colorized. On concentration there was obtained 0.5 g. of the pyridazine, m.p. 260°.

Anal. Calcd. for $C_{18}H_{12}ON_2$: C, 79.41; H, 4.42; N, 10.33. Found: C, 79.45; H, 4.72; N, 10.93.

This phthalazine was found to be identical with an authentic sample of the phthalazine from 2-(1-naphthoyl)-benzoic acid (m.p. and mixed m.p.). Both products afforded 2-(1-naphthoyl)-benzoic acid on acid hydrolysis.

Acknowledgment.—The authors wish to express their appreciation to J. M. Tinker and M. A. Perkins of this Laboratory and to Prof. L. F. Fieser of Harvard University for many helpful discussions during the course of this work.

WILMINGTON 99, DEL.

[CONTRIBUTION FROM THE MCPHERSON CHEMICAL LABORATORY, THE OHIO STATE UNIVERSITY]

The Synthesis and Resolution of 1,12-Dimethylbenzo[c]phenanthrene-5-acetic Acid[1]

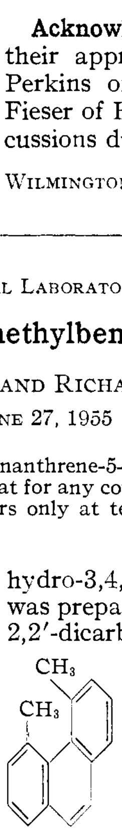
BY MELVIN S. NEWMAN AND RICHARD M. WISE

RECEIVED JUNE 27, 1955

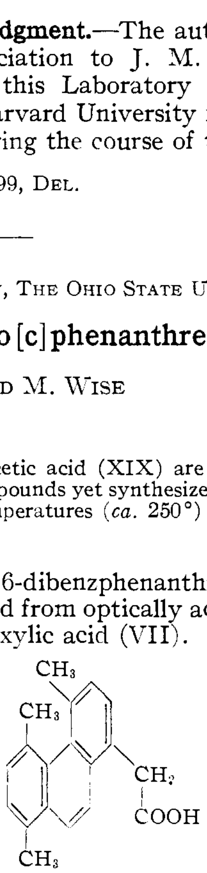
The synthesis and resolution of 1,12-dimethylbenzo[c]-phenanthrene-5-acetic acid (XIX) are described. The optical stability of the enantiomorphic forms of XIX is greater than that for any compounds yet synthesized which owe their optical activity to intramolecular overcrowding. Racemization occurs only at temperatures (*ca.* 250°) at which decomposition begins.

It was predicted[2] in 1940 that molecules containing the 4,5-dimethylphenanthrene system, I, might be capable of optical resolution due to the effect of the interference of the methyl groups in the hindered positions. Three alternatives were suggested relative to the geometry of the molecule as a whole in this system[2]: "(1) the methyl groups lie bent away from each other but in the same plane as the aromatic rings; (2) the aromatic rings are distorted in some way; (3) the methyl groups are bent out of the plane of the aromatic rings." If the first alternative were correct, there would be no asymmetry and the molecule would not be resolvable. However, if the second or third alternative, or a combination of the two, were correct, the molecule would be capable of resolution.

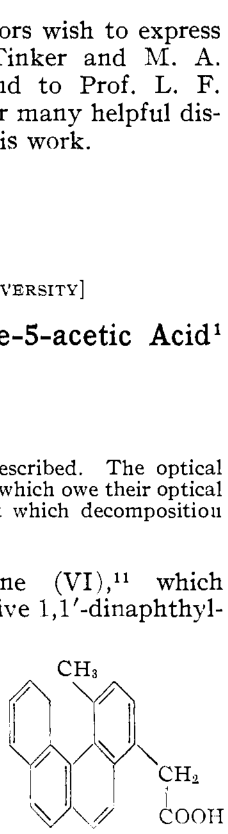
That (2) or (3) is the correct explanation has been shown by the successful resolution of 4,5,8-trimethyl-1-phenanthrylacetic acid (II),[3] 4-(1-methylbenzo[c]phenanthryl)-acetic acid (III)[4] and 4′,4″,6′,6″ - tetramethyl - 3,4,5,6 - dibenzphenanthrene-9,10-dicarboxylic acid (IVb).[5] Although the nitrogen-containing compound, 1,10-dimethylbenzo[c]cinnoline (Va), could not be resolved,[6,7] the corresponding 4,7-diamino-1,10-dimethylbenzo-[c]cinnoline (Vb) was resolved.[8] Other compounds showing this type of optical activity[9] and containing no methyl groups also have been synthesized and resolved; *e.g.*, 3,4,5,6-dibenzphenanthrene-9,10-dicarboxylic acid (IVa)[10] and 9,10-dihydro-3,4,5,6-dibenzphenanthrene (VI),[11] which was prepared from optically active 1,1′-dinaphthyl-2,2′-dicarboxylic acid (VII).



