acted rather poorly with anti-hog A and anti-human A sera,[19] horse blood group B preparations have been shown[20] to be almost as effective as human B preparations in the precipitin reaction with human isoimmune serum. This might in some way be a reflection of the finding that human B preparations give practically only glucosamine on mild acid hydrolysis.

The six bovine materials studied (Table IIIB) also showed a behavior characteristic of the species rather than of ABO specificity. While all six preparations showed some decrease in glucosamine–galactosamine ratios following mild acid hydrolysis, the composition of the dialyzable hexosamine showed no apparent relation to ABO activity. Rather, all six cattle preparations showed hexosamine ratios in the dialysate ranging only from 1.3 to 3.2, and in most cases not significantly different from those of the original unhydrolyzed material. Since bovine materials have been shown to react relatively poorly in the precipitin reaction with anti-hog A and anti-human A[4] and B,[20] it is not altogether surprising that these materials exhibit a behavior toward mild acid hydrolysis unlike that of the hog and human materials. Moreover, since bovine substances possess a common bovine specificity[4] and contain the so-called J factor of cattle,[17,18] it appears likely that a correlation between the hexosamine ratio of the dialysate and some specificity other than A, B or O might be a possibility. No explanation is apparent from the data presented for the capacity of cow B substances to precipitate human antibody to horse B substance.[4]

(19) E. A. Kabat, H. Baer, R. L. Day and V. Knaub, *J. Exp. Med.*, **91**, 433 (1950).

(20) Unpublished data.

NEW YORK, N. Y.

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF NORTHWESTERN UNIVERSITY]

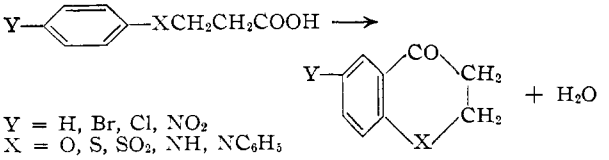
Chromanones, Thiochromanones and 2,3-Dihydro-4(1H)-quinolones

BY CHARLES D. HURD AND SHIN HAYAO

RECEIVED MAY 19, 1954

Polyphosphoric acid is an effective reagent for bringing about the ring closure of 3-aryloxypropionic acids into 4-chromanones, 3-arylmercaptopropionic acids into 4-thiochromanones and N,N-diaryl-β-alanines into 2,3-dihydro-1-aryl-4(1H)-quinolones. 8-Methyl-4-thiochromanones were included in the study. Phosphoryl chloride causes cyclization of N-*p*-chloro- and N-*p*-bromophenyl-N-*p*-tolylsulfonyl-β-alanine into 6-halo-2,3-dihydro-1-*p*-tolylsulfonyl-4(1H)-quinolone but the yields are low. Also, 3-(*p*-nitrophenoxy)-propionic acid produces 6-nitro-4-chloro-2H-benzopyran in good yield on heating with phosphoryl chloride, a process involving not only ring closure but also halogenation at the carbonyl. With 3-phenylmercaptopropionic acid, however, phosphoryl chloride gives rise to 3-chloro-4-thiochromanone. Aspects of this unusual C–H chlorination are discussed. Both physical and chemical evidence was used in establishing structures. Reactions carried out on the thiochromanones were oxidation to the 1-dioxides by hydrogen peroxide, halogenation at position 3 by bromine or sulfuryl chloride and hydrazone formation. 6-Nitro-4-chromanone reacts with sulfuryl chloride to yield 3-chloro-6-nitro-4-chromanone. This α-chloro ketone reacts with thiourea to produce a yellow crystalline solid, presumably a thiazolobenzopyran derivative. The 3-substituted propionic acids from which these heterocyclics are synthesized are prepared conveniently from propiolactone.

These cyclizations are known: 3-aryloxypropionic acids[1,2] into chromanones by phosphorus pentoxide,[1] 3-arylmercaptopropionic acids into thiochromanones by sulfuric acid[3] and N,N-diphenyl-β-alanine into 2,3-dihydro-1-phenyl-4(1H)-quinolone by phosphorus pentoxide in boiling xylene.[4] This general equation covers these ring closures



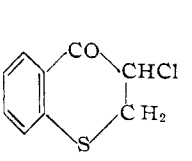
Y = H, Br, Cl, NO_2
X = O, S, SO_2, NH, NC_6H_5

Recently it has been shown that the precursors of these heterocyclics may be made from propiolactone, since the latter reacts with sodium phenoxide to yield 3-phenoxypropionic acid,[2] sodium phenyl sulfide to yield 3-phenylmercaptopropionic acid[2] and arylamines to yield N-aryl-β-alanines.[5]

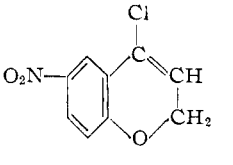
In view of this, we became interested in studying the reaction further, using polyphosphoric acid and phosphoryl chloride as reagents for effecting these ring closures.

