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Some Observations on the Interconversion of *cis* and *trans* Forms of α,β-Unsaturated Ketones

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Pyridine dehydrobromination of *erythro*-α,β-dibromo ketones obtained from a benzalacetone derivative (*trans*-2-keto-4-phenyl-3-butenyl benzoate (Ia)) and a chalcone derivative (*trans*-4-nitrochalcone (Ib)) yielded almost exclusively the *trans* forms (Va and Vb) of the resulting α-bromo-α,β-unsaturated ketones. Potassium acetate dehydrobromination afforded the expected mixture of *cis*- and *trans*-α-bromo-α,β-unsaturated ketones from these *erythro*-α,β-dibromo ketones and the *trans* product from a related *threo*-dibromo ketone. Pyridine induced the isomerization of the *cis* forms of 4-nitrochalcone (IIb) and 2-keto-3-bromo-4-phenyl-3-butenyl benzoate (IVa). Pyridine containing dissolved pyridine hydrobromide induced isomerization of *cis*-α-bromo-4-nitrochalcone (IVb) to the *trans* form Vb under conditions which failed to cause reaction when pyridine alone was present. The pyridine–pyridine hydrobromide combination appears to be more effective than iodine in promoting isomerization of this type of *cis* compound. Sodium iodide-induced debromination is apparently not stereospecific when applied to α,β-dibromo ketones; as is true of *erythro*-dibromides, two *threo*-α,β-dibromo ketones yielded *trans* products when debrominated in this manner.

In connection with an investigation of the stereochemistry of conjugate addition reactions[2] it became necessary to prepare some α,β-unsaturated ketones and their α-bromo derivatives in both *cis* and *trans* forms. The observations made in the course of this preparative work are recorded separately here because of their general implications with respect to the preparation and interconversion of such *cis* and *trans* isomers.

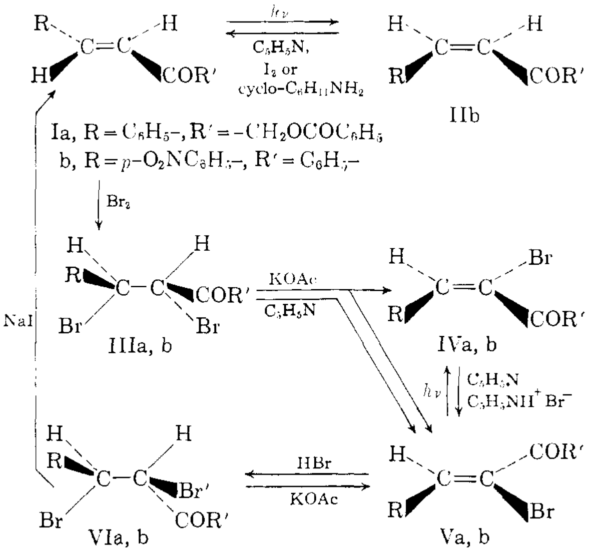
The initial objective of the work was preparation of crystalline *cis* and *trans* forms of an α-bromobenzalacetone derivative and of both a chalcone and the derived α-bromochalcone. It was decided to make use of the *cis* and *trans*-4-nitrochalcones (IIb and Ib)[3,4] and α-bromo-4-nitrochalcones (IVb and Vb),[5,6] compounds which were known to be accessible, although not easily so in each instance. On the other hand, the benzalacetone derivatives used in this work, the *cis*- and *trans*-2-keto-3-bromo-4-phenyl-3-butenyl benzoates (IVa and Va) and the parent unsaturated ketone *trans*-2-keto-4-phenyl-3-butenyl benzoate (Ia), were not known previously and were prepared for the first time for this investigation.

The transformations utilized or investigated are outlined in Chart I. The results observed in these reactions are described in the paragraphs which follow.

Results

(1) The ketone Ia, *trans*-2-keto-4-phenyl-3-butenyl benzoate, was obtained in 93% yield by treatment of iodomethyl styryl ketone[7] with sodium benzoate. *trans*-4-Nitrochalcone (Ib), prepared by condensation of p-nitrobenzaldehyde with acetophenone,[3] was converted in part into the *cis* form IIb by sunlight irradiation as had been reported by Black and Lutz.[4] A new procedure based upon ether extraction was developed for separation of the *cis* isomer IIb. It was observed that IIb was largely converted back into the *trans* compound Ib when treated with iodine in benzene or acetone solution, when dissolved in pyridine or triethylamine, or when treated with cyclohexylamine in benzene solution.

CHART I



(2) The dibromides IIIa and IIIb were obtained by addition of bromine to the *trans* unsaturated ketones Ia and Ib. They are considered to be *erythro* forms, as indicated in the formula given, not only because they were prepared by what is probably a *trans* addition of bromine to Ia and Ib, but also because, as discussed below, these compounds (unlike the *threo*-dibromide VIa) could be made to yield significant amounts of the *cis*-α-bromo-α,β-unsaturated ketones (IVa and IVb) (*trans* elimination) when dehydrobrominated with potassium acetate. Lutz, Hinkley and Jordan[8] advanced similar evidence in favor of an *erythro* configuration for the major dibromide formed by

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[2] See P. L. Southwick and J. E. Anderson, THIS JOURNAL, **79**, 6222 (1957), for an explanation of the nature of this investigation.

