# Acylquinolinium Ions. Formation and Reactions of 2-Benzamidocinnamaldehyde[1]

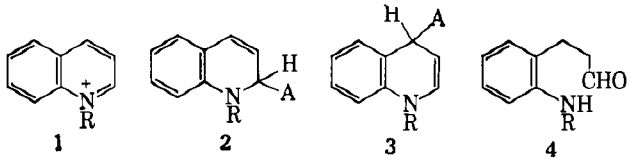
I. W. ELLIOTT

*Department of Chemistry, Fisk University, Nashville, Tennessee*

*Received July 25, 1963*

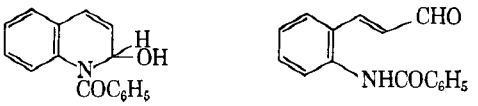
Spectroscopic evidence is presented in support of the open-chain form, 2-benzamidocinnamaldehyde, for the product of the reaction between quinoline, benzoyl chloride, and sodium hydroxide. Several substituted quinolines are converted to the corresponding cinnamaldehydes in low yield, but lepidine, 6-nitro-, 7-nitro-, and 3-acetamidoquinoline could not be cleaved successfully. Ultraviolet light promotes the decomposition of 2-benzamidocinnamaldehyde. The corresponding acid fails to undergo photodimerization, but a photodimer of carbostyril is reported.

Quinolinium salts (**1**) add a variety of anions to either the 2- or 4-position to give dihydro derivatives (**2** or **3**).[2,3] Among the compounds of type **2** are the Reissert compounds (**2**, R = acyl; A = CN) and the pseudobases (**2**, R = alkyl; A = OH).[4,5] The



**1** **2** **3** **4**

pseudobases generally are assumed to exist in the isomeric open-chain form (**4**) in basic solution, but a recent spectroscopic study of the pseudobase from 1-cyanoquinolinium ion (**2**, R = CN; A = OH) showed no evidence for the aminoaldehyde.[6] By analogy with the pseudobases, the product of the reaction of quinoline with benzoyl chloride in aqueous sodium hydroxide has been represented by the isomeric pair **5** and **6**. We were interested in determining whether **5** or **6** best constituted the reaction product and offer spectroscopic evidence in support of structure **6**.



**5** **6**

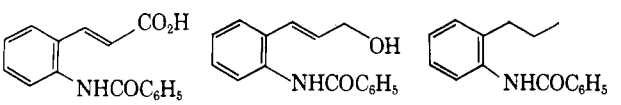
Reissert originally proposed that 1-benzoyl-1,2-dihydro-2-quinolinol (**5**) was formed from quinoline under Schotten–Baumann conditions, but he later revised the structure to 2-benzamidocinnamaldehyde (**6**) on the basis that the compound forms an oxime, and a phenylhydrazone, and is oxidized by silver oxide to the corresponding cinnamic acid (**7**).[4] However, the chemical behavior does not discriminate between **5** and **6** if a facile equilibrium exists between the two isomers.

In addition to the chemical evidence offered by Reissert, the ultraviolet and infrared spectra provide new information in support of the aldehyde **6**. 2-Benzamidocinnamaldehyde exhibits absorption maxima at 225, 256, and 285 mμ in the ultraviolet region, and the spectrum of this compound is similar in the positions of the maxima and the intensities of absorption with that for 2-benzamidocinnamic acid (**7**).[7] In the infrared spectrum the aldehyde **6** shows absorption bands at 3.05 (N–H), 3.67 (aldehyde C–H), 5.87 (conjugated aldehyde), and 6.05 μ (amide carbonyl group). These spectral features are in accord with **6** but not **5**.

