The Reaction of Unsaturated Acid Chlorides with Substituted Thioureas

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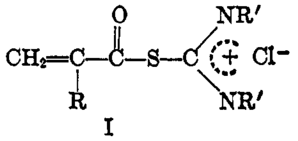
Received December 18, 1963

Acrylyl and methacrylyl chloride have been found to react with ethylenethiourea to yield 2,3,6,7-tetrahydro-5H-imidazo[2,1-*b*]-1,3-thiazin-5-one hydrochloride and its 6-methyl analog, respectively. Similarly, *sym*-diphenylthiourea yields the thiazine derivative, 2,3,5,6-tetrahydro-2-phenylimino-3-phenyl-4H-1,3-thiazin-4-one hydrochloride, and its 5-methyl analog. The free bases of the above compounds were also characterized. The reaction of acrylyl chloride with *sym*-diphenylthiourea, in the presence of triethylamine, yields a low molecular weight polymer with a degree of polymerization (DP) of 6–7.

The reaction of thioureas with acyl chlorides to yield N-acylthioureas has been reported[2-4]; the initial product, an S-acylisothiouronium chloride, undergoes rearrangement to the N-substituted compound upon heating, with the evolution of hydrogen chloride.

In addition to reactions with alkylating or acylating agents, thiourea has also been shown to be capable of addition to an activated double bond, in the presence of an acid. Thus, addition has been effected to α,β-unsaturated acids to give S-(β-carboxyalkyl)isothiuronium chloride,[5] to acrylonitrile and acrylamides to yield S-(β-cyanoethyl)- and S-(β-carboxamidoethyl)-isothiuronium salts,[6] and to 2- and 4-vinylpyridines to yield S-[2-(2- and 4-pyridinium)ethyl]isothiuronium salts.[7] Reaction of α,β-unsaturated diacid diesters with thiourea in the presence of hydrogen chloride or bromide yielded 2-imino-4-oxo-3,5-H-1,3-thiazin-6-carbonic acid ester[8] *via* ring closure.

In an attempt to prepare the unsaturated isothiuronium salts Ia–d, as potential antiradiation drugs, acrylyl and methacrylyl chloride reacted with N,N′-ethylene- and N,N′-diphenylthiourea. The product isolated in all instances was not the S- or N-acylthiourea, but rather a heterocyclic compound derived from a ring-closure reaction.

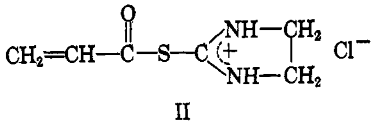


$\mathrm{CH_2{=}C(R){-}C(=O){-}S{-}C(NR')_2^{+}\ Cl^-}$

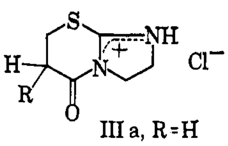
I

a, R = H; R′ = CH_2
b, R = CH_3; R′ = CH_2
c, R = H; R′ = C_6H_5
d, R = CH_3; R′ = C_6H_5

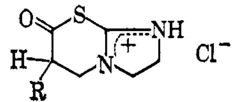
Elemental analysis for the product of the reaction of acrylyl chloride with N,N′-ethylenethiourea, for example, was in close agreement with three possible structures, II, IIIa, and IVa. Structure II was ruled out on the basis of infrared and ultraviolet spectra (by comparison with S-benzyl-N,N′-ethyleneisothiuronium chloride) and nuclear magnetic resonance spectra (which indicated the lack of vinyl protons and the presence of more than one type of methylene proton). Structure IVa was eliminated by the unequivocal synthesis of 2,3,6,7-tetrahydro-5H-imidazo[2,1-*b*]-1,3-thiazin-5-one hydrochloride (IIIa) from β-carboxyethyl-N,N′-ethyleneisothiuronium chloride (V).[9] The compound thus prepared proved identical with that obtained by reaction of acrylyl chloride and N,N′-ethylenethiourea. In a similar fashion, 6-methyl-2,3,6,7-tetrahydro-5H-imidazo[2,1-*b*]-1,3-thiazin-5-one hydrochloride (IIIb) was synthesized by using methacrylyl chloride.