[3] H. Wieland, *Ber.*, **37**, 1148 (1904).

[4] W. B. Black and R. E. Lutz, *ibid.*, **75**, 5990 (1953).

[5] E. P. Kohler and C. R. Addinall, *ibid.*, **52**, 3728 (1930). The potassium acetate dehydrobromination described by these authors was reported to produce a high yield of *cis* isomer when conducted under modified conditions; see ref. 6.

[6] W. B. Black and R. E. Lutz, *ibid.*, **77**, 5134 (1955).

[7] P. L. Southwick, L. A. Pursglove and P. Numerof, *ibid.*, **72**, 1604 (1950).

[8] R. E. Lutz, D. F. Hinkley, Jr., and R. H. Jordan, *ibid.*, **73**, 4647 (1951).

addition of bromine to *trans*-chalcone. Like the *erythro*-chalcone dibromide,[8] IIIa and IIIb are higher melting than the corresponding *threo* forms VIa and VIb.

(3) Treatment of the dibromides IIIa and IIIb with potassium acetate in ethanol or a mixture of methanol and acetone yielded mixtures of dehydrobromination products containing both *cis* and *trans* forms of the corresponding α-bromo-α,β-unsaturated ketones. From the dibromide IIIa the ratio of isolated *cis* product IVa to isolated *trans* product Va was slightly over 1 to 2, whereas in the case of the chalcone dibromide IIIb[5] the *cis–trans* ratio of isomers (ratio of IVb to Vb) isolated from the product was close to 1 to 1.

On the other hand, when either of the dibromides IIIa or IIIb was dehydrobrominated by dissolving the compound in pyridine, the *trans* form Va or Vb was obtained in high yield (92.5% for Va, 83.7% for Vb), and at the most only a trace of the *cis* isomer could be detected.

Configurations of the *cis* and *trans* isomers IVa and Va were assigned on the basis of the observations that, as described below, treatment of the assumed *cis* form with pyridine converted it largely into the assumed *trans* form, whereas photoequilibration through the agency of sunlamp irradiation converted the assumed *trans* form in part into the assumed *cis* form. Moreover, on the basis of these configurational assignments the ultraviolet spectra of the compounds are in accord with the generalization, which is based upon the observations of Lutz and co-workers,[6,8] on several such pairs of geometrical isomers, that among α-bromo-β-phenyl-α,β-unsaturated ketones the *trans* isomer (phenyl and carbonyl in the *trans* relationship) has a more intense long wave length band than does the *cis* isomer.

(4) The dibromides VIa and VIb, diasteroisomers of IIIa and IIIb, were prepared by addition of hydrogen bromide to the *trans*-α-bromo-α,β-unsaturated ketones Va and Vb. Potassium acetate dehydrobromination of the compound VIa regenerated the *trans*-α-bromoketone Va in 80% yield; little or none of the *cis* isomer IVa was formed. These results are consistent with the assumption that both hydrogen bromide addition and elimination occur very predominantly in a *trans* manner, and with the conclusion that the dibromide VIa has the *threo* configuration, like the chalcone dibromide prepared in a similar fashion by Lutz, *et al.*,[8] and assigned the *threo* configuration on similar grounds. No dehydrobromination experiment was performed on VIb, but it is presumed also to be a *threo*-dibromide.

(5) When treated with sodium iodide in acetone the *threo*-dibromides VIa and VIb yielded mainly the *trans* forms Ia and Ib of the corresponding unsaturated ketones. *trans* Elimination of the two bromine atoms, the normal preferred course for this type of reaction,[9] should have led to the *cis*-ketones IIa and IIb. Since, as described above, it was found that the *cis*-4-nitrochalcone (IIb) is isomerized to the *trans* form by iodine, it is possible that the *cis* product was formed initially in these debromination reactions, but was isomerized under the conditions of the reaction by the iodine released. Another possibility is that the debromination was not a concerted process, but that attack by the iodide ion on the α-bromine resulted in formation of an intermediate enolate ion, as is probably true to a considerable extent in alkaline dehydrobromination.[8]

(6) The *cis* form IVa of the α-bromobenzalacetone derivative was readily isomerized to the *trans* form Va by pyridine used as a solvent, although not by a dilute ethanol solution of pyridine. On the other hand, the *cis* form of α-bromo-4-nitrochalcone (IVb) was *not* readily isomerized into the *trans* form Vb by treatment with triethylamine or pyridine or, according to a previous report,[6] by heating with iodine, or by sunlight irradiation in the presence of iodine. However, when dissolved in pyridine containing some pyridine hydrobromide, the *cis* form was converted into an equilibrium mixture containing *ca.* 93% of the *trans* isomer Vb, as measured spectroscopically and confirmed by the melting point of the material isolated from the equilibrated mixture. When equilibrated in the same way the *trans* isomer Vb yielded a mixture in which only *ca.* a 3% content of the *cis* isomer was evident (from spectroscopic data). It is noteworthy that although pyridine plus the pyridinium ion effected isomerization of the *cis* form IVb, triethylamine plus the triethylammonium ion (introduced by addition of acetic acid) failed to cause a comparable degree of isomerization under similar conditions.

