hydroxide in ethanolic dioxane were isolated by removal of solvent and recrystallization from ethanol, m.p. 176.5–177.5°. The unsaturated sulfone XXIV gave a positive Baeyer (potassium permanganate) test for unsaturation.

Anal. Calcd. for $C_{23}H_{18}O_2S$: C, 77.07; H, 5.06. Found: C, 77.02; H, 5.06.

BOULDER, COLORADO

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF COLORADO]

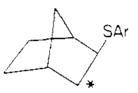
Bridged Polycyclic Compounds. IV. The Stereochemistry of the Free Radical Addition of *p*-Thiocresol to a Bicyclo[2,2,1]heptene and a Bicyclo[2,2,2]octene[1]

BY STANLEY J. CRISTOL AND ROBERT P. ARGANBRIGHT

RECEIVED JUNE 24, 1957

The addition of *p*-thiocresol to *endo-exo*-1,2,3,4,6,10,10-heptachloro-1,4,4a,5,8,8a-hexahydro-1,4,5,8-dimethanonaphthalene (IV) has been shown to give entirely *cis-exo* addition of the *p*-thiocresoxy radical and the hydrogen atom involved. Free-radical addition of thiocresol to 11-chloro-9,10-dihydro-9,10-ethenoanthracene (V) gave a mixture of isomers of which about $^1/_3$ resulted from *trans* addition and $^2/_3$ from *cis* addition. These results suggest that the product of addition of a thiocresoxy radical to these olefins is a classical free radical, rather than a sulfur-bridged radical.

Some time ago it was shown[2] that the sole 1:1 addition product of *p*-thiocresol to norbornene is *exo*-2-*p*-thiocresoxynorbornane, no rearrangement to the 7-isomer being observed. On the basis of this observation, it was suggested that the intermediate[3] in the addition reaction was the classical radical I rather than the carbon-bridged mesomeric radical II. At that time[2] it was pointed out that structure III was a possible one for the intermediate; this was based upon an analogous suggestion[4] made to explain the *trans* addition observed with hydrogen bromide to 1-bromocyclohexene and 1-methylcyclohexene. During the intervening period of time, a number of papers[5–9] have appeared which make a formulation such as III unlikely, but we wish to report work which makes such a formulation untenable, assuming that a structure such as III would lead to stereospecific *trans* addition.[4] The stereochemistry of the addition reaction could, of course, not be determined with norbornene itself (except with an isotopic label), so we undertook the addition of *p*-thiocresol to a substituted norbornene, 6-chloro-aldrin (IV) (*endo-exo*-1,2,3,4,6,10,10- heptachloro-1,4,4a,5,8,8a-hexahydro-1,4,5,8-dimethanonaphthalene) as well as to a substituted bicyclo[2,2,2]octene, 11-chloro-9,10-dihydro-9,10-ethenoanthracene (V).



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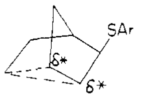

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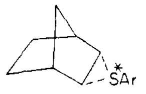

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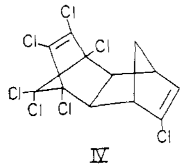

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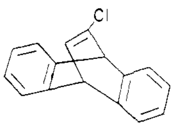

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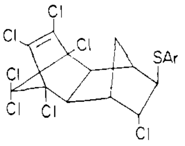

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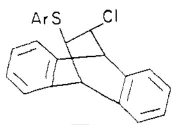
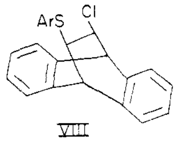


VII



VIII

Addition of *p*-thiocresol to 6-chloro-aldrin gave only one product in isolable quantities. This product was identical with that obtained from the addition of *p*-toluenesulfenyl chloride to aldrin which has been shown[1] to have the *trans* relationship between the chlorine atom and the sulfide group. Thus addition in this system is largely, if not completely, *cis* addition, and this result indicates that neither a bridged sulfur radical analogous to III nor a π-complex[6,10] are important intermediates in the addition of mercaptans to such olefins. The fact of clean *cis* addition appears to be a reflection of the generally observed *exo* addition[1,2,11] to norbornene derivatives, which has been formulated as a rule. The rule applies for the addition of the first ion, radical or atom to the bicyclic double bond, but the position and stereochemistry of the second addend depends upon the type of intermediate formed. For example, with ionic addition, Wagner–Meerwein rearrangements or *trans* additions may occur when the second group is added. However, in this radical addition, the transfer of the hydrogen atom from mercaptan to the radical analogous to I also occurs from the *exo* side. Another example of this is to be found in

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(1) Previous paper in series: S. J. Cristol, R. P. Arganbright, G. D. Brindell and Roger M. Heitz, THIS JOURNAL, **79**, 6035 (1957).

