13.01; N, 10.27. Found: C, 61.68; H, 3.49; Cl, 13.0; N, 10.14.

2-Carbethoxyamino-5-chlorobenzophenone α-Oxime (III).—A heated solution of 2 g. of II in 30 ml. of ethanol was evaporated *in vacuo* to give an oil which solidified upon trituration with hexane. Recrystallization from a small volume of alcohol afforded 1.1 g. of III, m.p. 128°.

Anal. Calcd. for $C_{16}H_{15}ClN_2O_3$: C, 60.29; H, 4.74; Cl, 11.14; N, 8.79. Found: C, 60.30; H, 4.78; Cl, 11.1; N, 8.86.

One-half gram of III was heated at its melting point until the liquid solidified. After recrystallization from alcohol, 0.2 g. of V was obtained, m.p. 312°.

Compound III (0.6 g.) ws dissolved in 10 ml. of 1 *N* sodium hydroxide by warming on a steam bath.[4] The solution was acidified with glacial acetic acid and extracted with ethyl acetate. The organic layer was dried, concentrated, and the residue was triturated with hexane to obtain 0.4 g. of white solid, m.p. 126–128°. The melting point was not depressed upon mixing with III.

2-Amino-5-chlorobenzophenone α-Oxime, Ethyl Carbonate Ester (IV).—A solution of 6 g. of I and 3.5 ml. of triethylamine in 100 ml. of ethyl acetate was cooled to 5°. Ethyl chlorocarbonate (2.3 g.) was added in one portion and the mixture was stirred vigorously for 20 min. The mixture was filtered and the filtrate was evaporated *in vacuo.* Upon recrystallization of the residue from alcohol, 3.0 g. of white crystals of IV was obtained, m.p. 149–151°.

Anal. Calcd. for $C_{16}H_{15}ClN_2O_3$: C, 60.29; H, 4.74; Cl, 11.14; N, 8.79. Found: C, 60.39; H, 5.05; Cl, 12.0; N, 8.67.

6-Chloro-4-phenyl-2(1H)-quinazolinone 3-Oxide (VII).—A solution of 5 g. of VI (m.p. 130–133°) and 5.6 ml. of triethylamine in 75 ml. of ether was cooled to 5°. With stirring, 11.2 g. of 18% phosgene in benzene solution was added dropwise, keeping the temperature below 10°. After stirring for an additional 0.5 hr., the mixture was washed with water and concentrated *in vacuo.* Recrystallization of the residue from alcohol gave 2.1 g. of yellow solid, m.p. 270° dec. $\lambda_{max}^{CHCl_3}$ 242, 262(s), 322, 336, 345, 364, 380 mμ ε 19,500, 12,700, 6,000, 6,100, 6,120, 7,200, 6,900.

Anal. Calcd. for $C_{14}H_9ClN_2O_2$: C, 61.66; H, 3.33; Cl, 13.01; N, 10.27. Found: C, 61.69; H, 3.30; Cl, 12.90; N, 10.52.

6-Chloro-4-phenyl-2(1H)-quinazolinone (VIII) from VII.—A mixture of 1.4 g. of VII, 3.5 ml. of phosphorus trichloride and 20 ml. of chloroform was heated under reflux for 1 hr. The solvent was evaporated *in vacuo.* The residue was triturated with saturated sodium bicarbonate solution and recrystallized from ethanol yielding 0.85 g. of yellow VIII, m.p. 310–312°. Upon mixing with an authentic sample (below) of 6-chloro-4-phenyl-2(1H)-quinazolinone the m.p. was undepressed. The infrared spectra were identical.

Compound VIII from 2-Amino-5-chlorobenzophenone.—Two grams of 2-amino-5-chlorobenzophenone and 0.5 g. of urea were heated at 195° until the mixture solidified. The solid was triturated with hexane and recrystallized from alcohol to yield 1.3 g. of VIII, m.p. 312°.

Anal. Calcd. for $C_{14}H_9ClN_2O$: C, 65.50; H, 3.53; Cl, 13.82; N, 10.91. Found: C, 65.54; H, 3.70; Cl, 13.48; N, 11.08.

The Stereochemistry of the Hydrogenation of *cis*- and *trans*-1-Nitro-2-phenylcyclohexane Using W-2 Raney Nickel Catalyst

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Hydrogenation of *cis*-1-nitro-2-phenylcyclohexane over W-2 Raney nickel occurs with retention of configuration if conditions are used that avoid epimerization of the nitro compound prior to reduction.

