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*-stilene oxide[10] gave 4.7 g (72%) of **9** as white prisms: mp 82–86°; nmr peaks ($CDCl_3$) at $\delta$ 2.50 (4 H singlet, $NH_1OH_1NH_2$), 2.62 (4 H multiplet, $CH_2CH_2$), 3.62, 4.60 (2-proton AB quartet, $J$ = 8.5 cps, CHCH).

*Anal.* Calcd for $C_{16}H_{20}N_2O$: 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 ($CHCl_3$) 1660, 1520 cm$^{-1}$ (NHCO).

*Anal.* Calcd for $C_{16}H_{18}N_2O$: 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*-benzylbenzoate[11] 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 (38%) 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.

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[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).

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# Maleimide Syntheses by Amine Reaction with Acetylenedicarboxylate Esters

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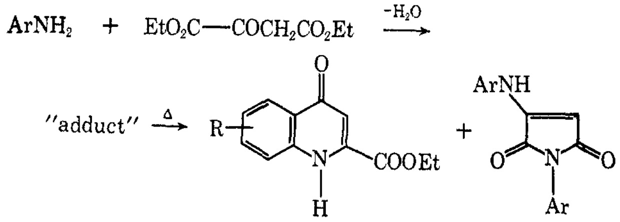
*Received February 18, 1970*

In the course of our study of amine–acetylene ester reactions we reported that certain aniline–acetylenedicarboxylate adducts could undergo facile ammonolysis to $\alpha$-anilinomaleimides.[1] Related N-aryl-$\alpha$-anilinomaleimides were observed as by-products in the pyrolytic quinoline cyclization of the condensation adducts from anilines and ethyl ethoxalylacetate (**1**).[2] Landquist[3] 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 anilinofumarate enamines.[5,6] It would be reasonable to expect the same anilinofumarates as principal products of anilines and ethoxalylacetate. Adducts prepared in this fashion have been variously described as either iminosuccinates[3,7] or anilinomaleates[2] but without any firm experimental evidence for either structure.

We have repeated Surrey and Cutler's synthesis[2] 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 $\delta$ 5.31 ppm in the aniline adduct and at $\delta$ 5.41 ppm in the *m*-chloroaniline product. Huisgen has shown that the normal position of such fumarate vinyl resonances is $\delta$ 5.4 ppm and for maleate vinyls approximately $\delta$ 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.

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[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.*, **68**, 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).

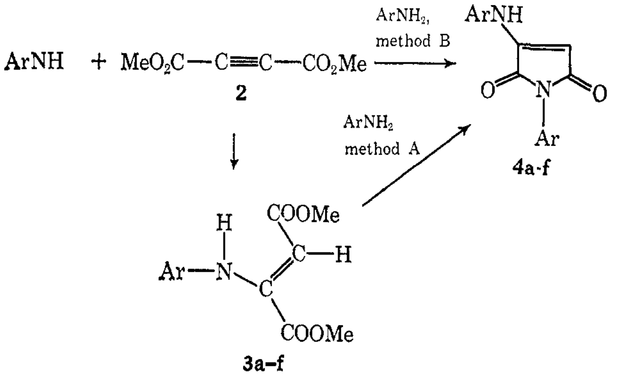
TABLE I

MALEIMIDE SYNTHESES

| Compd no. | $RNH_2$ (R =) | + | Coreactant | Method | % yield[a] | Mp, °C |
|---|---|---|---|---|---|---|
| **4a** | 3-Cl-4-$MeOC_6H_3$- | | **2** | B | 66 | 269-270 |
| **4b** | 4-$MeOC_6H_4$- | | **2** | B | 62 | 221-223[b] |
| **4b** | 4-$MeOC_6H_4$- | | **3b**[c] | A | 73 | 221-223 |
| **4c** | 4-$FC_6H_4$- | | **2** | B | 69 | 274-276 |
| **4c** | 4-$FC_6H_4$- | | **3c**[d] | A | 58 | 274-276 |
| **4d** | 4-$BrC_6H_4$- | | **2** | B | 61 | 260-262[e] |
| **4e** | 3-$ClC_6H_4$- | | DEADC[f] | B | 54 | 221-223[g] |
| **4f** | $C_6H_5$- | | **2** | B | 50 | 230-232[h] |
| **5a** | H | | **3** (Ar = 4-$ClC_6H_4$)[c] | C | 44 | 249-251 |
| **5b** | H | | **3b**[c] | C | 40 | 204-206 |
| **5c** | H | | **3f**[c] | C | 51 | 210-212[i] |