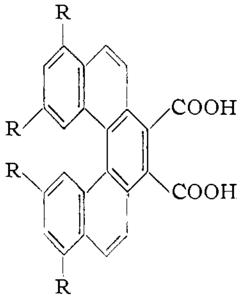
I



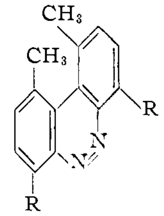
II



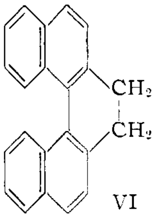
III



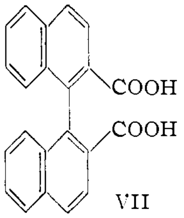
IVa, R = H
b, R = CH_3



Va, R = H
b, R = NH_2



VI



VII

Compound VI is an example of a molecule which bridges the gap between the biphenyl type and the intramolecular overcrowding type of optical activity.

The recent X-ray crystallographic investigation of the structures of overcrowded aromatic compounds by Schmidt and co-workers[12-15] has clari-

---

[1] The material herein presented is taken from the Ph.D. thesis of R. M. Wise, Ohio State, 1955. Allied Chemical and Dye Fellow, 1952–1953. This work was also supported in part by a grant from the Office of Ordnance Research and Development, contract DA-33-019-ord-1240.

[2] M. S. Newman, THIS JOURNAL, **62**, 2295 (1940).

[3] M. S. Newman and A. S. Hussey, *ibid.*, **69**, 3023 (1947).

[4] M. S. Newman and W. B. Wheatley, *ibid.*, **70**, 1913 (1948).

[5] F. Bell and D. H. Waring, *J. Chem. Soc.*, 2689 (1949).

[6] G. Wittig and O. Stichnoth, *Ber.*, **68**, 928 (1935).

[7] G. Wittig and H. Zimmermann, *ibid.*, **86**, 629 (1953).

[8] W. Theilacker and F. Baxmann, *Ann.*, **581**, 117 (1953).

[9] The term adopted for the phenomenon of this type of optical activity is "optical activity due to intramolecular overcrowding," see ref. 5. Originally it was called "optical activity of the 4,5-phenanthrene type," ref. 3.

[10] F. Bell and D. H. Waring, *Chemistry and Industry*, **27**, 321 (1949). The optical activity was shown only by the racemization of the morphine salt. The free acid obtained showed no rotation.

[11] D. M. Hall and E. E. Turner, *ibid.*, **31**, 1177 (1953).

[12] E. Harnick, F. H. Herbstein, G. M. J. Schmidt and F. L. Hirshfeld, *J. Chem. Soc.*, 3288 (1954).

[13] E. Harnik and G. M. J. Schmidt, *ibid.*, 3295 (1954).

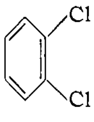
[14] F. H. Herbstein and G. M. J. Schmidt, *ibid.*, 3302 (1954).

[15] F. H. Herbstein and G. M. J. Schmidt, *ibid.*, 3314 (1954).

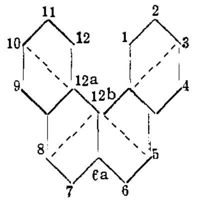
fied the question of whether the asymmetry in an overcrowded molecule is caused by (2) distortion of the aromatic rings or (3) non-coplanar methyl groups (or a combination of the two). An approach of 3.0 Å. or less between non-bonded atoms frequently results in repulsion forces sufficient to produce detectable distortions within a molecule. The X-ray workers have found that this compression can be relieved both by a bending of the exocyclic bonds of the aromatic ring and by the assumption of a non-planar configuration by the aromatic system. The ultraviolet spectra fail to distinguish between the possibilities although the loss of fine structure in the wave length region 310 to 360 mμ in overcrowded polynuclear compounds has been attributed to intramolecular overcrowding.[16]

Four general types of overcrowded molecules are considered by these investigators[12]: group I, substituted benzenes such as *o*-dichlorobenzene (VIII): group II, aromatic polycyclics such as benzo[c]phenanthrene (IX): group III, tetraphenylethylenes bridged at all 2-positions such as dianthrone (X): group IV, molecules containing adjacent phenyl rings such as 1,4,5,8-tetraphenylnaphthalene (XI).

