tions with actinometer solution[21] (with optimum concentrations to give a quantum yield of 0.60 at 2537 Å.—about 0.01 *M* in uranyl sulfate and 0.025 *M* in oxalic acid). Titration of an aliquot portion (10 ml.) of this solution required 41.6 ml. of 0.0114 *N* potassium permanganate solution (0.0474 *N* oxalic acid). The stirred actinometer solution (80 ml. in the reaction tube) was irradiated for 2400 seconds (0–2°, with the apparatus immersed in an ice–water-bath) after which an aliquot portion (10 ml.) required 39.2 ml. of the permanganate solution (0.11 millimole of oxalic acid consumed in the 80-ml. solution). The remaining solution (70 ml.) was then irradiated for an additional 1800 seconds and titration of a 10-ml. aliquot required 37.2 ml. of the permanganate solution (0.080 millimole of oxalic acid used in the 70-ml. solution).

The reaction tube was then filled to the same level with a solution of diazomethane (from N-nitroso-N-methylurea, 18 g., 0.174 mole) in carbon tetrachloride (100 ml., n^{20}D 1.4600). The outer tube was filled with actinometer solution, and the apparatus was immersed in an ice–water-bath which held the reaction temperature at 0–2°. Irradiation of the reaction mixture for two successive periods (300 seconds each) gave nitrogen (149 ml. at S.T.P.) from reaction of diazomethane (6.65 millimoles) in each time period. The calculated gross quantum yield was 298. During the reaction experiment and the quantum output determination the light was completely absorbed by the contents of the reaction tube. The oxalic acid concentration of the actinometer solution in the outer tube did not change.

The Reaction of Diazomethane with Methyl Dichloroacetate.—In a stream of nitrogen (5.2 l.), diazomethane (17.3 g., 0.41 mole) was swept over a period of two hours into methyl dichloroacetate (166 g., 1.19 moles) illuminated internally with the mercury discharge tube. Two additional hours of illumination were needed before nitrogen evolution ceased. Total nitrogen volume measured by the Precision Wet Test meter (15.7 l.) indicated its yield (10.5 l. at 25° and 750 mm., 0.42 mole, 100% yield) from the diazomethane generation and light reactions. Methyl ether (2.5 g.) and polymethylene (0.04 g.) were obtained.

The reaction mixture was distilled to give recovered methyl dichloroacetate (b.p. 45.5–46° at 14 mm., 152 g.) and a product fraction (b.p. 46–67° at 14 mm., 16.94 g.). A residue (1.8 g.) remained in the distilling flask. The product was redistilled to give the following fractions: 1, b.p. 47–49° at 14 mm., 1.83 g.; 2, b.p. 49–64° at 14 mm., 3.22 g.; 3, b.p. 54–59.5° at 14 mm., 2.88 g., and 4, b.p. 59.5–68° at 14 mm., 2.27 g. Analysis of these fractions indicated that they contain little of the expected methyl α,α-bis-(chloromethyl)-propionate ($C_6H_{10}O_2Cl_2$, fraction 1 is apparently in part unreacted methyl dichloroacetate), and that the dominant product is probably methyl α,α-bis-(chloromethyl)-butyrate ($C_7H_{12}O_2Cl_2$).

Anal. Calcd. for $C_6H_{10}O_2Cl_2$: Cl, 38.3; mol. wt., 185; for $C_7H_{12}O_2Cl_2$: Cl, 35.6; mol. wt., 199. Found: fraction 1, Cl, 42.0; mol. wt., 185; fraction 2, Cl, 35.8; mol. wt., 190; fraction 3, Cl, 35.6; mol. wt., 198; fraction 4, mol. wt., 203.

Fractions 2 and 3 were combined and reduced with excess lithium aluminum hydride (0.1 *N* solution in ether). The resulting alcohol gave an α-naphthylurethan (m.p. 159.5–160°) which gave the correct analysis for that of 2,2-bis-(chloromethyl)-butanol-1.

Anal. Calcd. for $C_{17}H_{19}O_2NCl_2$: C, 60.01; H, 5.63; Cl, 20.84. Found: C, 59.49; H, 5.61; Cl, 20.92.

CHICAGO, ILLINOIS

(21) W. G. Leighton and G. S. Forbes, THIS JOURNAL, **52**, 3139 (1930).