The spectroscopic data suggest further that the aldehyde is isolated as the *trans* isomer although the ring cleavage might yield directly the *cis* form. The comparable intensities of the ultraviolet spectra of the aldehyde **6** and the known *trans* acid **7** may be interpreted as due to a similar stereochemistry.[8] The presence of a band at 10.19 μ in the infrared spectrum of **6** is ascribed to the out-of-plane hydrogen deformation vibration of a *trans* olefin; this band appears consistently in other unsaturated compounds of this series (*e.g.*, the acid **7** and the alcohol **8**). Moreover, there is no absorption in the region attributed to a *cis* double bond. The infrared spectrum of the crude aldehyde shows the same features as the recrystallized product, indicating that the *cis*-to-*trans* isomerization in an easy process and is probably facilitated both by conjugation and by the bulky *ortho* substituent. The predominant *trans* configuration for the aldehyde may in large part preclude a mobile equilibrium between **5** and **6**.

2-Benzamidocinnamaldehyde (**6**) is readily reduced to the cinnamyl alcohol (**8**) by sodium borohydride. The structure of the alcohol is confirmed by its elemental analysis and spectra. Although the aldehyde **6** was too insoluble in the available solvents to obtain the n.m.r. spectrum, the alcohol **8** was sufficiently soluble in deuteriochloroform. The *J*-value for the olefinic protons was found to be 17 c.p.s., consistent with a *trans* configuration.

Catalytic hydrogenation of either 2-benzamidocinnamaldehyde (**6**) or 2-benzamidocinnamyl alcohol (**8**) at moderate pressures gave a mixture of products that was difficult to separate. When **8** was reduced in the presence of acid, hydrogenolysis occurred to afford 2-(*n*-propyl)benzanilide (**9**).



**7** **8** **9**

(1) Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for support of this work.

(2) W. Bradley and S. Jeffrey, *J. Chem. Soc.*, 2770 (1954).

(3) N. J. Leonard and R. L. Foster, *J. Am. Chem. Soc.*, **74**, 2110 (1952); A. Kaufmann and A. Albertini, *Ber.*, **42**, 3776 (1909).

(4) A. Reissert, *ibid.*, **38**, 1603, 3415 (1905).

(5)(a) W. E. McEwen and R. L. Cobb, *Chem. Rev.*, **55**, 511 (1955); (b) N. Campbell, "Chemistry of the Carbon Compounds," Vol. IVA, E. H. Rodd, Ed., Elsevier Publishing Co., Amsterdam, 1957, p. 597.

(6) M. D. Johnson, *J. Chem. Soc.*, 283 (1962).

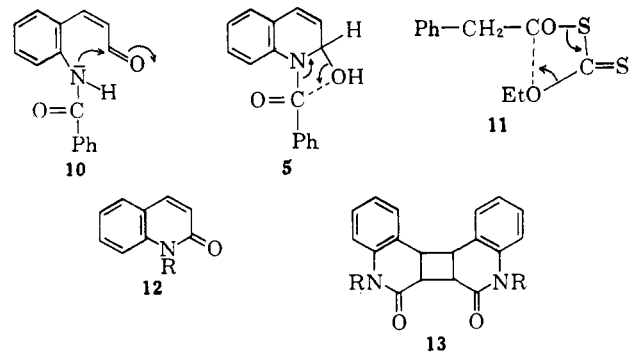
(7) The structure of the acid **7** is shown by acid hydrolysis to carbostyril[4] and by an independent synthesis from 2-aminocinnamic acid: see G. Heller, *Ber.*, **43**, 1918 (1910).

(8) A. E. Gillam and E. S. Stern, "An Introduction to Electronic Absorption Spectroscopy in Organic Chemistry," E. Arnold, Ltd., London, 1954, p. 223.

Cleavage of the quinoline ring system by aroyl halides in alkaline solution has not been studied extensively although the reaction provides a convenient one-step route to polyfunctional compounds of possible synthetic utility. This ring opening is extended to several substituted quinolines to give the corresponding 2-benzamidocinnamaldehyde in low yield. The apparent disadvantage of the small yield is partially offset by the fact that the unchanged quinoline can be recovered. The compounds that were successfully converted to the aldehyde are 6-methyl-, 6-chloro-, 6-methoxy-, and 6-bromoquinoline. The same method applied to lepidine, 3-acetamido-, 6-nitro-, or 7-nitroquinoline failed to afford the cinnamaldehyde derivatives.