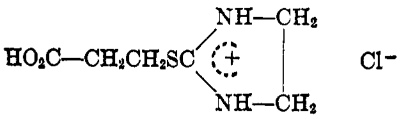
II



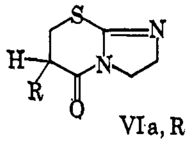
III a, R=H
b, R=CH_3



IVa, R=H
b, R=CH_3



The bases VIa and b were prepared from the salts by reaction with diethylamine. Attempts to prepare these compounds directly by conducting the reaction in the presence of triethylamine resulted in polymer formation. These polymers could not be characterized.



VIa, R=H
b, R=CH_3

Reaction of acrylyl or methacrylyl chloride with *sym*-diphenylthiourea gave the thiazine derivatives, 2,3,5,6-tetrahydro-2-phenylimino-3-phenyl-4H-1,3-thiazin-4-one hydrochloride (VIIa) and its 5-methyl analog, VIIb, respectively. These salts are unstable to heat and readily decompose affording their conjugate bases, VIIIa and b, with the evolution of hydrogen chloride. The structure of VIIIa was proved by an un-

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[1] Taken from a portion of the dissertation submitted to the faculty of the Polytechnic Institute of Brooklyn in partial fulfillment of the requirements for the degree of Doctor of Philosophy in Chemistry, 1964.

[2] A. E. Dixon and J. Taylor, *J. Chem. Soc.*, 720 (1920).

[3] M. L. Moore and F. S. Crossley, *J. Am. Chem. Soc.*, **62**, 3273 (1940).

[4] J. E. Baer and R. G. Lockwood, *ibid.*, **76**, 1163 (1954).

[5] H. Behringer and P. Zillikens, *Ann.*, **574**, 140 (1951).

[6] L. Bauer and T. L. Welsh, *J. Org. Chem.*, **26**, 1443 (1961).

[7] L. Bauer and L. A. Gardella, Jr., *ibid.*, **26**, 82 (1961).

[8] R. Zimmerman, *Angew. Chem.*, **74**, 906 (1962).

[9] M. C. Wani, Ph.D. thesis, Indiana University, 1962, p. 92. Information also kindly furnished by Professor E. Campaigne in report to Office of Surgeon General.

TABLE I

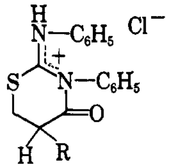
N.M.R. SPECTRA

Compound	Solvent	Proton	Chemical shift, τ	J, c.p.s.
VIa[a]	D_2O[b]	$=N-CH_2-CH_2-N=$	6.04[c]	
		$-CH_2-S-$	6.73	ca. 4.9[d]
		$-CH_2-C=O$	7.02	ca. 4.9[d]
VIb	D_2O[b]	$=N-CH_2-CH_2-N=$	6.08[c]	
		$-CH_3$	8.52[e]	6.4
		$-S-CH_2-CH-C=O$	6.78[f]	
IIIa	D_2O[b]	$=N-CH_2-CH_2-N=$	5.72, 5.55	ca. 3.7[d]
		$-CH_2-C=O$	6.69	ca. 5.5[d]
		$-CH_2-S-$	6.24	ca. 5.5[d]
IIIb	D_2O[b]	$=N-CH_2-CH_2-N=$	5.78, 5.16	ca. 2.1[d]
		$-CH_3$	8.44[e]	6.5
		$-S-CH_2-CH-C=O$	6.86–6.24, 6.41[g]	
VIIIa	$CDCl_3$[h]	$-CH_2-CH_2-$	7.18[c]	
		o-H's of C_6H_5	3.55–3.18[f]	
		m- and p- H's of C_6H_5	3.18–2.50[f]	
VIIIb	$CDCl_3$[h]	$-CH_2-CH-$	7.07[f]	
		$-CH_3$	8.65[e]	4.9
		o-H's of C_6H_5	3.38–3.05[f]	
		m- and p-H's of C_6H_5	3.05–2.50[f]	

