	47.98	48.19	5.64	5.76
8	2-CH_3	5-CH_3	4-I	9	I	56	210–214	1	$C_{20}H_{31}O_2I$	55.82	57.22[g]	7.22	7.35
9	H[h]	4-OCH_3	3-I	9	I	76	212–215	1	$C_{19}H_{29}O_3I$	52.78	53.03	6.77	6.65
10	H	4-OC_2H_5	3-I	9	I	78	218–221	1	$C_{20}H_{31}O_3I$	53.81	53.53	7.00	7.06
11	H	4-OCH_3	3-I	10	III	64	212–215	1	$C_{20}H_{31}O_3I$	53.81	54.19	7.00	7.26
12	H	4-OC_2H_5	3-I	10	I, III	60, 70	215–217	1	$C_{21}H_{33}O_3I$[i]	54.77	55.23	7.22	7.02

[a] The yields are calculated on the basis of distilled products. [b] Also prepared by the acetyl chloride esterification of the iodo acids (Table I), yields 84–92%. [c] See (*f*) Table I. [d] M. p. 51–51.5° after recrystallization from petroleum ether. [e] Ethyl γ-(2-methyl-4-methoxyphenyl)-butyrate was prepared from the acid by acetyl chloride esterification, yield 94%; b. p. 143–145° (1 mm.); $n^{25}D$ 1.5012. [f] *Anal.* Calcd. I, 35.1. Found: I, 35.1. [g] A small amount of the ethyl ω-(2,5-dimethylphenyl)-caprate contaminated the iodo compound and repeated fractionation failed to remove this impurity. [h] The ethyl ω-(*p*-methoxyphenyl)-caprate was prepared by the acetyl chloride procedure in 86% yield, b. p. 167–169° (1 mm.). *Anal.* Calcd. for $C_{19}H_{30}O_3$: C, 74.47; H, 9.87. Found: C, 74.96; H, 10.08. [i] *Anal.* Calcd.: I, 27.6. Found: I, 27.7.

ture, rubber nipples or stoppers softened and either contaminated the product or collapsed.

Preparation of Silver Salts.—To a solution of 0.05 mole of the arylaliphatic acid in 100 cc. of ethyl alcohol, there was added 2 g. (0.05 mole) of sodium hydroxide dissolved in 5 cc. of water. The resulting solution was neutralized to phenolphthalein and the silver salt precipitated by adding 8.5 g. (0.05 mole) of silver nitrate in 10–15 cc. of water. The precipitate was digested for a few hours on a steam-bath, cooled and filtered. After washing with water, either directly on the funnel or by triturating in a mortar, the silver salt was dried to constant weight at 110° or preferably at 50–60° in a vacuum oven. Just prior to use, the silver salt was powdered in a heated mortar.

Halogenation Method I.—To a solution of 0.1 mole of the iodinated acid or ester and 100 cc. of C. P. acetic acid, there were added alternately with stirring (glass stirrer) in small portions, 25.4 g. (0.1 mole) of powdered iodine and 16.6 g. (0.1 mole) of silver acetate. In general, iodination proceeded rapidly at room temperature. In those cases (Table II, no. 10–12) in which iodination proceeded somewhat more slowly, the addition of the iodinating reagents was regulated so that the previous charge had reacted completely before the next charge was added. The iodinated mixture was then stirred for one hour at room temperature, filtered and the filtrate diluted with water. The oily product which separated was extracted with ether, the ether extracts washed free of acetic acid and the iodinated acid or ester purified by recrystallization or distillation.

Method II.—To a suspension of 0.05 mole of the anhydrous silver salt of the arylaliphatic acid in 100 cc. of anhydrous carbon tetrachloride in a 500-cc., three-necked flask equipped with an efficient stirrer, there was added dropwise at room temperature 16 g. (0.1 mole) of bromine dissolved in 10 cc. of carbon tetrachloride. The bromine reacted immediately with the precipitation of silver bromide. After the bromine addition was completed, the reaction mixture was stirred for an additional hour, the silver bromide filtered off and the solvent distilled off *in vacuo*. The iodinated acid was purified by distillation or recrystallization.