Hydrogenation over W-2 Raney nickel catalyst has proved, in our experience, to be one of the most effective methods of reducing a nitro group in a β-nitro acetate to an amino group. To use this reaction as a means of establishing the configuration of certain β-nitro acetates[2] it became necessary to establish its stereochemical course. The reduction of *cis*- and *trans*-1-nitro-2-phenylcyclohexanes was chosen as a model system since both the nitro compounds[3] and the corresponding amines[4] have been well characterized and are closely analogous to the systems in question.[2]

trans-1-Nitro-2-phenylcyclohexane was found to yield *trans*-1-amino-2-phenylcyclohexane on hydrogenation over W-2 Raney nickel catalyst or on reduction using zinc and sulfuric acid in methanol.

The nature of the product formed by hydrogenation of *cis*-1-nitro-2-phenylcyclohexane was found to depend on the conditions used. When the nitro compound was dissolved in warm (60° to 70°) alcohol, W-2 Raney nickel added, and the mixture hydrogenated (the conditions used for the *trans* isomer) a mixture of *cis*- and *trans*-1-amino-2-phenylcyclohexanes resulted. On the other hand, when *cis*-1-nitro-2-phenylcyclohexane was added to cold (0–20°) ethanol, W-2 Raney nickel added, and the mixture hydrogenated, the product was *cis*-1-amino-2-phenylcyclohexane. The thioureide derivative, prepared for purposes of identification, did not possess bands at 9.35, 10.27, and 13.19 μ that are present in the spectrum of the corresponding derivative of the *trans* isomer. The reduction was stereospecific to the extent of at least 86%, judging from the absence of these bands.

Hydrogenation of *cis*-1-nitro-2-phenylcyclohexane over palladium on charcoal in methanol containing a few drops of sulfuric acid also proceeded with retention of configuration, as did

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[1] National Science Foundation Cooperative Fellow, 1961–1962.

[2] Paper IV, F. G. Bordwell and E. W. Garbisch, Jr., *J. Org. Chem.*, in press.

[3] H. E. Zimmerman and T. E. Nevins, *J. Am. Chem. Soc.*, **79**, 6559 (1957).

[4] R. T. Arnold and P. N. Richardson, *ibid.*, **76**, 3649 (1954).

reduction with zinc and sulfuric acid in methanol. On the other hand, hydrogenation over platinum in ethanol gave a mixture of *cis* and *trans* amines.

Kornblum, Fishbein, and Smiley[5] have shown that reduction of the nitro group in optically active 2-nitroöctane occurs with retention of configuration using iron and acetic acid or hydrogen and a platinum catalyst in acetic acid. It seems clear in the light of these studies and the present work that the nitro group can be reduced to amino in nonalkaline media without alteration of the configuration of the carbon atom to which it is attached. Evidently the intermediate nitroso compound is *not* tautomerized to the oxime under these conditions.

In contrast, the reduction product from 2-nitrooctane was reported to be completely racemized when lithium aluminum hydride was used as a reducing agent,[5] and was 92% racemized in a hydrogenation over platinum in ethanol. The nitro compound recovered from an interrupted reduction was 99% racemized. The racemization accompanying reduction over platinum in ethanol[5] is presumably the result of prior epimerization of the nitro compound brought about by the small amount of alkali[6] in the commercial catalyst. Similarly, since Zimmerman and Nevins[3] have shown that *cis*-1-nitro-2-phenylcyclohexane is rapidly epimerized to the *trans* isomer by the action of sodium bicarbonate in ethanol, it seems likely that epimerization of the nitro compound is preceding reduction in those of our reductions where *trans* amine is formed from *cis* nitro compound. It is, in fact, remarkable that hydrogenation of the *cis* nitro compound with retention of configuration is possible with W-2 Raney nickel, since this is a relatively basic catalyst. Yet the result was reproducible when a fresh sample of W-2 nickel prepared by a different investigator was used. Therefore, the present results show that under mild conditions this method can be used in determining configuration. Previous structure assignments, made on the basis of an assumed retention of configuration during reductions of this kind,[2,7] now seem secure.

Experimental

***trans*-1-Nitro-2-phenyl-4-cyclohexene.**[8]—A solution of 45 g. (0.30 mole) of β-nitrostyrene in 75 ml. of toluene containing 100 mg. of hydroquinone was placed in a 450-ml. steel bomb and flushed by repeatedly pressurizing and depressurizing with about 50 p.s.i. of nitrogen. 1,3-Butadiene (140 ml.) was added from a pressure charger and the bomb was rotated and heated at 115 ± 3° for 40 hr. After cooling and releasing the residual butadiene, the semisolid mixture was removed by solution in ether. After removal of the solvents under reduced pressure the residue was crystallized from 200 ml. of methanol; 40 g. of material melting at 102–103° was thus obtained. Recovery of additional material from the mother liquor brought the total yield to 42 g. (69%).