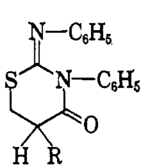
[a] Taken at 66°. [b] CH_3CN, calibrated against tetramethylsilane in D_2O, used as internal standard. [c] Singlet. [d] Symmetrical A_2B_2 system, $J_{AB} = J_{AB}'$. [e] Doublet. [f] Complex multiplet. [g] Main peak. [h] Tetramethylsilane used as internal standard.

equivocal synthesis from β-iodopropionic acid and *sym*-diphenylthiourea.[10]

When acrylyl chloride reacted with *sym*-diphenylthiourea in the presence of triethylamine a low molecular weight polymer was obtained. Elemental analysis and a molecular weight determination of the compound indicated a repeating unit composed of two acrylyl groups and one *sym*-diphenylthiourea moiety with a DP of 6–7. Structure[11,12] IX or X is suggested for the repeating unit on the basis of spectral evidence.



VII a, R=H
b, R=CH_3



VIII a, R = H
b, R = CH_3

A similar reaction with methacrylyl chloride did not lead to polymer formation.

Alkaline hydrolysis of compounds VIIIa and b, as well as the polymer, led to formation of *sym*-diphenylthiourea. The polymer yielded, in addition, a polymeric acid. It is interesting that no *sym*-diphenylurea could be isolated. Bhargava and Ram[13] reported that alkaline hydrolysis of the five-membered analog of VIIIa, 3-phenyl-2-phenylimino-4-ketotetrahydrothiazole, gives *sym*-diphenylurea. The hydrolysis of compound VIIIa (as well as VIIIb and the polymer) could take place *via* a hydrolytic route.

The infrared, ultraviolet, and nuclear magnetic resonance spectra of these compounds were reasonably definitive. The key peaks in the infrared appear to depend upon the structure of the heterocycle involved. These are to be found in the Experimental section.

It may be noted that the substitution of a phenyl group for an alkyl group on the lactam nitrogen, such as in VIIIa and b resulted in a shift of the carbonyl stretching frequency of the lactams by 25–30 cm.$^{-1}$. The shift in the same frequency of these compounds upon protonation may be attributed to a delocalization of the electron density over a three-atom system which includes both nitrogen atoms. This inductive effect would be similar to that experienced by the carbonyl group of an ester.

The ultraviolet spectra of the compounds are to be found in the Experimental section. Note that the spectra of the bases and of the polymer are similar for the most part. The protonated derivatives exhibited a bathochromic shift of wave length.

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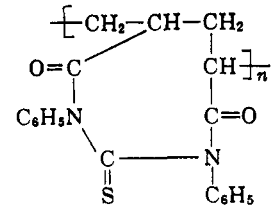
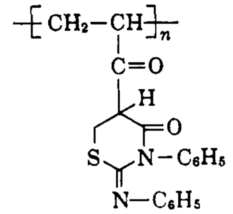
[10] Langlet, *Ofversigt K. Vetensk.-Akad. Forhandligar*, 41 (1895); Beilstein's Handbuch Der Organischen Chemie, **27**, 248 (1919).