Polyphosphoric acid proved to be very effective. Examples tested with it were 3-phenylmercaptopropionic acid (I) into 4-thiochromanone, 3-(*p*-nitrophenoxy)-propionic acid (II) into 6-nitro-4-chromanone and N,N-diphenyl-β-alanine into 2,3-dihydro-1-phenyl-4(1H)-quinolone. Polyphosphoric acid has been used previously[6] for intramolecular acylations to give isocyclic rings, but it has not been used in the synthesis of heterocyclic compounds.

Phosphoryl chloride also promoted cyclizations of I and II, but the compounds formed contained chlorine, that from I being 3-chloro-4-thiochromanone (III) although in poor yield, and that from



III



IV

(1) D. Chakravarti and J. Dutta, *J. Indian Chem. Soc.*, **16**, 639 (1939).

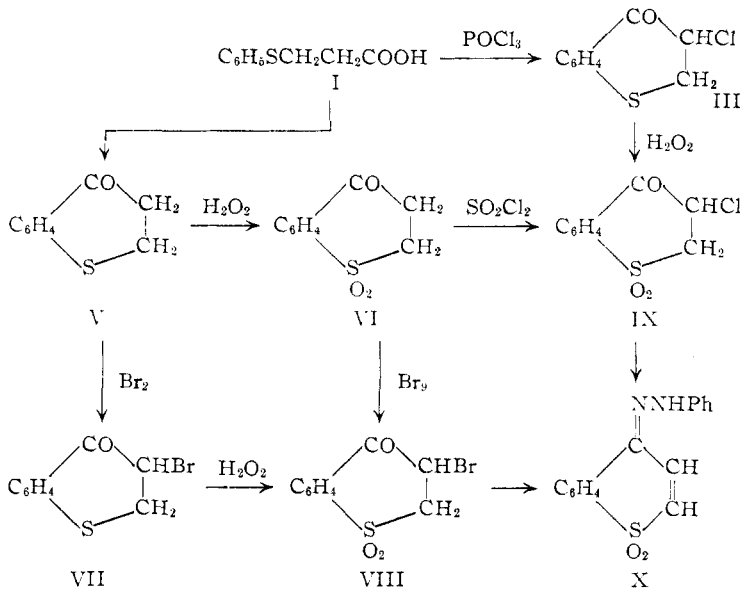
(2) T. L. Gresham and co-workers, THIS JOURNAL, **71**, 661 (1949).

(3) (a) F. Krollpfeiffer and H. Schultze, *Ber.*, **56**, 1819 (1923); (b) *ibid.*, **58**, 1654 (1925); (c) F. Arndt and co-workers, *ibid.*, **58**, 1612 (1925).

(4) R. C. Cookson and F. G. Mann, *J. Chem. Soc.*, 67 (1949).

(5) (a) T. L. Gresham and co-workers, THIS JOURNAL, **73**, 3168 (1951); (b) C. D. Hurd and S. Hayao, *ibid.*, **74**, 5889 (1952).

(6) H. R. Snyder and F. X. Werber, *ibid.*, **72**, 2965 (1950).



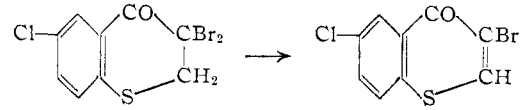
II being 6-nitro-4-chloro-2H-benzopyran (IV) in good yield. This difference in behavior of the S- and O-heterocyclics is striking. Clemo and Perkin[7] once reported a similar conversion by phosphoryl chloride of N-phenyl-N-tosyl-β-alanine into 1,2,3,4-tetrahydro-3-chloro-1-tosyl-4-quinolone (analogous to III), but Backeberg[7] showed that this substance actually was 1,2-dihydro-4-chloro-1-tosylquinoline (analogous to IV). In view of this, and particularly in view of the fact that halides of phosphorus usually cause replacement of carbonyl oxygen rather than of methylene hydrogen, we were particularly careful to prove the structures of our substances beyond question. Our evidence is as follows.

4-Thiochromanone (V) was oxidized smoothly by hydrogen peroxide to the 1-dioxide VI, and also was easily brominated to 3-bromo-4-thiochromanone (VII). This bromo compound is known,[3b] but the fact that it yielded the same 1-dioxide VIII as was obtained from VI by bromination is proof of the position of the bromine in VII for bromination is known not to occur[8] in acid media alpha to the sulfone group.

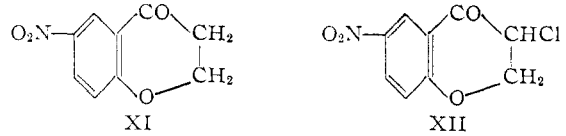
That the chlorine in III was at position 3 was demonstrated by oxidizing it with hydrogen peroxide to 3-chloro-4-thiochromanone 1-dioxide (IX) as the only crystalline product. IX was also obtained from VI by halogenation with sulfuryl chloride. Both VIII and IX gave the same phenylhydrazone X, as would be expected by their analogous structures. Osazone formation would have been conceivable, but there is precedent with α-halocyclohexanones[9] for the elimination reaction which was observed.

