3.34 (t, 2 H), 2.07 (s, 3 H), 1.88 (s, 3 H); $^{13}$C NMR (CDCl$_3$) $\delta$ 183.46, 183.11, 169.18, 145.09, 135.56, 134.32, 134.09, 133.63, 132.98, 132.56, 130.10, 128.97, 127.44, 126.83, 123.48, 49.84, 33.23, 29.27, 19.02; MS, *m/e* (relative intensity) 323 (1.4, M$^+$), 249 (10.0), 239 (14.0), 139 (14.1), 70 (100). Anal. Calcd for $C_{19}H_{17}NO_2S$: C, 70.56; H, 5.30; N, 4.33. Found: C, 70.43; H, 5.30; N, 4.21.

**2,3-Dihydro-8*H*-anthra[9,1-*ef*][1,4]thiazepin-8-one (5).** The crude solid **1b** (0.200 g, 0.75 mmol) was refluxed in toluene (20 mL) for 20 h. The reaction mixture was allowed to cool slightly and then introduced onto a column of silica gel. Elution with $CH_2Cl$ and concentration yielded an orange solid as the major component (0.105 g, 56%). Crystallization from ethanol afforded **5** as orange needles: mp 180–182 °C dec; $^1$H (NMR (CDCl$_3$) $\delta$ 7.47–8.22 (m, 7 H), 4.07–4.18 (m, 2 H), 3.80–3.90 (m, 2 H); $^{13}$C NMR (CDCl$_3$) $\delta$ 183.40, 163.03, 139.62, 137.88, 137.48, 136.09, 135.41, 133.68, 131.41, 130.77, 130.24, 126.77, 126.53, 125.03, 52.14, 42.78; MS, *m/e* (relative intensity) 265 (48.3, M$^+$) 264 (57.5), 237 (100), 163 (52.6). Anal. Calcd for $C_{16}H_{11}NOS$: C, 72.43; H, 4.18; N, 5.28. Found: C, 72.45; H, 4.32; N, 5.22.

**7*H*-Dibenzo[*de,h*]quinolin-7-one (6).** The crude amine **1b** (0.300 g, 1.06 mmol) was refluxed in glacial acetic acid (10 mL) for 1 h. The cooled reaction mixture was poured into water (100 mL), and the precipitate was collected by filtration, washed with water, and dried in vacuo. Column chromatography (silica gel, 1:1 $CCl_4/CH_2Cl_2$) afforded **6** as a yellow solid (0.165 g, 66%). Crystallization from an ethanol–methanol–water mixture gave yellow needles: mp 183–185 °C (lit.[8] mp 184–186 °C; $^1$H NMR (CDCl$_3$) $\delta$ 8.88–8.95 (m, 1 H), 8.77–8.81 (m, 1 H), 8.65–8.70 (m, 1 H), 8.40–8.47 (m, 1 H), 8.15–8.19 (m, 1 H), 7.62–7.94 (m, 4 H); $^{13}$C NMR (CDCl$_3$) $\delta$ 183.91, 149.25, 144.50, 137.22, 135.59, 134.41, 133.75, 132.82, 130.90, 130.76, 130.25, 129.55, 127.95, 125.71, 123.29, 121.23; MS, *m/e* (relative intensity) 231 (100, M$^+$), 230 (14.5), 203 (38.1), 88 (14.6).

**Acknowledgment.** This research was supported by Grant CA 24543 from the National Cancer Institute.

**Registry No.** **1a**, 86709-68-4; **1b**, 86709-69-5; **1c**, 82-44-0; **1e**, 4465-58-1; **1f**, 569-06-2; **1g**, 86709-70-8; **1h**, 86709-71-9; **2**, 86709-72-0; **3**, 86709-73-1; **4**, 86709-74-2; **5**, 86709-75-3; **6**, 65543-67-1; 2-aminoethanol, 141-43-5; 2-(benzylidineamino)ethanol, 770-37-6; 2-aminoethanethiol hydrochloride, 156-57-0.

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[8] Bayer, O. In "Methoden der Organische Chemie (Houben-Weyl)"; Georg Thieme Verlag: Stuttgart, 1979; Band 7 (3c), p 347 and references cited therein.

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# Isolation of the Intermediates in a Benzoin-Type Condensation

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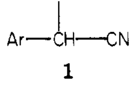
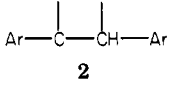
The mechanism of the benzoin condensation for aromatic aldehydes is well established, at least in alcoholic solution.[1] Two important cyanohydrin intermediates, **1** and **2**, exist in this reaction. Several workers have demonstrated that **1** accumulates in significant amounts during the course of the condensation, and it has been isolated both as a salt and as its conjugate acid.[1a,b] However, **2** is readily converted to a product, and, not surprizingly, a literature search has failed to turn up any report of its isolation.