**Photochemical Transformations.**—Light-catalyzed dimerization of $\alpha,\beta$-unsaturated carbonyl compounds is well-known although generally applied to acid derivatives and ketones.[9] Aldehydes have not been included in these studies. In the attempt to prepare a photodimer of 2-benzamidocinnamaldehyde (**6**), we observed that a benzene solution of **6** slowly turned yellow when exposed to ultraviolet radiation for several days. The solution contained no dimeric product, but quinoline was isolated from the reaction mixture. To test whether the degradation was truly light-catalyzed or occurred merely when a benzene solution of **6** was allowed to stand, parallel solutions of 2-benzamidocinnamaldehyde in dry benzene were allowed to reflux for 24 hr. One solution was exposed to ultraviolet light, and the second solution was kept in the dark. Only in the irradiated sample was quinoline formed and isolated as the picrate. The decomposition of 2-benzamidocinnamaldehyde was substantially complete as indicated by the failure of the light-exposed solution to afford the 2,4-dinitrophenylhydrazone of **6**. In the "dark" experiment the reverse was found. The aldehyde **6** was largely unchanged, and no quinoline could be detected.

One plausible hypothesis for the degradation of **6** to yield quinoline and benzoic acid would require a prior *trans*-to-*cis* isomerization to bring the aldehyde carbonyl into juxtaposition with the amide function. The *cis* isomer (**10**) could then form the tautomeric carbinol (**5**), and hydroxyl group transfer and formation of the heteroaromatic ring can be accounted for through a four-membered transition state in **5**. The proposed intermediate (**5**) is structurally analogous to one (**11**) suggested by Barton for thermal decomposition of S-acyl xanthates.[10]




(9) A. Mustafa, *Chem. Rev.*, **51**, 1 (1952); P. DeMayo, "Advances in Organic Chemistry," Vol. 2, R. A. Raphael, E. C. Taylor and H. Wynberg, Ed., Interscience Publishers, Inc., New York, N.Y., 1960, p. 367.

(10) D. H. R. Barton, M. V. George, and M. Tomoeda, *J. Chem. Soc.*, 1967 (1962).

2-Benzamidocinnamic acid (**7**) could not be induced to dimerize when exposed to ultraviolet radiation, but, when 2-benzamidocinnamic acid is converted to carbostyril (**12**, R = H), the later formed a photodimer. In a parallel experiment, a solution of N-methyl-2-quinolone (**12**, R = $CH_3$) in benzene readily dimerized.[11] After the completion of this work Taylor and Paudler reported the preparation of a photodimer of N-methyl-2-quinolone and showed it to have structure **13**.[12] Our additional evidence for the saturated (cyclobutane) nature of the photodimers is obtained from the ultraviolet spectrum of the more soluble dimer (**13**, R = $CH_3$) that is very different from the starting N-methyl-2-quinolone.[13] The absorption band in the infrared spectra arising from the amide carbonyl vibration shows a consistent shift to shorter wave lengths on dimerization for the two carbostyrils (**13**) and coumarin (Table I).

TABLE I

INFRARED BAND FOR C=O STRETCHING VIBRATION

| Compound | Monomer, $\mu$ | Dimer, $\mu$ |
|---|---|---|
| Coumarin | 5.80 | 5.66 |
| Carbostyril | 6.00 | 5.81 |
| N-Methylcarbostyril | 6.03 | 5.95 |

## Experimental

**2-Benzamidocinnamaldehyde** (**6**).—The reaction between quinoline (24 g.), benzoyl chloride (70 ml.), and 10% aqueous sodium hydroxide (200 ml.) by the method of Reissert gave the aldehyde (13% yield) that was recrystallized from acetonitrile as colorless feathery crystals, m.p. 185.5–186.0° (lit.[4] m.p. 186–187°); $\lambda_{max}^{EtOH}$ 285 m$\mu$ (log $\epsilon$ 4.28), 256 (4.22), and 225 (4.29); $\lambda_{min}$ 265 m$\mu$ (log $\epsilon$ 4.19), 243 (4.18); infrared spectrum (Nujol and perfluorocarbon mulls), 3.05, 3.67, 5.87, 6.05, and 10.19 $\mu$.