(2) S. J. Cristol and G. D. Brindell, *ibid.*, **76**, 5699 (1954).

(3) M. S. Kharasch, A. T. Read and F. R. Mayo, *Chemistry & Industry*, 752 (1938).

(4) H. L. Goering, P. I. Abell and B. F. Aycock, THIS JOURNAL, **74**, 3588 (1952).

(5) H. L. Goering and L. L. Sims, *ibid.*, **77**, 3465 (1955).

(6) (a) P. S. Skell and R. C. Woodworth, *ibid.*, **77**, 4638 (1955); (b) P. S. Skell, R. C. Woodworth and J. H. McNamara, *ibid.*, **79**, 1253 (1957).

(7) H. L. Goering, D. I. Relyea and D. W. Larsen, *ibid.*, **78**, 348 (1956).

(8) F. G. Bordwell and W. A. Hewett, Abstracts of the 126th Meeting of the American Chemical Society, New York, N. Y., Sept., 1954, p. 6-O.

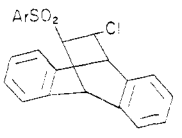
(9) F. G. Bordwell and N. P. Neureiter, Abstracts of the 131st Meeting of the American Chemical Society, Miami, Florida, April, 1957, p. 10-O.

(10) H. C. Brown and J. D. Brady, THIS JOURNAL, **74**, 3570 (1952).

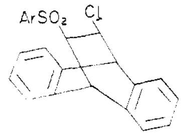
(11) See for example: K. Alder and G. Stein, *Ann.*, **504**, 216 (1933); R. B. Woodward and H. Baer, THIS JOURNAL, **70**, 1161 (1948); G. Stork, E. E. van Tamelen, L. J. Friedman and A. W. Burgstahler, *ibid.*, **75**, 384 (1953); K. Alder and H. Wirtz, *Ann.*, **601**, 138 (1956).

the work of Berson,[12] who observed exclusive *cis-exo* addition of bromine to *endo-cis*-1,2,3,6-tetrahydro-3,6-endomethanophthalic anhydride.[13]

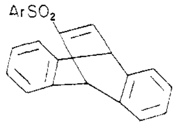
When *p*-thiocresol was allowed to react with 11-chloro-9,10-dihydro-9,10-ethenoanthracene (V), a mixture of products was obtained which was separated by chromatography on activated alumina into two products. These were shown to be geometrically isomeric *β*-chlorothioethers by oxidation to the sulfones followed by elimination of hydrogen chloride with base to give identical olefins. The very fast eliminations with alkali[14] indicate that the isomers are the *β*-chlorosulfones IX and X and that no rearrangement occurred during addition.



IX



X



XI

Of these two isomeric chlorothioethers, one was obtained in greater amount and was found to be identical with that obtained by the addition of *p*-toluenesulfenyl chloride to 9,10-dihydro-9,10-ethenoanthracene; this compound has been shown to have the *trans* structure VII.[1] The compound formed in lesser amount may therefore be assigned the *cis* structure VIII. Hence the reaction gives more *cis* than *trans* addition.

The product comprised 67–86% of the *trans* isomer and 14–33% of the *cis* isomer when a 2:1 ratio of mercaptan to olefin was used and when the mercaptan was added dropwise to the olefin. The apparent variation in the ratio of products may be due to the isolation techniques used. If the inverse method of addition was used, the reaction did not go to completion, presumably since the propagation step was interrupted when insufficient olefin was present. The total isolated yield of product was only 37–43% of the theoretical yield.

