Phenanthro[9,10-*c*]thiophene. Syntheses and Reactions[1]

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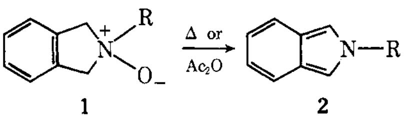
The reaction of 9-bromomethyl-10-chloromethylphenanthrene with alcoholic sodium sulfide has been found to yield not only 1,3-dihydrophenanthro[9,10-*c*]thiophene (**9**) as reported by earlier investigators, but also phenanthro[9,10-*c*]thiophene (**7**) in somewhat larger amount. Oxidation of **9** yielded the expected 1,3-dihydrophenanthro[9,10-*c*]thiophene 2-oxide (**8**) which, surprisingly, was also obtained from **7** by addition of the elements of water during attempted oxidation with *N*-bromosuccinimide in acetone–water solution. Sulfoxide **8** underwent facile elimination to afford **7** which gave a mixture of endo and exo Diels–Alder adducts on prolonged heating with *N*-phenylmaleimide in xylene.

Some time ago it was shown that isoindoline *N*-oxides (**1**, R = alkyl or aryl) lose the elements of water when pyrolyzed or treated with acetic anhydride to afford 2-substituted isoindoles (**2**) in good yield.[2] Subsequently, this method was extended to the preparation of several polynuclear heterocyclic compounds where thiophene was annelated to benzene[3] and naphthalene.[4,5] For example, Cava and his coworkers[3,4] observed that 1,3-dihydrobenzo[*c*]thiophene 2-oxide (**3**) underwent dehydration to give benzo[*c*]thiophene (isothianaphthene) (**4**) and, in similar fashion, 1,3-dihydronaphtho[1,2-*c*]thiophene 2-oxide (**5**) afforded napththo[1,2-*c*]thiophene (**6**). We now describe the first example of the reverse reaction: namely, the addition of the elements of water to phenanthro[9,10-*c*]thiophene (**7**) to form 1,3-dihydrophenanthro[9,10-*c*]thiophene 2-oxide (**8**). Furthermore, two new syntheses of **7** are reported together with a clarification of the results of the reaction used by earlier investigators[6] to prepare 1,3-dihydrophenanthro[9,10-*c*]thiophene (**9**).



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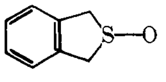

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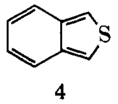

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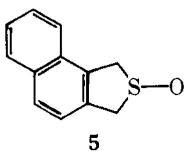

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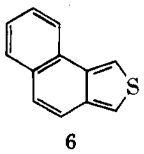

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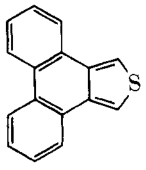

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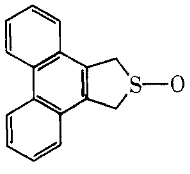

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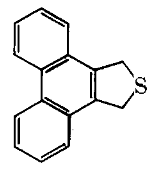

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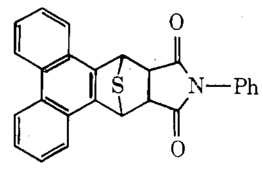

10, exo
11, endo

In connection with our general study of the chemistry of *o*-quinonoid heteroaromatic compounds and because of a specific interest in the effect of benzannelation[7] on the stability of these heterocycles, we had occasion recently to prepare 1,3-dihydrophenanthro[9,10-*c*]thiophene (**9**). Stille and Foster[6] had earlier described the synthesis of **9** by treatment of 9-bromomethyl-10-chloromethylphenanthrene with ethanolic sodium sulfide; they reported **9** to have mp 164–166°. Using their procedure we observed the formation of both phenanthro[9,10-*c*]thiophene (**7**) and the expected 1,3-dihydro derivative **9**. Similar results were obtained when the cyclization was subsequently repeated with 9,10-bis(bromomethyl)phenanthrene. Chromatographic separation of the reaction mixture afforded **7** (13%), mp 168–169°, and **9** (10%), mp 180–181°. The uv and nmr spectra of **7** and **9** served to distinguish these compounds. The uv spectrum of **9** was strikingly similar to that of 9,10-dimethylphenanthrene while **7**, as expected, exhibited absorption at longer wavelength due to the additional conjugation. Phenanthro[9,10-*c*]thiophene (**7**) showed only low-field absorption for aromatic protons in its nmr spectrum whereas the corresponding dihydro derivative **9** displayed typical benzylic signals in addition to peaks for aromatic protons.