Discussion

The significance of the foregoing observations is considered briefly: (1) With respect to the stereochemistry of bromine addition, hydrogen bromide addition, and sodium or potassium acetate-induced dehydrobromination, these results are strictly parallel to those reported by Lutz, Hinkley and Jordan[8] in their study of the stereochemistry of corresponding bromine derivatives of chalcone itself. Thus it appears that the pattern of behavior elucidated by those authors for the chalcone derivatives may be expected to extend to analogous benzalacetone derivatives as well as to chalcone derivatives bearing substituents in the aromatic rings. (2) The combination of pyridine and a pyridine salt is extremely effective as an agent for inducing equilibration of *cis* and *trans* isomers of α,β-unsaturated ketones.[10] For this reason pyridine may be an advantageous dehydrobromination agent for use with dibromides of such ketones when the product desired is the more stable form of the corresponding α-bromo-α,β-unsaturated ketone, but when the desired result is stereospecific *trans* elimination to give the unstable geometrical isomer,

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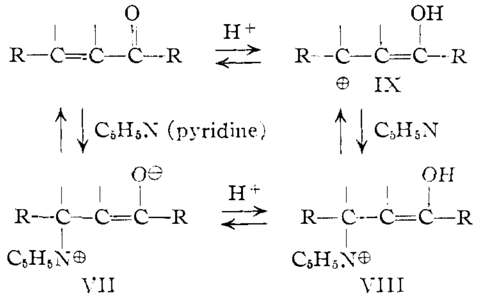
[9] S. Winstein, D. Pressman and W. G. Young, THIS JOURNAL, **61**, 1695 (1939).

[10] Many years ago Pfeiffer (P. Pfeiffer, *Ber.*, **43**, 3039 (1910)) showed that the pyridine–pyridinium salt combination was an efficient agent for isomerizing the *cis* form of α-halogen-α,β-unsaturated acids, whereas pyridine alone was less effective. Pfeiffer and others have noted that the dehydrobromination of α,β-dibromo acids with pyridine and other organic bases tends to yield a higher proportion of the stable form of the α-bromo-α,β-unsaturated acid than does dehydrobromination with solutions of strong alkalies; *cf.* T. C. James, *J. Chem. Soc.*, **97**, 1565 (1910), and L. N. Owen and M. U. S. Sultanbawa, *ibid.*, 3105 (1949).

sodium acetate or potassium acetate appear to be the best dehydrobromination agents presently known.

There would seem to be little doubt that when pyridine and other nitrogen bases induce geometrical isomerization of α,β-unsaturated ketones they do so through an attack at the β-carbon atom by which enolates such as VII and, in some cases, the related enols VIII are formed reversibly. It is apparent that such an attack by the base would be assisted by the shift of electrons away from the β-carbon which would result from protonation of the carbonyl oxygen to give IX (one contributing form shown). It is therefore reasonable to expect that the presence of an amine salt to serve as a proton source might be required to produce the isomerization reaction in the case of compounds not readily attacked by the organic base alone, as is evidently true of *cis*-α-bromo-4-nitrochalcone with respect to attack by pyridine.



The fact that the triethylamine–triethylammonium acetate combination does not isomerize *cis*-4-nitro-α-bromochalcone (IVb) readily, whereas the pyridine–pyridine hydrobromide combination does, probably can be explained on the basis of steric hindrance to the approach of the triethylamine nitrogen to the β-carbon. It must, however, also be noted that the triethylammonium ion is a weaker acid than the pyridinium ion; hence protonation of the carbonyl oxygen may also be less effective when the former agent is involved.

(3) In connection with some studies on the stereochemistry of the addition of N-halogen amines to α,β-unsaturated ketones,[11] it was desired to have an α-bromo-α,β-unsaturated ketone which was stable in the *cis* form. The observation of Black and Lutz[6] that sunlight irradiation of *trans*-α-bromo-4-nitrochalcone (Vb) in the presence of iodine converted that compound into a mixture (m.p. 114–120°) evidently consisting largely of the *cis* isomer IVb had suggested that the *cis* isomer of this pair was the more stable of the two, for the procedure had often been used for equilibrating *cis* and *trans* isomers. However, our results show that the *trans* isomer is the more stable compound in the equilibrating system containing pyridine and a pyridine salt, and suggest that the equilibrium attained in the presence of iodine with sunlight irradiation is a type of photoequilibrium.

