in admixture with an authentic sample and having an infrared spectrum identical with that of an authentic sample.

In a parallel experiment in which 1.71 g. of tropylium bromide in 30 ml. of water was treated with 1.0 g. of chromic oxide in 10 ml. of water and allowed to stand for 48 hr., benzaldehyde was isolated in 71% yield. No benzoic acid was isolated.

Reaction of Cycloheptatrienylium Bromide with Silver Oxide.—A solution of 1.71 g. of tropylium bromide in 50 ml. of water was stirred for 24 hr. with 2.0 g. of silver oxide. Filtration followed by ether extraction afforded 0.491 g. (46.3%) of benzaldehyde which was identified by comparison of its infrared spectrum and 2,4-dinitrophenylhydrazone with those of an authentic sample.

Dihydroheptafulvalene (Ditropyl). (a).—A solution of 0.513 g. of tropylium bromide (purified by crystallization from absolute ethanol) in 6 ml. of water was shaken vigorously with 0.200 g. of zinc dust. The mixture became warm and the yellow color of the solution was rapidly discharged. Extraction with four 5-ml. portions of pentane, followed by evaporation of the solvent, afforded a colorless crystalline residue of dihydroheptafulvalene, 0.266 g. (97.4%), m.p. 61° after one recrystallization from pentane. Sublimation at 65–75° at 0.5 mm. gave a colorless crystalline sublimate of unchanged melting point.

Anal. Calcd. for $C_{14}H_{14}$: C, 92.3; H, 7.7. Found: C, 92.1; H, 7.7.

(b).—A solution of 28.8 g. of bromine in 120 ml. of carbon tetrachloride was added in 45 min., with stirring, to a solution of 16.6 g. of tropilidene in 180 ml. of carbon tetrachloride cooled in ice-water. Solvent was removed at room temperature under reduced pressure and the residual crude dibromotropilidene was heated at 70–80° at 20 mm. for 24 hr. The resulting yellow-brown cake was dissolved in 100 ml. of water, filtered from a small amount of insoluble tar and shaken vigorously with 12.0 g. of zinc dust. Slight warming occurred, but on addition of 10 ml. of pentane and shaking, the reaction became strongly exothermic. After being shaken intermittently over a period of 15 min., the mixture was extracted with three 50-ml. portions of pentane. Concentration of the extract to 25 ml. and cooling overnight at −40° afforded 11.4 g. of ditropyl as a heavy, slightly discolored crystalline mass, m.p. 56–58°, for a total yield of 39% based on tropilidene.

Hydrogenation of Dihydroheptafulvalene.—Ditropyl, 0.182 g., was hydrogenated in 10 ml. of glacial acetic acid over 50 mg. of platinum oxide. Four molar equivalents of hydrogen was absorbed in 40 min. Filtration of the catalyst and dilution with water precipitated the hydrocarbon which was extracted with four 10-ml. portions of pentane. The pentane extract was washed twice with 2 *N* sodium bicarbonate and twice with water. Evaporation of the dried (magnesium sulfate) pentane extract and evaporative distillation of the residual oil at 80–90° at 0.5 mm. afforded dicycloheptyl as a colorless oil, $n^{25}D$ 1.4910, having an infrared spectrum identical with that of an authentic sample (prepared by Dr. J. R. Mayer[17]).

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[CONTRIBUTION FROM THE ENTOMOLOGY RESEARCH BRANCH, AGRICULTURAL RESEARCH SERVICE, UNITED STATES DEPARTMENT OF AGRICULTURE]

Constituents of *Heliopsis* Species. V. Heliopsin, a Second Insecticidal Amide from the Roots of *H. helianthoides* var. *scabra*.

BY MARTIN JACOBSON

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Heliopsin, an unsaturated isobutylamide closely related to scabrin, has been isolated from the roots of *Heliopsis helianthoides* var. *scabra*. It is a powerful sialagogue as toxic as pyrethrins to house flies. Hydrogenation, hydrolysis, oxidation, and ultraviolet and infrared absorption spectra of heliopsin show it to be the N-isobutylamide of either 2,4,8,10,12,16- or 2,4,8,12,14,16-octadecahexaenoic acid. The geometrical configuration of heliopsin has been partially determined.