The 2,4-dinitrophenylhydrazone of **6** was obtained as rust colored plates, m.p. 263–264°.

*Anal.* Calcd. for $C_{22}H_{17}N_5O_5$: C, 61.25; H, 3.98; N, 16.24. Found: C, 61.38; H, 3.67; N, 16.32.

A thiosemicarbazone of 2-benzamidocinnamaldehyde was prepared in acetic acid and isolated as yellow needles, m.p. 203–204°.

*Anal.* Calcd. for $C_{17}H_{16}N_4OS$: C, 62.94; H, 4.92; N, 17.27; S, 9.88. Found: C, 63.08; H, 5.28; N, 17.29; S, 10.06.

**2-Benzamidocinnamic Acid.**—Silver hydroxide oxidation of the aldehyde afforded the acid in high yield as reported. The acid was recrystallized from acetic acid as colorless needles, m.p. 263–265° (lit.[3] m.p. 261–262°); $\lambda_{max}^{EtOH}$ 265 m$\mu$ (log $\epsilon$ 4.30), 227 (4.31); infrared spectrum (Nujol), 3.02, 5.87, 6.01, 6.10, 6.20 (sh), 8.13, 10.20, 10.45, 10.65 $\mu$.

**2-Benzamido-5-chlorocinnamaldehyde.**—Adaptation of Reissert's method of ring cleavage to 6-chloroquinoline gave the corresponding aldehyde in 3% yield; the product was recrystallized from acetic acid as colorless needles, m.p. 190–191°.

*Anal.* Calcd. for $C_{16}H_{12}O_2NCl$: C, 67.25; H, 4.24; N, 4.90; Cl, 12.41. Found: C, 67.36; H, 4.10; N, 5.11; Cl, 12.46.

The 2,4-dinitrophenylhydrazone of 2-benzamido-5-chlorocinnamaldehyde was prepared in acetic acid and melted at 278–279° dec.

*Anal.* Calcd. for $C_{22}H_{16}O_5N_5Cl$: C, 56.75; H, 3.46; N, 15.03. Found: C, 56.77; H, 3.54; N, 15.23.

**2-Benzamido-5-methylcinnamaldehyde.**—From 23 g. of 6-methylquinoline, by the usual procedure, there was isolated 9.2 g. of aldehyde, m.p. 201–202°.

*Anal.* Calcd. for $C_{17}H_{15}NO_2$: C, 76.96; H, 5.70; N, 5.28. Found: C, 77.06; H, 5.81; N, 5.09.

The 2,4-dinitrophenylhydrazone melted at 275–276°.

(11) M. S. Barry, M. A. thesis, Fisk University, 1960.

(12) E. C. Taylor and W. W. Paudler, *Tetrahedron Letters*, **No. 25**, 1 (1960); Dr. Taylor has kindly compared a sample of our photodimer, prepared in homogeneous benzene solution, with his, from irradiation of an aqueous or cyclohexane suspension, and found them to be identical.

(13) H. Ley and H. Specker, *Ber.*, **72**, 192 (1939).

*Anal.* Calcd. for $C_{23}H_{19}N_5O_5$: C, 62.02; H, 4.30; N, 15.72. Found: C, 61.95; H, 4.34; N, 15.55.

**5-Bromo-2-benzoylaminocinnamaldehyde.**—From 5 g. of 6-bromoquinoline, by the usual method, a crude oily product was obtained that was recrystallized from acetonitrile as colorless crystals, 0.3 g., m.p. 191–193°.