Reduction of *trans*-1-Nitro-2-phenylcyclohexane.—*trans*-1-Nitro-2-phenylcyclohexane was prepared by the catalytic hydrogenation of *trans*-1-nitro-2-phenyl-4-cyclohexene using a platinum catalyst in acetic acid according to the method described by Zimmerman and Nevins.[3] Six grams (wet weight) of W-2 Raney nickel catalyst was added to a warm solution of 1.4 g. of nitro compound in 75 ml. of ethanol and the mixture hydrogenated for 55 min. under 50 p.s.i. hydrogen pressure (97% hydrogen uptake). The catalyst was collected on a diatomaceous earth filter and washed with ethanol.[9] The ethanol was removed under reduced pressure and finally with a stream of nitrogen. The solid residue was triturated with 0.93 g. of freshly distilled phenyl isothiocyanate and the resulting solid was washed successively with 5-ml. portions of hexane and ethanol. The product thus obtained weighed 1.7 g. (80%) and melted at 176–180°. One crystallization from ethanol (89% recovery) raised the m.p. to 185–186° (184–185° reported[4]). The phenylthioureide had infrared bands at 9.35, 10.27, and 13.19 μ. The N-acetyl derivative, m.p. 130–131° (130° reported[4]), was also prepared.

trans-1-Amino-2-phenylcyclohexane was also obtained (as the phenylthioureide) in an experiment where the reduction was carried out by merely refluxing the ethanol solution of the nitro compound in the presence of the catalyst; the yield was much lower.

When 0.772 g. of the nitro compound in 10 ml. of ethanol was stirred with 1.5 g. of zinc dust and treated over a 30-min. period with 10 ml. of 30% sulfuric acid, the *trans* amine was formed in 66% yield (judging from the yield of crude phenylthioureide).

Reduction of *cis*-1-Nitro-2-phenylcyclohexane.[10]—Four grams (wet weight) of W-2 Raney nickel was added to a freshly prepared suspension of 1.13 g. of the *cis* nitro compound in 50 ml. of cold (0° to 5°) ethanol. The mixture was hydrogenated for 140 min. under 50 p.s.i. hydrogen pressure (95% hydrogen uptake). During this time it gradually reached room temperature. On processing by the method used for the *trans* nitro reduction product there was obtained 1.29 g. (76%) of phenylthioureide derivative, m.p. 126–135°. One crystallization from ethanol (88% recovery) gave material melting at 136–137° (137–138° reported[4]). Infrared bands characteristic of the *trans* isomer at 9.35, 10.27, and 13.19 μ were absent in both the crude and recrystallized products. These bands were detectable in known mixtures containing as little as 5% of *trans* isomer.

Preparation of the thioureide derivative from a weighed sample of amine by this procedure gave 84% yield. Since the crude derivative from the reduction product, obtained in 76% yield, contained less than 5% of *trans* isomer (by infrared analysis), the reduction is stereospecific to the extent of at least 86%.

In a similar experiment in which the hydrogenated mixture was heated for 30 min. at the reflux point after hydrogenation, *cis* amine, free of *trans* isomer, was also isolated (showing that epimerization of the *cis* amine does not occur under these conditions).

When the *cis* nitro compound was dissolved in warm (60° to 70°) ethanol prior to hydrogenation, as in the hydrogenation of the *trans* nitro compound, the reduction product was a mixture of *cis* and *trans* amine as judged by the melting point of the phenylthioureide derivative (142–165°) and the appearance of bands in its spectrum at 9.35, 10.27, and 13.19

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(5) N. Kornblum, L. Fishbein, and R. A. Smiley, *J. Am. Chem. Soc.*, **77**, 6261, 6266 (1955).

(6) H. Yao and P. H. Emmett, *ibid.*, **83**, 799 (1961).

(7) G. Drefahl, H. Crahmer, and W. Thomas, *Ber.*, **91**, 282 (1958); G. Drefahl and H. Crahmer, *ibid.*, **91**, 745, 750 (1958).

(8) The procedure is essentially that of W. C. Wildman and R. B. Wildman, *J. Org. Chem.*, **17**, 581 (1952), but use of a steel autoclave has the advantage of greater ease of manipulation over the sealed tube.

(9) The catalyst is extremely pyrophoric and should be kept wet with solvent at all times.

(10) The *cis* isomer was obtained by acidification of the salt of 1-nitro-2-phenylcyclohexane according to the method of Zimmerman and Nevins.[3] Much lower yields were obtained in runs made on quantities larger than the 1-g. scale specified.

μ that are characteristic of the derivative of the *trans* amine.

