at once. It was crystallized from alcohol; m. p. 260–261° dec., $[\alpha]^{27}\mathrm{D}$ −7.4° in chloroform; yield 1.3 g.

Anal. Calcd. for $C_{32}H_{50}NI$: C, 66.75; H, 8.79; N, 2.44. Found: C, 66.59; H, 8.66; N, 2.12.

(b) A solution of 1.1 g. of I in absolute alcohol was treated with concentrated hydriodic acid. The iodide precipitated at once. It was crystallized from alcohol and was identical with that above, m. p. 260–261°; $[\alpha]^{25}\mathrm{D}$ −7.8° in chloroform; yield 0.9 g.

Attempted Rearrangement of Cholesterylpyridinium *p*-Toluenesulfonate.—A solution consisting of 1.0 g. of cholesterylpyridinium *p*-toluenesulfonate and 1 g. of *p*-toluenesulfonic acid in 15 g. of pyridine was heated at the reflux temperature for twenty-four hours. The reaction mixture was worked up as described under the preparation of I. There was no evidence of decomposition and 0.9 g. of the starting substance was recovered unchanged; m. p. 229–231°. This was converted to the iodide, m. p. 260–261°; $[\alpha]^{24}\mathrm{D}$ −7.5° in chloroform.

Cholesterylisothiuronium *p*-Toluenesulfonate (II).—(a) A solution of 5.4 g. (0.01 mole) of cholesteryl *p*-toluenesulfonate, 9.0 g. of thiourea and 5 cc. of pyridine in 50 cc. of absolute ethanol was heated under reflux for three hours. The resulting solution was diluted with water until a precipitate started forming, cooled and filtered. The residue was then suspended in acetone, the acetone heated to boiling, and the insoluble product filtered from the solution; yield 4.0 g. (65%) of salt; m. p. 230–234°. Recrystallization from alcohol raised the melting point to 233–235°; $[\alpha]^{24}\mathrm{D}$ −27.1° in pyridine.

Anal. Calcd. for $C_{35}H_{56}N_2O_3S_2$: C, 68.15; H, 9.15; N, 4.54. Found: C, 68.26; H, 9.16; N, 4.31.

(b) From a similar reaction using 0.01 mole of cholesteryl *p*-toluenesulfonate, 0.02 mole of thiourea and 50 cc. of 95% alcohol, 2.26 g. (40%) of II, m. p. 231–233°, was obtained. This reaction mixture was acid to litmus and contained some cholesteryl ethyl ether, m. p. and mixed m. p. 89.0–89.5°.

(c) A reaction mixture consisting of 2.0 g. of *i*-cholesteryl methyl ether,[6] 2.0 g. of *p*-toluenesulfonic acid, 4.0 g. of thiourea in 50 cc. of ethyl alcohol was refluxed four hours. Compound II was isolated as described above; m. p. 233°; yield 1.3 g. (42%); $[\alpha]^{24}\mathrm{D}$ −26.9° in pyridine. From this reaction mixture 0.3 g. of unchanged *i*-cholesteryl methyl ether, m. p. 75–77°, was also obtained.

Cholesteryl Mercaptan.—A solution of 2.46 g. (0.004 mole) of II and 0.68 g. (0.012 mole) of sodium hydroxide in 50 cc. of ethyl alcohol was heated under reflux. After the solution became homogeneous 5 cc. of water was added and the heating continued for two hours. The reaction mixture was then poured into 100 cc. of ice water and the resulting suspension acidified with 1 cc. of glacial acetic acid and stirred until the precipitate coagulated. The compound was separated and crystallized from acetone–methanol; m. p. 94–96°; yield 1.5 g. (93%). Recrystallization from acetone raised the melting point to 97.0–97.5°; $[\alpha]^{25}\mathrm{D}$ −26.6° in chloroform.[7]

Anal. Calcd. for $C_{27}H_{46}S$: C, 80.53; H, 11.51. Found: C, 80.25; H, 11.80.

Cholesteryl Disulfide.—A solution consisting of 0.50 g. (0.00125 mole) of cholesteryl mercaptan in 10 cc. of hexane was oxidized with 0.32 g. (0.00125 mole) of iodine. Ten cubic centimeters of 5% potassium hydroxide was added and the mixture shaken. The mixture was then diluted and extracted with hexane. The hexane was then evaporated and the residue crystallized from benzene–ethyl alcohol and from acetone–benzene; m. p. 141–143°.[7]

Summary

Cholesterylpyridinium *p*-toluenesulfonate was prepared from cholesteryl *p*-toluenesulfonate and from *i*-cholesteryl methyl ether. Cholesterylisothiuronium *p*-toluenesulfonate was prepared from the same substances. The evidence indicates that these salts are derivatives of the normal cholesteryl structure.