[CONTRIBUTION FROM AVERY LABORATORY, UNIVERSITY OF NEBRASKA]

Ethylenimine Ketones. XI.[1] Steric Controls in the Formation of Isomeric Ethylenimine Ketones

BY NORMAN H. CROMWELL, ROGER P. CAHOY, WILLIAM E. FRANKLIN AND GERALD D. MERCER

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A study of the reaction of α-bromo-α,β-unsaturated ketones with primary amines indicates that the ethylenimine ketone *cis/trans* product ratio which results is nearly the same as that observed for the analogous reactions with the corresponding α,β-dibromoketones. Evidence is presented to support a rationale to explain the ethylenimine ketone *cis/trans* product ratio based on relative group sizes in the intermediate α-bromo-β-aminoketones and favored conformations in transition states. The reaction of N-bromocyclohexylamine and cyclohexylamine with *p*-phenylcrotonophenone by various procedures produced the *cis*-ethylenimine ketone which is the major, though not exclusive, product from the reaction of α-bromo-*p*-phenylcrotonophenone and cyclohexylamine, indicating that similar steric controls operate in these diverse reactions. Several new examples of the N-iodo amine reaction with α,β-unsaturated ketones to produce only *trans*-ethylenimine ketones have been performed. An explanation of the relative adsorptivity of *cis*- and *trans*-ethylenimine ketones on activated alumina is presented.

A comparison of the ratios of the amounts of the *cis* and *trans* isomeric forms of ethylenimine ketones resulting from the reactions of primary amines with 4′-phenylchalcone dibromide[2] and *p*-phenylcrotonophenone dibromide[1] suggests that steric controls are operating during the formation of the products. With the former dibromide,[2] cyclohexylamine produced 47% of the *cis* isomer and 44% of the *trans* isomer[2] of 1-cyclohexyl-2-phenyl-3-(*p*-phenylbenzoyl)-ethylenimine, while methylamine gave 20% of the *cis* and 70% of the *trans* isomer[2] of 1-methyl-2-phenyl-3-(*p*-phenylbenzoyl)-ethylenimine with the same dibromide.[2] With the latter dibromide,[1] cyclohexylamine formed 59% of the *cis*- and 33% of the *trans*-1-cyclohexyl-2-methyl-3-(*p*-phenylbenzoyl)-ethylenimine.[1]

(1) For paper X, see N. H. Cromwell and R. J. Mohrbacher, THIS JOURNAL, **75**, 6252 (1953).

(2) N. H. Cromwell and M. A. Graff, *J. Org. Chem.*, **17**, 414 (1952).

It has been postulated that the first step in the reaction of a primary amine with an α,β-dibromoketone is the formation of the α-bromo-α,β-unsaturated ketone. This is then followed by a 1,4-addition of the amine to produce the α-bromo-β-aminoketones.[3] It has been pointed out[2] that these intermediate α-bromo-β-aminoketones must exist as varying mixtures of the diastereoisomeric *erythro* and *threo* forms. An internal SN2 type ring closure would then be expected to produce the mixed *cis*- and *trans*-ethylenimine ketones. A study of the mechanism and stereochemistry of three-ring cleavage and closure[4] has revealed the fact that each ring closure of the halo amino ketones involves a Walden inversion. This suggests that the ethylenimine ketone *cis/trans* ratio is determined by the product ratio of the intermediate

(3) N. H. Cromwell and D. J. Cram, THIS JOURNAL, **65**, 301 (1943).

(4) N. H. Cromwell, *et al.*, *ibid.*, **75**, 5384 (1953).

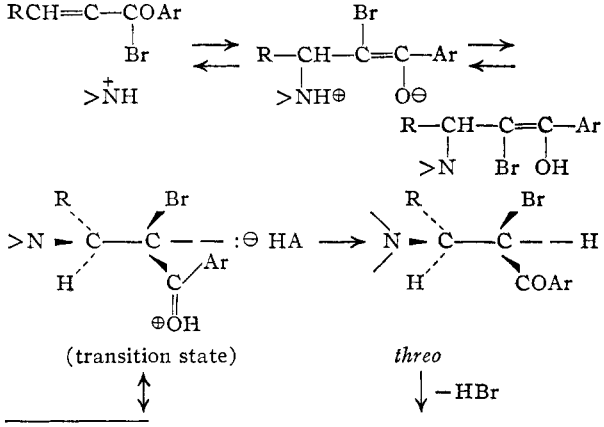
erythro and *threo* forms of the α-bromo-β-aminoketones resulting from the 1,4-addition of the amine to the α-bromo-α,β-unsaturated ketones.