To confirm further that the lower melting component of the product mixture is indeed phenanthro[9,10-*c*]thiophene (**7**), it was compared with an authentic sample (mp 168–169°) whose preparation was first reported by Hinsberg.[8] Both specimens were identical in all respects; hence, it is almost certain that the material melting at 164–166° and believed by Stille and Foster[6] to be 1,3-dihydrophenanthro[9,10-*c*]thiophene (**9**) was actually a mixture of **7** and **9**. The origin of **7** in the reaction of the 9,10-bis(halomethyl)phenanthrenes with sodium sulfide is obscure at this time, but it is possible that it is formed from **9** by oxidation during work-up of the reaction product. Compound **7**, like the previously reported nitrogen analog,[7,9] is an exceptionally stable *o*-quinonoid heterocycle and survives prolonged standing at room temperature. It will react slowly with *N*-phenylmaleimide (NPM), as noted below, suggesting that any difference in stability between **7** and **9** may be quite small. If this is the case, it would be reasonable to expect that oxidation of **9** to **7** should occur under relatively mild conditions. In this connection, it is interesting to note that the very reactive benzo[*c*]thiophene (**4**) was first synthesized by high-temperature catalytic dehydrogenation of its considerably more stable 1,3-dihydro derivative.[10]

Oxidation of sulfide **9** with sodium periodate in aqueous ethanol afforded the expected 1,3-dihydrophenanthro-

[9,10-*c*]thiophene 2-oxide (**8**) in 92% yield. When subjected to these same conditions, phenanthro[9,10-*c*]thiophene (**7**) was found to be inert, but quite surprisingly it underwent addition of the elements of water when treated with *N*-bromosuccinimide in aqueous acetone to give sulfoxide **8** in 77% yield. This material was shown by mixture melting point determination and spectral comparison to be identical with a specimen prepared from sulfide **9**. Using the procedures of Cava and coworkers[4] for effecting the dehydration of sulfoxides, we found that treatment of **8** with acetic anhydride or, more conveniently, pyrolysis of **8** in the presence of neutral alumina afforded phenanthro[9,10-*c*]thiophene (**7**) in 43% yield.

The high degree of stability possessed by **7** necessitated the use of rather drastic conditions to effect the Diels–Alder reaction; addition to NPM occurred only after a solution of the reactants in xylene was heated at reflux for 3 days. The reaction product was separated by column chromatography into two stereoisomeric adducts, exo isomer **10** (67%) and endo isomer **11** (9%). The assignment of structures **10** and **11** to the adducts was made on the basis of their nmr spectra which are similar in many respects to those of the related exo and endo NPM adducts of naphtho[1,2-*c*]thiophene.[4]

Experimental Section

Melting points were determined on a Mel-Temp melting point apparatus and are corrected. Infrared spectra were recorded on a Perkin-Elmer Model 137 Infracord. Ultraviolet spectra were obtained on a Cary 17 spectrophotometer. Nuclear magnetic resonance spectra were taken on Varian Model T-60 and HA-100 spectrometers. Elemental analyses and molecular weight determinations were performed by Dornis and Kolbe Microanalytical Laboratory, Mülheim, Germany.

Reaction of 9-Bromomethyl-10-chloromethylphenanthrene with Sodium Sulfide. Phenanthro[9,10-*c*]thiophene (7) and 1,3-Dihydrophenanthro[9,10-*c*]thiophene (9). A solution of 19.0 g (0.08 mol) of sodium sulfide nonahydrate in 500 ml of ethanol was heated at reflux for 48 hr in an apparatus fitted with a Soxhlet extractor holding 5.0 g (0.015 mol) of 9-bromomethyl-10-chloromethylphenanthrene.[6] The reaction mixture was poured into 1 l. of water and the resulting suspension was collected by filtration. The crude solid was extracted with five 100-ml portions of boiling ethanol and the combined extracts were evaporated *in vacuo* to give 1.1 g of yellow solid. Chromatography on a column of silica gel with petroleum ether as eluent gave two fractions. The first fraction, on recrystallization from benzene–cyclohexane, afforded 450 mg (13%) of **7** as colorless, felted needles, mp 168.5–169°; uv λ_{max} (EtOH) (ϵ) 253 nm (58,800), 262 (58,000), 275 (7100), 290 (7900), 305 (7100), 320 (4700), and 334 (2000); nmr ($CDCl_3$) δ 7.20–8.40 (m).

