cyanamide, be desiccated for several days over phosphorus pentoxide before using.

Ethylisourea Hydrochloride.—This compound was prepared, with modifications, by the procedure of Stieglitz and Noble.[7] Dry hydrogen chloride was passed into a solution of 10 g. of cyanamide in 100 cc. of absolute ether until no more precipitate came down. The cyanamide dihydrochloride was filtered, washed with ether and stored in a desiccator over phosphorus pentoxide. The yield was 95%.

Cyanamide dihydrochloride, 23 g. (0.2 mole), and cyanamide, 8.4 g. (0.2 mole), were suspended in 70 cc. (1.2 mole) of absolute alcohol and heated in a pressure bottle for one hour at 55–65°. One-half of the alcohol was removed at the water pump and 150 cc. of absolute ether was added. An oil which first appeared soon solidified into a white crystalline mass. The weight of the crystals of ethylisourea hydrochloride was 40 g. (80%).

Benzenesulfonyl Ethylisourea.[8]—The best yields of this compound were obtained in the following manner: to a mixture of 10 g. (0.08 mole) of ethylisourea hydrochloride and 14 g. (0.08 mole) of benzenesulfonyl chloride in 50 cc. water, was added a solution of 6.4 g. (0.16 mole) of sodium hydroxide in 30 cc. of water. The reaction mixture was kept cold in an ice-bath and stirred during the addition of the alkaline solution. One-third of the alkaline solution was added and the reaction mixture was set aside until it showed acid to litmus. The second third was added likewise. The reaction mixture remained permanently alkaline after the third portion of alkali was added. After standing in the cold for twenty-four hours the reaction mass was filtered and washed with cold water. The crude air-dried product weighed 11.7 g. (65%). It crystallized from dilute alcohol in fine colorless plates and melted at 101°.

Benzenesulfonyl Urea.—The benzenesulfonyl ethylisourea, 5 g., was covered with 25 cc. of concentrated hydrochloric acid. The isourea dissolved almost immediately as the hydrochloride. The flask containing the solution was immersed in a boiling water-bath for five minutes. The solution was then cooled in an ice-bath and the product filtered and washed. The dried product weighed 4.3 g. (practically quantitative). It crystallized from alcohol as fine white needles and melted at 169°.[9]

TABLE I

ARYLSULFONYL ETHYLISOUREAS, Ar—$SO_2N{=}C(OC_2H_5)$-NH_2

Ar	M. p., °C.	Formula	Nitrogen, % Calcd.	Found	
Benzene	101	$C_9H_{12}O_3N_2S$	12.27	12.17	12.17
p-Toluene	79	$C_{10}H_{14}O_3N_2S$	11.56	11.53	11.41
α-Naphthalene	145	$C_{13}H_{14}O_3N_2S$	10.06	10.11	9.84
Arylsulfonyl ureas, Ar—$SO_2NHCONH_2$					
Benzene	169	$C_7H_8O_3N_2S$	13.98	13.94	13.91
p-Toluene	192	$C_8H_{10}O_3N_2S$	13.08	13.01	12.95
α-Naphthalene	211	$C_{11}H_{10}O_3N_2S$	11.19	11.17	11.16

Summary

Some unsuccessful methods for the preparation of arylsulfonyl ureas have been mentioned.

The successful procedure was that of the hydrolysis of the corresponding arylsulfonyl ethylisourea by means of concentrated hydrochloric acid.

p-Toluenesulfonyl and α-naphthalenesulfonyl ethylisoureas, and *p*-toluenesulfonyl and α-naphthalenesulfonyl ureas have not been previously described in the literature.

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[7] Stieglitz and Noble, *Ber.*, **38**, 2243 (1905).

[8] Basterfield and Whelan, THIS JOURNAL, **49**, 3179 (1927).

[9] Billeter, *Ber.*, **37**, 694 (1904).

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[CONTRIBUTION FROM THE BAKER LABORATORY OF CHEMISTRY AT CORNELL UNIVERSITY]

Carcinogenic Hydrocarbons. IV. The Bromination of Hydrindene and a Briefer Synthesis of Cholanthrene[1]

BY WILLIAM F. BRUCE

One of the intermediates in the preparation of cholanthrene by the method of Fieser and Seligman[2] is 4-bromohydrindene, which they obtained from *o*-bromocinnamic acid. We have investigated the possibility of preparing this intermediate more directly by bromination of commercial hydrindene. Both of the possible nuclear monobromohydrindenes are formed in the bromination. The physical properties of these two compounds are too much alike to permit from available physical data alone a conclusion concerning the nature of the mixture.