As was mentioned above, IX was prepared from both VI and III. The identity of this material from either source was witnessed by the identical melting point behavior and by identical infrared spectra. The samples, when pressed with solid potassium bromide, showed a carbonyl band at 5.80 μ (1724 cm.$^{-1}$), two bands for the sulfone group at 7.70 and 8.76 μ, and an aliphatic carbon–chlorine band at 14.46 μ. For comparison, 4-thiochromanone 1-dioxide (VI) had absorptions at 5.92 μ (1689 cm.$^{-1}$) for carbonyl, and 7.69, 8.76 μ for sulfone, with no band around 14.5 μ. Here, the hypsochromic shift of 35 cm.$^{-1}$ was observed for the carbonyl band in passing from VI to IX. It is known[10] that the same shift of carbonyl band occurs when comparing a cyclic ketone with the α-chloro analog if the C–Cl bond is of an equatorial type.

Just as V may be converted directly into the 3,3-dibromo derivative[3b,c] so also we found that treatment of 6-chloro-4-thiochromanone and 8-methyl-4-thiochromanone with two moles of bromine gave rise to 3,3-dibromo-6-chloro-4-thiochromanone and 3,3-dibromo-8-methyl-4-thiochromanone, respectively. On heating with pyridine these substances readily lost hydrogen bromide



As stated above, IV was prepared by condensing 3-(*p*-nitrophenoxy)-propionic acid (II) with phosphoryl chloride. It was made also by reaction of 6-nitro-4-chromanone (XI) with phosphorus pentachloride, whereas reaction of XI with sulfuryl chloride caused formation of XII which differed in properties from IV.



The IV gave the same m.p. and infrared spectrum whether it was prepared from XI or II. The spectrum (in potassium bromide) showed no carbonyl band between 5.8 to 6.0 μ, but it did show a band at 6.01 μ indicative of carbon-to-carbon double bond. On the other hand, XI (in chloroform) showed a carbonyl absorption at 5.83 μ. IV gave no 2,4-dinitrophenylhydrazone, and the starting material was recovered. IV was unaffected by chlorine when heated with pyridine and here again the starting material was recovered. An acetone solution of IV decolorized aqueous potassium permanganate immediately, showing the presence of a double bond. XI did not decolorize permanganate.

The reaction of XII with thiourea was investigated. An orange colored solid resulted having an empirical formula of $C_{10}H_9N_2O_4S$. Two possible

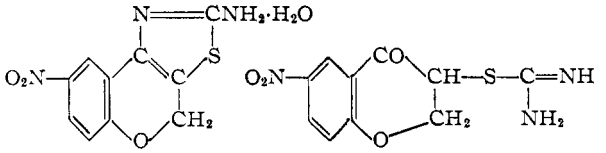
(7) G. R. Clemo and W. H. Perkin, Jr., *J. Chem. Soc.*, **125**, 1608 (1924); **127**, 2297 (1925); O. G. Backeberg, *ibid.*, 618 (1933).

(8) R. L. Shriner and S. O. Greenlee, *J. Org. Chem.*, **4**, 242 (1939).

(9) W. W. Rinne and co-workers, THIS JOURNAL, **72**, 5759 (1950); F. Ramirez and F. A. Kirby, *ibid.*, **74**, 4331 (1952).

(10) R. N. Jones, D. A. Ramsay, F. Herling and K. Dobriner, *ibid.*, **74**, 2828 (1952); N. J. Leonard and G. C. Robinson, *ibid.*, **75**, 2143 (1953); E. J. Corey, *ibid.*, **75**, 2301 (1953).

structures are XIIIa, a monohydrate of a 2-aminothiazole derivative, and XIIIb, a substituted isothiourea. The free base XIII was precipitated from a solution of its hydrochloride with concentrated ammonium hydroxide, and since there was



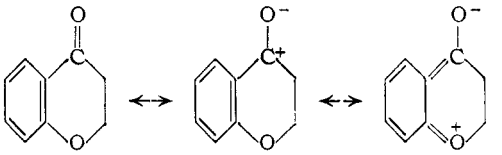
XIIIa XIIIb

no cleavage into a mercaptan this favors the more stable 2-amino-8-nitro-4H-thiazolo[5,4-c]benzopyran structure XIIIa. Its infrared spectrum showed the –OH band (2.83 μ), –NH– (3.00 μ), and =C=N– (6.10 μ). Also, there was no absorption around 5.9 μ for a conjugated carbonyl band. These facts all support structure XIIIa and confirm the conclusion that the chlorine in XII was at 3.