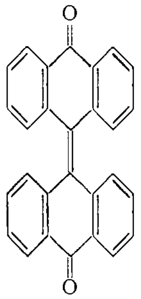
A crystallographic analysis of octamethylnaphthalene[17] has shown that the 1- and 8-methyl carbon atoms are displaced from the mean molecular plane by 0.73 Å. and the 2-methyl carbon atoms are displaced from the mean plane by 0.25–0.40 Å. It is not definitely established whether the naphthalene ring remains flat or is somewhat twisted. Hence, it is not known in which of the four groups it should be placed.



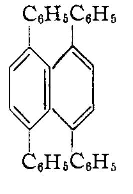
VIII



IX



X



IX

A planar model of benzo(c)phenanthrene (IX) shows a distance of 2.4 Å. between the carbon atoms in the 1- and 12-positions. This distance is much shorter than that found between non-bonded carbon atoms in any of the overcrowded molecules.[18] Therefore, the ring system must be distorted in order to relieve this strain.[19] A few of the points of interest revealed in the crystallographic study are indicated in formula IX. Double bonds are omitted as they would be without the usual significance since the bending of the rings affects C–C bond distances and bond orders. For example, the bond distance between atoms 6a and 12b is 1.55 Å. In the valence bond treatment using a planar model this bond would have a large double bond character. The rings are bent along the axes indicated by the dotted lines. Furthermore "The crystallographic evidence indicates resolution of 3,4-benzphenanthrene into (+)- and (−)-crystals. We have not yet succeeded in growing crystals either of large enough size or with sufficiently well-developed ***hkl*** faces to take advantage of this spontaneous resolution for the measurement of the optical activity of 3,4-benzphenanthrene."[14]

It is not known how the structure of benzo(c)phenanthrene in solution may vary from that in the solid state. The relatively high melting point[4] and high heat of fusion[20] of 1-methylbenzo(c)phenanthrene compared with the other monomethyl benzo(c)phenanthrenes show that the crystal forces must be quite strong since, thermodynamically, this compound should be less stable than the others because of its greater strain. The intermolecular van der Waals forces in the solid state are probably important in determining the physical properties and structure of these molecules.

As a result of the X-ray crystallographic work it is seen that the asymmetry introduced into a molecule by intramolecular overcrowding is caused by a combination of the two alternatives previously mentioned; that is, by a folding of the benzene rings, and, if there are groups present in the hindered positions, by the assumption of non-coplanar positions for these groups. How much the exocyclic groups may be bent before the aromatic system becomes non-planar is not known.

Optical activity due to intramolecular overcrowding can be compared with that which certain well-known biphenyl compounds exhibit.[21] In both cases the optical stability depends on the steric requirements of the groups in the interfering positions. The larger the groups are, the more difficult it is for racemization to occur. However, there is an important difference. In the biphenyl series the phenyl rings themselves almost certainly remain flat and coaxial although they are not coplanar.[4] The strain introduced by bulky groups in the *ortho* positions is relieved by rotation of the rings on the single bond connecting them. In overcrowded molecules the strain introduced by the groups in the crowded positions is relieved by a folding of the aromatic rings and by bending of the substituents out of the plane of the ring.

All of the compounds possessing optical activity due to intramolecular overcrowding prepared thus

---

(16) R. N. Jones, THIS JOURNAL, **63**, 313 (1941).

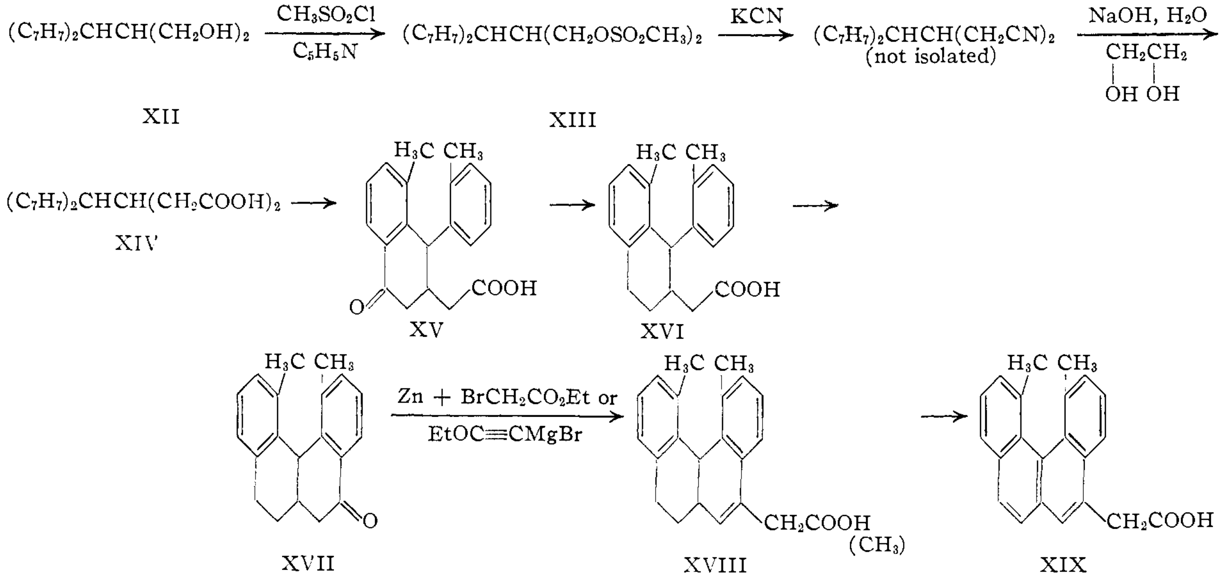
(17) D. M. Donaldson and J. M. Robertson, *J. Chem. Soc.*, 17 (1953).