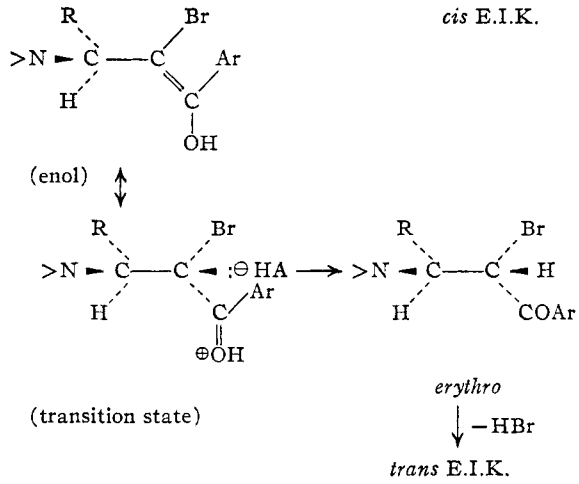
It was thus to be expected that the α-bromo-α,β-unsaturated ketones, analogous to the above-mentioned dibromides, would produce nearly the same *cis/trans* ratios of isomeric ethylenimine ketones with the corresponding amines. This has now been shown to be the case.

α-Bromo-*p*-phenylcrotonophenone (II), prepared by the dehydrohalogenation of the corresponding dibromide, reacted with cyclohexylamine to give a 95% yield of the mixed isomers of 1-cyclohexyl-2-methyl-3-(*p*-phenylbenzoyl)-ethylenimine. A chromatographic separation of this mixture employing activated alumina produced a 34% yield of the higher melting *trans* isomer VIb and a 62% yield of the lower melting *cis* isomer VIa. The reaction of α-bromo-4′-phenylchalcone (I) with methylamine gave a 92% yield of the mixed isomers which was separated into a 68% yield of the low-melting *trans* isomer VIIb and a 31% yield of the *cis* isomer VIIa.

These results suggest that the relative size of the groups (alkyl or aryl and amino) on the β-carbon atom of the α-bromo-β-aminoketones determines the diastereoisomer product ratio, which is directly proportional to the ethylenimine ketone *cis/trans* product ratio.

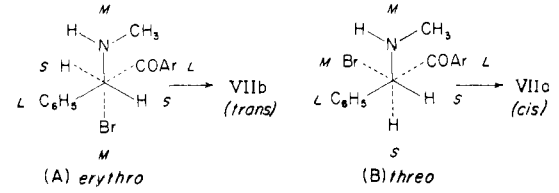
It must be emphasized that ring closure of the α-halo-β-aminoketones to produce the ethylenimine ketones is in general a faster reaction than enolization at the α-carbon atom and possible consequent racemization[4] or reversal[3] of addition to produce the amine and the α-halo-α,β-unsaturated ketone under these reaction conditions. Thus it may be assumed that, in contrast with the previously reported stereochemistry for the ketonization of exocyclic enols,[5] protonation must be with an α-carbon which in these cases is more nearly in the tetrahedral sp^3-hybridized state of the final product than it is in the sp^2-trigonal state of the enol. Thus the kinetically favored product in these cases is the *more stable* (less sterically crowded) configuration of the resulting α-bromo-β-aminoketone.





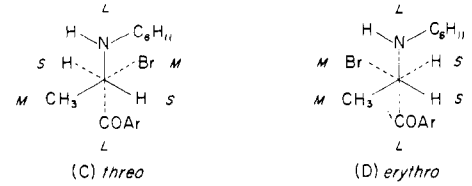
If the mechanism of the addition reaction involved a protonation of the classical enol structure, then the rule of asymmetric induction[6] might be expected to predict the outcome of these reactions. That this is clearly not the case is shown by the results reported here.

A comparison of the most favored conformations, based on relative group size, for the *erythro* and *threo* configurations of the β-amino-α-bromoketone precursors of VIIb and VIIa clearly indicates that conformation A for the *erythro* form would be less sterically crowded than conformation B for the *threo* form.



relative size of groups: (S) small, (M) medium, (L) large

A comparable comparison of the most favored conformations of the *threo* and *erythro* forms of the α-bromo-β-aminoketone precursors of the ethylenimine ketones VIa and VIb suggests that conformation C for the *threo* form would be less sterically crowded than conformation D for the *erythro* isomer.

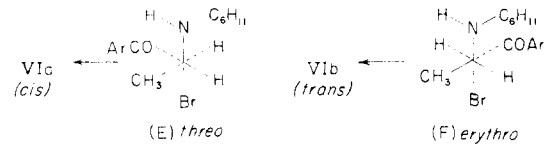


Neither conformation C nor D forms the transition states for ring closure to produce VIa and VIb, respectively. A 120° rotation of the α-carbon which has the halogen atom produces conformations E

(5) H. E. Zimmerman, *J. Org. Chem.*, **20**, 549 (1955), has pointed out that under non-equilibrating conditions the kinetically determined formation of the *less stable* ketonic isomer, *cis*-1-phenyl-2-benzoylcyclohexane, from the 1,4-addition of phenylmagnesium bromide to 2-benzoylcyclohexene implies that the transition state of protonation must be geometrically and energetically more similar to that of the enolic than of the final ketonic state. Our results, reported here, indicate that the transition state for the protonation step in the 1,4-addition of amines to acylic α-bromo-α,β-unsaturated ketones must be geometrically and energetically similar to that of the final α-bromo-β-aminoketone.