*Anal.* Calcd. for $C_{16}H_{12}NO_2Br$: C, 58.20; H, 3.66; N, 4.24. Found: C, 58.46; H, 3.70; N, 4.11.

**5-Methoxy-2-benzamidocinnamaldehyde.**—The reaction between 6-methoxyquinoline (25 g.), benzoyl chloride (50 ml.), and cold 10% sodium hydroxide (220 ml.) gave a difficultly separable oil. After careful decantation of the aqueous layer the oil was washed twice with 10% hydrochloric acid, then with water, and redissolved in methanol containing a small quantity of acetonitrile. The aldehyde slowly separated as pale yellow needles, 3.5 g., m.p. 197–198° after several recrystallizations.

*Anal.* Calcd. for $C_{17}H_{15}NO_3$: C, 72.56; H, 5.38; N, 4.98. Found: C, 71.90; H, 5.20; N, 5.32.

The 2,4-dinitrophenylhydrazone, m.p. 269–271°, was prepared in acetic acid.

*Anal.* Calcd. for $C_{23}H_{19}N_5O_6$: C, 59.86; H, 4.15; N, 15.18. Found: C, 60.12; H, 3.89; N, 15.16.

**2-Benzamidocinnamyl Alcohol.**—To 2.0 g. of 2-benzamidocinnamaldehyde suspended in 40 ml. of hot ethanol was added all at once 1.0 g. of sodium borohydride. A yellow color quickly developed and soon faded. After 10 min. water was added until the clear solution became turbid, the mixture was heated to boiling for 2 min. and allowed to cool. The mixture deposited glistening colorless crystals, 1.8 g., m.p. 141–143°. Recrystallization from aqueous ethanol raised the m.p. to 144–145°; $\lambda_{max}$ 234 mμ (ε 22,800); infrared spectrum (Nujol), 3.07, 6.04, 10.35 μ.

*Anal.* Calcd. for $C_{16}H_{15}NO_2$: C, 75.86; H, 5.97; N, 5.53. Found: C, 76.07; H, 6.30; N, 5.37.

**Hydrogenolysis of 2-Benzamidocinnamyl Alcohol to 2-(*n*-Propyl)benzanilide.**—A solution of 2.2 g. of 2-benzamidocinnamyl alcohol in 125 ml. of methanol was added to a suspension of prereduced platinum from 0.1 g. of Adam's catalyst in 50 ml. of methanol containing 1 ml. of concentrated hydrochloric acid. The initial pressure of hydrogen was 45 p.s.i. and after 0.75 hr. the uptake of hydrogen virtually ceased. The catalyst was removed by filtration, and the filtrate was concentrated to one-third of the original volume under reduced pressure. The solution was heated to boiling, and water was slowly added to the point of turbidity. The solution was covered and allowed to cool slowly, affording 1.1 g. of colorless needles, m.p. 114–115°; ultraviolet spectrum inflections at $\epsilon_{225}$ 12,200 and $\epsilon_{270}$ 4400; infrared spectrum (KBr), 3.27, 3.39 (asym. $CH_3$ str.), 3.49 (asym. $CH_2$ str., sym. $CH_3$ str.), 3.55 (sym. $CH_2$ str.), 6.15, 6.70, 7.30 μ.

*Anal.* Calcd. for $C_{16}H_{17}NO$: C, 80.30; H, 7.16; N, 5.85. Found: C, 80.61, 80.35; H, 7.35, 7.29; N, 5.60.

**Photochemical Degradation of 2-Benzamidocinnamaldehyde.**—A solution of 0.6 g. of 2-benzamidocinnamaldehyde in 300 ml. of dry benzene was divided into two equal portions. The first solution (A) was refluxed for 24 hr. in a 500-ml. Pyrex conical flask and continuously exposed to ultraviolet radiation from a Hanovia utility model lamp. The second portion (B) was refluxed for the same period in the dark. At the end of this time solution A was colored faintly yellow; B was colorless. After cooling, a 50-ml. aliquot of A was treated with 10 ml. of a saturated solution of picric acid. Crystals began to form after 5 min. These were collected at the end of 2 hr. and identified by melting point and mixture melting point determinations as quinoline picrate (0.08 g., 57% yield, or 100% compared with a standard solution of quinoline in benzene).