(18) The authors do not consider the hydrogens at these positions since they are not detectable by X-ray studies.

(19) The original paper[14] should be consulted for details of structure of IX.

(20) R. R. Brattain, Shell Development Co., Emeryville, Calif., unpublished results.

(21) See R. L. Shriner, R. Adams and C. S. Marvel in Gilman, "Organic Chemistry," Vol. I, 2nd Ed., John Wiley and Sons, Inc., New York, N. Y., 1943, pp. 343–370, and G. M. Badger, "The Structures and Reactions of the Aromatic Compounds," Cambridge University Press, London, England, 1954, pp. 411 ff.



far readily racemize at room temperature with the exception of the non-aromatic compound VI and possibly the cinnoline derivative Vb. It was not stated[8] how stable Vb is at room temperature, but on warming the compound for one hour at 60° in methanol, complete racemization occurred. The molecule VI is reported[11] to be optically stable in benzene at 60° and slowly racemized in benzene in a sealed tube at 100°. However, the fully aromatic compound IVa containing the same basic ring structure as VI is highly optically unstable[11] as the morphine salt rapidly racemizes in solution at room temperature to produce inactive acid. The attempted synthesis of 7,10,11,14-tetramethyldibenzo(c,g)phenanthrene-3,4-dicarboxylic acid,[10] which should be optically stable, failed.

In this paper we report the synthesis and resolution of 1,12-dimethylbenzo[c]phenanthrene-5-acetic acid (XIX). The optically active acid and its methyl ester are highly stable from the point of view of optical activity but unexpectedly are thermally unstable.

The synthesis of XIX follows that by which 1,12-dimethylbenzo[c]phenanthrene was previously prepared,[22] but significant improvements have been made. Previously the bishomologation of ethyl 2,2'-dimethylbenzhydrylmalonate to β-(2,2-dimethylbenzhydryl)-glutaric acid (XIV) was accomplished by two methods: a double Arndt–Eistert reaction (yield 40%); and by reduction to 2-(2,2'-dimethylbenzhydryl)-propane-1,3-diol (XII) successive conversion of XII to the bis-*p*-nitrobenzenesulfonate and the corresponding dinitrile, which was not purified but hydrolyzed directly to XIV (22% over-all yield). In this work, the over-all yield to the glutaric acid XIV was improved to 85% as shown in the chart, XII to XIV, and the further steps which led to the desired acid XIX are shown.

The acid XIX was partly resolved by forming a salt with cinchonidine and recrystallizing the latter from ether. An acid with maximum rotation was obtained by recrystallization of the acid regenerated from the partly resolved cinchonidine salt. The active acid XIX was converted to the methyl ester with diazomethane for racemization experiments when it was found that the acid was quite optically stable when heated for seven days in refluxing mesitylene but suffered some decomposition. The ester proved optically stable on heating under nitrogen for extended periods at temperatures up to 250°. At 250° signs of decomposition accompanied slight racemization. After heating at 300° for 30 minutes, the ester, recovered after two chromatographic purifications, was optically inactive. Extensive decomposition, as evidenced by darkening, had occurred. Thus for the first time, a compound which owes its optical activity to intramolecular overcrowding has been shown to be optically stable at ordinary and reasonably high temperatures.

Experimental[23]

2-(2,2'-Dimethylbenzhydryl)-1,3-propanediol-bis-(methanesulfonate) (XIII).—To a solution of 114.0 g. (0.422 mole) of the diol XII[24] in 600 ml. of dry pyridine cooled to −5° was added dropwise with stirring over a period of one-half hour 130 ml. of methanesulfonyl chloride. After standing for four hours in the cooling bath (much pyridine hydrochloride crystallized) the mixture was poured into 2.5 l. of water with stirring. The oil which separated readily solidified. This was separated by filtration, washed well with dilute hydrochloric acid and water, and dried to give 174.2 g. (96.6%) of cream-colored XIII. The analytical sample, crystallized four times from absolute ethanol, melted at 134.1–135.1°.