In Part I of this series[1] the isolation of scabrin, an unsaturated insecticidal amide from the roots of *Heliopsis helianthoides* (L.) B.S.P. var. *scabra* Dunal. (formerly *H. scabra*), was reported, and reference was made to the presence in the roots of a second highly insecticidal material. The latter has now been obtained in the pure state and its structure has been elucidated.

A petroleum ether extract of the roots,[2] after purification by solvent partition with nitromethane, was chromatographed on adsorption alumina (80 to 200 mesh). The scabrin was readily removed by elution with benzene,[1] and elution with benzene–ethyl ether (1:1) removed the second toxic fraction (corresponding to fraction B) as a yellow oil showing blue fluorescence in ultraviolet light. Repeated attempts to purify the fraction on ordinary adsorption alumina and on silicic acid columns were unsuccessful, but purification was finally achieved by chromatography on neutral alumina (Woelm) and elution with benzene–ethyl ether (9:1) to give a pale yellow, non-fluorescent, viscous oil for which the name "heliopsin" is proposed.

Heliopsin, obtained in 0.06% yield (based on dry root), distilled at 198–200° (0.08 mm.) accompanied by extensive decomposition, and could not be induced to crystallize. A trace of the material, when placed on the tongue, produced an intense paralytic effect on the tongue and lips after an induction period of approximately 20 minutes, whereas scabrin gave a similar effect in 10 minutes.[3] It proved to be as toxic as the pyrethrins to house flies.[4] It is quite unstable at room temperature, changing to a red inactive resin after about a week, but it is stable in the cold for several months under nitrogen or in sealed ampoules, particularly when kept in solution.

Analysis and molecular-weight determination indicated the formula $C_{22}H_{33}NO$ for heliopsin. Acid hydrolysis yielded an acid which was too unstable to be characterized, and a nitrogenous base which was identified as isobutylamine. On reduction with platinum it absorbed hydrogen equivalent to 5.8 double bonds to give N-isobutylstearamide, m.p. 77–78°. Heliopsin was thus established as the N-isobutylamide of an unsaturated

(1) M. Jacobson, THIS JOURNAL, **73**, 100 (1951).

(2) The plant material was very kindly collected on the Mescalero Indian Reservation in the White Mountains of New Mexico by A. H. Berkman, Texas Western College, El Paso.

(3) Because of this induction period, heliopsin was previously mistakenly reported as being without sialagogue effect.

(4) The tests against house flies were carried out by W. A. Gersdorff and P. G. Piquett, of the Entomology Research Branch.

18-carbon straight-chain acid, and it remained only to determine the points of unsaturation in the molecule.

Oxidation of heliopsin with alkaline permanganate resulted in the isolation of acetic, oxalic, succinic and N-isobutyloxamic acids only, showing unsaturation at C-2 and C-16. As the infrared spectrum indicated the absence of acetylenic linkages, the position of four double bonds still remained to be accounted for. The ultraviolet absorption spectrum showed a single maximum at 259 mμ (ε 34,000), which is in agreement with data expected for a chromophore—CH=CHCH=CH-CONH— and indicates the absence of two conjugated double bonds in the middle of a chain.[5] There are only two structures for heliopsin consistent with this data—namely, N-isobutyl-2,4,8,-10,12,16-octadecahexaenamide (I) or N-isobutyl-2,4,8,12,14,16-octadecahexaenamide (II).

$$CH_3CH{=}CH{-}(CH_2)_2{-}CH{=}CHCH{=}CHCH{=}CH{-}(CH_2)_2{-}CH{=}CHCH{=}CHC(=O){-}R \quad (I)$$

$$CH_3CH{=}CHCH{=}CHCH{=}CH{-}(CH_2)_2{-}CH{=}CH{-}(CH_2)_2{-}CH{=}CHCH{=}CHC(=O){-}R \quad (II)$$

where R = $NH{-}CH_2{-}CH{-}(CH_3)_2$

Oxidation of either of these structures would theoretically yield 3 moles of oxalic acid and 2 moles of succinic acid; in fact, permanganate oxidation of heliopsin gave 2.17 moles of the former and 1.56 moles of the latter.