$\mathrm{Ar{-}CH(O^-){-}CN}$

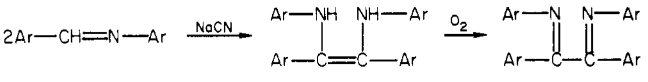
1



$\mathrm{Ar{-}C(OH){-}CH(O^-){-}Ar}$

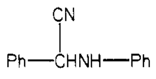
2

Schiff bases undergo a reaction that gives a benzoin-type product (**3**), which is rapidly oxidized to **4**.[2] The reaction is assumed to proceed via the same mechanism as the benzoin condensation, but there has been no supporting evidence for this assumption.



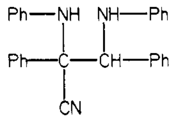
$$\mathrm{2Ar{-}CH{=}N{-}Ar} \xrightarrow{\mathrm{NaCN}} \underset{3}{\mathrm{Ar{-}C(NH{-}Ar){=}C(NH{-}Ar){-}Ar}} \xrightarrow{O_2} \underset{4}{\mathrm{Ar{-}C({=}N{-}Ar){-}C({=}N{-}Ar){-}Ar}}$$

This note reports the use of a phase-transfer agent, tetrabutylammonium chloride, in the reaction of NaCN with *N*-benzylideneaniline. When the reaction was run in a two-phased solid–liquid system with toluene as the organic solvent, **3** and **4** were obtained in moderate yield. The only other compound isolated was a decomposition product of **3**. In contrast, when performed in a two-phased methylene chloride–$H_2O$ system, the reaction proceeded to give not only **3** (isolated as **4**) but also **5** and **6**, which are the conjugate acids of the corresponding analogues of **1** and **2**. In fact, **6** is formed in nearly quantitative yield when the reaction is run in a toluene–$H_2O$ mixture. This high yield of **6** is explained by its extreme insolubility in toluene, thus shifting all equilibria toward its formation. A reversible sequence of reactions was demonstrated by interconverting **5** and **6**, as well as converting each into **3**.[3]



$\mathrm{Ph{-}CH(CN){-}NH{-}Ph}$

5



$\mathrm{Ph{-}C(NH{-}Ph)(CN){-}CH(NH{-}Ph){-}Ph}$

6

Compound **5** is well-known, and it has been prepared in many ways.[4] The structure for **6** is supported by analysis and by its UV, NMR, and mass spectra. Interestingly, **6** does not exhibit a nitrile absorption in the IR. This is not unexpected, since nitriles that have an electron-withdrawing substituent $\alpha$ to the nitrile often have very weak or undetectable absorption in the 2000–2400-cm$^{-1}$ region.[5] The presence of the CN functional group was demonstrated by generation and identification of CN$^-$ from **6** in a basic solution.

The mass spectrum confirms the $\alpha$-amino nitrile structure in **6**. The spectrum consists largely of two fragments at *m/e* 362 and 180. The first is due to loss of HCN from the parent molecule and the second is probably Ph–$\overset{+}{C}{\equiv}N$-Ph, resulting from fragmentation of the *m/e* 362 molecule. A molecular ion at *m/e* 389 is observable, but its intensity is very weak. The spectrum is entirely consistent with mass spectra reported for other aromatic $\alpha$-amino nitriles.[6]

There has been a prior report of **6**. It was obtained as a byproduct during the reaction of carvone with **5** under

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[1] (a) Lapworth, A. *J. Chem. Soc.* **1903**, *83*, 995. (b) Lapworth, A. *Ibid.* **1904**, *85*, 1206. (c) Kuebrich, J. P.; Schowen, R. L.; Wang, M.; Lupes, M. *J. Am. Chem. Soc.* **1971**, *93*, 1214.

[2] (a) Strain, H. *J. Am. Chem. Soc.* **1928**, *50*, 2218. (b) Strain H. *J. Am. Chem. Soc.* **1929**, *51*, 269. (c) Becker, H. D. *J. Org. Chem.* **1970**, *35*, 2099.

[3] Since **5** and **6** are the conjugate acids of the true intermediates, the extent of conversion of **5** and **6** into **3** depends on the basicity of the reaction medium. See Experimental Section.