A better total yield in the reaction was obtained by partial separation and then oxidation of the mixture of *β*-chlorothioethers remaining, followed by separation of the isomeric *β*-chlorosulfones. In this manner, a 71% total yield was obtained, of which $^1/_3$ was the *cis*-sulfone and $^2/_3$ was the *trans*-sulfone.

There is a possibility that the isomer ratio would change if the mercaptan to olefin ratio were changed, but there are no such data on this particular olefin at present. Such an effect was found in the reaction of mercaptans with 1-chlorocyclohexene[7] but would not be expected here if the explanation offered by Goering and his co-workers for their results is correct.

In this bicyclo[2,2,2]octene system, then, as well as in the bicyclo[2,2,1]heptene system, there is evidence for neither intermediates of type III nor of type II, and it must be concluded that the intermediate in addition (and perhaps other) free-radical reactions is best represented by a classical radical (I) as originally postulated.[2,3]

Acknowledgments.—The authors are indebted to the National Science Foundation for support of this work. They are further indebted to the Shell Development Co. for samples of aldrin dichloride. Analyses are by Galbraith Laboratories.

Experimental

Addition of *p*-Thiocresol to *endo-exo*-1,2,3,4,6,10,-10-Heptachloro-1,4,4a,5,8,8a-hexahydro-1,4,5,8-dimethanonaphthalene (IV).—To a stirred solution of 5.87 g. (0.0147 mole) of IV[15] (m.p. 62–64°) dissolved in 50 ml. of *n*-hexane was added dropwise 2.48 g. (0.020 mole) of *p*-thiocresol. The temperature was held below 40° by cooling. The solvent was then evaporated until only about 10 ml. remained. The precipitate, which weighed 6.17 g., was filtered. It had a melting point of 129.6–130.2° (sealed tube). From the filtrate was recovered 0.32 g., m.p. 120–137°. The total yield was 85%. After recrystallization from ethanol, the product VI melted at 129–130°. This melting point was not depressed when a sample was admixed with a sample, m.p. 129–130°, of *exo*-2-*p*-thiocresoxy-*endo*-3,5,6,7,8,9,9-heptachloro-*exo-endo*-1,2,3,4,4a,5,8,8a-octahydro-1,4,5,8-dimethanonaphthalene.[1]

Addition of *p*-Thiocresol to 11-Chloro-9,10-dihydro-9,10-ethenoanthracene (V).—A solution of 4.30 g. (0.018 mole) of 11-chloro-9,10-dihydro-9,10-ethenoanthracene (V)[16] dissolved in 40 ml. of *n*-hexane was added dropwise to 4.47 g. (0.036 mole) of *p*-thiocresol dissolved in 20 ml. of *n*-hexane. After the addition was complete, the solution was heated at reflux for 1 hr. Then about 45 ml. of the solvent was distilled and the precipitate which formed was removed by filtration. Its weight was 2.75 g. and its melting point was 114–142°. From the filtrate was recovered 1.47 g. with a melting point of 174–185°. The remaining liquid was chromatographed on 20 g. of activated alumina using about 500 ml. of each of the following solvents in order: 80:20 petr. ether (boiling range 30–60°)-carbon tetrachloride, carbon tetrachloride, chloroform. Cuts of 50 ml. were taken of the eluent. From the solvent mixture was recovered 1.7 g. of *p*-thiocresol and some *p*-tolyl disulfide. Then 0.26 g. of material melting at 121–122° was isolated from the seventh through the eleventh cuts of the same solvent. The final recovery of products after further recrystallization was 1.6 g. of *trans*-11-*p*-thiocresoxy-12-chloro-9,10-dihydro-9,10-ethanoanthracene (VII) melting at 193–195° and 0.20 g. of the *cis* isomer VIII melting at 157–159°. Also recovered was 0.65 g. of the unreacted olefin. The total yield of products was only 28%.

Anal. Calcd. for $C_{23}H_{19}ClS$: C, 76.12; H, 5.28. Found (product VII): C, 75.95; H, 5.40. Found (product VIII): C, 76.00; H, 5.12.

Product VII was tested in a mixed melting point with the product obtained from the addition of *p*-toluenesulfenyl chloride to 9,10-dihydro-9,10-ethenoanthracene,[1] and no depression was observed. The sulfones obtained from the two products were also identical by this test. Hence VII is the *trans* isomer.