We therefore employed the oxidation method which v. Braun[3] used for the determination of the isomers from the bromination of tetralin. The mixture of bromohydrindenes was oxidized and the relative amounts of 3-bromo and 4-bromophthalic acid were determined by esterification under conditions which do not affect the sterically hindered carboxyl group of the 3-bromo com-

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[1] Previous paper, Bruce and Todd, THIS JOURNAL, **61**, 157 (1939). For previous studies of the bromination of hydrindene, see Perkin and Revay, *J. Chem. Soc.*, **65**, 251 (1894); Meyer and Meyer, *Ber.*, **51**, 1583 (1918); Borsche and Pommer, *ibid.*, **54**, 102 (1921).

[2] Fieser and Seligman, THIS JOURNAL, **57**, 2174 (1935).

[3] Von Braun, Braunsdorf, Engelbertz, E. Hahn, G. Hahn, Hainbach, Kredel and Larbig, *Ber.*, **56**, 2332 (1923).

pound. This procedure gave approximately one part of acid ester to two parts of neutral ester. This result indicated that the monobromohydrindene mixture consisted of one-third α-bromohydrindene and two-thirds β-bromohydrindene. The use of dry hydrogen chloride in place of sulfuric acid as catalyst resulted in the formation of a completely neutral product, as might be expected on the basis of Victor Meyer's study of steric hindrance. Since chemical effects have frequently combined to complicate the interpretation of results based on steric hindrance,[4] we wished to secure additional evidence concerning the nature of the mixture.

In order to secure further solid derivatives, the cyanohydrindenes prepared from the brominated product were hydrolyzed by hydrochloric acid to the corresponding acids. The α-acid, prepared by Fieser and Hershberg,[5] melts at 152.5–153.5° and the amide at 173–173.5°. These values are nearly reversed for the β acid which melts at 177°,[6] 178–179°,[7] or 183°,[8] while the amide melts at 130°.[9] Our cyanohydrindenes yielded an acid melting at 172–174° after crystallization from acetic acid, and a lower melting fraction liquefying at 140–145° obtained from the mother liquors and amounting to about one-quarter of the whole. The amide, either prepared from the acid or isolated from the high boiling residue in the preparation of the nitrile, melted at 143-144.5°. These data support the conclusions of the esterification procedure, since all the observations can be explained by assuming a mixture of the two bromohydrindenes with the β-form predominating.

To establish whether such a mixture can be used in the preparation of cholanthrene, the α-naphthoyl derivatives were made by the usual methods.[1] By pyrolysis of these ketones cholanthrene was obtained in an over-all yield of 8% from the bromohydrindene mixture. Based only on the α form, this yield is 24%, assuming one-third of the mixture is α. It is therefore evident that the presence of the β form did not greatly interfere with the course of the reaction. The principal loss of material occurred during pyrolysis, which resulted in much non-volatile residue. This modification of the synthesis of cholanthrene allows a significant saving in time and expense.

Since any means by which the proportion of the α bromo isomer in the bromination mixture can be increased will enhance the value of this procedure, we wish to call attention to some preliminary results which indicate that marked improvement in the $\alpha:\beta$ ratio can be obtained. By adding hydrindene to the calculated amount of bromine dissolved in acetic acid, instead of the more usual reverse procedure, we found that the majority of the product was the α form as judged by the oxidation procedure. This procedure we consider reliable in view of our own results and the fact that v. Braun has studied it for a series of pure substituted tetralins. We intend to use it for a further study of the effect of conditions on the bromination of hydrindene, tetralin and related compounds. Even with the less favorable ratio, however, the synthesis of cholanthrene is facilitated by starting with hydrindene.