[4] See, for example: (a) Everset, A. E.; McCombie, H. *J. Chem. Soc.* **1911**, *99*, 1756. (b) von Walther, R.; Hubner, R. *J. Prakt. Chem.* **1916**, *93*, 119. (c) McEwen, W. E.; Grossi, A. V.; MacDonald, R. J.; Stamegna, A. P. *J. Org. Chem.* **1980**, *45*, 1301.

[5] Bellamy, L. J. "The Infrared Spectra of Complex Molecules"; Chapman and Hall: London, 1975; p 297.

[6] Sandhu, J. S.; Mohan, S.; Schroll, G. *Acta Chem. Scand.* **1971**, *25*, 590.

0022-3263/83/1948-3343$01.50/0 © 1983 American Chemical Society

strongly basic conditions.[7] Undoubtedly, some of **5** decomposed to *N*-benzylideneaniline, which then proceeded to react to give the condensation product. Since the benzoin condensation of Schiff bases was not known at the time, the significance of the reaction was not recognized.

The formation of **3** thus appears to occur via a benzoin-type condensation. The isolation of **6** is peculiar to reaction with Schiff bases. For example, the benzoin condensation of benzaldehyde was studied with a phase-transfer agent in a $H_2O$–organic system, and a high yield of benzoin was observed with no mention of isolation of any other compounds.[8] The greater basicity of the Schiff base intermediate evidently allows it to be trapped in the presence of a proton donor, whereas aldehyde intermediates more readily decompose.

## Experimental Section

Melting points were determined on a Thomas-Hoover melting point apparatus and are corrected. Infrared spectra were obtained from a Perkin-Elmer Model 137 spectrophotometer, and ultraviolet spectra were run on a Hitachi Perkin-Elmer Model 139 UV–visible spectrophotometer. NMR spectra were recorded on a Varian Associates Model A-60 instrument. Elemental analyses were performed by Integral Microanalytical Laboratories, Raleigh, NC, and the mass spectrum was run by Gollob Analytical Services, Berkeley Heights, NJ.

**Reactions of *N*-Benzylideneaniline with NaCN and Tetrabutylammonium Chloride (TBACl).** The following represent typical results. (a) A mixture of 0.50 g (0.010 mol) of NaCN and 0.28 g (0.0010 mol) of TBACl was dried under reduced pressure at 100 °C for 1 h and then finely ground. The solids were added to a solution of 1.81 g (0.010 mol) of *N*-benzylideneaniline[9] dissolved in 5.0 mL of toluene (dried over Na), and the resulting mixture was stirred vigorously at room temperature under an atmosphere of dry $N_2$. Within 1 to 2 h, a fluorescent yellow solid began to precipitate from solution. After 4.5 h, the reaction was stopped, and the yellow solid filtered and washed with water to give 0.63 g (35%) of crude **3**, mp 175–190 °C (lit.[2c] mp 205–210 °C). Recrystallization improved the melting point only slightly, but an IR spectrum was identical with that of **3** prepared by the method of Becker.[2c]

The filtrate from isolation of **3** was evaporated to dryness under reduced pressure, and the oily residue was allowed to stand open to air overnight.[10] The oil was then chromatographed on 20 g of Florisil.[11] Elution with hexane gave 0.35 g (19%) of crude **4**, which was recrystallized from 95% ethanol to yield bright yellow crystals with mp 140–144 °C (lit.[2c] 146–148 °C) whose IR spectrum was identical with that of authentic **4**.

Continued elution with 10% acetone–hexane resulted in the isolation of 0.11 g of benzanilide, a reported decomposition product of **3**.[2b] A significant amount of more polar material was isolated from the column, but none of this material could be crystallized or easily purified.[12]

(b) To a mixture of 0.50 g (0.010 mol) of NaCN, 0.28 g (0.0010 mol) of TBACl, and 1.81 g (0.010 mol) of *N*-benzylideneaniline were added 5.0 mL of toluene and 2.0 mL of $H_2O$. Vigorous stirring was continued for 5 h, after which time a thick, white precipitate had collected. The weight of crude material was 1.90 g (98%), which, after washing thoroughly with 95% ethanol and crystallization from toluene, gave 1.42 g of **6**, mp 199–202 °C. This material was sufficiently pure for most purposes, but it held onto toluene tenaciously, so purer samples were obtained by recrystallization from benzene. One additional recrystallization from benzene gave material melting from 207 to 209 °C (lit.[7] mp 210–211 °C): IR (Nujol) 3300 (NH), 1595 (aromatic) cm$^{-1}$; UV $\lambda_{max}$ (isooctane) 240 nm ($\epsilon$ 32 000) 283 (3900); MS, *m/e* (relative intensity) 389 (0.07), 362 (51), 347 (5), 285 (7), 270 (6), 182 (26), 181 (32), 180 (100), 152 (3), 104 (8), 77 (39), 51 (11), 27 (5); NMR ($CDCl_3$) $\delta$ 4.82 (br s, 1 H), 5.80 (br, 2 H), 6.6–7.3 (m, 20 H). The broad absorption at $\delta$ 5.80 disappeared when $D_2O$ was added.