(4) There remains the interesting question of why, although *cis*-4-nitrochalcone is isomerized by iodine or pyridine (without pyridinium ion) and *cis*-α-bromochalcone by heating with iodine,[8] *cis*-α-bromo-4-nitrochalcone (IVb) is apparently not affected by these agents. An additive effect of electron withdrawal by both bromine and *p*-nitrophenyl groups might be expected to diminish the susceptibility of the olefinic bond to electrophilic attack by molecular iodine and perhaps also to attack of the free radical type by iodine atoms resulting from photochemical dissociation. However by the same token, a reduced electron density in the olefinic bond should facilitate attack by pyridine. That it evidently does not do so would seem to indicate that a strong polarization of the olefinic bond is more effective in promoting nucleophilic attack than electron withdrawal from both ends of the bond as in compound IVb.

Experimental[12–14]

2-Keto-4-phenyl-3-butenyl Benzoate (Ia).—Benzoic acid (4.04 g., 0.033 mole) was dissolved in a solution of 1.4 g. (0.035 mole) of sodium hydroxide in *ca.* 15 ml. of water; dilute hydrochloric acid was added dropwise until a faint, permanent turbidity appeared. The solution was added to a refluxing solution of 9 g. (0.033 mole) of iodomethyl styryl ketone[7,15] in 90 ml. of ethanol. The mixture was refluxed for one-half hour and then cooled to room temperature. A crop of 8.2 g. (93%) of crude 2-keto-4-phenyl-3-butenyl benzoate, m.p. 100–105°, separated. Repeated crystallization from ethanol yielded fluffy, pale-yellow needles, m.p. 120–121.5°; ultraviolet spectrum (95% ethanol): λ_{max} 228 mμ (ε 27,300), 290–293 mμ (ε 27,900); λ_{min} 249 mμ (ε 5,470); infrared spectrum (chloroform): 3.30w, 3.43w, 5.79i, 5.86is, 5.92i, 6.19i, 6.34m, 6.69w, 6.89m, —10.25m.

Anal. Calcd. for $C_{17}H_{14}O_3$: C, 76.67; H, 5.30; mol. wt., 266. Found: C, 76.65; H, 5.34; mol. wt. (ebullioscopic, benzene), 265.

The oxime[16] crystallized from methanol–water mixtures as ivory-colored plates, m.p. 125–127°

Anal. Calcd. for $C_{17}H_{15}O_3N$: C, 72.58; H, 5.38; N, 4.98. Found: C, 72.27; H, 5.28; N, 4.64.

erythro-**2-Keto-3,4-dibromo-4-phenylbutyl Benzoate** (IIIa).—A solution of 12 g. (0.075 mole) of bromine in 40 ml. of chloroform was slowly added to a stirred solution of 20 g. (0.075 mole) of 2-keto-4-phenyl-3-butenyl benzoate (m.p. 110–116°) in 400 ml. of chloroform. The temperature was kept between 5° and 10° by an ice-bath. After the addition was completed, stirring was continued for another 1.5 hours while the temperature of the solution was maintained at 5°. A crop of solid separated when the solution was concentrated to *ca.* 50 ml. under reduced pressure. The solid was washed with ether to give 24.4 g. (76.3 %) of white powder, m.p. 167–168° dec. An additional 4.3 g. (13.4%) of tan product was isolated by further evaporation of the original chloroform solution. Repeated crystallization from carbon tetrachloride afforded fluffy, white needles, m.p. 184–186° dec.

Anal. Calcd. for $C_{17}H_{14}O_3Br_2$: C, 47.91; H, 3.31. Found: C, 48.13; H, 3.25.

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[11] P. L. Southwick and W. L. Walsh, THIS JOURNAL, **77**, 405 (1955).

[12] Ultraviolet spectra were determined with a Beckman spectrophotometer, model DU, or a Cary recording spectrophotometer; infrared spectra with a Perkin-Elmer recording infrared spectrophotometer, model 21. Infrared absorption bands, given in microns, are quoted over the range 2.5–7.00 μ, and the position of the longer wave length band (10.20–10.35 μ), diagnostic of *trans* hydrogens on the olefinic bond is given when observed. Intensities of infrared bands are indicated by the letters i (intense, 0–30% transmittance), m (medium 30–60% transmittance) and w (weak, 60–90% transmittance), which follow the figures for wave length. The letter s indicates that the absorption appears as a shoulder rather than a distinct maximum. Determinations were made on solutions containing 30–100 mg./ml.

[13] Melting points are corrected.

[14] Microanalyses by Dr. G. Weiler and Dr. F. B. Strauss, 164 Banbury Road, Oxford, England; Geller Laboratories, Bardonia, N. Y., and Micro Tech Laboratories, Skokie, Ill.

[15] P. L. Southwick and H. L. Dimond, THIS JOURNAL, **76**, 5667 (1954).

[16] R. L. Shriner and R. C. Fuson, "The Systematic Identification of Organic Compounds," 3rd ed., John Wiley and Sons, Inc., New York, N. Y., 1948, p. 202. Method A was used.

