

(m, 2, CH₂CH₂CH₂) and 1.35 (s, 2, NH; disappears with D₂O) ppm.

Titration with perchloric acid in glacial acetic acid gave equiv wt 107.7 (calcd 107.5).

Anal. Calcd for C₁₃H₁₇N₃: C, 72.51; H, 7.96; N, 19.53. Found: C, 72.05; H, 8.11; N, 19.67.

Registry No.—4, 7032-12-4; hydrazine, 302-01-2; phenylhydrazine, 100-63-0; 5, 24978-50-5; 7, 24978-51-6; 8, 24978-52-7; 9, 25080-59-5.

Acknowledgment.—Generous support from the American Tobacco Co., Richmond, Va., is gratefully acknowledged.

Reduction of

2-(2-Imidazolin-2-yl)benzophenone

W. METLESICS, T. ANTON, L. BENJAMIN,
V. TOOME, AND R. IAN FRYER¹

Chemical Research Department, Hoffmann-LaRoche, Inc.,
Nutley, New Jersey 07110

Received December 16, 1969

In the course of the structural investigation of compounds obtained by the condensation of *o*-benzoylbenzaldehyde with aliphatic diamines,² we decided to study the reduction of these products. The equilibrium between the two tautomeric forms of the imidazoline derivatives **1a** and **1b** has been previously discussed.² Reduction with borohydride gave a nearly quantitative yield of the tautomeric dihydro compound **3a-b**.

The uv absorption of **3** is similar to that of **4** and different from that of **6** (Table I). This is probably

TABLE I
ULTRAVIOLET ABSORPTION DATA

Compd	Solvent	λ_{\max} , m μ ^a	$\epsilon \times 10^{-3}$
3	2-Propanol	260 (s), 275 (i), 284 (i)	2.52, 2.20, 1.65
	CHCl ₃	260 (i), 275 (i), 283 (s)	3.00, 2.28, 1.68
	0.1 N HCl	235 (i), 273 (i)	7.60, 1.40
	0.1 N KOH	265 (i), 283 (i)	2.10, 0.95
6	2-Propanol	230, 270 (i)	12.50, 3.80
	0.1 N HCl	236, 270 (i)	16.65, 3.30
4	0.1 N HCl	235 (i), 262 (i), 269 (i)	7.30, 2.0, 1.60
	0.1 N KOH	266, 265	13.25, 3.90
4	0.1 N HCl	235 (i), 262 (i), 269 (i)	7.30, 2.0, 1.60
	0.1 N KOH	263 (i), 269 (i)	2.20, 1.72

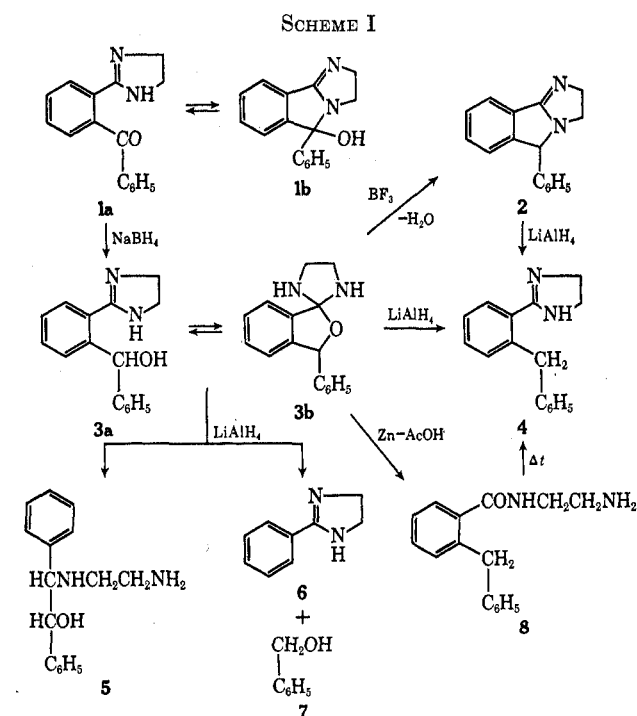
^a s, shoulder; i, inflection.