Anal. Calcd for $C_{16}H_{10}S$: C, 82.01; H, 4.30; S, 13.68; mol wt, 234. Found: C, 82.06; H, 4.28; S, 13.60; mol wt, 232 (osmometry).

The second fraction from the column was recrystallized from benzene–petroleum ether to give 350 mg (10%) of **9** as colorless needles: mp 180–181°; uv λ_{max} (EtOH) (ϵ) 254 nm (55,000), 277 (11,000), 287 (8340), and 300 (9100); nmr ($CDCl_3$) δ 6.9–8.1 (m, 8, aromatic) and 4.0 (s, 4, benzylic).

Anal. Calcd for $C_{16}H_{12}S$: C, 81.31; H, 5.12; S, 13.57; mol wt, 236. Found: C, 81.22; H, 5.15; S, 13.57; mol wt, 239 (osmometry).

Phenanthro[9,10-*c*]thiophene (7) by the Hinsberg Condensation.[8] A solution of 6.0 g (0.029 mol) of phenanthrenequinone and 6.0 g (0.029 mol) of diethyl thiodiglycolate in 600 ml of benzene was prepared by warming the mixture to 70°. This solution was cooled to 40° and added to a solution of 6.0 g (0.11 mol) of sodium methoxide in 45 ml of methanol which was immersed in an ice bath. The resulting dark green solution was stirred under an atmosphere of dry nitrogen at room temperature for 5 days and then added to 1 l. of water. The reddish-orange two-phase mixture was concentrated at reduced pressure to a volume of 300 ml and filtered to remove 2.1 g (35%) of unreacted phenanthrenequinone. Acidification of the filtrate with hydrochloric acid afforded 2.5 g of an orange solid which was collected by filtration; recrystallization from aqueous ethanol gave 1.70 g of phenanthro[9,10-*c*]thiophene-1,3-dicarboxylic acid, mp 240° dec.[11] Decarboxylation of the diacid by sublimation at 160° (1.0 mm) or by heating at 260° until evolution of carbon dioxide ceased afforded 0.90 g of crude **7**. Chromatography of this material on silica gel with benzene as eluent and subsequent recrystallization from benzene gave a pure sample of **7**, mp 168–169°, identical with the specimen prepared above by the method of Stille and Foster.

1,3-Dihydrophenanthro[9,10-*c*]thiophene 2-Oxide (8). A. From Compound 9. To a boiling solution of 60 mg (0.26 mmol) of **9** in 15 ml of ethanol was added a solution of 64 mg (0.30 mmol) of sodium periodate in 2.5 ml of water. The resulting solution was heated at reflux for 20 hr, cooled, diluted by addition of 25 ml of water, and extracted with two 25-ml portions of chloroform. The combined chloroform extracts were dried over magnesium sulfate and concentrated under reduced pressure to yield 80 mg of crude solid, mp 210–215°. Recrystallization from benzene–hexane of the material thus obtained gave 60 mg (92%) of pure **8**, mp 215–216°. This compound was shown by mixture melting point determination and ir and nmr spectral comparison to be identical with **8** prepared below from **7**.

B. From Compound 7. A solution of 1.10 g (4.7 mmol) of **7** in 175 ml of 85% aqueous acetone was warmed to 50° and maintained at this temperature while a solution of 0.91 g (5.1 mmol) of *N*-bromosuccinimide in 40 ml of 50% aqueous acetone was added with stirring over a 10-min period. The resulting yellow solution was stirred for 1 hr at room temperature and the acetone was then removed under reduced pressure. Filtration gave 1.1 g of light yellow needles, mp 197–202°. Recrystallization from benzene–hexane yielded 0.91 g (77%) of **8** as colorless needles: mp 215–216°; ir (mull) 1050 cm^{-1} (SO); uv λ_{max} (EtOH) (ϵ) 255 nm (53,500), 277 (8700), 287 (6300), 300 (7900); nmr ($CDCl_3$) δ 7.3–7.9 (m, 8, aromatic), 4.65 (s, 4, benzylic).

Anal. Calcd for $C_{16}H_{12}OS$: C, 76.16: H, 4.79; S, 12.71. Found: C, 76.10; H, 4.82; S, 12.76.

Pyrolysis of Sulfoxide 8. Formation of 7. An intimate mixture of 1.0 g (4.0 mmol) of **8** and 300 mg of neutral alumina (Merck, activity grade I) was heated in a sublimation apparatus at 180° (25 mm). The colorless crystals which collected on the cold finger were recrystallized from benzene to give 0.40 g (43%) of **7**, mp 167–168°. This material was shown to be identical with the samples of **7** prepared above.