A mixture of 0.46 g. of the nitro compound, 25 ml. of methanol, 10 drops of sulfuric acid, and 0.1 g. of 10% palladium on charcoal was hydrogenated for 250 min. (72% hydrogen uptake). The catalyst was collected and washed and the filtrate was neutralized with 20% sodium hydroxide solution. Extraction with ether followed by drying and preparation of the phenylthioureide gave 45% recovery of material melting at 115–124° whose spectrum contained no bands characteristic of the *trans* phenylthioureide. After crystallization from ethanol this material melted at 137–138°.

On hydrogenation of the *cis* nitro compound in ethanol using platinum oxide catalyst there was obtained 68% of a mixture consisting of *cis* and *trans* amines (judging from the melting point of the phenylthioureide derivative, 140–167°, and from the presence of relatively strong bands at 9.35, 10.27, and 13.19 μ in its spectrum).

Ring Closure of Ylidenemalononitriles

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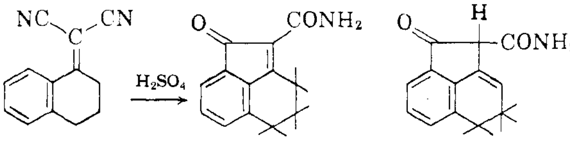
Ylidenemalononitriles are readily available by the reaction of aldehydes or ketones with malononitrile. Treatment of aromatic aldehyde derivatives in concentrated sulfuric acid, followed by quenching the reaction mixture over ice, results in hydrolysis of one nitrile group to produce α-cyanocinnamamides. Similar treatment of ketone derivatives may result in cyclization to form indenones and/or indanones. The rate of ring closure is increased by increase of size of group R in III. When R is incapable of prototropic rearrangement with the endocyclic double bond, as *t*-butyl or phenyl, only the indenones V are formed. When R carries a hydrogen on the α-carbon, mixtures of the endocyclic and exocyclic isomers V and VI may be obtained. Ring closures to produce three fused-ring systems are also possible, starting with two-ring ketones like α-tetralone. A series of cyclized compounds derived from III (R = H, CH_3, C_2H_5, *i*-C_3H_7, *t*-C_4H_9, C_6H_5) have been prepared, and the separation, identification, ultraviolet spectral characteristics, and certain reactions of derivatives V and VI are discussed.

The observation that sulfuric acid treatment of α-tetrylidenemalononitrile (I) led to a five-membered cyclized product[3] suggested further study of this facile ring closure to determine the scope and limitations of the reaction. The structure of the keto amide was reported as IIa,[3] but we have now established that the compound actually is 2-carbamoyl-3,4-trimethylene-1-indenone (IIb). I was prepared from α-tetralone using a method described by Mowry.[4] Although he named the product 1,2,3,4 - tetrahydro - 1 - naphthylidenemalonitrile, Mowry presented no evidence favoring either the structure having the exocyclic double bond I or the isomer having the endocyclic double bond, 1-dicyanomethyl-3,4-dihydronaphthalene.



I IIb IIa

Ring closure of *cis*-cinnamic acid derivatives are known[5] in Stobbe condensation products, but have not been reported with simple cinnamic acids or with arylidenemalonic acids or esters. Cyclization of aromatic derivatives of nitriles to form six-membered rings are known.[6,7] The present report deals with the formation of five-membered ring ketones.

A series of ylidenemalononitriles III was synthesized in which the group R in the β-position was H, CH_3, C_2H_5, *i*-C_3H_7, *t*-C_4H_9, or C_6H_5 (Table I). This series of α-cyano-β-substituted cinnamonitriles was designed to help prove the structure of I by a comparison of the ultraviolet absorption spectra and to shed light on two important aspects of the ring closure; one, the influence of the steric effect of bulky groups; and two, the possibility that prototropy, with concommitant rearrangement of the double bond so as to be exocyclic to the ring being formed, might play a role in ring formation. This latter possibility cannot be ruled out in previous reports of the ring closure of cinnamic acid derivatives.[5]

A comparison of the ultraviolet spectral data of the ylidenemalononitriles III served as a method of locating the double bond in I; that is, whether endo-or exocyclic to the six-membered ring. If the olefinic bond is in the endocyclic position, the chromophore should have a λ_{max} value corresponding to a 1-substituted 3,4-dihydronaphthalene. An example is 1-methyl-3,4-dihydronaphthalene, which exhibits a λ_{max} at 258 mμ (ϵ = 6,300).[8] If, however, the double bond is exocyclic, then the λ_{max}

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(1) Bristol Postdoctoral Fellow, 1960–1961.

(2) Taken in part from a thesis submitted to Indiana University in partial fulfillment of the requirements for the degree Doctor of Philosophy, June, 1962, by D. M., Bristol Predoctoral Fellow, 1960–1962. This work was presented before the Organic Division at the 140th National Meeting of the American Chemical Society in Chicago, Ill., September, 1961.

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