[a] Satisfactory analytical values (±0.35) for C, H, N were reported for compounds **4a-c** and **5a-c**. Ed. [b] Lit.[3] mp 225-226°. [c] Prepared as in ref 5. [d] See ref 9. [e] Lit. mp 260°: F. D. Chattaway and G. D. Parkes, *J. Chem. Soc.*, **123**, 663 (1923). [f] Diethyl acetylenedicarboxylate. [g] Lit.[2] mp 220-221°. [h] Lit. mp 232-233°: L. Clarke and E. K. Bolten, *J. Amer. Chem. Soc.*, **36**, 1906 (1914). [i] Lit. mp 206.5-207°: M. T. Bogert and R. A. Gortner, *ibid.*, **32**, 119 (1910).

Excellent yields of six N-aryl-α-anilinomaleimides have been obtained by pyrolysis of these anilinofumarates in the presence of a fourfold molar excess of the corresponding aniline (see Table I, Method A). Isolation of the intermediate adducts, **3**, however, appeared to offer little advantage over the direct combination of acetylenedicarboxylate with a fivefold excess of the aniline (Method B). In the latter technique, the initially vigorous reaction of the amine was allowed to subside before the mixture was heated at reflux (220–245°) for 5 min.



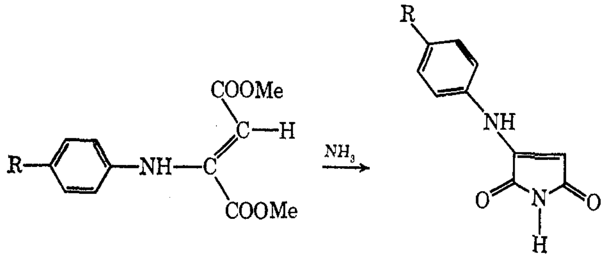
**a**, Ar = 3-Cl-4-$MeOC_6H_3$
**b**, Ar = 4-$MeOC_6H_4$
**c**, Ar = 4-$FC_6H_4$
**d**, Ar = 4-$BrC_6H_4$
**e**, Ar = 3-$ClC_6H_4$
**f**, Ar = $C_6H_5$

It has not been possible to prepare pure "mixed" maleimides in which the aryl moiety at the α carbon is different from that on the imino nitrogen. Thus, the reaction of *p*-anisidine with dimethyl 3,5-dichloroanilinofumarate[9] gave a maleimide mixture and with dimethyl 4-chlorophenoxyfumarate gave 57% of **4b**. Further evidence for a disproportionation–recombination was obtained when **3b** and *o*-chloroaniline produced a 34% yield of **4b** as the only isolable product.

It was possible to subject aniline–acetylenedicarboxylate adducts to ammonolysis in methanol solutions and to obtain α-anilinomaleimides (Method C).

This ammonolysis and the aniline thermolysis (Methods A and B) must naturally involve geometric isomerization of the enamine linkage prior to maleimide formation. Such conversions are not without precedent, since it has been recently shown that the rotational barrier about an enamine bond is less than one-third that of a normal C=C.[10] Presumably the ammonia–methanol medium used to generate the maleimides could effect a base catalyzed *trans-to-cis* isomerism of the enamine.

All the maleimide products displayed a characteristic imide carbonyl absorption. A weak C=O band at 1770 ± 5 and an intense band at 1705 ± 5 cm⁻¹ could be observed in all the products. This strong–weak carbonyl set is a well known feature of five-membered imides.[11] Solubility difficulties precluded a comprehensive nmr analysis of all the maleimide products, but **4b**, **4d**, **4f**, **5b**, and **5c** were sufficiently soluble in Sulfolane-W[12] to give suitable spectra. All were distinguished by a unit proton resonance at δ 5.60 ± 0.2 ppm for the maleimide vinyl-H therefore eliminating the possibility of imino tautomers in this series.



**5a**, R = Cl
**b**, R = MeO
**c**, R = H

### Experimental Section[13]

**General Technique for Maleimide Synthesis. Method A.**—Anilinofumarates (0.01 mol), prepared by published methods

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[9] N. D. Heindel, I. S. Bechara, P. D. Kennewell, J. Molnar, C. J. Ohnmacht, S. M. Lemke, and T. F. Lemke, *J. Med. Chem.*, **11**, 1218 (1968).

(10) Y. Shvo, E. C. Taylor, and J. Bartulin, *Tetrahedron Lett.*, 3259 (1967).

(11) K. Nakanishi, "Infrared Absorption Spectroscopy," Holden-Day, San Francisco, Calif., 1962, p 47.