Experimental Part

Bromination of Hydrindene.—Bromination was carried out without solvent, in carbon tetrachloride, and in acetic acid. The latter gave less residue and higher yield than the other procedures. A solution of 118 g. (1 mole) of hydrindene, boiling from 172–175° at 743 mm., in 300 cc. of glacial acetic acid in a 1-liter flask was cooled to 10°. The acetic acid partially solidified, and with mechanical stirring a solution of 166 g. of bromine (1.1 mole) in 100 ml. of acetic acid was added over a period of three hours. Cooling was continued so that solid acetic acid was always present.[10]

After the reaction mixture had stood overnight, it was diluted with 500 ml. of water. A yellow oil separated and was washed with dilute sodium bisulfite followed by water. The oil was distilled with steam, giving 144 g. of water-insoluble oily distillate. Toward the end of the distillation, long white needles of a solid product formed in the aqueous layer, but dissolved in the oil when brought in contact with it. Fractionation of the oil *in vacuo* gave 30 g. of unchanged hydrindene boiling from 78–83° at 22 mm., 76.5 g. of a fraction boiling from 124–126° at 22 mm., 35 g. of material boiling from 126–135° at 22 mm., and 10 g. of residue. Refractionation of the 35-g. fraction gave 25 g. of liquid boiling from 129–131° at 24 mm. This was combined with the main fraction to give 101.5 g. of product. On distillation through a 1-meter Fenske column, it gave 97.5 g. of monobrominated product boiling from 128–131° at 25 mm.; d^{27} 1.416; $n^{27}\text{D}$ 1.5790; melting point (time–temperature cooling curve method) -15.2 to $-17.5°$. There remained 27 g. of residue which partly solidified. The solid on crystallization from 60–80° petroleum ether gave 8 g. of needle-shaped crystals melting at 120–2°.[11]

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[4] Rupp, *Ber.*, **29**, 1625 (1896); Meyer and Sudborough, *ibid.*, **27**, 3146 (1894); Graebe, *Ann.*, **238**, 327 (1887).

[5] Fieser and Hershberg, This Journal, **59**, 396 (1937).

[6] Gattermann, *Ann.*, **347**, 386 (1906).

[7] Von Braun, Kirschbaum and Schulmann, *Ber.*, **53**, 1160 (1920).

[8] Borsche and Bodenstein, *ibid.*, **59**, 1909 (1926).

[9] Borsche and John, *ibid.*, **57**, 656 (1924).

[10] Rapid addition of bromine without control of the temperature, as in the bromination of toluene, produced a marked rise in temperature and much more high boiling residue.

[11] Probably a monobromindene: Borsche and Pommer, *Ber.*, **54**, 102 (1921).

The yield of monobrominated product, based on hydrindene actually used, was 75%.

When the bromination was carried out as above described, except that 0.25 g. of steel wool was added as catalyst and the acetic acid solution was distilled without the addition of water, 118 g. of hydrindene gave 20 g. of unchanged material, 83 g. boiling from 102–3° at 7 mm. and a tarry residue weighing 70 g.

Oxidation.—In a 200-ml. round bottomed flask fitted with a mechanical stirrer was put 50 ml. of boiling water and 4.25 ml. (6 g.) of bromohydrindene. In 1-g. portions, 11 g. of powdered potassium permanganate was added. The mixture was stirred and heated for one hour. After filtering out the oxide of manganese, 4 ml. of concentrated sulfuric acid was added, together with 0.5 g. of permanganate. The colorless solution was evaporated to near dryness on a steam-bath. The residue was made alkaline and extracted with ether to remove unchanged bromohydrindene. After the material was acidified strongly by 2 ml. of concentrated hydrochloric acid, ether extracted 2.8 g. of colorless acid, which after evaporation of the ether and washing the residue with benzene, melted at 153–155° with decomposition, determined by the method of successive approximations. On titration 88.5 mg. used 7.40 ml. of 0.0954 N sodium hydroxide; neut. equiv. 125.3, calcd. for $C_8H_6O_4Br$ 122.5. After one crystallization from water, the substance melted with decomposition at 177–179° (cor.) by the method of successive approximations.

Esterification of the Acids.—Following von Braun's technique,[3] a solution of 1.3 g. of the acid in 6 cc. of absolute ethyl alcohol and 0.3 ml. of concentrated sulfuric acid was refluxed for 2.5 hrs. After cooling and adding 8 ml. of water to the solution, an oil precipitated; it was extracted by ether. The ethereal solution was washed with dilute sodium carbonate three times. The residue after evaporation of the ether and drying in a desiccator weighed 0.85 g. From the carbonate solution after acidifying, 0.5 g. of acid ester was extracted.