The *cis*- and *trans*-2-Keto-3-bromo-4-phenyl-3-butenyl Benzoates (IVa and Va). Potassium Acetate Dehydrobromination of IIIa.—A solution of 3.9 g. (0.04 mole) of potassium acetate in 25 ml. of ethanol was added dropwise over a period of 1.75 hr. to a refluxing slurry of 25.0 g. (0.0597 mole) of the dibromide (m.p. 174–180° dec.) in 400 ml. of ethanol. The mixture was refluxed for another 20 minutes and then cooled to room temperature. Potassium bromide and 11.3 g. of unreacted starting material was filtered from the mixture. The filtrate was concentrated to *ca.* 50 ml. by vacuum distillation. The residue was dissolved in ether and washed with aqueous sodium bicarbonate and then water; the solution was dried over magnesium sulfate and evaporated under reduced pressure to give 10.0 g. (93.7%) of crude product.

The 31.5 g. of crude product isolated from four reactions similar to the above was separated by a combination of fractional crystallization from methanol and manual separation into 17.4 g. of large, yellow prisms, m.p. 69.5–73.5°, of *trans*-2-keto-3-bromo-4-phenyl-3-butenyl benzoate and 9.7 g. of pale-yellow needles, m.p. 95.5–98°, of *cis*-2-keto-3-bromo-4-phenyl-3-butenyl benzoate. Analytical samples were prepared by further crystallizations of these isomers from methanol; *trans* isomer, m.p. 72–74°; *cis* isomer, m.p. 98–99°; ultraviolet spectra (95% ethanol): *trans* isomer, λ_{min} 229 mμ (ϵ 38,200), 299 mμ (ϵ 34,000); $\lambda_{min.}$ 213 mμ (ϵ 19,800), 253 mμ (ϵ 8,500); *cis* isomer, λ_{max} 232 mμ (ϵ 42,700), 283.5 mμ (ϵ 13,650), 297.5 mμ (ϵ 13,800); λ_{min} 215 mμ (ϵ 27,300), 278 mμ (ϵ 13,200), 289 mμ (ϵ 13,300); infrared spectra (in carbon tetrachloride): *trans* isomer, 3.28w, 3.43w, 5.76i, 5.87i, 6.28i, 6.36ms, 6.72m, 6.92m; *cis* isomer, 3.28w, 3.43w, 5.79i, 6.22w, 6.32w, 6.35w, 6.70w, 6.90w.

Anal. Calcd. for $C_{17}H_{13}O_3Br$: C, 59.15; H, 3.79; Br, 23.15. Found (*trans* isomer): C, 59.52; H, 3.67. (*cis* isomer): C, 59.02; H, 3.79; Br, 23.2.

***trans*-2-Keto-3-bromo-4-phenyl-3-butenyl Benzoate (Va). Pyridine Dehydrobromination of IIIa.**—A solution of 5.0 g. of the dibromide (m.p. 174–180° dec.) in 60 ml. of pyridine stood at room temperature for an hour. The solution was poured into a stirred mixture of ice and excess concentrated hydrochloric acid. The slurry was extracted with ether. The extract was washed with water, dried over magnesium sulfate and evaporated under reduced pressure. Crystallization of the residue from methanol gave 3.7 g. (92.5%) of *trans*-2-keto-3-bromo-4-phenyl-3-butenyl benzoate, m.p. 71–73°.

***threo*-2-Keto-3,4-dibromo-4-phenylbutyl Benzoate (VIa).**—A stream of hydrogen bromide was bubbled for one hour through a cooled solution of 6.6 g. (0.019 mole) of *trans*-2-keto-3-bromo-4-phenyl-3-butenyl benzoate in 50 ml. of carbon tetrachloride. After the mixture had stood at room temperature for a day, 1.7 g. (21%) of the *erythro*-dibromide IIIa was filtered out. Evaporation of the filtrate gave 6.4 g. (79%) of residue. One crystallization from carbon tetrachloride yielded 4.6 g. of tan solid, m.p. 107–111°. Repeated crystallization from methanol gave white needles, m.p. 113–115°.

Anal. Calcd. for $C_{17}H_{14}O_3Br_2$: C, 47.91; H, 3.31; Br, 37.51. Found: C, 47.56; H, 3.20; Br, 37.7.

Dehydrobromination of *threo*-2-Keto-3,4-dibromo-4-phenylbutyl Benzoate (VIa) with Potassium Acetate.—A solution of 1.1 g. (0.0112 mole) of potassium acetate in 15 ml. of ethanol was added over a 10-minute period to a refluxing solution of 4.6 g. (0.0108 mole) of the dibromide (m.p. 107–111°) in 40 ml. of ethanol. Separation of isomers was attempted as in the dehydrobromination of the *erythro*-dibromide IIIa. Crystallization of the crude product from methanol gave 2.9 g. (80%) of *trans*-2-keto-3-bromo-4-phenyl-3-butenyl benzoate, m.p. 71–73.5°. Concentration of the mother liquor gave an additional small portion of solid which appeared to consist of both dehydrobromination products IVa and Va.