Anal. Calcd for $C_{27}H_{23}N_3$: C, 83.26; H, 5.95; N, 10.79. Found: C, 83.46; H, 6.18; N, 10.38.

Brief heating of a mixture of **6** and alcoholic NaOH resulted in rapid decomposition. After dilution with water, the solution gave a heavy Prussian blue precipitate when tested in the usual way for cyanide ion.

When the above reaction with NaCN and TBACl was performed with a methylene chloride–$H_2O$ medium rather than a toluene–$H_2O$ medium, the results were considerably different. Compound **6** was obtained as described above, but its yield was variable in different runs—on the order of 0.2–0.4 g (10–20%) of crude material.

The organic layer of the filtrate from the isolation of crude **6** was separated and washed with water. After drying over $CaCl_2$, the solvent was removed under reduced pressure, and the residue was taken up in a small amount of hot methanol. The solution was filtered to remove a small amount of **6**. The methanol was then allowed to evaporate slowly in air overnight to give an oil, which was chromatographed on 15 g of Florisil. Elution with 1% acetone–hexane, followed by recrystallization of the eluted solid from ethanol, gave 0.15 g (8%) of **4**, mp 140–142 °C. Continued elution with 10% acetone–hexane gave, after crystallization from petroleum ether (bp 60–90 °C), 0.10 g (15%) of **5** melting at 80–82 °C (lit.[4b] mp 85 °C): IR (Nujol) 3320 (NH), 2220 ($C\equiv N$), 1595 (aromatic) cm$^{-1}$. The IR spectrum of a sample prepared by the method of von Walther[4b] was identical with that of **5**, and the NMR spectrum of **5** was identical in all respects with that reported for **5** by McEwen.[4c]

**Reaction of Compounds 5 and 6 with NaCl and TBACl.** When **6** was treated with NaCN in a methylene chloride–$H_2O$ medium in the same manner as *N*-benzylideneaniline (except for a longer reaction period of 7 h), only about 1% of starting material was recovered. Use of the same workup procedure and chromatography described above resulted in the isolation of a very small amount of **4** (2%) and a 25% yield of **5**. A great deal of uncharacterized, highly polar material was formed.

Reaction of **6** with NaCN in a methylene chloride–1 M NaOH medium gave a higher yield of **4** (10%), and the amount of **5** stayed about the same.

Compound **5** was unreactive when stirred with NaCN in methylene chloride–$H_2O$ in the presence of TBACl. There was a nearly complete recovery of starting material. Use of 1 M NaOH in place of the water resulted in the formation of a small amount of **4** (1%) and **6** (25%), as well as substantial recovery of starting material (25%).

**Registry No.** 3 (Ar = Ph), 24099-48-7; 5, 4553-59-7; 6, 86712-42-7; *N*-benzylideneaniline, 538-51-2.

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[7] Clarke, R. W. L.; Lapworth, A. *J. Chem. Soc.* **1907**, *91*, 694.

[8] Solodar, J. *Tetrahedron Lett.* **1971**, 287.

[9] Bigelow, L.; Batough, H. "Organic Syntheses"; Wiley: New York, 1941; Collect. Vol. I, p 80.

[10] Since **3** is difficult ( if not impossible) to isolate from solution in a pure state, this procedure ensures that any **3** in solution is converted to **4**. A similar procedure is used in subsequent reactions.

[11] The adsorbent was 60–200 mesh supplied by Matheson, Coleman and Bell.

[12] For the structure of compounds that could be formed under these reaction conditions, see: El-Gawad, I.; Harhash, A; El-Zahab, M. *Z. Naturforsch., Anorg. Chem., Org. Chem.* **1980**, *35B*, 712.

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# An Efficient Synthesis of Substituted Isoquinolines

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There are a number of synthetic methods for preparing isoquinolines,[1] but all require two or more isolation steps and most suffer from harsh conditions, less than ideal

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[1] A quick review of isoquinoline synthesis methods is given by Boger et al.: Boger, D. L.; Brotherton, C. E.; Kelley, M. D. *Tetrahedron* **1981**, *37*, 3977.

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