(6) D. J. Cram and F. A. Abd Elhafez, THIS JOURNAL, **74**, 5828 (1952).

and F, respectively, which take part in the internal SN2 type ring closures to produce the *cis* form VIa and *trans* isomer VIb, respectively.



Although neither E nor F is a favored conformation, the *threo* configuration is expected to be present in larger amounts in this reaction mixture since a transition state for its formation similar to conformation C should have a lower free energy than that of any of the possible transition state conformations of the *erythro* configuration.

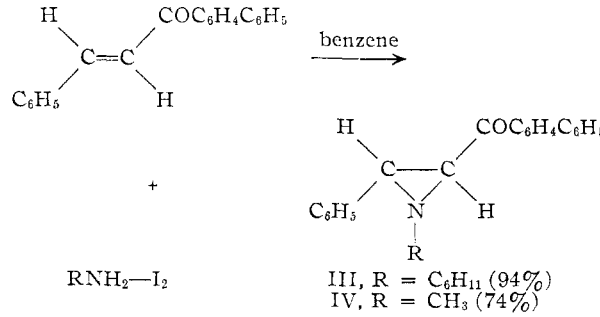
When the amino group and the alkyl or aryl group on the β-carbon atom in the α-bromo-β-aminoketones have comparable space requirements, the *cis/trans* product ratio in these reactions is expected to be more nearly equal to one. Thus 1-cyclohexyl-2-phenyl-3-(*p*-toluyl)-ethylenimine was isolated as the *cis* and *trans* isomers in yields of 45 and 40%, respectively, from the reaction of cyclohexylamine with α-bromobenzal-*p*-methylacetophenone.[7] Approximately the same results were obtained when the corresponding dibromide was used as a starting material. It is to be expected that nearly the same *cis/trans* product ratio of the isomeric ethylenimine ketones will result whether the starting bromo ketone is either geometrical isomer of the α-bromo-α,β-unsaturated ketone or either diastereoisomer of the corresponding α,β-dibromoketone.

The reaction of *p*-phenylcrotonophenone dibromide with methylamine produced a good yield of the *cis*- and *trans*-1,2-dimethyl-3-(*p*-phenylbenzoyl)-ethylenimines. These isomers appeared to be present in nearly equal amounts in the mixture, but only the higher melting (probably *cis*) form Va was obtained pure. The *trans* isomer Vb was quite unstable, undergoing decomposition on the alumina during chromatographic separation. The *cis* isomer Va reacted with phenylhydrazine in glacial acetic acid to produce the known[1] 1-phenyl-3-(*p*-biphenylyl)-5-methylpyrazole. The halo amine method discussed below, employing methylamine, iodine and *p*-phenylcrotonophenone, gave a good yield of the unstable *trans* isomer Vb.

Similar steric controls as discussed here for the addition of amines to α-bromo-α,β-unsaturated ketones might be expected to apply to some analogous reactions wherein two asymmetric centers are being created. Related steric controls which operate to determine the *cis/trans* ratio for the aryl aroyl ethylene oxides in the Darzens condensation have been discussed.[8]

In sharp contrast with the results discussed above are those experienced with the interesting iodo amine reaction with α,β-unsaturated ketones discovered by Southwick.[9] It was found[9b] that *trans*-chalcone reacted with a mixture of iodine and cyclohexylamine to produce only the *trans*-1-cyclohexyl-2-phenyl-3-benzoylethylenimine, the structure of which had been previously established.[7] In a recent investigation[1] it was found that only the *trans* form of 1-cyclohexyl-2-methyl-3-(*p*-phenylbenzoyl)-ethylenimine results when *trans-p*-phenylcrotonophenone is treated with iodine and cyclohexylamine.

In the present investigation *trans*-1-cyclohexyl-2-phenyl-3-(*p*-phenylbenzoyl)-ethylenimine (III) was the only product isolated from the reaction of 4′-phenylchalcone and a mixture of iodine and cyclohexylamine. Also only *trans*-1-methyl-2-phenyl-3-(*p*-phenylbenzoyl)-ethylenimine (IV) resulted when 4′-phenylchalcone was treated with a mixture of iodine and methylamine. The structures of both of these ethylenimine ketones had been established previously.[2]



It has been suggested[2,9c] that these results could be accounted for by the occurrence of a *trans* addition of the N-iodo amine to the *trans* forms of the α,β-unsaturated ketones.