Reaction of *threo*-2-Keto-3,4-dibromo-4-phenylbutyl Benzoate (VIa) with Sodium Iodide.—A solution of 0.32 g. of the dibromide (m.p. 112–115°) and excess sodium iodide in acetone stood at room temperature in the dark for 4 hours. The sodium bromide was filtered from the solution, and the filtrate was concentrated under reduced pressure. The mixture was treated with aqueous sodium sulfite and extracted with ether. The extract was washed with water, dried over magnesium sulfate, and evaporated. The residue consisted of 0.11 g. (55%) of yellow powder, m.p. 83–100°. Two crystallizations from methanol afforded a yellow solid, m.p. 111–113°, which appeared to be a crude sample of the previously isolated form of 2-keto-4-phenyl-3-butenyl benzoate (Ia).

***cis*-4-Nitrochalcone (IIb),**—*trans*-4-Nitrochalcone was prepared from acetophenone and *p*-nitrobenzaldehyde by the procedure of Wieland.[3] The following general procedure was adopted for the preparation of the *cis* isomer. A saturated benzene solution of the *trans* isomer was exposed to sunlight for 2 to 4 days. The solution was chilled in a refrigerator and then filtered to remove the bulk of the less soluble, unchanged *trans* isomer. The solution was evaporated to dryness under reduced pressure on a steam-cone, with care to avoid excessive heating. Crude *cis*-4-nitrochalcone was isolated by repetition of a procedure involving extraction of the residue with ether, evaporation of the ether extract, and ether extraction of the residue from evaporation of the preceding ether extract. When the residue resulting from several such operations was freely soluble in ether (crude yields of 25–40%), it was crystallized from methanol, giving small, pale-yellow needles, m.p. 88–90°. Repeated crystallizations from methanol afforded an analytical sample, m.p. 89–91°.

Anal. Calcd. for $C_{15}H_{11}O_3N$: C, 71.14; H, 4.37; N, 5.53. Found: C, 71.14; H, 4.38; N, 5.10.

This compound has been reported to melt at 98–98.5°.[4] The sample described here may be a different polymorphic form. The ultraviolet spectrum did not indicate the presence of any significant amount of the *trans* isomer in the sample; *cf.* ultraviolet data in references 4 and 6; ultraviolet spectrum (95% ethanol): λ_{max} 262.5 mμ (ϵ 12,600), 301 mμ (ϵ 18,000); $\lambda_{min.}$ 237.5 mμ (ϵ 10,200), 265 mμ (ϵ 12,500); infrared spectrum (chloroform): 3.30w, 6.00i, 6.20m, 6.27i, 6.32m, 6.59i, 6.71w, 6.91m.

***trans*-α-Bromo-4-nitrochalcone. (Vb). Pyridine Dehydrobromination of IIIb.**—A solution of 35 g. (0.085 mole) of *erythro*-4-nitrochalcone dibromide (IIIb), m.p. 150–152.5°,[3] in 85 ml. of pyridine stood for 24 hours at room temperature. The reaction mixture was poured into a mixture of ice and 185 ml. of concentrated hydrochloric acid. The resulting slurry was extracted twice with ether. The combined ether extracts were washed with water, dried over magnesium sulfate, and evaporated.

The residue was crystallized from benzene to give large, glassy, yellow prisms, which appeared in several crops as the solution was concentrated by evaporation. This product melted over the range 60–82°. It represents a form of the *trans* isomer which may perhaps be solvated with benzene. It was recrystallized from methanol to which some acetone (a minimum amount) was added to prevent separation of the compound as an oil. Several crops of crystals totaling 23.6 g. (a 83.7% yield) were obtained as the solvent mixture was concentrated by evaporation. Final crystallizations were performed with the same solvent mixture.

Two crystalline forms of the compound were encountered. The first to be observed melted at 64.5–66.5°, and formed large, light-yellow prisms.

Anal. Calcd. for $C_{15}H_{10}O_3NBr$: C, 54.24; H, 3.03; N, 4.22. Found: C, 54.49; H, 3.10; N, 4.11.

Melting points reported previously for this isomer were 62°,[5] and 54–56°.[6]

Later the compound usually crystallized from the same solvent mixture in the form of large, yellow prisms, m.p. 73–75°. Infrared spectra in chloroform of the two forms were identical and a mixture of the two melted at the higher m,p.; ultraviolet spectrum (95% ethanol): λ_{max} 245 mμ (ϵ 13,950), 310 mμ (ϵ 20,500); $\lambda_{min.}$ 236 mμ (ϵ 13,200), 267 mμ (ϵ 12,300); infrared spectrum (chloroform): 3.30w, 5.98i, 6.25m, 6.56i, 6.70w, 6.91m.

Anal. Calcd. for $C_{15}H_{10}O_3NBr$: C, 54.24; H, 3.03; N, 4.22. Found: (form of m.p. 73–75°) C, 54.36; H, 3.47; N, 4.0.

A trace of *cis*-α-bromo-4-nitrochalcone could usually be isolated from the mother liquors of the first crystallization.