The infrared spectrum of heliopsin is consistent with structures I or II, being characteristic of a monosubstituted amide conjugated with a diene system (NH stretching 3250, 3030; amide A carbonyl 1625; amide B 1545; C=C stretching 1655, 1612 cm.$^{-1}$).[5a]

The geometrical stereochemistry of heliopsin can be partly, but not completely settled. The C=C stretching vibration (1655 cm.$^{-1}$) lies in a region characteristic of a *trans*-2,*trans*-4-isobutylamide. This is supported by the fact that there is only one peak at 995 cm.$^{-1}$ without a second in the 960–970 cm.$^{-1}$ region (the nearest is at 939 cm.$^{-1}$). Therefore, even though heliopsin failed to give a crystalline maleic anhydride adduct, the 2,4-diene system almost certainly has the *trans,trans* configuration. The ultraviolet extinction coefficient (34,000) is also in agreement, since Crombie[6] has shown, in a study of the isomeric N-isobutyl-2,4-decadienamides, that any *cis*-containing combination of linkages in the 2,4-diene system of these type compounds would give rise to a value of less than 26,000. The presence of moderately strong bands at 818 and 725 cm.$^{-1}$ in the infrared spectrum of heliopsin indicates that the isolated double bond is probably *cis*.

An attempt to convert heliopsin to the all-*trans* isomer by exposure to ultraviolet light was unsuccessful, most of the material being recovered unchanged after three hours of exposure.

(5) (a) L. Crombie, *Nature*, **174**, 832 (1954); (b) L. Crombie, *J. Chem. Soc.*, 995, 999 (1955); (c) L. Crombie and J. D. Shah, *ibid.*, 4244 (1955).

(6) L. Crombie, *ibid.*, 1007 (1955).

Experimental[7]

Isolation of Heliopsin.—A petroleum ether (b.p. 30–40°) extract of 12.9 kg. of ground roots was partitioned with nitromethane, and the neutral fraction of the nitromethane-soluble portion was chromatographed on adsorption alumina (80 to 200 mesh) according to the procedure previously reported[1] for the isolation of scabrin. The viscous, blue-fluorescing, orange oil (8.1 g., 0.063% based on dry root), which was eluted with benzene–ethyl ether (1:1) (corresponding with fraction B), was dissolved in a small quantity of dry benzene and put on a 17- by 1-inch column of Woelm alumina (non-alkaline, activity grade 1). Elution with benzene containing 10% of anhydrous ethyl ether slowly brought down the column a yellow, non-fluorescent band, leaving at the top of the column a dark yellow band with strong blue fluorescence. Further development brought out the non-fluorescent band which, on removal of solvent under reduced pressure, consisted of 7.5 g. (0.058%) of pale yellow, viscous oil (heliopsin). Chromatographic adsorption on a fresh column of neutral alumina and development with benzene brought the fraction down the column as a sharp, well defined yellow band which was considered to be pure.

The fluorescent, dark yellow band remaining at the top of the column could be rapidly eluted with methanol. Removal of the solvent and recrystallization of the resulting yellow solid from ethanol gave 0.5 g. of yellow crystals showing strong blue fluorescence in ultraviolet light and in solution. The compound melted at 235° and was identical with the non-toxic fluorescent crystals previously obtained[1] from the roots.

Heliopsin was a pale yellow, viscous oil distilling in a nitrogen atmosphere at 198–200° (0.08 mm.) with extensive decomposition. It could not be induced to crystallize.

Anal. Calcd. for $C_{22}H_{33}NO$: C, 80.68; H, 10.16; N, 4.28; mol. wt., 327.5. Found: C, 80.41; H, 10.21; N, 4.18; mol. wt. (Rast), 321.2.