Diels–Alder Reaction of 7 with *N*-Phenylmaleimide. Formation of Adducts 10 and 11. A solution of 900 mg (3.8 mmol) of **7** and 700 mg (4.0 mmol) of *N*-phenylmaleimide in 100 ml of dry xylene was heated under reflux for 72 hr. Evaporation of the resulting suspension *in vacuo* afforded 1.6 g of crude solid which was dissolved in benzene and chromatographed on silica gel using benzene as eluent. Three fractions were obtained. The first fraction gave 350 mg of a mixture consisting of unreacted **7** and *N*-phenylmaleimide. The second fraction yielded 1.03 g (67%) of exo adduct **10**, as a white solid, mp 253–255°, which on recrystallization from benzene–petroleum ether afforded an analytically pure sample: mp 254.5–255° dec; nmr (DMSO-d_6) δ 7.20–8.95 (m, 13, aromatic), 5.90 (s, 2, bridgehead), and 3.58 (s, 2, α to imide C=O).

Anal. Calcd for $C_{26}H_{17}NO_2S$: C, 76.64; H, 4.20; N, 3.44; S, 7.87; mol wt, 408. Found: C, 76.45; H, 4.15; N, 3.44; S, 7.86; mol wt, 410 (osmometry).

The third fraction gave 135 mg (9%) of endo adduct **11**. Recrystallization from benzene–petroleum ether yielded 110 mg of pure **11** as colorless plates: mp 225–226°; nmr (DMSO-d_6) δ 7.60–8.89 (m, 11, aromatic), 6.95 (m, 2, aromatic H ortho to N), 5.85 (m, 2, bridgehead), and 4.48 (m, 2, α to imide C=O).

Anal. Calcd for $C_{26}H_{17}NO_2S$: C, 76.64; H, 4.20; N, 3.44; S, 7.87; mol wt, 408. Found: C, 76.43; H, 4.42; N, 3.49; S, 7.85; mol wt, 410 (osmometry).

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Registry No.—**7**, 235-95-0; **8**, 53449-54-0; **9**, 53449-55-1; **10**, 53449-56-2; **11**, 53495-82-2; 9-bromomethyl-10-chloromethylphenanthrene, 35974-44-8; sodium sulfide, 16721-80-5; phenanthrenequinone, 84-11-7; diethyl thiodiglycolate, 925-47-3; phenanthro[9,10-*c*]thiophene-1,3-dicarboxylic acid, 19799-45-2; *N*-bromosuccinimide, 128-08-5; *N*-phenylmaleimide, 941-69-5.

References and Notes

(1) Presented in part at the Fifth Northeast Regional Meeting of the American Chemical Society, Rochester, N.Y., Oct 1973.

(2) For a review, see J. D. White and M. E. Mann, *Advan. Heterocycl. Chem.*, **10**, 119 (1969).

(3) M. P. Cava and N. M. Pollack, *J. Amer. Chem. Soc.*, **88**, 4112 (1966).

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(7) J. Kopecký, J. E. Shields, and J. Bornstein, *Tetrahedron Lett.*, 3669 (1967); J. E. Shields and J. Bornstein, *J. Amer. Chem. Soc.*, **91**, 5192 (1969).
(8) O. Hinsberg, *Chem. Ber.*, **43**, 901 (1910). For a review of the Hinsberg thiophene ring synthesis, see D. E. Wolf and K. Folkers, *Org. React.*, **6**, 410 (1951).
(9) J. S. Dewar, A. J. Harget, N. Trinajstić, and S. D. Worley, *Tetrahedron*, **26**, 4505 (1970).
(10) R. Mayer, H. Kleinert, S. Richter, and K. Gewald, *J. Prakt. Chem.*, **20**, 244 (1963).
(11) Hinsberg, ref 8, p 903, reported the diacid decomposed at 270°, but noted this value depended on the purity of the compound and the method of heating.