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[7] Wagner-Jauregg and Lennartz (ref. 2) reported for cholesteryl mercaptan m. p. 99.5°, $[\alpha]_{\mathrm{D}}$ −23.85°; and for cholesteryl disulfide; m. p. 144.5°.

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Substituted Styrenes. III. The Preparation of Some *m*- and *p*-Substituted α-Methylstyrenes

BY DEXTER SEYMOUR AND KATHERINE B. WOLFSTIRN

In connection with some studies undertaken in this laboratory on the effect of ring substituents in styrenes on their reactivity toward certain types of free radicals,[1a,b] it was necessary to synthesize a series of substituted α-methylstyrenes. *p*-Bromo, *p*-chloro and *p*-methoxy-α-methylstyrenes were synthesized by known methods. Some peculiarities in the preparation of the last mentioned were noted and are discussed further in the experimental part.

p-Fluoro-α-methylstyrene was prepared in a straightforward way from *p*-fluorobromobenzene and acetone through the Grignard reagent. *p*-Cyano-α-methylstyrene was prepared by taking advantage of the rather large difference in reactivity toward the Grignard reagent between a nitrile and a ketone grouping. A somewhat obscure paper[2] which came to our attention later records this fact also. Methylmagnesium bromide was added to a stoichiometric amount of *p*-cyanoacetophenone and the crude alcohol was dehydrated with acetic anhydride. Careful fractionation of the product gave 44% of *p*-cyano-α-methylstyrene, 20% of unreacted *p*-cyanoacetophenone and about 25% of non-volatile polymeric material. *m*-Bromo-α-methylstyrene was prepared in 54% yield by addition of two moles of methylmagnesium bromide to methyl *m*-bromobenzoate followed by dehydration with acetic anhydride.

Although the reaction is reported in the literature,[3] we were unable to prepare the Grignard reagent from *p*-dimethylaminobromobenzene even

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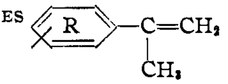
[1] (a) Walling, Seymour and Wolfstirn, THIS JOURNAL, in press; (b) Walling, Seymour and Wolfstirn, *ibid.*, submitted for publication.

[2] Carter, *Iowa State Coll. J. Sci.*, **15**, 63 (1940); *cf. British Chem. Abs.*, **AII**, **254** (1941).

[3] Ehrlich and Sachs, *Ber.*, **36**, 4297 (1903).