Anal. Calcd. for $C_{20}H_{26}O_6S_2$: C, 56.3; H, 6.2. Found: C, 56.6, 56.5; H, 6.2, 6.3.

β-(2,2'-Dimethylbenzhydryl)-glutaric Acid (XIV).—To 174 g. of the ester XIII, dissolved in 900 ml. of dimethylformamide, was added 114 g. of potassium cyanide and 2.3 g. of potassium iodide in 340 ml. of water. After heating on a water-bath at 90–100° with stirring for three hours the solution was poured into three liters of ice-water. The tan sticky ball which formed solidified after two hours and turned pink when dry.

This crude dinitrile and 111 g. of sodium hydroxide were

---

(22) M. S. Newman and M. Wolf, THIS JOURNAL, **74**, 3225 (1952).

(23) All melting points are corrected. Analyses by Galbraith Laboratories, Knoxville, Tenn.

(24) Prepared in quantitative yield by reduction of ethyl 2,2',-dimethylbenzhydrylmalonate with lithium aluminum hydride; ref. 22.

suspended in 1100 ml. of ethylene glycol. Ammonia was vigorously evolved upon heating the mixture to reflux. The condenser was removed until the temperature of the dark red solution rose to 185°. After twenty minutes at this temperature the bulky disodium salt began to precipitate and in a few minutes it almost filled the flask. The mixture was refluxed for one more hour, cooled and filtered. The disodium salt was dissolved in water and the solution extracted with ether–benzene. Acidification of the aqueous solution yielded 119.4 g. (86.5%) of colorless acid XIV m.p. 205–207°. The glycol filtrate was worked up to yield 11.5 g. of tan acid. Recrystallization of this from benzene-acetone gave a first crop of colorless crystals, m.p. 207.5–208.5°,[25] and a second crop of 0.53 g., m.p. 202.0–203.5°. A total of 127 g. (91.8% based on malonate) of good XIV was obtained.

1,2,3,4-Tetrahydro-8-methyl-4-oxo-1-*o*-tolyl-2-naphthaleneacetic Acid (XV).—This was prepared by cyclization of the diacid chloride of XIV with stannic chloride as reported in the literature.[22]

It was found that treatment of XIV with polyphosphoric acid[26] at 130° for 45 minutes with rapid stirring afforded the double cyclization product 5,6,6a,7,8,12b-hexahydro-1,12-dimethylbenzo(c)phenanthrene-5,8-dione in 82% yield (once recrystallized).[27]

1,2,3,4-Tetrahydro-8-methyl-1-*o*-tolyl-2-naphthaleneacetic Acid (XVI). (A) Wolff–Kishner Reduction (Huang-Minlon Modification.[28]—A mixture of 7.00 g. (0.0227 mole) of the keto-acid XV, 60 ml. of diethylene glycol, 4.9 g. of potassium hydroxide and 15 ml. of 95% hydrazine was refluxed for 1.5 hours at 148°. The condenser was removed and the temperature of the pale yellow solution allowed to rise to 198° at which temperature the refluxing was continued for four more hours. The cooled purple solution was diluted with 60 ml. of water, extracted with ether–benzene to remove the color, and the alkaline solution acidified to afford 6.09 g. (91.2%) of pale pink crystalline acid XVI, m.p. 165–168°. A recrystallization from acetone yielded a first crop of 4.63 g. of colorless rhombic crystals, m.p. 168.6–169.8°, a second crop of 1.03 g., m.p. 165–167°, and a third crop of 0.18 g., m.p. 166–168° (87.4%). Mixtures of these three crops with XV melted at 150–163°. The analytical sample, crystallized three times from acetone, melted at 168.9–169.9°.

Anal. Calcd. for $C_{20}H_{22}O_2$: C, 81.6; H, 7.5. Found: C, 81.5, 81.8; H, 7.6, 7.7.

(B) Clemmensen Reduction (Martin Modification).[29]—The reaction was carried out in the usual manner on 4.00 g. of XV. A few ml. of glacial acetic acid was added to increase the solubility of XV in the aqueous layer. There was obtained 2.87 g. (74.9%) of recrystallized XVI. A mixed melting point of the acids prepared by methods A and B gave no depression.