Propiolactone reacts smoothly with *p*-chloro- or *p*-bromoaniline to give the corresponding N-aryl-β-alanine[5b] in good yield. Elderfield and Maggiolo[11] have prepared N-*p*-chlorophenyl-β-alanine in a lower yield from ethyl acrylate and *p*-chloroaniline, and they cyclized its tolylsulfonyl derivative by heating with phosphoryl chloride to yield 6-chloro-2,3-dihydro-4(1H)-quinolone. We repeated this ring closure and obtained a product seemingly identical except that its melting point was 11–12° higher. The *p*-bromo derivative also was prepared and cyclized in the same way.

The conversion of I into III by phosphoryl chloride, presumably *via* 4-thiochromanone, suggests that the literature should reveal examples of similar chlorination of ketones into α-chloro ketones. We did not look exhaustively but we could find only one, namely, acetophenone which is converted by cold phosphorus pentachloride into benzoyldichloromethylphosphonic acid,[12] $C_6H_5COCCl_2PO(OH)_2$, (after hydrolysis) along with normal products of chlorination, α,α-dichloroethylbenzene and α-chlorostyrene.

The sulfur atom is the obvious distinguishing feature between thiochromanone and chromanone. It has been established[13] that the sulfur of *p*-substituted thiophenols (*i.e.*, *para* NO_2, CH_3SO_2, COOR, CN, etc.) undergoes less resonance interaction with the nucleus than is shown in the oxygen resonance of corresponding *p*-substituted phenols. One may assume that thiochromanone and chromanone exhibit a similar disparity, with the sulfur of the former showing less resonance interaction with the *o*-carbonyl than the oxygen of the latter does. This oxygen resonance would tend to inhibit tautomerism, hence would deactivate the methylene hydrogens alpha to the carbonyl. With less resonance interaction of sulfur in the thiochromanone there would be greater tautomeric activity of a methylene hydrogen and this is in



keeping with the fact that chlorination did occur at the methylene hydrogen; but the fact that ketones do not usually behave this way means that the explanation at best is only partial.

Experimental[14]

3-Arylmercaptopropionic Acids.—These acids were prepared from sodium aryl sulfides and propiolactone, adapting Gresham's procedure[2] for 3-phenylmercaptopropionic acid, aryl as *p*-bromophenyl: m.p. 114–115° (lit.[3c] 119°), yield 61%; aryl as *p*-chlorophenyl: m.p. 88–89.5° (lit.[3a] 90–91°), yield 83%; aryl as *p*-tolyl: m.p. 65–66° (lit.[3a,15] 70°, 71–72°), yield 96%.

4-Thiochromanone,[3a] 3-bromo-4-thiochromanone,[3b] 6-bromo-4-thiochromanone[3c] and 6-chloro-4-thiochromanone[3b] were prepared by cyclizing the 3-arylpropionic acid in sulfuric acid according to directions in the literature.

4-Thiochromanone 2,4-dinitrophenylhydrazone: orange-red needles, m.p. 237–238° dec.

Anal. Calcd. for $C_{15}H_{12}N_4O_4S$: C, 52.32; H, 3.49. Found: C, 52.25; H, 3.58.

4-Thiochromanone 1-Dioxide (VI).—A suspension of 16.8 g. of I in 150 g. of polyphosphoric acid was heated on a steam-bath for an hour to give a dark brown solution. After this was poured into crushed ice a brown oil separated. The mixture was made basic with solid sodium carbonate, then was extracted with ether. The ether layer was dried over sodium sulfate, the ether removed, and the remaining sirup (10 g.) was dissolved in 60 ml. of glacial acetic acid. To this solution of V was added 35 ml. of 30% hydrogen peroxide and it was heated at 100° for an hour to give a light yellow solution. On dilution with ice-water there was formed 9.1 g. (84% yield, based on 10 g. of V) of the sulfone melting at 128–129.5° (lit.[3c] 131–132°). A mixed m.p. with an authentic sample (m.p. 129–130°, yield 71.5%), prepared by use of sulfuric acid as a condensing agent followed by oxidation, was undepressed.

3-Bromo-4-thiochromanone 1-Dioxide (VIII). Method A.—To a solution of 0.75 g. of 3-bromo-4-thiochromanone in 10 ml. of acetic acid was added 2 ml. of 30% hydrogen peroxide. From this solution there was obtained 0.7 g. of the sulfone melting at 181–184° (darkening at 161°). It was recrystallized thrice from aqueous acetone to give colorless needles of m.p. 204–204.5° (lit.[3c] m.p. 199–200°).

Anal. Calcd. for $C_9H_7BrO_3S$: C, 39.27; H, 2.55. Found: C, 39.57; H, 2.62.

Method B.—To a solution of 6.0 g. of VI in 80 ml. of glacial acetic acid was added dropwise during 15 minutes at 60°, 4.9 g. of bromine in 20 ml. of acetic acid. The bromine color disappeared rapidly and a colorless solid separated. The solution was stirred at 50–60° for 4 hours and then was poured into crushed ice to give 7.6 g. (90.5%) of colorless solid of m.p. 198–200°. The sample was recrystallized twice from aqueous acetone to give needles of m.p. 203–203.5°. The mixed m.p. with the sample from A was undepressed.