due to steric hindrance in compounds **3** and **4**. These results indicate the presence of C₆H₅C=N moiety in **3**, but do not allow a quantitative estimate of the equilibrium **3a** \rightleftharpoons **3b**. The near ir spectrum of **3** was recorded in CHCl₃ at three different concentrations. All spectra exhibit a band at 1.494 μ (ϵ 0.8) (NH of **3a**), a broad small band at 153 μ (NH of **3b**), and a very broad band at 1.4 μ area (strongly bonded OH of **3a**). This gives

an approximate ratio for **3a**:**3b** of 9:1. For comparison, the near ir spectrum of salicylideneaniline (Frinton Laboratories) was recorded. With this compound the OH also forms a very strong intramolecular bonding and no absorption for nonbonded OH was detected. Compounds **4** and **6** exhibit only one kind of NH and no OH. Polarograms of **3** and **6** were recorded in 0.1 N KOH. The half-wave potential $E^{1/2}$ (reduction of -C=N-) of both compounds is similar (-1.755 and -1.730 V, respectively, vs. Ag|AgCl electrode) but the intensity of the molar diffusion currents (I_d) is different ($I_d \times 10^{-3}$ for **3** = 9.38 μ A; and $I_d \times 10^{-3}$ for **6** = 12.72 μ A), indicating the presence of some **3b** in 0.1 N KOH. On the assumption that reduction at the mercury dropping electrode is faster than the tautomeric equilibrium rate and that the diffusion coefficients are essentially the same for compounds **3** and **6**, these data also suggest a predominance of **3a**.

As expected, the results of chemical reactions were compatible with either structural possibility. Thus, hydrolysis gave 3-phenylphthalide and treatment of **3** with an acidic catalyst gave the imidazoisoindoline **2**.

Reduction of compound **2** with lithium aluminum hydride in boiling tetrahydrofuran yielded the 2-benzylphenylimidazoline **4** as the major product. The same product was obtained by heating the amide **8**, a compound which in turn was obtained either from the reaction of *o*-benzyl benzoate and ethylenediamine or by the reduction of compound **3** with zinc in acetic acid (Scheme I).



On prolonged treatment (>60 hr) of compound **3** with lithium aluminum hydride in boiling tetrahydrofuran a mixture of products was obtained which consisted of compounds **4**, **5**, **6**, and **7** in a molar ratio of 1:9:13:12. Compound **5** could be isolated directly from the reaction mixture in 24% yield as the least ether soluble product. Compound **6** was obtained

(1) To whom inquiries should be addressed.

(2) W. Metlesics, T. Anton, M. Chaykovsky, V. Toome, and L. H. Sternbach, *J. Org. Chem.*, **33**, 2874 (1968).

from the mother liquor as a maleate and identified with an authentic specimen. Compound 4 was isolated after chromatographic separation on an alumina column. Benzyl alcohol (7) was identified by mass spectroscopy after chromatographic separation.

Compounds 5, 6, and 7 are products of a carbon-carbon cleavage.³ The formation of the 1,2-diphenyl-ethanolamine derivative 5 requires a carbon-carbon cleavage, a carbon-nitrogen cleavage, and the migration of a benzyl group. Although no mechanism is proposed for this reaction, the result is perhaps best explained by assuming an initial carbon-nitrogen cleavage in structure 3b. Such a hydrogenolysis is unlikely for structure 3a since the imidazoline derivatives 4 and 6 were found to be stable under the reduction conditions used.

From nmr data ($J = 6$ cps) the *erythro* configuration was proposed for compound 5.⁴ For comparison this compound was prepared by the reaction of *trans*-stilbene oxide and ethylene diamine. This established both the structure and the configuration of 5 since it is known that the reaction of stilbeneoxides with amines generally proceeds by a *trans* addition.⁵ The formation of 5 appears to be stereospecific since treatment of the corresponding *threo* isomer 9 (prepared by the reaction of *cis*-stilbene oxide with ethylenediamine) under the same LiAlH_4 conditions gave no trace of compound 5. In order to see whether 5 could be prepared from the imidazoline 6 with benzyl alcohol or with benzaldehyde, various combinations of the reactants were mixed and heated under reflux in tetrahydrofuran either alone or together with lithium aluminum hydride or sodium carbonate or sodium hydride. Under the conditions used, we were unable to detect the presence of compound 5 in the reaction mixture by tlc examination.