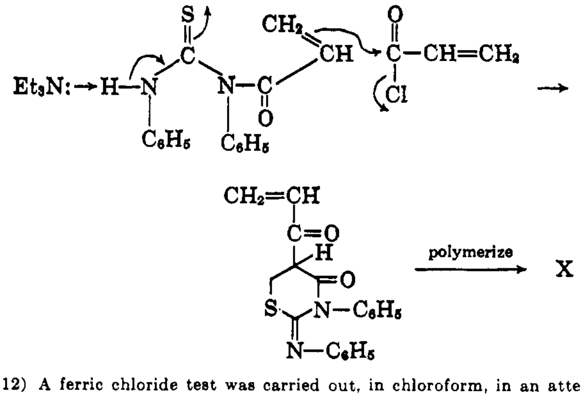
[11] Similarities in the infrared spectrum of the polymer with both *sym*-diphenylthiourea and VIIIa do not permit a definite assignment of structure. The formation of IX could be accomplished by a cyclopolymerization of N,N′-diphenyl-N,N′-diacrylylthiourea, whereas X could be formed by reaction of N,N′-diphenyl-N-acrylylthiourea with triethylamine and acrylyl chloride in the following way.



IX



X



[12] A ferric chloride test was carried out, in chloroform, in an attempt to distinguish between structures IX and X. However, anomalous results were obtained. The procedure followed was that to be found in N. D. Cheronis and J. B. Entrikin, "Semimicro Qualitative Organic Analysis," 2nd Ed., Interscience Publishers, New York, N. Y., 1957, p. 228, section B.

[13] P. M. Bhargava and P. Ram, *J. Indian Chem. Soc.*, **38**, 127 (1961).

The nuclear magnetic resonance spectra of the salts are more complex than that of their corresponding free bases. These differences are summarized in Table I. The n.m.r. spectrum of the polymer did not yield useful information, other than to indicate the lack of vinyl protons. The bands are too broad to be of diagnostic value in assigning a definite structure to the compound.

Experimental[14,15]

Reaction of Unsaturated Acid Chlorides with Ethylenethiourea. A. 2,3,6,7-Tetrahydro-5H-imidazo[2,1-*b*]-1,3-thiazin-5-one Hydrochloride (IIIa) and Its Free Base, VIa.—Ethylenethiourea (5.1 g., 0.05 mole) was added to 50 ml. of anhydrous acetone (dried over molecular sieves). A solution of acrylyl chloride (4.5 g., 0.05 mole) in 25 ml. of anhydrous acetone was added slowly to the reaction flask. The slurry was magnetically stirred for 3 hr. while in an ice bath. A drying tube protected the mixture from moisture. The yield of crude product was quantitative. A 3-g. sample yielded 2 g. (66.7%), m.p. >250° dec., upon one recrystallization from 95% ethanol. Four recrystallizations from the solvent gave analytically pure sample, m.p. >250° dec. (m.p. 277–278°, prepared by the reaction of ethylenethiourea and acrylic acid in the presence of hydrogen chloride followed by refluxing the product in ethanol[9]).

The infrared absorption spectrum of the salt showed absorption at 1730, 1715 (shoulder, s, C=O), 1600 (s, C=N), and 2650–3200 cm.$^{-1}$ (m, NH$^+$). The ultraviolet absorption spectrum showed $\lambda_{max}^{H_2O}$ 238 mμ (ϵ 13,180).

Anal. Calcd. for $C_6H_9ClN_2OS$: C, 37.41; H, 4.71; N, 14.54; S, 16.65. Found: C, 37.45; H, 4.81; N, 14.34; S, 16.62.

Recrystallization of the purified salt from absolute ethanol containing sufficient diethylamine to neutralize the acid gave its free base in a yield of 46.5%, m.p. 138–141°. Recrystallization of this base from absolute ethanol yielded colorless crystals, m.p. 142–144.5° (m.p. 144°, prepared by reaction of the hydrobromide of VIa with ammonium hydroxide[9]).

The infrared absorption spectrum of the base showed absorption at 1670, 1660 (shoulder, s, C=O), and 1600 cm.$^{-1}$ (s, C=N). The ultraviolet absorption spectrum showed $\lambda_{max}^{CH_3OH}$ 229 mμ (ϵ 11,600).[16]

Anal. Calcd. for $C_6H_8N_2OS$: C, 46.13; H, 5.16; N, 17.93; S, 20.53. Found: C, 46.25; H, 5.38; N, 17.65; S, 20.24.