Acid-Catalyzed Rearrangements of Humulene[1]

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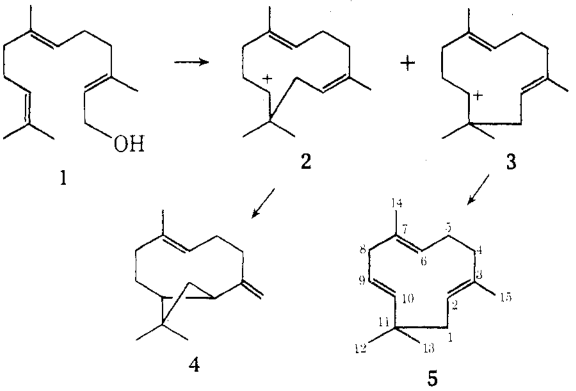
Upon extended treatment with acid, the sesquiterpene humulene yielded 20–25% α-caryophyllene alcohol and 70–75% mainly a new bicyclic sesquiterpene hydrocarbon. The structure of the material, as well as a series of its precursors, was established. The mechanism of the transformation was shown to proceed *via* a series of stepwise rearrangements.

In recent years considerable interest has been directed toward the biogenesis, rearrangement, and synthesis of polyisoprenoid natural products. The finding of the enzymatically induced cyclization of squalene epoxide to lanosterol called attention to the high degree of specificity of a polycyclization initiated by formation of a carbonium ion. The *in vitro* equivalent of the process, *i.e.*, regiospecific carbonium ion generation, has been utilized by Johnson[2] to convert polyolefins to steroids, by Marshall[3] to convert bicyclo[4.3.1]decanes to hydroazulenes, and by studies in this laboratory[4] of the acid catalyzed rearrangement of the cyclopropyl-ene system in the sesquiterpene thujopsene to yield sesquiterpenes of the widdrene and chamigrene series.

In the Hendrickson biogenetic hypothesis for bicylic and tricyclic sesquiterpenes,[5] key intermediates were the eleven-membered ring carbonium ions **2** and **3**, respectively.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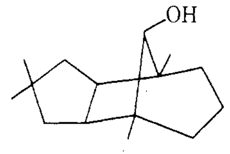
These ions were suggested to be the intermediates in the transformation of farnesol (**1**) to caryophyllene (**4**) and humulene (**5**). It was of particular interest that the ion **3** was related to humulene (**5**) by simple loss of a proton and such a relationship called attention to the possibility of the acid catalysis of the reverse process, **5** to **3**.

The acid-catalyzed rearrangement of α-humulene, itself, was first reported by Nickon[6] who reported that the hydrocarbon upon treatment with sulfuric acid in ether gave rise to alcohol **6** in 12–24% yield. The present studies were directed toward a more controlled reaction and investigation of all the products of the reaction. It was found that humulene (>97% pure) in refluxing dioxane–water containing 0.02 *M* perchoric acid yielded 20–25% of alcohol **6** (stable under the reaction conditions) and that the 75–80% of the remaining material was more than 90% of one hydrocarbon. This major material was isolated and its structure established.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The product (**7**) was isomeric with humulene (mass spectrum) and possessed an s-trans conjugated diene chromophore (uv max 245 nm, ε 12,000). The nmr spectrum showed signals for one vinyl hydrogen atom, one vinyl methyl group, one quaternary methyl group, and an isopropyl group. The presence of the isopropyl group was further confirmed by double resonance studies and by an M − 43 peak (93% of base peak) in the mass spectrum. These data indicated the absence of any additional double bond in the structure and with the conjugated diene accounting for only two degrees of ursaturation, the hydrocarbon **7** must be bicyclic. Furthermore, the quaternary methyl group most likely was at an angular position.

The material was dihydrogenated and vpc analysis of the crude reduction product showed the presence of 79% of hydrocarbon **8**, 17% of hydrocarbon **9**, and 4% of starting material. If the reaction mixture was allowed to remain under hydrogenation conditions for an extended period (6–8 hr) practically no further uptake of hydrogen occurred but the only product obtained was **9**. The isomeric dihydro derivatives were isolated by preparative vpc. The nmr spectrum of **8** showed signals for one vinyl proton, an isopropyl group, an angular methyl group, and a new secondary methyl group but no vinyl methyl group. The final product **9** which was resistant to further hydrogenation showed no vinyl proton signals in the nmr spectrum but did show double bond absorption in the Raman spectrum. This unsaturated bond cannot be between two rings since there is an angular methyl group. Furthermore, since there is no vinyl methyl group, it follows that the isopropyl group must be on the tetrasubstituted double bond.

Treatment of hydrocarbon **8** with osmium tetroxide yielded diol **10** which was cleaved with lead tetraacetate to give a keto acid **11a**. The ir spectrum of the keto acid and its methyl ester indicated the presence of a five-membered