In order to investigate the stereochemical role of the halogen in these reactions, we have begun a study of the formation of ethylenimine ketones from α,β-unsaturated ketones using various primary amines and halogens as well as the corresponding N-haloamines (N-iodo, N-bromo, N-chloro).[10] We report here the results of several such experiments employing *p*-phenylcrotonophenone, bromine, cyclohexylamine and N-bromocyclohexylamine.

It is very interesting and significant that *cis*-1-cyclohexyl-2-methyl-3-(*p*-phenylbenzoyl)-ethylenimine was the major, if not the only, product produced in excellent yield from, (a) treating a benzene solution of one molar equiv. of the unsaturated ketone and four molar equivs. of cyclohexylamine with one molar equiv. of bromine, (b) the reaction of a benzene solution of one molar equiv. each of the unsaturated ketone and cyclohexylamine with one molar equiv. of the preformed N-bromocyclohexylamine and (c) the reaction of a benzene solution of one molar equiv. of the preformed β-cyclohexylamino-*p*-phenylbutyrophenone with one molar equiv. of preformed N-bromocyclohexylamine. Thus it is apparent that the *cis* isomer in this series is produced by these N-bromocyclohexylamine reactions while the *trans*-ethylenimine ketone results from the N-iodocyclohexylamine reaction.[1]

Recalling that the *cis*-1-cyclohexyl-2-methyl-3-

(7) N. H. Cromwell, *et al.*, THIS JOURNAL, **73**, 1044 (1951).

(8) N. H. Cromwell and R. A. Setterquist, *ibid.*, **76**, 5752 (1954).

(9) (a) P. L. Southwick and W. L. Walsh, *ibid.*, **77**, 405 (1955); (b) P. L. Southwick and D. R. Christman, *ibid.*, **74**, 1886 (1952); (c) **75**, 629 (1953).

(10) Other current investigations in the laboratory of Prof. P. L. Southwick are also aimed at the further elucidation of the mechanisms of certain related reactions.

(*p*-phenylbenzoyl)-ethylenimine was the major, though not exclusive, product resulting from the reaction of either α,β-dibromo-*p*-phenylbutyrophenone[1] or the α-bromo-*p*-phenylcrotonophenone and cyclohexylamine, it seems evident that similar steric controls as discussed above operate in all of these reactions which involve bromine to favor the formation of the intermediate *threo*-α-bromo-β-cyclohexylamino-*p*-phenylbutyrophenone. Preliminary attempts to isolate this probable intermediate from the addition of N-bromocyclohexylamine to the unsaturated ketone were unsuccessful.

The mechanism of these N-bromo amine reactions appears to involve transition states in which Br^+ is associated with the α-carbon of the mesomeric ion which is again mainly in the sp^3-hybridized state, and thus the outcome of these reactions is subject to steric controls which are similar, though probably not quantitatively identical, to those which were described above for protonation.

It will be interesting to learn if the unknown α-iodo-*p*-phenylcrotonophenone will react with cyclohexylamine to give mainly the *trans* isomer. Further studies designed to establish the mechanisms and further elucidate the stereochemistry involved in these reactions are being undertaken.

A model chromatographic separation of a synthetic 50–50 mixture of *cis*- and *trans*-1-cyclohexyl-2-phenyl-3-(*p*-phenylbenzoyl)-ethylenimine[2] showed that the *trans* isomer was least strongly adsorbed on alumina and thus was found in the first eluates from the column. In general it has been found in the present investigation and previously[1] that the *trans*-ethylenimine ketones are less strongly adsorbed on alumina than are the *cis* isomers. This seems to indicate that the relative basic strength of the ethylenimine rings in these isomers is the determining factor. The *trans* forms have been shown by spectral[1,2,7] and chemical[11] methods to have a more polar carbonyl group than the corresponding *cis* isomers. Thus it might be expected that the three-ring carbonyl hyperconjugation[2] in the *trans* form which increases the polarity of the carbonyl group results in a parallel decrease in the electron density of the three-ring and consequent decrease in basicity of this grouping.

An improved procedure for the preparation of 4′-phenylchalcone was devised, and the α-bromo derivative was prepared in good yield from the dibromide by heating with sodium acetate.

Acknowledgment.—This investigation was supported in part by a grant from the National Science Foundation, NSF-G 1091.

Experimental

***trans*-4′-Phenylchalcone.**—To a solution of 29.43 g. (0.15 mole) of *p*-phenylacetophenone and 5.0 g. (0.125 mole) of sodium hydroxide in 300 ml. of dioxane and 25 ml. of methanol was added with stirring 25.0 ml. (0.247 mole) of benzaldehyde over a period of 1 hr. at 25–30°. Stirring was continued for two additional hours during which time part of the product precipitated from solution. This material was removed by filtration and the filtrate concentrated by evaporation and mixed with water to precipitate more product. Recrystallization from methanol and chloroform gave 35.3 g. (82.6% yield), m.p. 156–158°.[12]

(11) N. H. Cromwell, *et al.*, THIS JOURNAL, **73**, 2803 (1951).