A smoother reaction was obtained by adding the mercaptan dropwise to the olefin. By this modification a 37% total yield was obtained of which $^1/_3$ was the *cis* isomer and $^2/_3$ was the *trans* isomer.

A better yield was obtained using the above modification and direct oxidation of the reaction mixture followed by separation of the isomeric sulfones. For this purpose, 3.18 g. (0.0133 mole) of V was dissolved in 100 ml. of *n*-hexane, and 1.65 g. (0.0133 mole) of *p*-thiocresol in 50 ml. of the same solvent was added dropwise. The mixture was then heated on a steam-plate for 0.5 hr. and allowed to stand overnight. The solvent was removed by evaporation, and the remaining

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[12] J. A. Berson, THIS JOURNAL, **76**, 5748 (1954).

[13] An observation of a transfer from the *endo* side recently has been noted in these laboratories by Mr. J. A. Reeder.

[14] S. J. Cristol and R. P. Arganbright, THIS JOURNAL, **79**, 3441 (1957).

[15] R. E. Lidov, U. S. Patent 2,635,977 (April 21, 1953).

[16] S. J. Cristol and N. L. Hause, THIS JOURNAL, **74**, 2193 (1952).

material was dissolved in as small a volume of acetone as possible. Dry ethanol was added to effect a partial separation of the isomers. The precipitate which formed on standing was filtered and was found to be the almost pure *trans*-β-chlorothioether VII, yield 1.95 g., m.p. 186–190°. The solvent was evaporated from the filtrate leaving an oil.

The solid was dissolved in 200 ml. of glacial acetic acid, to which 20 ml. of 30% hydrogen peroxide was then added. The solution was heated for 0.5 hr. on a steam-bath and was then allowed to stand overnight. Addition of water formed a precipitate of 2.3 g. of *trans*-12-*p*-toluenesulfonyl-11-chloro-9,10-dihydro-9,10-ethanoanthracene (IX), m.p. 156–161°. Two recrystallizations from ethanol gave 1.73 g., m.p. and mixed m.p. with authentic material,[1] 160–162°.

The oil obtained above was treated similarly using 100 ml. of glacial acetic acid and 20 ml. of 30% hydrogen peroxide, yielding 1.06 g., m.p. 185–200°. Several recrystallizations from absolute ethanol gave 0.72 g. of white crystals of *cis*-12-*p*-toluenesulfonyl-11-chloro-9,10-dihydro-9,10-ethanoanthracene (X), m.p. 216–218°.

Anal. Calcd. for $C_{23}H_{19}ClO_2S$: C, 69.95; H, 4.85. Found: C, 70.13; H, 4.99.

The products from the treatment with alkali in ethanolic dioxane[14] of IX and X were isolated separately. Each of the samples of XI[1] melted at 176.5–177.5° and each did not depress the m.p. of the other sample.

BOULDER, COLORADO

[CONTRIBUTION FROM THE DEPARTMENT OF BIOCHEMISTRY, LOUISIANA STATE UNIVERSITY SCHOOL OF MEDICINE]

Two New Glucose Monoacetates, Apparently 6-O-Acetyl-α- and β-D-Glucose, and a Comparison of the Metabolism of Glucose, Acetylglucose and 6-O-Methylglucose[1]

BY RICHARD E. REEVES, ROLAND A. COULSON, THOMAS HERNANDEZ AND FLORINE A. BLOUIN

RECEIVED JUNE 21, 1957

Two new crystalline glucose monoacetates, apparently the α- and β-anomers of 6-O-acetyl-D-glucopyranose have been prepared. The mixed anomeric forms crystallize together under certain conditions and the properties of some of the mixtures are in agreement with those of a substance recently isolated from cultures of *Bacillus megaterium*. Injected acetylglucose is metabolized by the alligator almost as rapidly as is glucose while 6-O-methylglucose disappears from the blood at a much slower rate.