Experimental Section⁶

2,3-Dihydro-5-phenyl-5H-imidazo[2,1-*a*]isoindole Sulfate (2·H₂SO₄).—A solution of 0.4 g (0.0016 mol) of 3 in 40 ml of chloroform was treated with 0.25 ml of boron fluoride etherate. The solution was heated at reflux under nitrogen for 6 hr and then kept at 25° for 18 hr. After the addition of another 0.25 ml of boron fluoride etherate and heating at reflux for 3 hr, the solution was washed with aqueous sodium carbonate solution. Concentration of the dried chloroform solution gave a yellow oil which was dissolved in tetrahydrofuran.

Acidification with ethanolic sulfuric acid and addition of ethyl acetate gave a crystalline product which after recrystallization from a mixture of methanol and ethyl acetate gave 0.15 g (28%) of 2·H₂SO₄ as white prisms, mp 216–223° dec, mmp 219–224° dec with an authentic sample.²

(3) The cleavage of compound of type $\text{C}_6\text{H}_5\text{CHOHC} \llcorner$ on reduction with lithium-aluminum hydride has been described in the literature: see P. Reynaud and J. Matti, *Bull. Soc. Chim. Fr.*, **612**, (1951); P. Rona and U. Feldman, *J. Chem. Soc.*, 1737 (1958); P. T. Lansbury, *J. Amer. Chem. Soc.*, **83**, 429 (1961).

(4) Similar ethanolamine derivatives have been described in the literature and their stereochemistry was known and correlated with nmr data. See J. W. Huffmann and R. P. Elliott, *J. Org. Chem.*, **30**, 365 (1965), and G. G. Lyle and M. L. Durand, *ibid.*, **32**, 3295 (1967).

(5) R. E. Lutz, J. A. Freek, and R. S. Murphey, *J. Amer. Chem. Soc.*, **70**, 2015 (1948).

(6) Melting points were determined using a Mettler FP-1 instrument and are corrected. Uv and near-infrared spectra were determined using a Cary 14 spectrophotometer; ir spectra, using a Beckman IR-9 spectrophotometer and nmr spectra, using a Varian A-60 spectrometer at 60 Mc/sec. Polarographic reductions were carried out on a Metrohm Polarecord Model E 216. The identity of compounds was established by a comparison of spectral properties and by mixture melting point. The purity of compounds was checked by thin layer chromatography.

3'-Phenylspiro[imidazolidine-2,1'-phthalan] and/or 2-[2'-(α -Hydroxybenzyl)phenyl]-2-imidazoline (3). A. From 1 with Sodium Borohydride.—A solution of 5 g (0.135 mol) of sodium borohydride in 100 ml of ethanol was treated with 25 g (0.1 mol) of 1² added in small portions. The suspension was stirred at 25° for 18 hr and poured into 600 ml of ice water. Filtration gave 24.5 g (97%) of a crystalline product, mp 117–119°. A sample was recrystallized from a mixture of methylene chloride, ether, and petroleum ether (bp 30–60°) to give 3 as white prisms: mp 119–121°; nmr peaks (CDCl_3) at δ 3.47 (4 H singlet, $\text{CH}_2\text{-CH}_2$), 5.80 (1 H singlet, CH), 6.23 (2 H singlet, OH, NH); near-ir (CHCl_3) max 1.49 μ (ϵ 0.9) (NH).

Anal. Calcd for $\text{C}_{16}\text{H}_{16}\text{N}_2\text{O}$: C, 76.16; H, 6.39; N, 11.10. Found: C, 76.24; H, 6.43; N, 11.29.

B. From 1 by Catalytic Hydrogenation.—A suspension of 2.5 g (0.01 mol) of 1 and approximately 0.5 g of Raney nickel in 50 ml of ethanol was shaken in an atmosphere of hydrogen at 25° and 1 atm. After 22 hr, the uptake was 240 ml (ca. 0.01 mol). The solution was filtered and the filtrate was concentrated *in vacuo*. The residue was dissolved in ether to give 1.5 g (60%) of 3 as white prisms, mp 117–121°.