***cis*- and *trans*-α-Bromo-4-Nitrochalcones (IVb and Vb). Potassium Acetate Dehydrobromination of IIIb.**—A solution of 3.4 g. (0.0347 mole) of potassium acetate in a mixture of 50 ml. of methanol and 50 ml. of acetone was shaken intermittently with 13.6 g. (0.0330 mole) of *erythro*-4-nitrochalcone dibromide (IIIb), m.p. 150–152.5°,[3] for 2.5 hours at room temperature. Filtration gave 1.7 g. (43%) of potassium bromide. The filtrate was evaporated to dryness under reduced pressure, and the residue was washed with water. Fractional crystallization from methanol afforded 3.6 g. of the unchanged dibromide, 1.7 g. (21%) of the *cis* isomer, m.p. 109–119°, and 1.7 g. (21%) of the *trans* isomer. A purified sample of the *cis* isomer was prepared by further crystallization from methanol; small, pale-yellow needles, m.p. 128–130°. The melting point of this isomer was previously reported as 130°[5] or 127–129°.[6] A mixed melting point with the lower melting form (m.p. 66°) of the *trans* isomer was 57–61°; ultraviolet spectrum of the *cis* isomer IVb (95% ethanol): λ_{max} 264.5 mμ (ϵ 17,050), 302.5 mμ (ϵ 17,900); $\lambda_{min.}$ 237.5 mμ (ϵ 13,900), 277.5 mμ (ϵ 15,500); infrared spectrum (chloroform): 3.30w, 5.95i, 6.16w, 6.23m, 6.29ws, 6.54i, 6.68w, 6.87w.

***threo*-2,3-Dibromo-3-(*p*-nitrophenyl)-1-phenyl-1-propanone (VIb).**—Hydrogen bromide was passed through a solution of 4.0 g. (0.012 mole) of *trans*-α-bromo-4-nitrochalcone in 30 ml. of carbon disulfide for 1.5 hours. Evaporation of the solution gave 5.0 g. (100%) of a yellow oil which solidified on scratching with a glass rod. The crude product melted at 91–100°. Five crystallizations from methanol gave ivory-colored needles, m.p. 112–114°.

Anal. Calcd. for $C_{15}H_{11}O_3NBr$: C, 43.61; H, 2.68; N, 3.39. Found: C, 43.90; H, 3.20; N, 3.38.

Reaction of *threo*-2,3-Dibromo-3-(*p*-nitrophenyl)-1-phenyl-1-propanone (VIb) with Sodium Iodide.—A solution of 3.7 g. (0.009 mole) of the dibromide VIb (m.p. 102–109°) and 2.7 g. (0.018 mole) of sodium iodide in 35 ml. of anhydrous acetone stood for one hour at room temperature in a flask wrapped with aluminum foil. The mixture was treated with excess aqueous sodium sulfite and filtered to give 1.2 g. (55%) of a yellow solid, m.p. 162–164°. A mixed melting point with *trans*-4-nitrochalcone was 162–164°.

Isomerization of the Isomeric Forms of 2-Keto-3-bromo-4-phenyl-3-butenyl Benzoate. Irradiation of the *trans* Isomer.—A solution of 5.0 g. of the *trans* isomer in 315 ml. of ether was irradiated for 5 days in a quartz cell, cooled by a stream of water running over its surface, by a General Electric Mazda S-4 lamp set 4 cm. from a face of the cell. The solution was evaporated and crystallized from methanol to give 1.5 g. of the starting material, m.p. 71–73°, 0.8 g. of the *cis* isomer, m.p. 95.5–97.5°, and an oil which could not be crystallized.

Reaction of the *cis* Isomer with Pyridine.—A solution of 72 mg. of the *cis* isomer in 3 ml. of pyridine stood at room temperature for 35 minutes. The solution was poured into a mixture of ice and concentrated hydrobromic acid, and the resulting slurry was extracted with ether. The ether extract was washed with water, dried over magnesium sulfate, and evaporated to leave 50 mg. of solid, m.p. 55–62°. The residue was crystallized once from methanol to give a solid, m.p. 68–72°. A mixed melting point with a sample of *trans*-2-keto-3-bromo-4-phenyl-3-butenyl benzoate was 70–74°.

Treatment of the *cis* Isomer with Pyridine in Ethanol.—One milliliter of ethanol containing 1.14×10^{-4} mole of pyridine was added to a solution of 0.517 g. (0.0015 mole) of the *cis* isomer in 70 ml. of ethanol. The solution stood for 18 hours at 20°, and was evaporated to dryness under reduced pressure. The residue was dissolved in ether, and the solution was washed with water, dried over magnesium sulfate, and evaporated to give 0.406 g. of unchanged *cis* isomer, m.p. 91–93°.

In similar experiments, potassium acetate and acetic acid were equally uneffective in promoting isomerization.

Isomerization of *cis*-4-Nitrochalcone (IIb). With Iodine in Acetone.—A solution of 0.15 g. of the *cis* isomer, 0.15 g. of iodine, and 2 ml. of acetone stood at room temperature for 1 hour in a flask wrapped in aluminum foil. The solution was then poured into a concentrated aqueous solution of sodium sulfite, and the bulk of the acetone was removed under reduced pressure. The precipitated solid was filtered, washed with water, and dried in air; 0.14 g. of the *trans* isomer, m.p. 159–163°, was isolated.