A second 50-ml. portion of A was treated with 10 ml. of solution of 2,4-dinitrophenylhydrazine in hydrochloric acid–ethanol. No precipitate formed during a 2-hr. period.

The final 50 ml. of A was extracted with three 20-ml. portions of 5% potassium hydroxide and the aqueous layer acidified with concentrated hydrochloric acid and re-extracted with ether. Evaporation of the ether and recrystallization of the residue from water gave a few crystals identified as benzoic acid by infrared spectrum and melting point.

Solution B was similarly treated. A 50-ml. portion gave no precipitate with 10 ml. of saturated picric acid solution after 2 hr. The second 50-ml. portion of B when mixed with the 2,4-dinitrophenylhydrazine reagent rapidly formed a red precipitate, 0.09 g. [52%, or 90% based on comparison with a standard benzene solution (50 ml.) containing 0.10 g. of 2-benzanmidocinnamaldehyde], which was identified as 2-benzamidocinnamaldehyde-2,4-dinitrophenylhydrazone.

**Irradiation of N-methyl-2-quinolone.**[11]—A solution of 3.0 g. of N-methyl-2-quinolone in benzene was irradiated under an ultraviolet lamp for 15 days. During this period a solid precipitated from the solution. The precipitate, 1.7 g., was recrystallized from ethanol–benzene solution as colorless crystals, m.p. 213–214° (lit.[12] m.p. 211.5–212°); $\lambda_{max}^{EtOH}$ 260 mμ (log 3.83), shoulder at 225 (4.15); $\lambda_{min}$ 240 mμ (log ε 3.56); infrared spectrum (Nujol), 5.90, 7.70, 8.75, 11.80, 13.15 μ.

*Anal.* Calcd. for $C_{20}H_{18}N_2O_2$: C, 75.46; H, 5.69; N, 8.80; mol. wt., 322. Found: C, 75.76; H, 5.80; N, 9.09; mol. wt., 314.

**Photodimerization of Carbostyril.**—A solution of 5 g. of carbostyril in benzene was irradiated by an ultraviolet lamp for 2 months. A fine white precipitate slowly separated from the solution, and 2 g. of a very insoluble solid, m.p. 271–273°, was collected. Recrystallization of this product from a large volume of acetic acid gave first a tan amorphous product that did not melt below 320°. The main recrystallized fraction was a colorless microcrystalline solid, m.p. 274–275°.

*Anal.* Calcd. for $C_9H_7NO$: C, 74.56; H, 4.86. Found: C, 74.69; H, 5.06.

**Attempted Photodimerizations A. 2-Benzamidocinnamic Acid.**—Five grams of powdered 2-benzamidocinnamic acid was exposed for 3 weeks to ultraviolet radiation, and the sample was stirred daily to ensure complete exposure. At the end of this period the crude material and a recrystallized portion had the same melting point and mixture melting point as the starting acid.

A sample of 1.0 g. of acid was suspended in benzene and irradiated for 2 weeks. The recrystallized product proved to be unreacted starting material.

**B. Isocarbostyril.**—A solution of 1.0 g. of isocarbostyril in benzene was exposed to ultraviolet radiation for 2 months. The solution was concentrated and the solid obtained was unreacted isocarbostyril by melting point and mixture melting point determinations.

**Attempted Cleavage of Some Quinoline Derivatives.**—When the bases lepidine, 6-nitroquinoline, 7-nitroquinoline, or 3-acetamidoquinoline were allowed to react with benzoyl chloride in aqueous sodium hydroxide, no corresponding cinnamaldehyde could be isolated. In practically all cases benzoic anhydride was obtained in high yield. With lepidine, a high-melting amorphous solid was obtained that was not studied further.