5,6,6a,7,8,12b-Hexahydro-5-oxo-1,12-dimethylbenzo(c)-phenanthrene (XVII).—A mixture of 30.00 g. (0.1019 mole) of finely ground XVI and 350 g. of polyphosphoric acid was heated with rapid stirring for three hours in a glycerol-bath at 130–135°. The color changed gradually from colorless to dark green. The mixture was poured into ice and water and the product was extracted with ether–benzene. The organic layer was washed with water–5% potassium carbonate solution, and worked up to give 24.5 g. of very viscous orange-red neutral residue. Acidification of the carbonate extract afforded 5.0 g. (16%) of XVI. Upon distillation of the residue there was obtained 17.6 g. (62.5%) of pale yellow viscous ketone XVII, b.p. 180–200° at 0.15 mm., which yielded crystalline material from 95% alcohol. The crude distillate was suitable for the next step. The analytical sample, crystallized three times from 95% alcohol, formed fine colorless needles, m.p. 117.8–118.6°.

Anal. Calcd. for $C_{20}H_{20}O$: C, 86.9; H, 7.3. Found: C, 86.9, 87.1; H, 7.2, 7.4.

The oxime, crystallized four times from benzene, melted with decomposition at 210–224° as the rate of heating was varied.

Anal. Calcd. for $C_{20}H_{21}ON$: N, 4.8. Found: N, 4.8.

When the cyclization was carried out at higher temperatures such as 170–180° for shorter periods of time, impure products were obtained.

Cyclization of the acid chloride of XVI with aluminum chloride in tetrachloroethane at 25° for 44 hours afforded XVII in only 39% yield. No cyclization of the acid chloride with anhydrous stannic chloride in tetrachloroethane at 25° for 25 minutes occurred and keto acid was recovered. The results of a single attempt at ring closure of XVI with hydrogen fluoride were not promising.

1,12-Dimethylbenzo(c)phenanthrene-5-acetic Acid (XIX).—To 25 g. of 20-mesh granular zinc (previously washed with 2% hydrochloric acid, water, alcohol, acetone, dry ether and dried in a vacuum oven at 74° for one hour) was added 480 ml. of a 1:1 mixture of dry ether–benzene and 0.5 g. of iodine.[30] To this was added 15.6 g. (0.0564 mole) of XVII and 10 ml. of ethyl bromoacetate. As the reaction did not start when the solution was refluxed, 5 g. of dry zinc amalgam was added. The solution was refluxed without stirring and within five minutes the reaction started as noted by a cloudy appearance. The mixture was stirred and refluxed for 6.5 hours. During this period five 25-g. portions of fresh zinc and a few crystals of iodine were added and three 10-ml. portions of bromoester. Some yellow-orange solid was dissolved by the addition of 20 ml. of an equal mixture of methanol and glacial acetic acid. The product was worked up as in a previously described method[31] to give 21.50 g. of viscous orange residue (hydroxy ester as shown by infrared analysis). Dehydration of the residue was effected by heating at 190–200° with iodine for one-half hour. A mixture of 19.3 g. (0.055 mole) of dehydrated product and 3.53 g. (0.110 mole) of sulfur was immersed in a salt-bath at 205°. Hydrogen sulfide was evolved immediately. After five minutes the temperature was raised to 215° and then held at 215–225° for two hours. The very dark green residue was saponified and re-esterified to aid in removal of sulfur compounds. The resulting dark ester was chromatographed over alumina in Skellysolve B (petroleum ether, b.p. 65–70°). The 13.43 g. of yellow-orange residue was saponified with potassium hydroxide in 95% ethyl alcohol. Acidification afforded 11.73 g. of crude tan acid (66% based on XVII), m.p. 200–210°. A recrystallization from benzene–acetone gave a first crop of 5.24 g. (30%) of cream-colored acid, m.p. 224–226°, and a second crop of 2.01 g., m.p. 200–204°. Two recrystallizations of the first crop raised the melting point to 234.5–236.5°. The analytical sample of XIX obtained after four more recrystallizations from benzene–acetone formed fine colorless needles, m.p. 243.0–244.4° with darkening.

Anal. Calcd. for $C_{22}H_{18}O_2$: C, 84.1; H, 5.8. Found: C, 84.3, 84.1; H, 5.9, 5.9.

After several recrystallizations, the above second crop would not melt above 210–212°. Analysis indicated that this acid contained two more hydrogens than XIX but this fraction was not further studied.

The methyl esters of XIX, prepared with diazomethane, melted at 121–123° with softening at 119°. The analytical sample, recrystallized three times from methanol, yielded fine colorless prisms, m.p. 127.8–129.0°.

Anal. Calcd. for $C_{23}H_{20}O_2$: C, 84.1; H, 6.1. Found: C, 84.1, 84.0; H, 6.3, 6.2.

