In general, good yields of anilides were obtained when solutions of the Grignard reagents were treated with phenyl isocyanate; therefore, cleavage of 4-methyl-1,3-dioxane, a cyclic formal, by the Grignard reagents could not have occurred in appreciable amount.

Further studies of 4-methyl-1,3-dioxane and similar compounds as solvents for the preparation and reactions of Grignard reagents are anticipated.

Summary

Solutions of several aliphatic and aromatic halides in 4-methyl-1,3-dioxane reacted with magnesium to produce good yields of Grignard reagents.

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The Catalytic Synthesis of Benzothiophene

BY R. J. MOORE AND B. S. GREENSFELDER

Recently,[1] new chemical methods for the synthesis of benzothiophene have been proposed to provide starting material for possible use in pharmaceuticals, and as a precursor of thioindigo. These processes are, however, inefficient and too expensive for commercial use. In the course of a general investigation of dehydrocyclization, a catalytic synthesis was developed by which good yields of benzothiophene can be obtained, using styrene and hydrogen sulfide as starting materials. The over-all reaction is described by the following equation
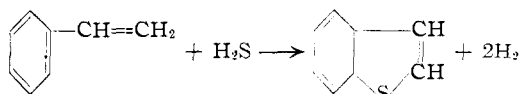
Experimental

The experiments discussed here were performed in a continuous flow reaction system at atmospheric pressure. The apparatus comprised a stainless steel catalyst tube heated by four sections of automatically controlled electric resistors and having the axial catalyst temperature profile flat within ±3°. The hydrocarbon was fed into the preheating section by a Hills–McCanna proportioning pump, while the gaseous reactants were measured by differential flowmeters. Reaction products were cooled to condense benzothiophene and unreacted styrene, and the vented product gases were sampled at intervals for analysis.

Ordinary commercial grade reactants were used, the styrene being only flash distilled to remove polymer and inhibitor. Hydrogen sulfide was charged directly from the cylinders as received.

Earlier work in these Laboratories showed in general that sulfur resistant dehydrogenation catalysts were suitable for this type of reaction; the most active of those tested was FeS/Al₂O₃ (ca. 5% iron on activated alumina). A suitable catalyst was prepared by sulfiding Alorco "Grade B" activated alumina at 600° with a mixture of two parts hydrogen sulfide and 1 part hydrogen at a rate of 100 vol./vol. catalyst/hr. until water no longer appeared as condensate. Usually one to two hours sufficed. Alternatively, activated alumina can be impregnated with ferric nitrate solution, and sulfided as above, after calcination to decompose the nitrate.

In order to minimize polymerization of the styrene, an excess of hydrogen sulfide was used, usually 4 moles of hydrogen sulfide per mole of styrene. A mole ratio of 8:1 was found to increase conversion but handling the corresponding volume of excess gas in the laboratory was impracticable.

The preferred operating temperature is related to the contact time and to the activity of the catalyst. As shown by the following typical results for runs of four hours duration, a temperature of 600 to 625° appears to be satisfactory.

TABLE I

Temp., °C.	Contact time, seconds[a]	Conversion of styrene to benzothiophene. mole %
500	20	20 (estd.)
500	40	43
600	20	60
625	20	63

[a] Calculated on basis of 100% void in catalyst bed.

It was observed that the catalyst gradually accumulated a deposit of carbonaceous material and lost activity during processing. The average conversion over the initial ten-hour process period was only 45–50% compared with 60% for four hours; beyond this time the rate of production fell off sharply. The carbonaceous deposit could be removed by burning with air, but excessively long times were required at relatively low temperatures in order not to overheat the catalyst, and complete re-sulfiding of the catalyst was necessary. It was found, however, that regeneration could be completed in two to four hours if steam were charged at 400 vol./vol. catalyst/hr. with air at such a rate that the catalyst temperature did not exceed 675°. Under these conditions the ferrous sulfide was only partially oxidized.

With the exception of small amounts of benzene and tar-like polymer, the crude product consisted of benzothiophene and unreacted styrene. It was estimated that conversion efficiency (yield) was of the order of 90%. The benzothiophene product was readily purified by distillation, b. p. 221°, since neither the feed nor the side reaction products boil in this range. The distilled material had a melting point of 31°, and on recrystallization from ethanol, 31.2°. Analysis showed 23.6% sulfur, calculated 23.8%.

The hydrogen sulfide-free vent gas was found to be predominantly hydrogen, with a small admixture of ethylene and a saturated hydrocarbon, presumably ethane.

Discussion

While no extensive investigation of the mechanism of this reaction was carried out, several inferences can be drawn from the experimental results. Assuming that 2-phenylethyl mercaptan is an intermediate in the conversion, its formation could be achieved in at least two ways at 600°: firstly, at equilibrium there should be an appre-

(1) Hansch and Lindwall, J. Org. Chem., 10, 381 (1945); Buu-Hoï and Cagniant, Ber.. 76B, 1269–1274 (1943); Tarbell and Fukushima, THIS JOURNAL, 68, 1456 (1946); Tarbell, Fukushima and Dam. ibid., 67, 1643 (1945).

ciable amount of the primary mercaptan formed by simple addition,[3] and secondly, conditions are favorable for the formation of free radicals, through which anti-Markownikoff addition is now assumed to proceed.[3] Dehydrocyclization of the adduct then would lead directly to the principal observed product.