Hydrolysis of 3 to 3-Phenylphthalide.—A solution of 0.2 g of 3 in 2 ml of 2 N hydrochloric acid was heated on a steam bath for 1.5 hr and then kept at 25° for 18 hr. The crystals which had separated were collected, mp 115–117°, and were identified by comparison with an authentic sample of 3-phenylphthalide.⁷

2-(2-Benzylphenyl)-2-imidazoline (4). A. From Compound 8.—A melt of 1.3 g of 8 was kept at 230–240° for 25 min. Distillation at 0.5 mm and 200° (bath temperature) gave an oil which was dissolved in ethyl acetate. Cooling gave 4 as white prisms, mp 111–113°.

Anal. Calcd for $\text{C}_{18}\text{H}_{18}\text{N}_2$: C, 81.32; H, 6.83. Found: C, 81.09; H, 7.02.

B. By Reduction of 2.—A solution of 1.25 g of lithium aluminum hydride in 25 ml of tetrahydrofuran was treated with 0.5 g of 2·H₂SO₄, and the mixture was refluxed for 70 hr. After cooling, 6 ml of water was added slowly and the mixture was filtered. The filtrate was concentrated *in vacuo* and the residual oil was placed on a column of 5 g of neutral alumina No. III (Woelm) and was eluted with methylene chloride. Evaporation of the solvent gave white prisms which after distillation in a bulb tube at 0.2 mm and 150° (bath temperature) gave 4, mp and mmp 107–110° with a sample prepared as described in part A.

C. From Compound 3.—See description in preparation of 5 by reduction of 3.

***erythro*-2-(2-Aminoethylamino)-1,2-diphenylethanol (5).** A. By Reduction of 3.—A suspension of 5 g (0.13 mol) of lithium aluminum hydride in 100 ml of tetrahydrofuran was treated with 10 g (0.04 mol) of 3 in small portions. The mixture was refluxed for 65 hr, cooled, and poured into 500 ml of ether. After the dropwise addition of 15 ml of water and filtration, the filtrate was concentrated to give 9.5 g of a partly crystalline residue. The crystals were collected on a filter and washed with ether. (For work-up of mother liquor, see below.) Recrystallization of the residue from methylene chloride and petroleum ether gave 2.5 g (24%) of 5 as white prisms: mp 123–125°; uv max (2-propanol) 259 m μ (ϵ 500); nmr peaks (CDCl_3) at δ 1.90 (4 H singlet, NH, NH_2OH), 2.52 (4-proton multiplet, CH_2CH_2), 3.83, 4.95 (2-proton AB quartet, $J = 6$ cps, CHCH).

Anal. Calcd for $\text{C}_{16}\text{H}_{20}\text{N}_2\text{O}$: C, 74.96; H, 7.86. Found: C, 74.69; H, 7.75.

The mother liquor of product 5 initially obtained was concentrated and the residue was dissolved in 35 ml of ethanol and 3.5 g of maleic acid was added. After 1 hr, 1 g of a crystalline precipitate was collected on a filter (maleate of 6). The mother liquor of this crop was diluted with 75 ml of ether and after standing for 18 hr gave an additional 4.9 g of the salt. This fraction was treated with aqueous sodium hydroxide and ether. The ether extract gave a material which after recrystallization from a mixture of benzene and petroleum ether yielded 6 as white prisms, mp 99–102° (lit.⁸ mp 101°).

The mother liquor obtained after removal of compound 5 and the maleate of compound 6 was concentrated and partitioned between aqueous sodium hydroxide and methylene chloride. The organic extract was placed on a column of 60 g of neutral

(7) F. Ullmann, *Justus Liebig's Ann. Chem.*, **291**, 23 (1896).

(8) G. Forssell, *Ber.*, **25**, 2132 (1892).

alumina No. III (Woelm) and eluted with methylene chloride. In the first fractions benzyl alcohol was identified by vapor phase chromatography and mass spectroscopy. The subsequent fractions containing crystalline material were combined and recrystallized from a mixture of ethanol and petroleum ether to give **4** as white prisms, mp 111–113°.