In the most recent bromination, 145 g. of distilled practical hydrindene and 0.2 g. of platinum oxide were shaken two hours under hydrogen to remove unsaturated material. The filtered product was added dropwise to a solution of 250 g. of bromine in 600 ml. of acetic acid at 15°. After standing overnight, the solution was worked up as before and gave 128 g. of product boiling at 112–114° at 13 mm. together with about 50 g. of unchanged hydrindene and 20 g. of high boiling material. Upon oxidation, 6 g. of bromohydrindene with 50 ml. of water and 11 g. of potassium permanganate gave 3 g. of unchanged material, 9 g. of manganese oxide and 2.6 g. of acid. Esterification of this acid gave 0.699 g. of neutral ester and 1.690 g. of acid ester.

Conversion to the Nitriles.—To 20 g. of cuprous cyanide in a bomb tube was added 32 g. of the mixture of one-third α-two-thirds β-bromohydrindene boiling from 102–103° at 7 mm., and after thorough mixing, 15 ml. of dry pyridine was added. The tube was sealed and heated at 190–200° overnight. The content of the tube was distilled directly under diminished pressure. On fractionation, 16 g. of uniform product boiling at 10 mm. between 132–134° was secured. This fraction had the following properties: d_{26} 1.053, compared with d_{27} 1.052 determined for a sample of the α-isomer prepared by the method of Bachmann[12]; $n^{27}{}_{\mathrm{D}}$ 1.5530. Fieser and Hershberg[6] found that 4-cyanohydrindene boils from 139–141° at 22 mm.

α-Naphthoylhydrindenes.—To a Grignard reagent made from 25 g. of α-bromonaphthalene and 3.0 g. of magnesium in 70 cc. of absolute ether was added 13 g. of the cyanohydrindene mixture in 10 ml. of benzene. On decomposition with ice and hydrochloric acid, 29 g. of ketimine hydrochlorides, dried in air, was obtained. The yield appeared quantitative. For purification 3 g. of the ketimine hydrochlorides was dissolved in 8 ml. of hot chloroform and 16 ml. of ethyl acetate was added. The clear solution was seeded and cooled. Turbidity soon appeared, and after standing overnight in an ice-box 2.5 g. of product was collected on a filter. The material decomposed at 191–195° with slow heating, and at 202–203° (207–208° cor.) when determined by the method of successive approximations. The ketones were secured from 20 g. of the ketimine hydrochlorides by boiling for four hours with 500 ml. of a solution of two parts of dilute hydrochloric acid (1:1) and one part of acetic acid. After extraction with benzene and distillation, 16 g. of ketones boiling from 210–215° at 1 mm. was secured.

Cholanthrene.—Pyrolysis of 5 g. of ketone mixture under the usual conditions (400–410° for half an hour) gave 2.4 g. of glassy amber distillate which was collected in three nearly equal fractions. These were dissolved separately in about 1 cc. of benzene, concentrated and diluted with 5 cc. of ether. The first fraction gave 0.25 g. of yellow solid softening at 140° and melting at 163–164°; the second gave 0.20 g. melting from 151–152°, softening at 140°; the third 0.1 g. melting from 167–168°, softening at 155°. On crystallization from *n*-propyl alcohol, these fractions melted at 168–169°, 168–169° and 170–171° (cor.), respectively. A mixed melting point with a sample of cholanthrene melting at 170–171° kindly provided by Professor Fieser showed no depression. From 2 g. of ketimine hydrochlorides by hydrolysis, and pyrolysis of the crude ketones without distillation, 0.2 g. of purified cholanthrene, melting at 170–171° (cor.), was obtained.

Summary

The bromination of hydrindene yields a mixture composed of one-third α and two-thirds β-bromohydrindene when bromine is added to a solution of the hydrocarbon in acetic acid. This mixture has been used to prepare cholanthrene with a yield of 24%, based on the α-isomer. A preliminary experiment shows that addition of hydrocarbon to a solution of bromine gives a much larger proportion of α-isomer than the procedure previously used.

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(12) Bachmann, *J. Org. Chem.*, **3**, 444 (1938).