B. 6-Methyl-2,3,6,7-tetrahydro-5H-imidazo-[2,1-*b*]-1,3-thiazin-5-one Hydrochloride (IIIb) and Its Free Base, VIb.—Compound IIIb was prepared by using a procedure similar to the above. Methacrylyl chloride replaced the acrylyl chloride used. The crude product was isolated in a yield of 95%. One recrystallization of a 6-g. sample from 95% ethanol yielded 3 g. (50%) of the compound, m.p. 260–280°. Recrystallization of the compound from the solvent to constant melting point gave a colorless solid, m.p. 275–280° dec.

The infrared absorption spectrum of the salt showed absorption at 1710 (s, C=O), 1600 (s, C=N), and 2630–3100 cm.$^{-1}$ (m, NH$^+$). The ultraviolet absorption spectrum showed $\lambda_{max}^{H_2O}$ 238 mμ (ϵ 13,020).

Anal. Calcd. for $C_7H_{11}N_2ClOS$: C, 40.68; H, 5.36; N, 13.55; S, 15.51. Found: C, 40.87; H, 5.32; N, 13.05; S, 15.75.

The free base of the above salt was prepared by stirring a slurry of 5 g. of the purified salt in 25 ml. of acetone containing a slight excess of diethylamine, for about 5 min. The solid remaining, diethylamine hydrochloride, was filtered. Evaporation of the supernatant liquid yielded a crude sample of the base. The compound was dissolved in hot benzene and filtered. Evaporation of the benzene followed by extraction of cyclohexane gave 2.5 g. (60.7% based on moles of salt used), m.p. 76–79°. Recrystallization of the base to constant melting point from cyclohexane yielded an analytical sample, m.p. 77–79.5°.

The infrared absorption spectrum of the base showed absorption at 1670 (s, C=O), and 1600 cm.$^{-1}$ (s, C=N). The ultraviolet absorption spectrum showed $\lambda_{max}^{CH_3OH}$ 231 mμ (ϵ 10,930).

Anal. Calcd. for $C_7H_{10}N_2OS$: C, 49.39; H, 5.92; N, 16.46; S, 18.84. Found: C, 49.64; H, 5.93; N, 16.15; S, 18.66.

All of the above compounds were found to be soluble in water and ethanol. Compound IIIa, upon being placed in refluxing toluene for 17 hr., did not lose hydrogen chloride and was recovered unchanged.

Reaction of Unsaturated Acid Chlorides with *sym*-Diphenylthiourea. A. 2,3,5,6-Tetrahydro-2-phenylimino-3-phenyl-4H-1,3-thiazin-4-one Hydrochloride (VIIa) and Its Conjugate Base, VIIIa.—Acrylyl chloride (9.0 g., 0.1 mole), dissolved in 50 ml. of chloroform, was slowly added to a solution of *sym*-diphenylthiourea (22.8 g., 0.1 mole) in 50 ml. of chloroform. The mixture was magnetically stirred for 3 hr. and was cooled in an ice bath. A drying tube protected the reaction mixture from moisture. Evaporation of the chloroform yielded a yellow semisolid.

The reaction was worked up in two ways. To obtain the salt VIIa, the mixture was extracted with benzene. A white powder (26.5 g., 83.3% yield) was obtained which was insoluble in the benzene. Upon standing, the powder became lumpy and somewhat difficult to handle. Attempted purification of the salt from a variety of solvents led to evolution of hydrogen chloride with the formation of the base, VIIa. Refluxing solvents led to the complete transformation of the salt to the base. To obtain the base, the salt could either be decomposed in isopropyl alcohol or the original semisolid isolated could be crystallized from the solvent. In the latter case, the combined fractions yielded 21.1 g. (75% yield) of product. Recrystallization of a 3.5-g. sample from isopropyl alcohol yielded 3.0 g. (85.6%) of the compound, m.p. 167–170°. Several recrystallizations from the solvent yielded an analytical sample, m.p. 168.5–170.5°.