3-Chloro-4-thiochromanone 1-Dioxide (IX). Method A.—To 28 ml. of phosphoryl chloride was added 18.2 g. (0.1 mole) of I and the suspension was heated on a steam-bath. It turned dark red at once. After 30 minutes it was poured into crushed ice. The dark sirup which resulted was extracted with ether, the ether layer washed with water, aqueous sodium carbonate and water, dried and the ether removed to give 16.7 g. of orange sirup. The latter was dissolved in 100 ml. of glacial acetic acid and 34 g. of 30% hydrogen peroxide was added. The solution was heated at 100° for an hour and treated with Norit. The light yellow filtrate was diluted with 500 ml. of water to give a milky suspension, which deposited 4.15 g. (4.3%) of light cream solid after standing for a day. It melted at about 170°

(11) R. C. Elderfield and A. Maggiolo, THIS JOURNAL, **71**, 1906 (1949).

(12) A. Béhal, *Bull. soc. chim.*, [2] **50**, 632 (1888).

(13) F. G. Bordwell and H. M. Andersen, THIS JOURNAL, **75**, 6019 (1953).

(14) Uncorrected melting points are given.

(15) F. Arndt, *Ber.*, **56**, 1276 (1923).

(softening at 145°). It was recrystallized thrice from aqueous acetone to give 1.1 g. of colorless needles of m.p. 198–199°. The sodium fusion test showed the presence of chlorine.

Anal. Calcd. for $C_9H_7ClO_3S$: C, 46.85; H, 3.04. Found: C, 47.05; H, 3.14.

Method B.—To a solution of 8.65 g. of VI in 100 ml. of chloroform was added 6.0 g. of sulfuryl chloride. The clear solution was refluxed for an hour and kept at room temperature overnight. Colorless needles separated. These were washed with water; yield 7.80 g., m.p. 194–195° (softening at 185°). A sample was recrystallized once from chloroform–acetone; m.p. 198.5–199°. A mixed m.p. with the sample from A was undepressed. Infrared spectra of both samples from A and B were identical. From the mother liquor, on removing solvent, there was obtained 1.85 g. of less pure product of m.p. 167–175°. One recrystallization from aqueous acetone caused it to melt at 194–196°; yield 0.7 g. Thus, the total yield was 8.5 g. (83%).

1,4-Benzothiapyrone 1-Dioxide Phenylhydrazone (X). A.—To a hot suspension of 2.31 g. of IX in 60 ml. of glacial acetic acid was added 3.25 g. of phenylhydrazine to give a light orange solution. It was heated at 100° bath for an hour, then was cooled in an ice-bath and diluted with water to give 1.7 g. of an orange powder of m.p. 183° (dec., softening at 175°). It was recrystallized twice from aqueous methanol to give a yellowish-brown solid of m.p. 199° dec. The chloroform solution of it was adsorbed on alumina in a column, and the light yellow band was eluted with chloroform to give a bright yellow solid of m.p. 204° dec. after evaporating the solvent. One recrystallization from chloroform–hexane raised the melting point to 212° dec.

Anal. Calcd. for $C_{21}H_{18}N_4O_2S$: C, 63.4; H, 4.23; N, 9.86. Found: C, 63.5; H, 4.26; N, 9.96.

B.—From 3.8 g. of VIII and 4.5 g. of phenylhydrazine in the same way as in A, 3.5 g. of a crude phenylhydrazone was obtained, m.p. *ca.* 140° dec. The purification of the product by means of chromatography gave a bright yellow solid of m.p. 198–199° dec. After two recrystallizations from chloroform–hexane the sample melted at 210–211° dec. The mixed m.p. with the sample from A was undepressed.

6-Bromo-4-thiochromanone 1-Dioxide.—A sample weighing 2.57 g. of 6-bromo-4-thiochromanone was oxidized with 30% hydrogen peroxide in acetic acid to give 2.6 g. (87%) of the corresponding sulfone of m.p. 148–154°. Two recrystallizations from aqueous methanol raised its m.p. to 155–156.5° (white silky needles).

Anal. Calcd. for $C_9H_7BrO_3S$: C, 39.27; H, 2.55. Found: C, 39.18; H, 2.61.

3-Chloro-6-bromo-4-thiochromanone 1-Dioxide.—Sulfuryl chloride, 2.0 g., was added to a solution of 3.0 g. of the above dioxide in 50 ml. of chloroform. It was refluxed for 2 hours, then cooled to cause the separation of colorless needles of m.p. 200–204°, yield 1.0 g. It was recrystallized twice from aqueous acetone to give needles of m.p. 205–206.5°.

Anal. Calcd. for $C_9H_6BrClO_3S$: C, 34.89; H, 1.94. Found: C, 34.94; H, 2.38.