(12) W. E. Bachmann and F. Y. Wiselogle, *ibid.*, **66**, 1559 (1934).

α-Bromo-4′-phenylchalcone (I).—A 26.5 g. (0.060 mole) sample of 4′-phenylchalcone dibromide[2] was refluxed with stirring for 4 hr. in a solution containing 4.92 g. (0.060 mole) of sodium acetate in 120 ml. of ethanol, 8 ml. of water and 30 ml. of dioxane. The dibromide dissolved completely after 2.5 hr. of refluxing. The precipitated sodium bromide was removed by filtration and the solvent evaporated under reduced pressure. The solid yellow residue was extracted with ether. The ether solution was washed with 5% aqueous sodium bicarbonate, then water, dried over anhyd. $MgSO_4$ and evaporated to a solid residue which was recrystallized from methanol and chloroform to give 17.8 g. (81.3% yield) of light-yellow colored needles, m.p. 101–102.5°.

Anal. Calcd. for $C_{21}H_{16}OBr$: C, 69.43; H, 4.16. Found: C, 69.73; H, 4.31.

α-Bromo-*p*-phenylcrotonophenone (II).—Following the procedure outlined in the previous preparation 37.3 g. (0.0973 mole) of *p*-phenylcrotonophenone dibromide[1] produced 22.55 g. (76.6% yield) of colorless plates, m.p. 84.5–86°, recrystallized from ethanol.

Anal. Calcd. for $C_{16}H_{14}OBr$: C, 63.80; H, 4.35. Found: C, 63.60; H, 4.59.

***trans*-1-Cyclohexyl-2-phenyl-3-(*p*-phenylbenzoyl)-ethylenimine (III).**—This known[2] compound was prepared by a modification of the procedure outlined by Southwick and Christman.[9b] A solution of 6.35 g. (0.025 mole) of iodine dissolved in 50 ml. of benzene was added over a period of 25 minutes to a solution of 7.1 g. (0.025 mole) of 4′-phenylchalcone and 9.9 g. (0.100 mole) of cyclohexylamine in 75 ml. of benzene. The color of the iodine solution was discharged as rapidly as it was introduced until 35 ml. had been added. After the addition was complete, the solution was reddish-brown in color, but after continued stirring for an additional hour, the color cleared to a light, yellow-orange. The precipitated cyclohexylamine hydroiodide was removed by filtration, the solution water washed and dried over anhyd. $MgSO_4$. Evaporation of the solvent resulted in a red oil which was crystallized from petroleum ether and benzene and then from methanol and chloroform to give 8.95 g. (94% yield) of yellow crystalline product, m.p. 116.5–118°. A mixed m.p. experiment with the *trans* form of 1-cyclohexyl-2-phenyl-3-(*p*-phenylbenzoyl)-ethylenimine[2] showed no depression.

***trans*-1-Methyl-2-phenyl-3-(*p*-phenylbenzoyl)-ethylenimine (IV).**—Employing the above procedure and using methylamine and ice-bath cooling 7.1 g. of 4′-phenylchalcone gave 6.12 g. (74% yield) of light yellow crystalline product, m.p. 119.5–120.5°, recrystallized from ethanol. A mixed m.p. experiment of this product IV with *trans*-1-methyl-2-phenyl-3-(*p*-phenylbenzoyl)-ethylenimine[2] showed no depression.

***cis*- and *trans*-1,2-Dimethyl-3-(*p*-phenylbenzoyl)-ethylenimines (Va) and (Vb).**—A suspension of 23.28 g. (0.061 mole) of *p*-phenylcrotonophenone dibromide in 65 ml. of benzene was cooled in an ice-bath and 220 ml. of a 0.240 *M* solution of methylamine in ether added with stirring over a period of 40 minutes. The reaction mixture was stirred for 4 hr. and then allowed to stand in the ice-chest for 20 hr. The oily methylamine hydrobromide was separated and the solution well washed with water, dried over anhyd. $MgSO_4$ and the solvent removed by evaporation. Addition of petroleum ether produced 12.86 g. (84.6% yield) of crude crystalline product, m.p. 69–76°; ultraviolet max., λ, 282 mμ (ϵ 29,400) in isoöctane; infrared C=O band, 1670 cm.$^{-1}$ (Nujol), 1660–1670 cm.$^{-1}$ (CCl_4).

Anal. Calcd. for $C_{17}H_{17}NO$: C, 81.24; H, 6.82; N, 5.57. Found: C, 80.88; H, 6.61; N, 5.42.