The infrared absorption spectrum of the salt showed absorption at 1740 (s, C=O), 1538 (s, C=N), and 2600–3050 cm.$^{-1}$ (m, NH$^+$). The base showed its abosrption at 1695 (s, C=O) and 1590 cm.$^{-1}$ (s, C=N). The ultraviolet absorption spectrum of the base showed $\lambda_{max}^{CH_3OH}$ 227 mμ (ϵ 22,300), and 268–281 (4000).[17]

Anal. Calcd. for $C_{16}H_{14}N_2OS$: C, 68.06; H, 5.00; N, 9.92; S, 11.36. Found: C, 68.34; H, 5.16; N, 9.40; S, 11.14.

The compound was unequivocally synthesized from β-iodopropionic acid and *sym*-diphenylthiourea in acetic anhydride using the method of Langlet,[10] m.p. 168.5–170.5°, lit. m.p. 106°. This compound was identified as the same compound as VIIIa by melting point, mixture melting point, and an infrared spectral comparison.

B. 5-Methyl-2,3,5,6-tetrahydro-2-phenylimino-3-phenyl-4H-1,3-thiazin-4-one Hydrochloride (VIIb) and Its Free Base, VIIIb.—A procedure similar to the above was followed in preparation of compounds VIIb and VIIIb. Methacrylyl chloride (10.4 g., 0.1 mole) was used in place of acrylyl chloride. The yield of the crude salt VIIb obtained by the above procedure was 20 g. (60.1% yield based on the salt). The properties of this compound were the same as that of VIIa. The base VIIIb may be obtained by decomposing the salt by crystallization from isopropyl alcohol. This afforded 14 g. of the free base, m.p. 128–131°. Several recrystallizations from the solvent yielded an analytical sample, m.p. 131–133°.

The infrared absorption spectrum of the salt showed absorption at 1740 (s, C=O), 1538 (s, C=N), and 2600–3050 cm.$^{-1}$ (s, NH$^+$). The base showed its absorption at 1700 (s, C=O and 1590 cm.$^{-1}$ (s, C=N). The ultraviolet absorption spectrum of the base showed $\lambda_{max}^{CH_3OH}$ 227.5 mμ (ϵ 23,000), 268–281 (4150).[17]

Anal. Calcd. for $C_{17}H_{16}N_2OS$: C, 68.89; H, 5.44; N, 9.45; S, 10.82. Found: C, 68.78; H, 5.65; N, 9.66; S, 10.54.

The ability to isolate the salts in the above two procedures is dependent upon the degree of decomposition that takes place during the course of the reaction.

The yield of the free bases depends upon the amount of impurities present in the solutions before their respective work-up.

Reaction of Unsaturated Acid Chlorides with *sym*-Diphenylthiourea in the Presence of Triethylamine.—Triethylamine (15.2 g., 0.15 mole) was added to a solution of *sym*-diphenylthiourea (11.4 g., 0.05 mole) in 50 ml. of chloroform. Acrylyl chloride (9.1 g., 0.1 mole), dissolved in 25 ml. of chloroform, was added dropwise to the solution. The mixture was magnetically stirred for 8 hr. and was cooled in an ice bath during the period of addition of the acid chloride. A drying tube was used to protect the reaction from moisture. Evaporation of the solvent left an orange semisolid from which triethylamine hydrochloride was separated upon the addition of acetone. Concentration of the acetone solution and dropwise addition to ten times its volume of isopropyl alcohol yielded 10.5 g. (78.9% yield) of a cream-colored

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[14] All melting points are uncorrected.

[15] Analyses were performed by Schwarzkopf Microanalytical Laboratory, Woodside, 77, N. Y.

[16] The λ_{max} for these compounds did not change when the solvent was changed to water.