6a,7,8,12b-Tetrahydro-1,12-dimethylbenzo(c)phenanthrene-5-acetic Acid XVIII (or Isomer).—In a single experiment a solution of 1.5 g. (0.021 mole) of ethoxyacetylene[32] in 5 ml. of dry ether was added dropwise at room temperature to 18 ml. of a 1.27 *M* ether solution of ethylmagnesium bromide (10% excess) in a nitrogen atmosphere. A gray-brown precipitate which formed was dissolved in 8 ml. of dry thiophene-free benzene after the addition was complete. To the solution cooled in an ice-bath was added dropwise with stirring 3.00 g. (0.0109 mole) of the ketone XVII in 50 ml. of a 1:1 mixture of dry ether and dry thiophene-free

---

(25) The melting point is reported as 207.5–208.0°, ref. 22.

(26) A sample of polyphosphoric acid was generously supplied by the Victor Chemical Co., Chicago, Ill.

(27) This method is much simpler and affords the dione in better yield than the aluminum chloride procedure previously reported, ref. 22.

(28) David Todd, "Organic Reactions," Vol. IV, John Wiley and Sons, Inc., New York, N. Y., 1948, pp. 378–422.

(29) E. L. Martin, "Organic Reactions," Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1942, pp. 155–209.

(30) R. L. Shriner, "Organic Reactions," Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1942, pp. 1–37.

(31) Reference 30, p. 18.

(32) E. R. H. Jones, G. Eglington, M. C. Whiting and B. L. Shaw, *J. Chem. Soc.*, 1860 (1954).

benzene. After the addition, the stirring was continued for six hours at room temperature. After hydrolysis with saturated ammonium chloride solution, the crude reaction product was refluxed for 3.5 hours with dilute hydrochloric acid in ethanol as the mild hydrolysis described[33] did not effect complete rearrangement to unsaturated ester in our case. Saponification with potassium hydroxide in 95% ethyl alcohol afforded 2.19 g. (63.5%) of crude XVIII. The analytical sample, m.p. 241.8–242.4° dec., was obtained after four recrystallizations from benzene–acetone. A mixture of XVIII with XIX melted at 222–230°.

Anal. Calcd. for $C_{22}H_{22}O_2$: C, 83.0; H, 7.0. Found: C, 83.1, 83.1; H, 7.2, 7.1.

Resolution of 1,12-Dimethylbenzo(c)phenanthrene-5-acetic Acid (XIX).[34]—To 2.00 g. of XIX dissolved in hot acetone was added 1.872 g., one equivalent, of *l*-cinchonidine dissolved in hot acetone. Removal of the solvent and trituration of the residue with Skellysolve F (petroleum ether, b.p. 35–40°) afforded a cream-colored solid, m.p. 105–130°, $[\alpha]^{24}_{\mathrm{D}}$ −32.5° (*c* 2 in chloroform). Approximately 600 ml. of warm ether failed to dissolve all the solid. The remaining cinchonidine salt (1 g.) melted at 140–142°, and had $[\alpha]^{24}_{\mathrm{D}}$ −153° (*c* 2 in chloroform). Recrystallization of this material from a large volume of ether at room temperature[35] gave 0.6 g., m.p. 139.8–141.0°, $[\alpha]^{23}_{\mathrm{D}}$ −170° (*c* 2 in chloroform). The analytical sample, recrystallized three times from ether, formed very fine needles in rosettes, m.p. 143.7–145.1° with softening at 140°. The analysis indicated a monohydrate.

Anal. Calcd. for $C_{41}H_{40}O_3N_2 \cdot H_2O$: C, 78.6; H, 6.8; N, 4.5. Found: C, 78.5, 78.6; H, 6.9, 7.1; N, 4.2, 4.4.

The original filtrate was concentrated at room temperature and 1.5 g. of white solid which precipitated was separated. The filtrate was concentrated to a viscous oil which formed a cream-colored solid, m.p. 120–124°, $[\alpha]^{23}_{\mathrm{D}}$ +43.0° (*c* 2.45 in chloroform), on trituration with Skellysolve F.

Each of the cinchonidine salts, $[\alpha]_{\mathrm{D}}$ −170° and +43.0°, was decomposed by the addition of aqueous alcoholic hydrochloric acid. The acid from the (−)-cinchonidine salt gave a rotation of −7.97°, $[\alpha]^{23}_{\mathrm{D}}$ −332° (*c* 1.20 in acetone). Repeated recrystallizations from ether yielded fine crystals, m.p. 207.3–208.4° with slight darkening, $[\alpha]^{25}_{\mathrm{D}}$ −362.7 ± 2.5° (*c* 0.35 in acetone). The acid from the (+)-cinchonidine salt gave a rotation of +6.05°, $[\alpha]^{23}_{\mathrm{D}}$ +187° (*c* 1.62 in acetone). From benzene–acetone some racemic acid crystallized, m.p. 238.5–240.0°. Repeated recrystallizations from ether of the acid obtained from the filtrate yielded fine crystals, m.p. 207.7–208.7° with slight darkening, $[\alpha]^{25}_{\mathrm{D}}$ +347.6 ± 3.6° (*c* 0.29 in acetone). The racemic acid has an m.p. of 243.0–244.4° dec.