From the mother liquor, after removing solvent, was obtained 2.3 g. of the crude starting material. After three recrystallizations from aqueous acetone it melted at 143–144°; recovery 1.65 g.

6-Chloro-4-thiochromanone 1-Dioxide.—The sulfide 6-chloro-4-thiochromanone, 5.0 g., was oxidized to its sulfone with hydrogen peroxide in acetic acid; yield 5.1 g. (76%), m.p. 155–156° after one recrystallization from aqueous acetone.

Anal. Calcd. for $C_9H_7ClO_3S$: C, 46.90; H, 3.04. Found: C, 46.89; H, 3.23.

3,3-Dibromo-6-chloro-4-thiochromanone.—To a warm solution of 7.6 g. (0.038 mole) of 6-chloro-4-thiochromanone in 100 ml. of glacial acetic acid was added dropwise 11.2 g. (0.07 mole) of bromine in 25 ml. of acetic acid during an hour at about 70°. It was stirred at this temperature for another hour and then at 25° for 2 hours. It was diluted with water (400 ml.) to give a yellow solid of m.p. 165° (dec., softening at 105°), yield 13.0 g. It was recrystallized thrice from benzene to yield 7.6 g. of canary yellow plates of m.p. 172° dec.

Anal. Calcd. for $C_9H_5Br_2ClOS$: C, 30.30; H, 1.40. Found: C, 30.55; H, 1.40.

The filtrates from the above recrystallizations were concentrated and diluted with hexane to give 3.9 g. of yellow micro crystals of m.p. 164–165° dec. This was found to be less pure dibromo compound from analysis (C, 30.71; H, 1.48).

3-Bromo-6-chloro-1,4-benzothiapyrone.—A solution of 2.4 g. of 3,3-dibromo-6-chloro-4-thiochromanone in 20 ml. of dry pyridine was heated on a steam-bath for 45 minutes and then poured into ice-water yielding 1.9 g. of precipitate of m.p. 164–164.5°. Two recrystallizations from benzene–hexane gave a pale tan solid of m.p. 168–169°.

Anal. Calcd. for $C_9H_4BrClOS$: C, 39.20; H, 1.45. Found: C, 39.38; H, 1.49.

6-Chloro-4-chromanone.—3-(*p*-Chlorophenoxy)-propionic acid,[2] 4.6 g., was dissolved in 50 ml. of concd. sulfuric acid to give a brownish-yellow solution, which was kept at 25° for two days and then poured into crushed ice. The 2.8 g. (66%) of resulting colorless precipitate melted at 100–101°. It was treated with aqueous sodium carbonate and insoluble solid was collected and recrystallized twice from aqueous methanol to yield a pure sample of m.p. 100–101° (lit.[1] m.p 106°).

Anal. Calcd. for $C_9H_7ClO_2$: C, 59.17; H, 3.84. Found: C, 59.22; H, 4.02.

6-Nitro-4-chromanone (XI). Method A.—A solution of 18.8 g. of 3-(*p*-nitrophenoxy)-propionic acid[2] in 100 g. of concd. sulfuric acid was kept at 25° for 33 hours and then poured into crushed ice to give a brown sirup, which soon changed to a yellow solid. The solid was treated with aqueous sodium carbonate. The alkali-insoluble solid weighed 2.85 g. (17% or 50% based on the acid cyclized). It was once recrystallized from aqueous acetone to give 2.80 g. of light tan crystals of m.p. 171–174°. Several recrystallizations from the same solvent raised its m.p. to 173–174° (lit.[1] m.p. 176–177°). The alkaline filtrate was acidified with dilute hydrochloric acid to give a white precipitate (12.5 g., 67% recovery), which was twice recrystallized from aqueous methanol to give the pure starting acid of m.p. 115–116.5° (lit.[2] m.p. 114–115°).

Method B.—A suspension of 18.0 g. of 3-(*p*-nitrophenoxy)-propionic acid in 350 g. of polyphosphoric acid was heated on a steam-bath for 4 hours with occasional stirring to give a dark brown solution, which was poured into ice-water to give a light brown oil, which gradually solidified to yield a light cream precipitate. It was collected and treated with aqueous sodium carbonate. The insoluble solid was collected, yield 12.0 g. (73%). It was once recrystallized from aqueous acetone to give 10.6 g. of yellowish tan crystals of m.p. 171–173°. The alkaline filtrate was acidified to give only 0.05 g. (0.28%, recovery) of the nitrophenoxypropionic acid, m.p. 113–115°.

2,4-Dinitrophenylhydrazone of XI: orange-red needles of m.p. 288–289° dec.

Anal. Calcd. for $C_{15}H_{11}N_5O_7$: C, 48.26; H, 2.95; N, 18.77. Found: C, 48.64; H, 3.04; N, 19.01.