(12) Gift of Shell Development Company.

(13) Nmr spectra were obtained on a Perkin-Elmer Hitachi R20A nmr spectrometer and are reported in δ ppm units from tetramethylsilane. Infrared spectra were obtained as paraffin oil mulls on a Perkin-Elmer 257 infrared spectrometer. We gratefully acknowledge the financial assistance of the National Science Foundation which made possible the purchase of these instruments. Combustion analyses were provided by the late Dr. Velmer B. Fish of these laboratories and by Dr. George I. Robertson, Florham Park, N. J.

from aryl amines and dimethyl acetylenedicarboxylate (2)[5,9] or aryl amines and ethyl ethoxalylacetate (1), were intimately mixed with 0.04 mol of the same aryl amine and heated to reflux for 10 min. The hot melt was cooled to room temperature and the resulting crystals thoroughly triturated with cold methanol. The maleimides were virtually insoluble in methanol but could be purified by sublimation [200° (0.1 mm)] or by recrystallization from acetic acid.

**Method B.**—The dimethyl acetylenedicarboxylate (0.01 mol) was added to 0.05 mol of the aryl amine and the initially vigorous reaction allowed to subside. The medium was then heated at reflux for 10 min and the maleimide product isolated as above.

**Method C.**—A solution of 0.01 mol of the appropriate anilinofumarate, synthesized as described by Huisgen,[5] was prepared in 100 ml of anhydrous methanol. The solution was saturated with anhydrous ammonia gas at 0° and sealed. After standing at room temperature for 1 week it was opened, resaturated with ammonia, and sealed for an additional week. The methanol was then chilled and the precipitated maleimide filtered off, dried, and sublimed *in vacuo*.

**Dimethyl 4-Chlorophenoxyfumarate.**—Following the procedure outlined for phenol,[14] 4-chlorophenol (30 mmol) was dissolved in 25 ml of ether containing 30 mmol of N-methylmorpholine. To this solution was added 30 mmol of 2 dissolved in 25 ml of ether. The mixture was allowed to stand at room temperature for 3 days, the ether removed by distillation, and the oily residue dissolved in benzene. The benzene phase was washed well with water, dried ($MgSO_4$), and concentrated to an oil which on cooling deposited 3.08 g (38%) of pale yellow crystals. An analytical sample was prepared by recrystallization from 1:1 benzene:hexane: mp 57–59°; ir (Nujol mull) 1740 and 1725 (C=O) and 1660 $cm^{-1}$ (C=C); nmr ($CDCl_3$) $\delta$ 3.67 (s, 3, $OCH_3$), 3.72 (s, 3, $OCH_3$), 6.60[15] (s, 1, $=CHCOOCH_3$), and 6.8 to 7.4 ppm (m, 4, ArH).

*Anal.* Calcd for $C_{12}H_{11}ClO_5$: C, 53.33; H, 4.07. Found: C, 53.42; H, 4.10.

Reaction of this 4-chlorophenoxy adduct with *p*-anisidine according to Method A gave a 57% yield of **4b**.

**Registry No.**—**4a**, 25024-00-4; **4b**, 24978-24-3; **4c**, 24978-25-4; **4d**, 24978-26-5; **4e**, 24978-27-6; **4f**, 13797-26-7; **5a**, 24978-29-8; **5b**, 24978-30-1; **5c**, 17244-42-7; dimethyl 4-chlorophenoxyfumarate, 24355-81-5.

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(14) E. Winterfeldt and H. Preuss, *Chem. Ber.*, **99**, 450 (1966).

(15) The observation that fumarate vinyls in phenoxy adducts fall at $\delta$ 6.45–6.68 ppm while maleate vinyls appear at 5.00–5.05 ppm permits assignment of fumarate geometry to this material. See ref 14 and N. D. Heindel and L. A. Schaeffer, *J. Org. Chem.*, in press, for similar examples.

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# Glyoxal Derivatives. II. Reaction of Glyoxal with Aromatic Primary Amines

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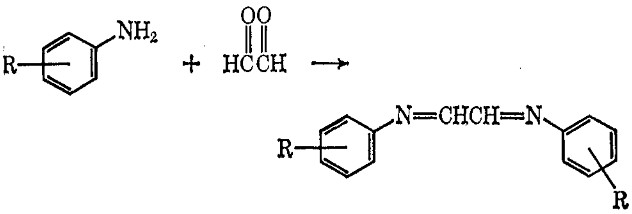
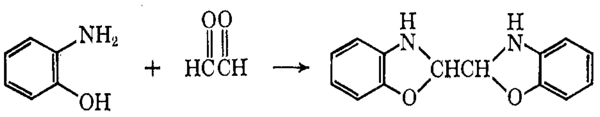
We have recently reported on the reaction of glyoxal with aromatic and aliphatic primary amines.[1] In that case, the products were N-substituted 1,2-diimines. In this paper we continue with our observations on the reaction of aromatic primary amines with glyoxal.