[17] Plateau.

polymer. The polymer was purified by dissolution in methanol and reprecipitation from isopropyl alcohol. Repetition of this procedure yielded an analytical sample. The compound was soluble in acetone, chloroform, and acetonitrile.

The infrared absorption spectrum of the polymer showed absorption at 1695, 1718 (shoulder, s), and 1595 cm.$^{-1}$ (s, C=N). The ultraviolet absorption spectrum showed $\lambda_{max}^{CH_3CN}$ 230 mμ (ϵ 18,130) and 277 (5130).

Anal. Calcd. for $(C_{19}H_{16}N_2O_2S)_n$: C, 67.83; H, 4.79; N, 8.33; S, 9.53. Found: C, 67.63; H, 4.85; N, 8.49; S, 9.45; mol. wt. (T.E.M.), 2300. This corresponds to an average value of *n* as 6.8.

The above reaction was also carried out using methacrylyl chloride in place of acrylyl chloride. However, no characterizable product was obtained.

The infrared spectra of all the compounds were taken in potassium bromide on a Perkin-Elmer Model 21 spectrophotometer. Ultraviolet spectra were recorded on a Cary Model 14 spectrophotometer and the nuclear magnetic resonance spectra were determined on a Varian instrument operating at 60 Mc.

Acknowledgment.—The authors gratefully acknowledge financial assistance from the Office of the Surgeon General under Contract No. DA-49-193-MD-2032.

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cis Addition of Performic Acid to Indene and Nuclear Magnetic Resonance Spectra of 1,2-Disubstituted Indanes

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Received December 27, 1963

The addition of performic acid to indene has been shown to give *cis*-2-formyloxy-1-hydroxyindane (IV). The unexpected location of the formate group at C-2 was proved by chemical and n.m.r. evidence. The conversions of IV, its *trans* isomer (VI), and both *cis*- (I) and *trans*-1,2-dihydroxyindane (III) to 2-indanone by treatment with aqueous acid are discussed and a mechanism is proposed which differs from the mechanism previously proposed. The n.m.r. spectra of fifteen indane compounds are listed, and the data are interpreted in terms of nonplanar five-membered rings.

The addition of performic acid to indene in an aqueous formic acid medium has been found to give two major products, *cis*-1,2-dihydroxyindane (I) and *cis*-2-formyloxy-1-hydroxyindane (IV). Our study of the products from performic acid oxidation of indene stemmed from our interest in the synthesis of 2-indanone oxime and its subsequent reduction[2a] to 2-aminoindane hydrochloride, a potent nonnarcotic analgesic.[2b] Horan and Schiessler[3] recently described the preparation of 2-indanone in high yield by performic acid oxidation followed by dilute sulfuric acid treatment of the intermediate (incorrectly assumed to be 1-formyloxy-2-hydroxyindane). Thin-layer chromatographic examination of samples of the performic acid oxidation reaction showed that indene reacted rapidly with the performic acid to give approximately equal amounts of I and IV, only traces (less than a total of 3–5%) of the corresponding *trans* isomers III and VI, and a small amount of a less polar material (possibly 1,2-diformyloxyindane).[4] Under the reaction conditions, *cis* and *trans* isomers were not equilibrated, so the *cis* products clearly resulted from a *cis* addition rather than from a secondary equilibration. It is not possible to say whether I or IV is the primary product, or whether both products form simultaneously, because equilibration of I and IV occurs fairly rapidly in the reaction mixture.