The ratio of the products in the crude reaction mixture, obtained after reduction and (a) after removal of the inorganic material and (b) after concentration of the solution, was determined with a 0.25 in. o.d. × 6 ft column containing 4% polyethylene glycol, mol wt 20,000, and 2% KOH on Chromosorb W support in a F & M Model 810 gas chromatograph with a dual flame detector. The column temperature was programmed for 150 to 250°, 6°/min. Nitrogen was used as carrier gas at 100 ml/min. The molar ratio of 4:5:6:7 was found to be approximately 1:9:13:12.⁹

B. Preparation of 5 from *trans*-Stilbene Oxide.—A solution of 5 g of *trans*-stilbene oxide in 15 ml of ethylenediamine was refluxed for 18 hr. The mixture was cooled, poured into water, and extracted with methylene chloride. The dried extract was concentrated to give **5** as white prisms which on recrystallization from a mixture of methylene chloride and petroleum ether gave 4.5 g (69%) of the pure product, mp 121–123°.

threo-2-(2-Aminoethylamino)-1,2-diphenylethanol (9).—In an exactly analogous manner as that used for the preparation of compound **5**, 5 g of *cis*-stilbene oxide¹⁰ gave 4.7 g (72%) of **9** as white prisms: mp 82–86°; nmr peaks (CDCl₃) at δ 2.50 (4 H singlet, NH₂OH, NH₂), 2.62 (4 H multiplet, CH₂CH₂), 3.62, 4.60 (2-proton AB quartet, *J* = 8.5 cps, CHCH).

Anal. Calcd for C₁₈H₂₀N₂O: C, 74.96; H, 7.86; N, 10.93. Found: C, 75.10; H, 8.00; N, 10.95.

N-(2-Aminoethyl)-2-benzylbenzamide (8). **A. By Reduction of 3.**—A solution of 5 g (0.02 mol) of **3** in 50 ml of acetic acid was treated with 10 g of zinc dust. The temperature of the mixture rose during the addition to 35° and after that was kept at 25° for 16 hr. Filtration gave a solution which was poured on ice, basified with sodium hydroxide, and extracted with methylene chloride. The dried extract was concentrated and the residue on distillation at 0.2 mm (bath temperature ca. 150°) gave **3** g (59%) of **8** as white, waxy prisms: mp 84–86°; ir (CHCl₃) 1660, 1520 cm⁻¹ (NHCO).

Anal. Calcd for C₁₆H₁₈N₂O: C, 75.56; H, 7.13. Found: C, 75.64; H, 7.23.

A solution of 10 g of **8** in 50 ml of methanol was treated with 20 ml of a 6 *N* methanolic hydrogen chloride solution. The precipitate was collected after 30 min and recrystallized from methanol to give 8.7 g (76%) of the hydrochloride of **8** as white needles: mp 200–201°; ir (KBr) 1645, 1540 cm⁻¹.

B. By the Condensation of Methyl *o*-Benzylbenzoate with Ethylenediamine.—A mixture of 35 g (0.16 mol) of methyl *o*-benzylbenzoate¹¹ and 350 ml of ethylenediamine was heated under reflux for 6 hr. The mixture was concentrated *in vacuo* and the residual oil was dissolved in aqueous sodium hydroxide to give a clear solution which was extracted with methylene chloride. The dried extract was concentrated and gave 14.5 g (33%) of **8** as a tan solid, mp 79–83°.

Registry No.—**1a**, 16780-90-8; **3a**, 25293-56-5; **3b**, 24811-71-0; **4**, 25293-58-7; **5**, 25286-80-0; **6**, 936-49-2; **8**, 25286-81-1; **9**, 25286-83-3.

Acknowledgment.—We are indebted to the following members of the Physical Chemistry Department under the direction of Dr. P. Bommer: Dr. F. Scheidl for microanalytical data; Mr. H. Jenny, Mr. S. Traiman, and Dr. F. Vane for spectroscopic data and interpretations. We also thank Mr. F. Jenkins for able assistance in the preparations.