In earlier work it has been found that *p*-(N,N-dimethylamino)aniline,[2] *p*-aminophenol,[3] 2-hydroxy-5-chloroaniline, and 2-hydroxy-5-nitroaniline[4] react with glyoxal to give N-substituted aromatic 1,2-diimines.



Chwala and Bartek[5] report that *p*-anisidine and glyoxal sulfate react in the presence of sodium acetate to give the diimine corresponding to the above 1,2-diimines. Bayer has reported that *o*-aminophenol gave a 1,2-diimine;[6] however, Murase demonstrated that it was actually a cyclization product.[3]



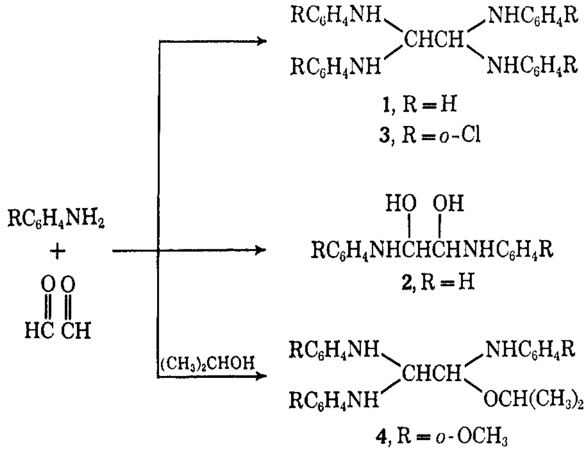
Other reports[7,8] state that aniline and glyoxal give only tars.

Somewhat related is the report by Malik, *et al.*,[9] that phenylglyoxal hydrate reacts with various aromatic primary amines to give imines; however, Proctor and Rehman offer evidence that the products are actually $\alpha$-diamines or products incorporating alcohol solvent.[10]

## Results and Discussion

We have found that aromatic primary amines react with 40% aqueous glyoxal to give either 1,2-diimines, 1,2-dihydroxy-1,2-diamino compounds, or tri- and tetraaminoethane derivatives. Thus, glyoxal reacts with excess aniline in isopropyl alcohol to give a 47% yield of 1,1′,2,2′-tetrakis(phenylamino)ethane, **1**, or with two molar equivalents of aniline to give 1,2-bis(phenylamino)-1,2-dihydroxyethane, **2**, in 54% yield.

Similarly, *o*-chloroaniline reacts with glyoxal giving a 47% yield of 1,1′,2,2′-tetrakis(*o*-chlorophenylamino)ethane, **3**, and *o*-anisidine gives 1,1′,2-tris(*o*-methoxyphenylamino)-2-isopropoxyethane, **4**, in 41% yield when the reaction is carried out in isopropyl alcohol solvent. These reactions are summarized in eq 1.



**1**, R = H
**3**, R = *o*-Cl
**2**, R = H
**4**, R = *o*-OCH₃

(1)

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(1) (a) Preliminary communication: J. M. Kliegman and R. K. Barnes, *Tetrahedron Lett.*, 1953 (1969); (b) J. M. Kliegman and R. K. Barnes, *Tetrahedron*, in press.

(2) Y. Tominatsu, *Yakugaku, Zasshi*, **77**, 292 (1957).

(3) I. Murase, *Bull. Chem. Soc. Jap.*, **32**, 827 (1959).

(4) O. Leminger and M. Farsky, *Collect. Czech. Chem. Commun.*, **30**, 607 (1965).

(5) A. Chwala and W. Bartek, *Monatsh. Chem.*, **82**, 652 (1951).

(6) E. Bayer, *Chem. Ber.*, **90**, 2325 (1957).

(7) I. S. Bengelsdorf, *J. Amer. Chem. Soc.*, **75**, 3138 (1953).

(8) S. B. Needleman and M. C. C. Kuo, *Chem. Rev.*, **62**, 422 (1962).

(9) W. U. Malik, D. R. Gupta, and C. L. Taploo, *J. Chem. Eng. Data*, **11** (2), 211 (1966).

(10) G. R. Proctor and M. A. Rehman, *J. Chem. Soc. C*, **1967** (2696).