The ultraviolet absorption curve of heliopsin showed a single maximum at 259 mμ (ε 34,000). When a trace of the material was placed on the tongue there was a short induction period (about 20 minutes) before strong sialagogue action was noticed. It proved to be as toxic as pyrethrins to house flies.[4]

Hydrogenation of Heliopsin.—An absolute ethanol solution of 0.4358 g. of heliopsin was hydrogenated with 150 mg. of reduced platinum oxide catalyst. In 15 minutes 172.1 ml. (cor.) of hydrogen was taken up, and the reaction then ceased. (The theoretical requirement for 6 moles of hydrogen for the above weight of a substance of molecular weight 328 is 178.8 ml.) The reaction mixture was separated from the catalyst, and the solvent was removed at reduced pressure, leaving a white solid. One recrystallization from ethanol gave a quantitative yield of the saturated compound as clusters of colorless needles, m.p. 77–78°.

Anal. Calcd. for $C_{22}H_{45}NO$: C, 77.81; H, 13.36; N, 4.13. Found: C, 77.98; H, 13.32; N, 4.27.

The product was found to be identical with N-isobutylstearamide, m.p. 77–78°, and hydrogenated scabrin by mixed m.p. (77–78°) with authentic specimens.

Action of Maleic Anhydride.—Heliopsin (150 mg.) was sealed with maleic anhydride (100 mg.) and benzene (2 ml.) in a nitrogen atmosphere and heated at 115° for 3 hours. On cooling to 5° a viscous yellow oil separated which could not be induced to crystallize. Evaporation of the benzene gave only a resin.

Hydrolysis of Heliopsin.—A mixture of 1.00 g. of heliopsin, 15 ml. of ethanol and 2.5 ml. of concentrated hydrochloric acid was heated at 100° for 120 hours in a sealed tube. The cooled reaction mixture was diluted with water and then extracted with ether. Evaporation of the aqueous phase and extraction with boiling ethyl acetate gave 0.31 g. (94%) of shining colorless plates, m.p. 174–175°, shown to be identical with isobutylamine hydrochloride by the mixture melting point with authentic material, m.p. and mixed m.p. 174–175°.

The ether extract of the original reaction mixture was

(7) All melting points are corrected; boiling points are uncorrected.

washed free of mineral acid and dried, and the solvent was removed. The residue was refluxed for one hour with 0.5 g. of potassium hydroxide in 20 ml. of ethanol; the reaction mixture, after being cooled and acidified, was extracted with ether. The dried ether solution was freed of solvent, leaving a red, oily acid residue (0.73 g., 84%), which was completely soluble in sodium bicarbonate solution but which could not be characterized at this stage because of its instability.

Oxidation of Heliopsin.—To a stirred suspension of 2.0 g. of heliopsin in 200 ml. of water, maintained at 50°, 12.5 g. of finely powdered potassium permanganate (equivalent to 12 moles of oxygen) was added in small portions. As soon as the reaction mixture had become colorless, the manganese dioxide was filtered and washed thoroughly with warm water. The combined aqueous filtrates were concentrated down to 20 ml. and made acid to congo red with sulfuric acid. The solution was steam distilled to remove completely the volatile acids and extracted with ether in a continuous extractor for 66 hours. The ether solution was freed of solvent, and the partly crystalline residue was subjected to sublimation in a micro-sublimator. The colorless solid subliming at 100–110° (15 mm.) weighed 1.18 g. and melted at 185–186° dec.

Anal. Calcd. for $C_2H_2O_4$: neut. equiv., 45. Found: neut. equiv., 43.

The substance (72%, 2.17 moles) was identified as anhydrous oxalic acid by a mixture melting point determination with an authentic specimen (m.p. 186–187° dec.).

The sublimation residue, after recrystallization from ethyl acetate, yielded 0.93 g. of colorless crystals, m.p. 188–189°.

Anal. Calcd. for $C_4H_6O_4$: neut. equiv., 59. Found: neut. equiv., 58.

The substance was identified as succinic acid by a mixture melting point determination, m.p. 188.0–188.5°, and by preparation of the di-*p*-phenylphenacyl ester, m.p. 208°. An additional 190 mg. of succinic acid (total yield 78%, 1.56 moles) was obtained from the ethyl acetate mother liquors, together with a small amount of polymerized material.

The solution of steam-volatile acids obtained above was neutralized with sodium hydroxide solution, concentrated to a small volume on the steam-bath, and acidified to congo red with sulfuric acid. The solution was rapidly steam distilled until all material acid to congo red had distilled over. The distillate was neutralized with sodium hydroxide solution, the neutral solution was evaporated to dryness, and the *p*-phenylphenacyl ester was prepared. It melted at 110°, and a mixed melting point determination with authentic *p*-phenylphenacyl acetate, m.p. 110°, showed no depression.