Iodination of the silver salts was carried out essentially as described for the bromination. Finely powdered iodine or iodine dissolved in carbon tetrachloride was used.

Method III.—To 0.1 mole of the iodinated acid or ester in 100 cc. of acetic acid, there was added 0.1 mole of freshly distilled iodine chloride in 25 cc. of acetic acid. The mixture was heated on the steam-bath for two hours, diluted with 25–50 cc. of water and the color discharged with sulfur dioxide. The reaction mixture was then poured into water, the oil or crystalline product extracted with ether; and, after washing with water and drying, the ether was evaporated off. The residue was either distilled or crystallized for purification.

β-(3-Iodo-4-methoxyphenyl)-butyric Acid.—The requisite intermediate, β-methyl-*p*-methoxycinnamic acid, was obtained by the Reformatsky reaction of *p*-methoxyacetophenone and ethyl bromoacetate.[11] The hydroxy ester dehydrated on distillation and the crude ethyl β-methyl-*p*-methoxycinnamate was obtained in 91% yield, b. p. 134–144° (3 mm.). The free acid was obtained by saponification with alcoholic alkali in 84% yield; and, after recrystallization from methanol, melted at 153–155°, reported 153°. Reduction by the Raney alloy procedure[12] gave β-(*p*-methoxyphenyl)-butyric acid in 95% yield, m. p. 66.5–67.5°.

Anal. Calcd. for $C_{11}H_{14}O_2$: neut. equiv., 194. Found: neut. equiv., 194.5.

Iodination by method I gave a 78% yield of the iodo compound, m. p. 99.5–100.5° after recrystallization from aqueous ethanol.

Anal. Calcd. for $C_{11}H_{13}O_3I$: C, 41.27; H, 4.09. Found: C, 40.93; H, 4.27.

Ethyl 4-(3-Iodo-4-methoxyphenyl)-cyclohexylacetate.—The intermediate, 4-(*p*-methoxyphenyl)-cyclohexylacetic acid, was obtained by the reaction of anisole and Δ^1-cyclohexenylacetic acid, essentially as described for the preparation of *p*-phenylcyclohexylacetic acid,[13] yield 48%,

(11) Lendenbaum, *Ber.*, **50**, 1273 (1917).

(12) Schwenk, Papa, Whitman and Ginsberg, *J. Org. Chem.*, **9**, 175 (1944).

(13) Nenitzescu and Gavat, *Ber.*, **70**, 1884 (1947); Cook and Goulden, *J. Chem. Soc.*, 1559 (1937).

m. p. 133–134° after recrystallization from benzene–petroleum ether.

Anal. Calcd. for $C_{14}H_{20}O_3$: C, 72.55; H, 8.12. Found: C, 72.97; H, 8.25.

The ethyl ester was prepared by the acetyl chloride procedure, yield 84%, b. p. 167–168° (2 mm.). The ester was iodinated by method I and a 70% yield of iodo ester was obtained, m. p. 85.5–86° after recrystallization from benzene–petroleum ether.

Anal. Calcd. for $C_{17}H_{23}O_3I$: C, 50.75; H, 5.76; I, 31.6. Found: C, 50.70; H, 5.96; I, 31.9.

Acknowledgment.—The authors wish to express their appreciation to Miss Margaret Sherlock, Mrs. Hilda Breiger, Miss Virginia Paterson and Mrs. Anna Klingsberg for their assistance and to Dr. Richard Tislow and Mrs. Annette LaBelle for the pharmacological data on the compounds.

Summary

1. A series of iodinated alkoxyaryl aliphatic acids and esters have been prepared and examined as X-ray diagnostic agents for visualization of the gall bladder and body cavities, respectively.

2. Four iodination procedures were studied; namely, mercuric acetate–iodine, iodine chloride, silver acetate–iodine, and silver salt of alkoxyaryl aliphatic acid and iodine. The latter two procedures yielded the iodinated acids and esters in good yield under extremely mild conditions.