TABLE I

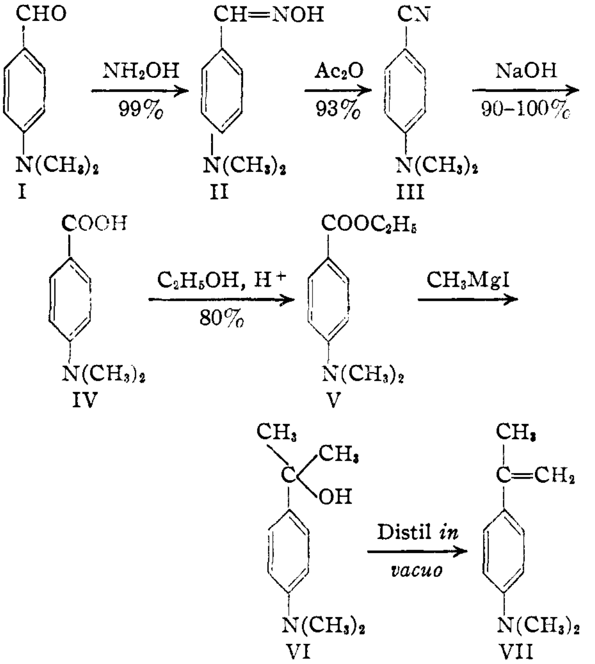
PHYSICAL PROPERTIES OF SUBSTITUTED α-METHYLSTYRENES



R	Yield, %	M. p., °C.	B. p., °C.	Pressure, mm.	n^{20}_D	d^{20}_4	Calcd %C	Calcd %H	Calcd %N	Found %C	Found %H	Found %N
p-F	55		97.5–101.5	95	1.5120	1.0150	79.40	6.66		78.66	6.71	
p-Cl	70	3.5	78.0–80.0	8	1.5559	1.0723	70.85	5.94	..[a]	71.04	6.03	..
p-Br	37		114.5–117.5	24	1.5834	1.3623	54.84	4.60		54.54	4.66	
m-Br	54		68–72	2	1.5779	1.3560	54.84	4.60		54.12	4.54	
p-OCH_3	66	34	63.0–65.5	0.5	....	0.9860[b]	...	..		...	..	
p-$N(CH_3)_2$	69	75.0–76.5	....	..	....	....	81.95	9.37	8.69	82.08	9.40	8.64
p-CN	44		86.0–87.5	2	1.5680	1.0017	83.90	6.34	9.78	83.98	6.31	9.72

[a] Calcd. for C_9H_9Cl: Cl, 23.23. Found: C, 23.22. [b] Density at 40° referred to water at 4°.

employing measures such as the "entrainment" method, and an alternative synthesis of *p*-dimethylamino-α-methylstyrene was carried out. The reactions employed were all straightforward and proceeded with the yields indicated. Several attempts to effect acid catalyzed alcoholysis of the nitrile III to produce the ester V directly met with no success and recourse was had to hydrolysis followed by Fisher esterification. The intermediate alcohol VI was not isolated but was dehydrated directly by vacuum distillation to the styrene VII. The over-all yield of recrystallized VII from V was 69%. The styrenes prepared, together with yields and physical properties, are listed in Table I.



Experimental[4]

***p*-Chloro-α-methylstyrene.**—This compound was prepared in 70% yield essentially by the method of Mowry, Huber and Ringwald.[5] The carbinol was dehydrated by refluxing sixty-four hours with about 100 mg. of iodine in toluene. After purification the product had b. p. 78.0–80.0° (8 mm.), n^{20}_D 1.5559, d^{20}_4 1.0723, *MR*D (calcd.) 44.56, *MR*D (found) 45.70.

***p*-Bromo-α-methylstyrene.**—This compound was prepared in 37% yield from *p*-bromophenylmagnesium bromide and acetone.[6] The best fraction had b. p. 114.5–117.5° (24 mm.), n^{20}_D 1.5834, d^{20}_4 1.3623, *MR*D (calcd.) 47.46, *MR*D (found) 48.34. Bergmann and Weigmann[6] give: b. p. 58–60° (2 mm.); n^{20}_D 1.5778.

***p*-Methoxy-α-methylstyrene.**—This compound was prepared from 249 g. (1.50 moles) of methyl anisate, 305 g. (3.20 moles) of methyl bromide and 81.6 g. (3.40 atoms) of magnesium.[6] The crude carbinol was dehydrated by distillation at reduced pressure.[7] The crude styrene so obtained was carefully redistilled through 17 cm. of glass helices with traces of *t*-butylcatechol and trinitrobenzene added as inhibitors. There was obtained 147 g. (66%) of pure product which had b. p. 63.0–65.5° (0.5 mm.), m. p. 34°, d^{40}_4 0.9860. The substance was observed to polymerize after several months even in the refrigerator in a brown bottle.

When methylmagnesium iodide was used in the preparation of the carbinol, or iodine or acetic anhydride were employed as dehydrating agents, the product was always what appeared to be the dimer of *p*-methoxy-α-methylstyrene with the following properties: b. p. 195–199° (1.5 mm.); n^{20}_D 1.5753.

Anal. Calcd. for $C_{20}H_{24}O_2$: C, 81.07, H, 8.11; mol. wt., 296. Found: C, 80.97; H, 8.91; mol. wt. (cryoscopic in benzene), 260.

Previous workers[6,7] apparently experienced little difficulty in this respect, however.[8]

***p*-Fluoro-α-methylstyrene.**—To the Grignard reagent prepared from 25.2 g. (1.05 atoms) of magnesium and 175 g. (1.00 mole) of *p*-fluorobromobenzene in 350 ml. of dry ether was added 63.8 g. (1.10 moles) of acetone in 700 ml. of ether and the mixture was allowed to stand two and one-half days. The mixture was hydrolyzed with saturated ammonium chloride solution and the ether removed from the product by distillation. Then 500 ml. of toluene and 100 mg. of iodine were added and the mixture was refluxed nineteen and one-half hours under a water separator. Fifteen milliliters (83%) of water separated. The toluene solution was washed with sodium thiosulfate and water and dried by distillation. The toluene was removed through a 17 cm. column packed with $^1/_8$" single turn glass helices and the residue fractionated. The middle fraction had b. p. 97.5–101.5° (95 mm.), n^{20}_D 1.5120, d^{20}_4 1.0150, *MR*D (calcd.) 39.59, *MR*D (found) 40.20. The yield was 74.5 g. (55%).