The distillation residue was neutralized with sodium hydroxide solution, concentrated on the steam-bath to 10 ml., acidified to congo red with sulfuric acid, and extracted with ether in a continuous extractor. The ether solution was dried and freed of solvent. The crystalline residue sublimed completely at 90–95° (15 mm.), and two recrystallizations from petroleum ether (b.p. 60–70°) gave 642 mg. (73%) of colorless feathery needles, m.p. 107°, containing nitrogen.

Anal. Calcd. for $C_6H_{11}NO_3$: N, 9.66; neut. equiv., 145. Found: N, 9.62; neut. equiv., 145.

The substance was identical with a synthetic sample of N-isobutyloxamic acid, m.p. and mixed m.p. 107°.

Exposure of Heliopsin to Ultraviolet Light.—One gram of heliopsin was dissolved in 50 ml. of petroleum ether (b.p. 60–70°)–ethyl ether (9:1) and irradiated with an ultraviolet lamp for 3 hours, during which time the solvent evaporated completely. The resulting orange viscous oil was taken up in a few milliliters of ether, in which a very small quantity remained insoluble, and the solution was evaporated to dryness. The viscous yellow oil remaining showed an infrared spectrum identical with that of heliopsin, and was considered to be unchanged material.

BELTSVILLE, MD.

[CONTRIBUTION NO. 980 FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF PITTSBURGH]

The Reaction of 1-Alkynes with Organometallic Compounds. VI.[1] The Mechanism of Reactions of Organomagnesium Compounds

BY RAYMOND E. DESSY,[2] J. H. WOTIZ AND C. A. HOLLINGSWORTH

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A mechanism has been postulated for the reaction of Grignard reagents (RMgX) with acetylenes. It is consistent with the deuterium-isotope effect, measured by comparing the rates of reaction of R′—C≡C—H and R′—C≡C—D, with the observed rate laws and agrees with previously reported data on the effects of varying R, R′ and X and the form of the organomagnesium compound according to the Schlenk equilibrium.

An investigation of the reaction

$$RMgX + R'—C{\equiv}C—H \xrightarrow[\text{ether}]{35^\circ} R'—C{\equiv}C—MgX + RH \quad (1)$$

has revealed that the rate of evolution of the hydrocarbon RH is a function of R′,[3] R and X.[4]

A correlation also had been noted between the log (reaction rate) and the decomposition potential (E_d) of the Grignard reagent.[5]

The effect of dioxane upon the rate of reaction 1 has been reported,[6] and the results have been shown to be compatible with the formulation of the Grignard reagent proposed by Schlenk.

$$2RMgX \rightleftharpoons R_2Mg + MgX_2 \quad (2)$$

The reaction

$$R_2Mg + 2R'—C{\equiv}C—H \xrightarrow[\text{ether}]{35^\circ} (R'—C{\equiv}C—)_2Mg + 2RH \quad (3)$$

has also been investigated,[6] and the effect of magnesium halide upon the rate of reaction reported.[7] The results have been shown to be compatible with the formulation of the Grignard reagent as indicated by equation 2.

The present paper reports the results of substituting a deuterium atom for the active hydrogen atom in the terminal acetylene used in the reactions 1 and 3. The rate laws obeyed by reactions 1 and

(1) Part V, *J. Org. Chem.*, **21**, 1063 (1956).

(2) National Science Foundation Predoctoral Fellow.

(3) J. H. Wotiz, C. A. Hollingsworth and R. E. Dessy, *J. Org. Chem.*, **20**, 1545 (1955).

(4) J. H. Wotiz, C. A. Hollingsworth and R. E. Dessy, THIS JOURNAL, **77**, 103 (1955).

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(6) J. H. Wotiz, C. A. Hollingsworth and R. E. Dessy, *ibid.*, **78**, 1221 (1956).

(7) J. H. Wotiz, C. A. Hollingsworth and R. E. Dessy, *J. Org. Chem.*, **21**, 1063 (1956).