6-Nitro-4-chloro-2H-benzopyran (IV). A.—A suspension of 11.9 g. of 3-(*p*-nitrophenoxy)-propionic acid in 25 ml. of phosphoryl chloride was heated on a steam-bath for 2 hours and then poured into crushed ice to give an orange-brown sirup, which gradually solidified to yield a red colored solid which, after treating with aqueous sodium carbonate, weighed 9.8 g. (90%). No solid was obtained when the basic filtrate was acidified. The crude product was once recrystallized from aqueous acetone (Norit) to give 6.3 g. of yellow needles of m.p. 129–132°. From the mother liquor another 2.0 g. of less pure product was secured. The sample was dissolved in benzene and chromatographed through alumina. The benzene eluate gave, after evaporation and a recrystallization from benzene–hexane, canary-yellow needles of m.p. 135–136°. Sodium fusion indicated the presence of chlorine.

Anal. Calcd. for $C_9H_6ClNO_3$: C, 51.06; H, 2.84; N, 6.61. Found: C, 51.14; H, 2.95; N, 6.83.

B.—An intimate mixture of 6.6 g. of XI and 20 g. of phosphorus pentachloride was heated for 3 hours at 115–120°. Phosphoryl chloride formed was removed at a water-pump. The remaining dark oil was treated with ice-water and then extracted with ether. The dark residue, after removing ether, was taken up in chloroform and chromatographed as

in A. The elution with benzene gave 2.2 g. of a bright yellow solid of m.p. 123° (softening at 110°). One recrystallization from aqueous acetone gave 2.0 g. of yellow microcrystals of m.p. 126° (softening at 120°). Sublimation of a sample at 130–150° (1 mm.) gave canary yellow needles of m.p. 134–135° after one recrystallization from benzene–hexane. The mixed m.p. with the sample from A was undepressed and infrared spectra of both samples were identical.

3-Chloro-6-nitro-4-chromanone (XII).—To a warm solution of 4.6 g. (0.022 mole) of XI in 100 ml. of chloroform was added 3.0 g. (0.022 mole) of sulfuryl chloride and it was refluxed for 4 hours, then was left at 25° for three days. The solution was evaporated to dryness on a steam-bath and the remaining brown sirup was treated with water. The colorless solid which formed immediately weighed 5.3 g. (97.5%), m.p. 100–101° (softening at 95°). The sample was recrystallized thrice from benzene–hexane to give needles of m.p. 107–108°.

Anal. Calcd. for $C_9H_6ClNO_4$: C, 47.47; H, 2.63; N, 6.15. Found: C, 47.36; H, 2.74; N, 6.17.

Reaction of XII with Thiourea.—A pale yellow solution of 1.6 g. (0.007 mole) of XII and 1.06 g. (0.014 mole) of thiourea in 50 ml. of 95% ethanol was refluxed for 1.5 hours. The intensely yellow solution, on concentration, gave a yellow solid. The reaction mixture was made basic with concd. ammonium hydroxide to give 0.55 g. of a bright orange solid of m.p. 210–215° (softening at 191°). It was twice recrystallized from methanol–hexane to give bright yellow micro crystals XIII of m.p. 213–215° dec. It was dried at 80° (0.3 mm.) for 2 hours and then was analyzed.

Anal. Calcd. for $C_{10}H_7N_3O_3S.H_2O$: C, 44.94; H, 3.37; N, 15.73. Found: C, 44.50; H, 3.15; N, 16.02.

6-Chloro-2,3-dihydro-4(1H)-quinolone.—Adapting the procedure of Elderfield and Maggiolo,[11] we prepared N-*p*-tolylsulfonyl-N-*p*-chlorophenyl-β-alanine from N-*p*-chlorophenyl-β-alanine[5b] and *p*-toluenesulfonyl chloride. It melted at 121–122° (lit.[11] m.p. 126–127°). From 8.85 g. of this acid, 0.6 g. of the pure quinolone was obtained, m.p. 125–126° (lit.[11] 112°). When their directions were followed, starting with *p*-chloroaniline and methyl acrylate, the quinolone (canary yellow needles) also melted high, at 123–124°. The mixture m.p. of the two was not depressed.

Anal. Calcd. for C_9H_8ClNO: C, 59.50; H, 4.40; N, 7.71. Found: C, 59.57; H, 4.69; N, 7.55.

2,4-Dinitrophenylhydrazone of this quinolone was prepared in the usual way to give orange red needles of m.p. 290° dec.

Anal. Calcd. for $C_{15}H_{12}ClN_5O_4$: C, 49.80; H, 3.32; N, 19.36. Found: C, 49.74; H, 3.32; N, 18.79.