Racemization Experiments.—The methyl ester obtained using diazomethane from acid $[\alpha]^{29}_{\mathrm{D}}$ −358° had a m.p. of 152–154° and $[\alpha]^{27}_{\mathrm{D}}$ −275° (*c* 0.0340 in chloroform). Rapid distillation of the methyl ester under nitrogen at 0.03 mm. and a bath temperature of 200–210° furnished a sample, m.p. 154–155°, $[\alpha]^{24}_{\mathrm{D}}$ −294° (*c* 0.0332 in chloroform).

The methyl ester ($[\alpha]^{27}_{\mathrm{D}}$ −275°, 19.5 mg.) was sealed under 0.05 mm. of nitrogen in a small Pyrex tube. This was immersed completely into a salt-bath kept at 246–250°. After 30 minutes the tube was taken out and cooled rapidly in cold air. The content of the tube was rinsed out thoroughly with chloroform diluted to 5 ml. and polarimeter readings were taken, $[\alpha]^{27}_{\mathrm{D}}$ −263° (*c* 0.039 in $CHCl_3$). The infrared spectrum of the recovered ester was found to be identical with that of the starting material. Crystallization from acetone furnished a sample, m.p. 152–154°.

A similar experiment at 250° for 2 hours resulted in a solution which was too dark to be read in the polarimeter. No crystalline ester could be obtained from this solution.

Similar heating at 294–297° for 30 minutes resulted in considerable darkening of the substance. This product was chromatographed over a short column of activated alumina in benzene–ligroin. After 2 chromatographs a pale yellow solution of the substance was obtained which showed no rotation, but the residue gave an infrared spectrum identical with that of the methyl ester.

We wish to acknowledge partial support for the work herein described by the Office of Ordnance Research, U. S. Army.

Columbus 10, Ohio

---

[33] I. Heilbron, E. R. H. Jones, M. Julia and B. Weedon, *J. Chem. Soc.*, 1823 (1949).

[34] All readings were taken using a Schmidt and Haensch polarimeter in a 2-dcm. tube.

[35] The solutions in these first experiments were not heated as the optical stability of the compound was not known. In later experiments recrystallization from acetone–ether was effective.

[Contribution from the Department of Chemistry, Duquesne University]

The Grignard Reaction and Infrared Spectra of Cyclic Sulfites

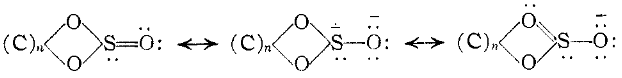
By H. Harry Szmant and William Emerson

Received May 23, 1955

The reaction of several cyclic sulfites with phenylmagnesium bromide gave phenyl sulfoxide in yields which did not vary greatly with the size of the sulfite ring or with the presence of substituents on the ring. Unlike non-cyclic sulfites, however, the cyclic ones gave some bromohydrins related to the glycol precursors of the sulfites. The infrared spectra of cyclic sulfites are discussed in the light of the known spectra of similar sulfur compounds.

It is well known that the behavior of the carbonyl function in cyclic ketones is greatly affected by the size of the ring.[1] This study was undertaken in the hope to uncover some variations in the behavior of cyclic sulfites as a function of ring size. If cyclic sulfites were to be affected by the size of the ring as are cyclic ketones, then reactivity (toward a Grignard reagent) and some physical properties (such as the stretching frequency of the >S=O bond) would be expected to vary with the relative resonance contributions of structures I–III.

The reaction of Grignard reagents with alkyl or aryl sulfites was reported some time ago as a method of preparation of sulfoxides,[2] but cyclic sulfites do not seem to have been studied in this connection. From the results listed in Table I it is evident that the yield of phenyl sulfoxide showed little variation when phenylmagnesium bromide reacts with alkyl, aryl or five- or six-membered cyclic sulfites. Also, in the case of ethylene sulfite the



I II III

---

[1] H. C. Brown, J. H. Brewster and H. Schechter, This Journal, **76**, 467 (1954).

[2] (a) W. Strecker, *Ber.*, **43**, 1131 (1910); (b) L. Bert, *Compt. rend.*, **178**, 1826 (1924); (c) H. Gilman, J. Robinson and N. J. Beaber, This Journal, **48**, 2715 (1926).