It is also possible to consider styrene as a conjugated diolefin[4] which reacts with hydrogen sulfide by 1,4-addition to form an adduct and then is catalytically dehydrocyclized. In view of the lack of confirmatory data, this is highly speculative, but it has the virtue of an ultimately simpler path, especially if cyclization is effected during the addition under the influence of the

(2) Barr and Keyes, *Ind. Eng. Chem.*, **26**, 1111 (1934).

(3) Mayo and Walling, *Chem. Rev.*, **27**, 351 (1940).

(4) Alder, *Die Chemie*, **55**, 53 (1942).

catalyst. In a parallel study of the reaction of butadiene and hydrogen sulfide to form thiophene, crotyl mercaptan (which would be formed by 1,4-addition) was isolated in experiments at 400° where the dehydrogenation activity of the catalyst was not sufficiently complete to convert the reactants to thiophene. Approximately equal quantities of thiophene and crotyl mercaptan were obtained in one case. No attempt was made, however, to isolate a corresponding styrene derivative in this investigation.

Summary

Catalytic dehydrocyclization of styrene and hydrogen sulfide at 600° over FeS/Al_2O_3 catalyst is described, leading to 60% mole conversion to benzothiophene.

An Improved Synthesis of the Selenium Analogs of Methionine and Homocystine[1]

BY HAROLD J. KLOSTERMAN AND EDGAR PAGE PAINTER[2]

A synthesis of amino acids with selenium substituted for sulfur in methionine and homocystine was recently described.[3] The selenium-containing amino acid from which these compounds were prepared was α-amino-γ-(benzylseleno)-butyric acid. The latter compound was prepared by reaction of sodium benzyl selenide with ethyl-α-benzamido-γ-chlorobutyrate. While these steps gave satisfactory yields, the synthesis of ethyl α-benzamido-γ-chlorobutyrate was very time consuming.

The recent paper by Livak, Britton, Vander-Weele and Murray[4] describing a new synthesis of methionine from 5-(β-bromoethyl)-hydantoin suggested a better method of preparing α-amino acids with selenium in the γ-position. The compound, 5-(β-bromoethyl)-hydantoin, readily prepared from γ-butyrolactone, reacted with sodium benzyl selenide to give 5-(β-benzylselenoethyl)-hydantoin in a yield of 72%. Saponification of the hydantoin by sodium hydroxide at a temperature of 155° gave α-amino-γ-(benzylseleno)-butyric acid in 85% yield. From the latter compound the selenium analogs of methionine and homocystine were prepared as previously described.[3]

Experimental

5-(β-Bromoethyl)-hydantoin.—This compound was prepared from α-amino-γ-hydroxybutyric acid by the method of Livak, *et al.*,[4] m. p. 141° (uncor.).

(1) Published by permission of the Director, North Dakota Agricultural Experiment Station.

(2) Present address: Division of Chemistry, College of Agriculture, University of California, Davis, California.

(3) Painter, THIS JOURNAL, **69**, 232 (1947).

(4) Livak, Britton, VanderWeele and Murray, *ibid.*, **67**, 2218 (1945).

Anal. Calcd. for $C_5H_7BrN_2O_2$: N, 13.53. Found: N, 12.49.

While the analysis of our compound, as well as the one of Livak, *et al.*, agrees well with that calculated for the monohydrate (12.44% N) we have been unable to remove a molecule of water by heating in vacuum or recrystallization from organic solvents.

5-(β-Benzylselenoethyl)-hydantoin.—To a solution of 69.5 g. (0.4 mole) of benzyl selenomercaptan[5] in 400 cc. of oxygen-free absolute ethanol, 9.2 g. of sodium was added in small pieces. After the sodium dissolved, a solution of 72 g. of 5-(β-bromoethyl)-hydantoin dissolved in 200 ml. of absolute ethanol was added and the mixture heated for one hour. The solution was cooled to room temperature, 25 ml. of concentrated hydrochloric acid added and then heated to boiling to ensure ring closure. The solvent was removed at reduced pressure and the salt extracted with water.

The residue was dried, then extracted with 2.5 liters of boiling toluene. After cooling in the refrigerator 75 g. of crude 5-(β-benzylselenoethyl)-hydantoin, melting at 101°, a yield of 72%, were obtained. After recrystallization by dissolving a portion of the crude product in boiling water and cooling, fine needles, melting point at 123-124°, were obtained. Recrystallization of this product from toluene did not change the melting point. The recovery by recrystallization from water was about 95% and the nitrogen content remained nearly constant.

Anal. Calcd. for $C_{12}H_{14}N_2O_2Se$: N, 9.43; Se, 26.58. Found: N, 8.95; Se, 25.0.

As is the case with 5-(β-bromoethyl)-hydantoin, the analyses agree better for the monohydrate, 8.89 nitrogen and 25.07% selenium.

α-Amino-γ-(benzylseleno)-butyric Acid.—A solution of 68 g. (0.23 mole) of crude 5-(β-benzylselenoethyl)-hydantoin in 600 cc. of 1.5 M sodium hydroxide was hydrolyzed by heating in an autoclave at 155° for thirty minutes. After the solution cooled to room temperature, a small amount of carbon was added and the solution filtered. The α-amino-γ-(benzylseleno)-butyric acid which precipitated when acid was added to a pH of 5.5

(5) Painter, *ibid.*, **69**, 229 (1947).