A 3.0-g. sample of the mixed *cis* and *trans* isomers was separated on a chromatographic column of activated alumina.[1] The first eluates contained most of the low melting *trans* isomer Vb, m.p. 61–67°, 0.93 g., while the latter ones consisted of the colorless higher-melting *cis* form Va, m.p. 84–85°, 1.2 g. The low melting form was quite unstable and further attempts to purify it led to partial decomposition; ultraviolet max. for Va, λ, 281 mμ (ϵ 19,800); infrared C=O band, 1674 cm.$^{-1}$ (Nujol), 1682 cm.$^{-1}$ (CCl_4).

Anal. Calcd. for $C_{17}H_{17}NO$: C, 81.24; H, 6.82; N, 5.57. Found for VIa: C, 81.08; H, 6.73; N, 5.44.

A 1.0-g. (0.004 mole) sample of Va in 25 ml. of abs. ethanol was treated with 0.48 g. (0.008 mole) of glacial acetic

acid and 0.43 g. (0.004 mole) of phenylhydrazine. The pyrazole was isolated in the usual way,[1,2] m.p. 128–129°, wt. 0.81 g. (67% yield). This product was identical with an authentic sample of 1-phenyl-3-(*p*-biphenylyl)-5-methylpyrazole.[1]

trans-**1,2-Dimethyl-3-(*p*-phenylbenzoyl)-ethylenimine (Vb).**—An 8.0 g. (0.036 mole) sample of *p*-phenylcrotonophenone in 40 ml. of benzene was treated with an ether solution of methylamine (0.144 mole) using ice-bath cooling. To this solution was added 9.26 g. (0.036 mole) of iodine dissolved in 120 ml. of benzene. The iodine color disappeared completely in 1 hr. The benzene layer was separated from the oily methylamine hydroiodide, washed with water, dried and evaporated to leave a red colored oil. This crude product was crystallized from petroleum ether (b.p. 40–50°) to give 7.0 g. of a nearly colorless product, m.p. 65–67°.

Anal. Calcd. for $C_{17}H_{17}NO$: C, 81.24; H, 6.82; N, 5.57. Found: C, 81.01; H, 6.93; N, 5.43.

This product decomposed in the air at room temperature to a red oil in a few hours.

cis- and *trans*-**1-Cyclohexyl-2-methyl-3-(*p*-phenylbenzoyl)-ethylenimines, VIa and VIb. A. Reaction of α-Bromo-*p*-phenylcrotonophenone with Cyclohexylamine.**—To a solution of 6.0 g. (0.020 mole) of α-bromo-*p*-phenyl-crotonophenone (II) in 50 ml. of dry benzene was added 4.5 g. (0.044 mole) of cyclohexylamine. The reaction mixture was stirred for 3 hr. and allowed to stand 12 hr. in the ice-chest. The reaction mixture was worked up and the crude product separated by a chromatographic method as previously described for the reaction using the analogous α,β-dibromo-*p*-phenylbutyrophenone.[1] The yield of crude, mixed product was 6.1 g. (95%), m.p. 110–118°. The first eluates from the chromatographic separation of a 3.0-g. sample of the mixed product produced 0.98 g. (34% of the total material recovered) of the *trans* isomer VIb, m.p. 141–142°. The final eluates contained the low melting, *cis* isomer VIa, m.p. 127–128°, wt. 1.8 g. (62% of the total material recovered). Both products were nearly colorless.

B. Reaction of *p*-Phenylcrotonophenone with Bromine and Cyclohexylamine.—A 5-g. (0.0225 mole) sample of the unsaturated ketone[1] was dissolved in 12 ml. of benzene and 9 g. (0.091 mole) of cyclohexylamine. The solution was cooled and 3.6 g. (0.0225 mole) of bromine in 50 ml. of benzene was added over a period of 20 minutes with stirring. The nearly colorless reaction mixture, after standing at room temperature for 12 hr., was filtered to remove 8.1 g. (0.045 mole) of cyclohexylamine hydrobromide. The filtrate was washed with water, dried and concentrated under reduced pressure to give 6.25 g. (0.0195 mole) of a colorless crystalline product, m.p. 112–124°. A chromatographic separation of 2 g. of this material produced 0.51 g. of a mixed product, m.p. 110–121°, in the first eluate and 1.47 g. of the pure *cis* isomer, m.p. 127–129°, in later eluates.