At the time this work was undertaken there appeared to be no record in the literature of a well-characterized mono- or diacetate of glucose. This is somewhat surprising in view of the great number of well characterized acetates of glucose derivatives. It was anticipated that the direct partial acetylation of glucose would yield a large number of isomers and that if a pure substance was isolated the definite establishment of its structure by chemical methods would be difficult because of the lability of the acetate group. Both difficulties were encountered. However, one pure monoacetate has been isolated repeatedly and a second substance, believed to be the anomer of the first, was obtained on two occasions.

Recently Duff, Webley and Farmer[2] have described as 6-O-acetylglucopyranose a crystalline glucose monoacetate, m.p. 133°, sp. rot. 48° (equil. H_2O). The physical properties of their substance agree closely with those observed by us for crystalline preparations thought to be mixtures of the α- and β-anomers of 6-O-acetylglucose. The chemical properties of their monoacetate are similar to those reported in the present investigation. Duff, *et al.*, obtained their substance as a metabolite from cultures of *Bacillus megaterium*. Evidence of the metabolic activity of our acetylglucose was obtained in experiments with the alligator.

Experimental

Preparation of Monoacetylglucoses.—Eighteen g. of powdered glucose was shaken with 40 ml. of pyridine and 5 ml. of acetic anhydride for one hour at room temperature. Another 5 ml. of acetic anhydride was then added and shaking was continued for 3 hours. Unreacted glucose (6.6 g.) was separated by filtration and the filtrate evaporated *in vacuo*, finally in a dish over sulfuric acid in a desiccator. The sirupy residue was dissolved in 15 ml. of methyl ethyl ketone and 10 ml. of alcohol and placed on a column 4 cm. in diameter containing 200 g. of Whatman cellulose powder. The column previously had been washed exhaustively with water, and then with 2 liters of methyl ethyl ketone–water azeotrope. At this stage a sample of the crude preparation spotted on paper and developed by the descending technique with *n*-butanol:alcohol:water (4:1:1) separated into three well resolved spots (aniline hydrogen phthalate spray reagent) of R_F 0.19, 0.45 and 0.72, respectively. The R_F of glucose in this system is 0.19.

The column was developed with methyl ethyl ketone–water azeotrope using an automatic fraction collector to collect 15–20 ml. samples. Drops of the collected fractions were spotted on paper, sprayed with aniline hydrogen phthalate and heated to show which tubes contained reducing sugars. On the basis of these tests, tubes 1–8 were discarded and tubes 9–25 were pooled and evaporated yielding 3.36 g. of a sirup of R_F 0.72 in the butanol system. This sirup has failed to crystallize on standing for two years.

High-rotating Form.—Tubes 26–34 contained no reducing sugar and were discarded. Tubes 35–65 were pooled and evaporated yielding 1.57 g. of a sirup with R_F 0.45 in the butanol system. This sirup partially crystallized upon standing. The crystals were dissolved in a little acetic acid and one volume of ether was added. Upon standing this solution yielded 0.46 g. of needle-like crystals which were recrystallized from the same solvent mixture. After drying in high vacuum at 100° over P_2O_5, the m.p. of this substance was 150–152°, sp. rot.[3] 90° (2 min.) changing to 51° (*c*, 1.6; H_2O). *Anal.* Calcd. $C_8H_{14}O_7$ (222.19): C, 43.24; H, 6.35. Found: C, 43.42; H, 6.51.

Low-rotating Form.—On two occasions the tubes containing the monoacetate fraction were not pooled, but were worked up separately or in small groups. The tubes containing the faster-moving part of the fraction yielded the high-rotating substance described above and those containing the slower moving part of the monoacetate fraction yielded a crystalline substance of low optical rotation. Recrystallization of this substance from methanol and acetone gave clusters of crystals, m.p. 148–149°, sp. rot. 22° (2 min.) changing to 51° (*c* 1; H_2O). *Anal.* Calcd. $C_8H_{14}O_7$ (222.19); C, 43.24; H, 6.35. Found: C, 43.21; H, 6.22. We have been able to convert partially the high-rotating form to the low-rotating form by recrystallization from water and acetone, and the low-rotating form has been com-

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[1] This work was supported, in part, by a grant from the Corn Industries Research Foundation.

[2] R. B. Duff, D. B. Webley and V. C. Farmer, *Biochem. J.*, **65**, 21P (1957).

[3] All specific rotations were determined at 25° using the sodium-D line.