With Iodine in Benzene.—A solution of 0.10 g. of the *cis* isomer, 0.10 g. of iodine and 2.5 ml. of benzene stood at room temperature for 2 hours. The solution was diluted with ether, washed with saturated aqueous sodium sulfite and then water, dried over magnesium sulfate, and evaporated under reduced pressure. There was recovered 0.09 g. of a yellow solid melting over the range, 87–162°. The major portion of the melting occurred near the upper limit, and evidently represented mainly the *trans* isomer.

With Cyclohexylamine in Benzene.—A solution of 0.10 g. of the *cis* isomer, 0.25 ml. of cyclohexylamine, and 2.5 ml. of benzene stood at room temperature for 2 hours. The solution was diluted with ether, washed with water, dried over magnesium sulfate, and evaporated to give 0.08 g. of a yellow solid, m.p. 86–160°. The melting occurred mainly near the upper limit, indicating that the *trans* isomer predominated in the mixture.

With Pyridine.—A solution of 0.10 g. of the *cis* isomer in 3 ml. of pyridine stood at room temperature for 13 hours. The solution was poured into a mixture of ice and excess concentrated hydrochloric acid. The solid was filtered, washed with water, and dried in air to give 0.10 g. of a yellow solid, m.p. 87–160°. Again most of the melting occurred near the upper limit, indicating a predominance of the *trans* isomer. Similar results were obtained using triethylamine in place of pyridine.

With Pyridine and Hydrochloric Acid.—A procedure identical with that described immediately above was employed except that one drop of 2 molar hydrochloric acid in absolute ethanol was added to the solution. The same kind of product mixture was obtained.

Isomerization of the *cis*- and *trans*-α-Bromo-4-nitrochalcones (IVb and Vb) with Pyridine and Pyridine Hydrobromide.—A solution of 0.5 g. of *cis*-α-bromo-4-nitrochalcone (IVb) in 4 ml. of pyridine to which 3 drops of 48% aqueous hydrobromic acid had been added was allowed to stand at room temperature for 17 hr. The mixture was poured into a beaker of ice containing 10 ml. of 48% hydrobromic acid and the resulting aqueous suspension was extracted with ether. The ether extract was washed with water, dried over magnesium sulfate and evaporated to leave 0.4 g. of residual yellow solid, m.p. 53–60°.

A calculation of the proportion of isomers present was based upon measurement of the ultraviolet spectrum and use of the expression

$$\frac{\epsilon^{t}{}_{310}f_t + \epsilon^{c}{}_{310}(1 - f_t)}{\epsilon^{t}{}_{265}f_t + \epsilon^{c}{}_{265}(1 - f_t)} = \frac{D_{310}}{D_{265}}$$

where f_t is the fraction of the *trans* compound in the mixture of isomers, D_{310}/D_{265} is the ratio of the observed optical density at 310 mμ to that at 265 mμ, and the molecular extinction coefficients used for the *cis* and *trans* isomers at the two different wave lengths were taken from curves for the pure isomers: $\epsilon^{t}{}_{310}$ 20,500, $\epsilon^{c}{}_{310}$ 16,700, $\epsilon^{t}{}_{255}$ 12,400, $\epsilon^{c}{}_{265}$ 17,050. A value of 0.93 for f_t (93% *trans* isomer) was obtained in this way from values of 0.459 for D_{310} and 0.289 for D_{265} measured on an ethanol solution calculated to be 2.36×10^{-5} molar if the isolated product contained nothing but the two geometrical isomers. This result must approximate the true proportion of *trans* isomer provided that the two isomers were the only components of the isolated product which made a significant contribution to the ultraviolet absorption at the wave lengths used. The curve for the mixture did, in fact, closely approximate that for the pure *trans* isomer, but the extinction near 310 mμ (ϵ 19,500) was slightly lower than that for the pure *trans* compound and the minimum at 267 mμ was lacking, presumably due to the presence of approximately 7% of the *cis* compound.

In an identical experiment 0.5 g. of the *trans* isomer yielded 0.4 g. of a yellow solid, m.p. 55–59°. The ultraviolet spectrum of an ethanol solution calculated to be 2.10×10^{-5} molar showed values of 0.411 for D_{310} and 0.252 for D_{265}. The value of f_t calculated from these figures was 0.97 (97% *trans* isomer).

Similar experiments using pyridine alone without the added hydrobromic acid left both isomers substantially unchanged over an 18-hr. reaction period. When triethylamine or triethylamine plus a small amount of acetic acid was used in place of pyridine and hydrobromic acid in experiments with the *cis* isomer the melting points of the isolated product mixtures were in the range 104–121°, indicating much unchanged *cis* isomer, and the ultraviolet spectra still had the gross appearance of the spectrum of the *cis* compound, with a prominent maximum at 265 mμ. However, the ratio D_{310}/D_{265} was considerably greater than that for the pure *cis* isomer, indicating the presence of appreciable amounts of the *trans* compound. No quantitative estimate of the proportion of isomers was attempted because some decomposition was evident in these experiments, especially in the mixture containing the acetic acid.

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