Anal. Calcd. for C_9H_9F: C, 79.40; H, 6.66. Found: C, 78.66; H, 6.71.

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[4] All melting and boiling points are uncorrected.

[5] Mowry, Huber and Ringwald, THIS JOURNAL, **69**, 851 (1947).

[6] Bergmann and Weizmann, *Trans. Faraday Soc.*, **32**, 1327 (1936), and earlier references given there.

[7] Skraup and Freundlich, *Ann.*, **431**, 267 (1923).

[8] Yamashita, *J. Chem. Soc. Japan*, **62**, 1216 (1941); *cf. Chem. Abs.*, **41**, 3070 (1947), reports, however, that *p*-methoxy-β-methylstyrene readily forms a dimer on treatment with iodine in toluene.

A bromine analysis indicated the presence of not more than 2 wt. per cent. *p*-fluorobromobenzene as impurity.

***p*-Cyano-α-methylstyrene.**—In a 2-liter three-necked flask previously flushed with dry nitrogen the Grignard reagent was prepared from 135 g. (0.95 mole) of methyl iodide and 24.0 g. (1.00 atom) of magnesium in 1250 ml. of dry ether. When reaction was complete, the reagent was filtered under nitrogen into a 2-liter dropping funnel attached to one neck of a 5-liter three-necked flask equipped with a Hershberg stirrer and a reflux condenser protected by a "Drierite" tube. In the flask was placed 133 g. (0.918 mole) *p*-cyanoacetophenone dissolved in 750 ml. of dry ether. The Grignard reagent was added to this solution dropwise over a period of one and one-half hours and the mixture was stirred two and three-quarter hours longer. The reaction mixture was worked up in the usual way and the crude carbinol dehydrated by boiling two hours with about 300 ml. of acetic anhydride. After hydrolysis of the excess anhydride, the products were taken up in chloroform, the solution dried, and the chloroform removed through 85 cm. of $^1/_8''$ glass helices. The residue was distilled at 1.5 mm. to separate volatile material from any polymeric products. The distillate was collected from 86–120° and there remained about 25 g. of non-distillable material in the flask. The distillate was fractionated at 2 mm. pressure using an 80-cm. 15-plate low hold-up column designed by Dr. H. Sargent of these Laboratories.[9] Three fractions were collected: (1) b. p. 82.0–86.0° (2 mm.), $n^{20}_{\rm D}$ 1.5618, wt. 4.4 g.; (2) b. p. 86.0–87.0° (2 mm.), $n^{20}_{\rm D}$ 1.5680, wt. 29.8 g.; (3) b. p. 87.0–87.5° (2 mm.), $n^{20}_{\rm D}$ 1.5680, wt. 28.0 g. The pot residue weighed 26.1 g. and gave 20.9 g. (15.7%) of *p*-cyanoacetophenone on crystallization from hexane-benzene. Fractions (2) and (3) of the distillate above which decolorized potassium permanganate in acetone and bromine in carbon tetrachloride were combined to yield 57.8 g. (44%) of *p*-cyano-α-methylstyrene, d^{20}_4 1.0017, $MR_{\rm D}$ (calcd.) 44.05, $MR_{\rm D}$ (found) 46.68.

Anal. Calcd. for $C_{10}H_9N$: C, 83.90; H, 6.34; N, 9.78. Found: C, 83.76, 83.98; H, 6.32, 6.31; N, 9.72.

***m*-Bromo-α-methylstyrene.**—The Grignard reagent was prepared from 67.8 g. (2.83 atoms) of magnesium and 265 g. (2.79 moles) of methyl bromide and to this was added an ether solution of 294 g. (1.40 moles) methyl *m*-bromobenzoate. The reaction mixture was worked up in the usual way and the carbinol was dehydrated by the acetic anhydride technique. After hydrolysis of the excess anhydride, the neutral products were extracted with chloroform, dried and the solvent removed through 17 cm. of glass helices. Fractionation of the residue gave 150 g. (54%) of *m*-bromo-α-methylstyrene, b. p. 68.0–72.0° (2 mm.), $n^{20}_{\rm D}$ 1.5779, d^{20}_4 1.3560, $MR_{\rm D}$ (calcd.) 47.46, $MR_{\rm D}$ (found) 48.20.