C. Reaction of *p*-Phenylcrotonophenone with Cyclohexylamine and N-Bromocyclohexylamine.—A 4.4-g. (0.02 mole) sample of the unsaturated ketone was dissolved in 10 ml. of benzene and 1.98 g. (0.02 mole) of cyclohexylamine. After standing for 30 minutes, 25 ml. of a benzene solution containing about 3.56 g. (0.02 mole) of N-bromocyclohexylamine[13] was added rapidly. After standing at room temperature for 14 hr., the cyclohexylamine hydrobromide, 3.4 g. (0.0189 mole), was removed and the filtrate worked up to give 6.35 g. (99% yield) of solid material, m.p. 114–122°. One recrystallization from petroleum ether (b.p. 60–70°) gave 6.3 g. of colorless crystalline solid, m.p. 120–128°. A 1.0-g. sample of this material was chromatographed to give as a first eluate 0.25 g. of a mixed product, m.p. 109–120°, and in later eluates 0.74 g. of the pure *cis* isomer, m.p. 128–129°.

D. Reaction of β-Cyclohexylamino-*p*-phenylbutyrophenone with N-Bromocyclohexylamine. The β-cyclohexylamino-*p*-phenylbutyrophenone was prepared from 2.2 g. of *p*-phenylcrotonophenone and 1.0 g. of cyclohexylamine in 8 ml. of abs. ethanol upon standing in the refrigerator fo three days. The yield was 2.9 g., m.p. 84.5–85.5°.

Anal. Calcd. for $C_{22}H_{27}NO$: C, 82.20; H, 8.47; N, 4.36. Found: C, 82.43; H, 8.61; N, 4.34.

A 1.6-g. (0.005 mole) sample of the β-aminoketone was dissolved without heating in 5 ml. of benzene and a solution of 0.89 g. (0.005 mole) of N-bromocyclohexylamine[13] in 15 ml. of benzene was added rapidly. After standing at room temperature for 12 hr. the working up of the reaction mixture produced 0.87 g. (97% yield) of cyclohexylamine hydrobromide and 1.33 g. (85% yield) of the pure *cis* isomer, m.p. 127–128°.

An attempt to add one molar equivalent of N-bromocyclohexylamine[13] to 2.22 g. of *p*-phenylcrotonophenone in benzene solution produced only small amounts of cyclohexylamine hydrobromide and 2.0 g. of unchanged unsaturated ketone.

Chromatographic Separation of *cis*- and *trans*-1-Cyclohexyl-2-phenyl-3-(*p*-phenylbenzoyl)-ethylenimines.—A 0.50-g. sample of a 50–50 mixture of the *cis* and *trans* isomers which had been separated previously by fractional crystallization[2] was re-separated by the chromatographic method.[1] The first eluates contained 0.24 g. (50% of the total material recovered) of the low melting *trans* isomer, m.p. 118–119°, while the final eluates produced the same amount of the higher-melting *cis* form, m.p. 144–146°. Both of these products were colorless.

(13) Using the procedure outlined for N-bromomorpholine, see ref. 7a, benzene solutions of N-bromocyclohexylamine were freshly prepared from one equiv. of bromine and two equiv. of cyclohexylamine and used immediately after removing the cyclohexylamine hydrobromide by filtration.

LINCOLN, NEBRASKA

[CONTRIBUTION FROM THE ORGANIC CHEMISTRY LABORATORY OF THE INDIAN INSTITUTE OF SCIENCE, BANGALORE]

Hydrolysis of Ethyl 4-(1-Carbethoxy-2-oxocyclopentyl)-2-pentenoate and Ethyl 4-(1-Carbethoxy-2-oxocyclopentyl)-valerate

BY D. K. BANERJEE AND T. R. KASTURI

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Hydrolysis of ethyl 4-(1-carbethoxy-2-oxocyclopentyl)-2-pentenoate (Ia) and ethyl 4-(1-carbethoxy-2-oxocyclopentyl)-valerate (Ib) with 10% sulfuric acid yielded the normal products Ic and Id, respectively. Treatment of Ia with hydrochloric acid yielded a mixture of II, a rearrangement product, and Ic.

In the course of a synthetic project currently in progress in our laboratory, the introduction of the bile acid side chain was contemplated by the condensation of a cyclopentanone-2-carboxylic ester derivative with ethyl 4-bromo-2-pentenoate followed by hydrolysis and reduction. Recently Herz[1] has shown that such condensation products, after reduction, on hydrolysis with hydrochloric acid yield rearranged products. We have now reinvestigated this step and it has been possible to obtain the desired normal hydrolysis product in good yield by using 10% sulfuric acid.

At first the hydrolysis of ethyl 4-(1-carbethoxy-2-oxocyclopentyl)-2-pentenoate(Ia)[1a] under the condition of Herz[2] was studied, as in this case

(1) (a) W. Herz, THIS JOURNAL, **78**, 1485 (1956); (b) **78**, 2529 (1956).

(2) These experiments were completed before the appearance of the second paper[1b] of Herz, where he has expressed the intention of studying the hydrolysis of Ia.