6-Bromo-2,3-dihydro-4(1H)-quinolone.—From 11.6 g. of N-*p*-bromophenyl-β-alanine and 9.1 g. of *p*-toluenesulfonyl chloride, following the procedure of Elderfield and Maggiolo for the *p*-chloro derivative, we obtained 10.4 g. of the tolylsulfonyl derivative of the acid. One recrystallization from ether–hexane gave colorless needles of m.p. 134–135°. As with the chloro analog, it was cyclized by hot phosphoryl chloride. The excess of phosphoryl chloride was removed at a water-pump and the residue was treated with aqueous sodium hydroxide (10%). The oily mixture was extracted with ether and a white solid appeared between two layers. It was collected (yield 0.4 g.) and recrystallized from methanol-acetone to give colorless crystals of m.p. 174–176°. It was not soluble in aqueous base or acid, and was considered to be 6-bromo-2,3-dihydro-1-*p*-tolylsulfonyl-4(1H)-quinolone from its analysis.

Anal. Calcd. for $C_{16}H_{14}BrNO_3S$: N, 3.68. Found: N, 3.49.

The ether layer was evaporated and the gummy residue was hydrolyzed in a mixture of acetic and hydrochloric acid[11] during 5 hours. The solution was evaporated to dryness *in vacuo* and treated with 20% sodium hydroxide solution to give 1.15 g. of a yellowish-brown solid. It was twice recrystallized from benzene–hexane to give yellow needles, m.p. 130–131.5°, of 6-bromo-2,3-dihydro-4(1H)-quinolone.

Anal. Calcd. for C_9H_8BrNO: N, 6.19. Found: N, 5.94.

2,3-Dihydro-1-phenyl-4(1H)-quinolone.—A mixture of 400 g. of polyphosphoric acid and 30.5 g. of N,N-diphenyl-β-alanine[5a] was heated at 100° with occasional stirring for 3 hours to give a dark brown-red solution, which was poured into ice-water to yield a yellowish-brown gum. It was extracted with benzene–ether (1:1). The organic layer was then extracted with a 5% solution of sodium hydroxide. The water solution was heated with Norit and acidified with dilute hydrochloric acid to recover 19 g. (62%) of the starting acid, m.p. 110–112° after one recrystallization from aqueous methanol. The organic layer was dried, the solvent removed, and the remaining red oil was distilled to give a bright yellow liquid of b.p. 185–193° (4 mm.), yield 5.3 g. (52% based on the acid cyclized). The distillate soon changed to a yellow solid of m.p. 69–70°. A sample was recrystallized twice from aqueous methanol to give canary-yellow needles of m.p. 83–84° (lit.[4] m.p. 83–84°).

3-(*o*-Tolylmercapto)-propionic Acid.—To 0.2 mole of *o*-tolyl sodium sulfide (from *o*-thiocresol) in 200 ml. of water at 0° was stirred in dropwise 0.2 mole of propiolactone during 5 minutes. After an hour at room temperature the solution was acidified, the precipitate collected, washed and redissolved in aqueous sodium carbonate solution. Any ether-soluble material was removed from the latter prior to acidification. The bulky, white precipitate was collected, washed with water and dried. An analytical sample was crystallized from aqueous methanol and from benzene–hexane; m.p. 93–94°.

Anal. Calcd. for $C_{10}H_{12}O_2S$: C, 61.2; H, 6.12. Found: C, 61.8; H, 6.21.

8-Methyl-4-thiochromanone.—The entire crude yield of the mercapto acid was dissolved in 100 ml. of the concd. sulfuric acid. A red color developed at once. After 2 days the mixture was poured into crushed ice; yield 17.6 g. after washing and drying, m.p. 59–62°. This is a 49% yield based on thiocresol. The solid was insoluble in sodium carbonate solution. Two recrystallizations from aqueous methanol yielded 12.7 g. of pale tan plates of m.p. 64–65°.

3,3-Dibromo-8-methyl-4-thiochromanone.—Two parts of bromine (22.8 g.) in 40 ml. of acetic acid were added dropwise with stirring into one part of 8-methyl-4-thiochromanone (12.7 g.) in 100 ml. of acetic acid. After a subsequent 2.5 hours of stirring (25°) and standing overnight it was poured into ice-water. The yellow solid, m.p. 84–87°, weighed 24.6 g., which is about quantitative. Two recrystallizations from benzene–hexane gave straw-colored plates of m.p. 90–90.2°.

Anal. Calcd. for $C_{10}H_8Br_2OS$: C, 35.7; H, 2.38. Found: C, 35.9; H, 2.24.

3-Bromo-8-methyl-4-benzothiapyrone.—A mixture of 1.3 g. of this dibromide and 10 ml. of pyridine was kept an hour at 100°, then was poured into dilute hydrochloric acid. The 0.8 g. of solid appearing was thrice crystallized from aqueous methanol, bringing the m.p. from 105–107° up to 111–112°. These were colorless needles.

Anal. Calcd. for $C_{10}H_7BrOS$: C, 47.1; H, 2.75. Found: C, 47.1; H, 2.73.

Acknowledgments.—One of us (S.H.) received a research fellowship from funds supplied by Swift and Company, without which this work could not have been done. Microanalyses were performed by Mrs. C. White and Miss H. Beck. Infrared spectra were obtained by Mr. W. Fateley.

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