Anal. Calcd. for C_9H_9Br: C, 54.86; H, 4.60. Found: C, 54.12; H, 4.54.

***p*-Dimethylaminobenzaldoxime.**—This material was prepared from 75 g. (0.50 mole) *p*-dimethylaminobenzaldehyde by the method of Sachs and Steinert.[10] There was obtained 80.9 g. (99%) of oxime melting at 142.5–144.0° and it was used without purification.

***p*-Dimethylaminobenzonitrile.**—Following the method of Sachs and Steinert,[10] 73.8 g. (0.45 mole) of *p*-dimethylaminobenzaldoxime was dehydrated with 300 ml. of 95% acetic anhydride to yield 61 g. (93%) of crude nitrile, melting at 74–75°. It was used directly in the next step.

***p*-Dimethylaminobenzoic Acid.**—One-hundred twenty-eight grams (0.877 mole) of *p*-dimethylaminobenzonitrile was refluxed for nineteen hours with a mixture of 750 ml. of 2 *M* sodium hydroxide and 450 ml. of 95% ethyl alcohol. Most of the alcohol was removed by distillation and 500 ml. of water was added. The warm solution was acidified to *p*H 2 with concentrated hydrochloric acid and the suspension was allowed to stand for thirty-six hours. The acid was collected by filtration and washed with water. Neutralizing to about *p*H 7 with ammonia afforded a further small amount of product. The dry *p*-dimethylaminobenzoic acid weighed 148 g. (102%, probably due to inorganic salts), and was esterified without further purification.

Ethyl *p*-Dimethylaminobenzoate.—A mixture of 196.5 g. (1.19 mole) of crude *p*-dimethylaminobenzoic acid and 2 liters of absolute ethanol was saturated with dry hydrogen chloride and refluxed overnight. Most of the alcohol was distilled and the residue was thrown into iced sodium hydroxide solution (200 g. in 1 liter of water) with good stirring. The crude ester was collected by filtration; after drying it weighed 172.7 g. (79% based on recovered acid). From the mother liquor there was recovered 9.1 g. (4.6%) of unreacted acid.

The crude ester was distilled at 1–2 mm., the fraction boiling at 125–142° being collected. This weighed 159 g. and was crystallized from 400 ml. of 66% by volume ethanol. The first crop of shiny white plates weighed 124 g. (57%) and melted at 65–66°. A second crop of less pure material, weighing 27.0 g. (12%) and melting at 58–61°, was obtained, by concentration of the mother liquor.

***p*-Dimethylamino-α-methylstyrene.**—The Grignard reagent was prepared from 341 g. (2.40 moles) of methyl iodide and 62.4 g. (2.60 atoms) of magnesium in 1200 ml. dry ether. To this refluxing solution was added 154.4 g. (0.800 mole) of ethyl *p*-dimethylaminobenzoate in 1200 ml. of ether over a period of one and one-half hours and refluxing was continued for twenty-one and one-half hours longer. The mixture was hydrolyzed with saturated ammonium chloride solution and worked up in the usual way. After removal of the ether, the crude product was distilled *in vacuo*, which caused the elimination of water. The styrene was collected from 95–121° at 1 mm.; it weighed 91.8 g. (71%). Recrystallization from 250 ml. of hexane gave 74.2 g. (58%) of *p*-dimethylamino-α-methylstyrene melting at 75.0–76.5°.

Anal. Calcd. for $C_{11}H_{15}N$: C, 81.95; H, 9.37; N, 8.69. Found: C, 82.08; H, 9.40; N, 8.64.

A further 14.6 g. (11%) of product melting at 72.0–74.0° was obtained from the mother liquor.

Summary

1. The preparation of *p*-chloro, *p*-bromo and *p*-methoxy-α-methylstyrenes is described.

2. *p*-Fluoro, *m*-bromo, *p*-cyano and *p*-dimethylamino-α-methylstyrenes have been prepared and their physical properties recorded for the first time.

PASSAIC, NEW JERSEY

RECEIVED OCTOBER 29, 1947

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[9] A description of this column will appear in a forthcoming article by Dr. Sargent.

[10] Sachs and Steinert, *Ber.*, **37**, 1740 (1904).