BLOOMFIELD, N. J. RECEIVED OCTOBER 8, 1949

[A COMMUNICATION FROM THE LABORATORY OF ORGANIC CHEMISTRY OF THE UNIVERSITY OF WISCONSIN]

The Copper–Chromium Oxide Catalyst for Hydrogenation[1]

BY HOMER ADKINS,[2] EDWARD E. BURGOYNE AND HENRY J. SCHNEIDER

The preferred catalyst for the hydrogenation of esters to alcohols and for certain other reactions contains copper, chromium, barium and oxygen. Recent physical data[3] have shown that the catalyst contains copper oxide and copper chromite, but that it is neither a simple copper chromite, nor a mechanical mixture of copper oxide and copper chromite.

That the true catalyst is not copper chromite has now been clearly established in this Laboratory and others[4] by the fact that the catalyst mass, after removal of cupric oxide either by reduction or by solution, is not active for the hydrogenations of ketones or esters at temperatures up to 275°. On the other hand, while copper chromite is certainly not the catalyst, it is an essential constituent since cupric oxide alone is rendered ineffective by its reduction to copper. Furthermore, the work now reported shows that the activity of the catalyst is dependent upon the ratio of copper oxide to copper chromite.

In order to improve the catalyst and to correlate activity with composition we have tested various samples of catalyst. The basis of comparison involved the hydrogenation of 0.10 mole of methyl laurate or palmitate in 100 ml. of pure, dry methanol, with 5 g. of catalyst, under a pressure of hydrogen so adjusted that it was approximately 6000 p. s. i. at the temperature of reaction.[5] The extent of hydrogenation, after three hours at the specified temperature, was determined by saponification of the residual ester. The results of representative hydrogenations are given in Table I. The catalysts differed principally in the method of decomposition of the basic copper ammonium chromate.

TABLE I

COMPARISON OF COPPER–CHROMIUM OXIDE CATALYSTS BY % HYDROGENATION OF ESTERS AT 175° FOR THREE HOURS

Catalyst	Methyl laurate	Methyl palmitate
C and E[a]	38	
REB[b]	34	
EEB 1[c]	37	
DW and A[d]	32	
TWR[e]	55	
HJS 1[f]	53	66
HJS 2[f]	62	78

[a] Prepared in 1934 by Calingaert and Edgar.[8] [b] Prepared by Robert E. Burks, Jr., by a modification of the procedure of Lazier and Arnold.[10] The decomposition of the basic copper ammonium chromate was carried out in small batches (40–50 g.) in a porcelain crucible of 40-ml. capacity surrounded by air at 350–375°. [c] Prepared as described in footnote 2, Adkins and Burgoyne, THIS JOURNAL, 71, 3528 (1949). [d] Prepared by Drake, Walton and Anspon. The decomposition was carried out as follows: "Three tablespoonfuls of copper ammonium chromate. . . is sprinkled on the bottom of a 2-l. casserole previously heated to a dull red heat and resting on a transite board. Additional material is sprinkled on the black patches where decomposition has taken place at such a rate as is necessary to maintain decomposition of the chromate without excessive violence or additional application of heat. When the casserole is half-full. . . it is stirred to red heat for ten to fifteen minutes while the powder is thoroughly stirred" (N. L. Drake, personal communication). [e] Prepared by T. W. Riener.[9] [f] See Experimental section.

It is not implied that a comparison of catalysts under any one set of conditions will show the relative value of these preparations under any other set of conditions. However, such a comparison as now reported has enabled us to prepare

(1) Supported in part by the Research Committee of the Graduate School from funds supplied by the Wisconsin Alumni Research Foundation.

(2) Deceased August 10, 1949.

(3) (a) Stroupe, THIS JOURNAL, **71**, 569 (1949); (b) Selwood, Hill and Boardman, *ibid.*, **68**, 2055 (1946), and personal communications.

(4) T. W. Riener, personal communication.

(5) Adkins and Billica, THIS JOURNAL, **70**, 3121 (1948).