The addition of deuterium bromide to indene was recently shown by Dewar and Fahey[5] to give 80% *cis*- and only 15–20% *trans*-1-bromo-2-deuterioindane. The proposed mechanism involved formation of an ion pair, consisting of a benzyl-type carbonium ion and a solvated bromide ion, which either collapsed directly to the *cis* adduct or isomerized and then collapsed to the *trans* adduct. The Dewar and Fahey mechanism[5] would predict the unknown *cis*-1-formyloxy-2-hydroxyindane as the primary product of performic acid addition to indene; this predicted product would have to undergo rapid acyl migration to give the isolated ester product (IV). The observed products I and IV cannot be explained by formation of an epoxide and its acid-catalyzed opening to a benzyl-type carbonium ion (or alternatively, attack of OH$^+$ to give this carbonium ion directly), followed by *cis* attachment of formate ion and subsequent acyl migration, because treatment of 1,2-epoxyindane[6,7] under the conditions of the performic acid oxidation gave a complex mixture of *cis*- and *trans*-disubstituted derivatives. One possible mechanism for the formation of IV is *cis* addition of performic acid to indene, either as a four-centered or as a

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[2] (a) W. E. Rosen and M. J. Green, *J. Org. Chem.*, **28**, 2797 (1963); (b) L. B. Witkin, C. F. Huebner, F. Galdi, E. O'Keefe, P. Spitaletta, and A. J. Plummer, *J. Pharmacol. Exptl. Therap.*, **133**, 400 (1961).

[3] J. E. Horan and R. W. Schiessler, *Org. Syn.*, **41**, 53 (1961).

[4] (a) W. Nagata and T. Terasawa [*Chem. Pharm. Bull* (Tokyo), **9**, 745 (1961)] reported the formation of some *cis*-2-benzoyloxy-1-hydroxy product from perbenzoic acid oxidation of 6-methoxy-3,4-dihydronaphthalene. The only *trans* isomer isolated was the *trans*-1-benzoyloxy-2-hydroxy product, presumably resulting from displacement of the intermediate epoxide with benzoate anion at C-1. The authors suggested that the *cis*-2-benzoyloxy-1-hydroxy product resulted from acyl migration of an initially formed *cis*-1-benzoyloxy-2-hydroxy isomer (*not* isolated). (b) After this paper had been submitted for publication, the authors became aware of the report by E. Vogel, W. Frass, and J. Wolpers [*Angew. Chem.*, **75**, 979 (1963)] on the *cis* hydroxylation of dibenzocyclooctatriene with performic acid.

[5] M. J. S. Dewar and F. C. Fahey, *J. Am. Chem. Soc.*, **85**, 2248 (1963).

[6] Originally, there was some doubt as to whether peracid addition to indene preceded epoxide formation or whether epoxide formation preceded disubstitution [see, for example, J. Böeseken and G. Elsen, *Rec. trav. chim.*, **48**, 363 (1929); J. Böeseken and G. C. C. C. Schneider, *J. prakt. Chem.*, **131**, 285 (1931)]. Recent workers have concluded that the epoxide is the initial product [*e.g.*, B. M. Lynch and K. H. Pausacker, *J. Chem. Soc.*, 1525 (1955)] and that disubstituted products result from opening of the epoxide ring [*cf.* R. E. Parker and N. S. Isaacs, *Chem. Rev.*, **59**, 737 (1959)]. Although exceptions to the normal *trans* opening of the epoxide ring have been observed [*e.g.*, C. C. Tung and A. J. Speziale, *J. Org. Chem.*, **28**, 2009 (1963)], such a *cis* opening of 1,2-epoxyindane would be expected to lead to *cis*-1-formyloxy-2-hydroxyindane.

[7] (a) The opening of 1,2-epoxyindane with aqueous acid to give mixtures of *cis*- and *trans*-1,2-dihydroxyindane was reported by Böeseken (ref. 22); (b) H. Bodot, J. Jullien, and E. Leblanc [*Bull. soc. chim. France*, 41 (1962)] described the treatment of 1,2-epoxyindane with hydrogen chloride in dioxane to give 9% 2-indanone, 21% *trans*-1-chloro-2-hydroxyindane, and 64% *cis*-1-chloro-2-hydroxyindane. They attributed the lack of specificity to an intermediate benzyl-type carbonium ion.