(9) Average of vapor phase chromatographic determinations in three independent reduction experiments. The fact that a slight excess of **6** over **7** was consistently found is best explained by assuming that some of the more volatile benzyl alcohol is lost in the work-up procedure.

(10) A. C. Cope, P. A. Trumbull, and E. R. Trumbull, *J. Amer. Chem. Soc.*, **80**, 2844 (1958).

(11) E. Barnett, J. Cook, and I. Nixon, *J. Chem. Soc.*, 508 (1927).

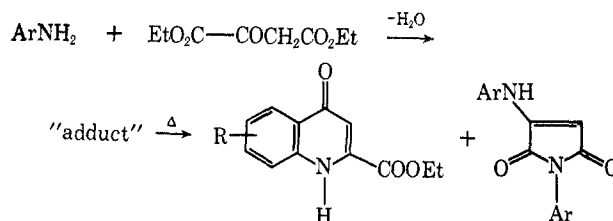
Maleimide Syntheses by Amine Reaction with Acetylenedicarboxylate Esters

NED D. HEINDEL

Chandler Laboratory of Chemistry,
Lehigh University, Bethlehem, Pennsylvania 18015

Received February 18, 1970

In the course of our study of amine-acetylene ester reactions we reported that certain aniline-acetylenedicarboxylate adducts could undergo facile ammonolysis to α -anilinomaleimides.¹ Related *N*-aryl- α -anilinomaleimides were observed as by-products in the pyrolytic quinoline cyclization of the condensation adducts



from anilines and ethyl ethoxalylacetate (**1**).² Landquist³ has demonstrated that if residual aryl amine were removed prior to thermolysis of these adducts, the maleimide normally formed could be minimized.

In contrast to the addition of arylhydrazines to dimethyl acetylenedicarboxylate, a reaction which produces both imine and enamine tautomers,⁴ the addition of aryl amines yields exclusively anilinfumarate enamines.^{5,6} It would be reasonable to expect the same anilinfumarates as principal products of anilines and ethoxalylacetate. Adducts prepared in this fashion have been variously described as either iminosuccinates^{3,7} or anilinomaleates² but without any firm experimental evidence for either structure.

We have repeated Surrey and Cutler's synthesis² of the adducts of aniline and *m*-chloroaniline with ethyl ethoxalylacetate, (**1**), and have found their products to be identical in all respects with the corresponding aniline plus diethyl acetylenedicarboxylate adducts (*i.e.*, *trans* enamines). These products were distinguished by a fumarate vinyl singlet at δ 5.31 ppm in the aniline adduct and at δ 5.41 ppm in the *m*-chloroaniline product. Huisgen has shown that the normal position of such fumarate vinyl resonances is δ 5.4 ppm and for maleate vinyls approximately δ 4.8 ppm.⁵ These differences have been explained on the basis of relative vinyl deshieldings by the ester carbonyls.⁸ Although Surrey and Cutler's "maleates" were distilled *in vacuo* to obtain analytical material, we have shown that the composition of the product is not changed by distillation.

(1) N. D. Heindel, V. B. Fish, and T. F. Lemke, *J. Org. Chem.*, **33**, 3997 (1968).

(2) A. R. Surrey and R. A. Cutler, *J. Amer. Chem. Soc.*, **66**, 514 (1946).

(3) J. K. Landquist, *J. Chem. Soc.*, 1038 (1951).

(4) N. D. Heindel, P. D. Kennewell, and M. A. Pfau, *Chem. Commun.*, 757 (1969), and *J. Org. Chem.*, **35**, 80 (1970).

(5) R. Huisgen, K. Herbig, A. Siegl, and H. Huber, *Chem. Ber.*, **99**, 2526 (1966).

(6) N. D. Heindel, I. S. Bechara, T. F. Lemke, and V. B. Fish, *J. Org. Chem.*, **32**, 4155 (1967).

(7) A. C. Mueller and C. S. Hamilton, *J. Amer. Chem. Soc.*, **65**, 1017 (1943).

(8) J. E. Dolfini, *J. Org. Chem.*, **30**, 1298 (1965).