NOTES

Reaction of Quinaldine with Aldehydes[1]

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Continuing the search for additional compounds which are capable of damaging or inhibiting the growth of cancer cells *in vivo*[2] we have attempted to prepare substituted 2-(2-hydroxy-2-phenylethyl)-quinolines by condensation of quinaldine with substituted benzaldehydes[3,4] during long exposure to bright light[5] and also, in several cases, under similar conditions with light excluded. The absence of light did not seem to alter greatly the course of reaction. It was found that the rates of reaction to form the desired alcohols were in the order 2,4-dichlorobenzaldehyde > 3,4-dichlorobenzaldehyde > 2,6-dichlorobenzaldehyde > benzaldehyde, whereas 3,4-methylenedioxybenzaldehyde yielded the known 2-(3,4-methylenedioxystyryl)-quinoline[6] instead of the alcohol, and no crystalline alcohol was obtained from *p*-isopropylbenzaldehyde, anisaldehyde, 2,3-dimethoxybenzaldehyde, 2,3-diethoxybenzaldehyde, *p*-dimethylaminobenzaldehyde or 2-thiophenaldehyde. In the latter cases most of the starting material was recovered after several months by vacuum distillation, although there was in each case some dark, liquid residue in the distilling flask which may have contained some of the alcohol. In the case of 4-methoxybenzaldehyde a small amount of crystalline material melting at 127.5°, apparently 2-(4-methoxystyryl)-quinoline,[7] was isolated from the residue. These results tend to support the views of Phillips and Murphy[8] concerning the relation of structure of aromatic aldehydes to reactivity in such condensations.

Experimental

Equimolar quantities of the aldehydes and quinaldine were mixed with warming to obtain clear solutions, then allowed to stand at 40° in stoppered flasks, either exposed to ultraviolet light or protected from it.

2-[β-Hydroxy-β-(2,4-dichlorophenyl)-ethyl]-quinoline.—Crude yield 90%, m.p. 139–140° after recrystallization.

Anal.[9] Calcd. for $C_{17}H_{13}Cl_2NO$: C, 64.17; H, 4.12. Found: C, 64.10; H, 4.12.

2-[β-Hydroxy-β-(3,4-dichlorophenyl)-ethyl]-quinoline.—Yield purified crystals 22%, m.p. 154°.

Anal. Calcd. for $C_{17}H_{13}Cl_2NO$: C, 64.17; H, 4.12. Found: C, 64.45; H, 4.32.

2-[β-Hydroxy-β-(2,6-dichlorophenyl)-ethyl]-quinoline.—Yield purified crystals, 35%, m.p. 154°. *Anal.* Calcd. for $C_{17}H_{13}Cl_2NO$: C, 64.17; H, 4.12. Found: C, 64.05; H, 4.24.

Infrared absorption spectra for 50% Nujol mulls of these compounds and of 2-[β-hydroxy-β-phenylethyl]-quinoline were determined and are available on microfilm.[10] None of them were effective in inhibiting the growth of Sarcoma 180 in the Sloan–Kettering screening technique.

We wish to express our thanks to Samuel P. Sadtler and Son for determining the infrared absorption spectra, to the Sloan–Kettering Institute for Cancer Research for screening tests and to Miss Emma Brown and Mr. Charles L. Chumley, Jr., for assistance in carrying out some of the laboratory procedures.

(1) This research was supported in part by a grant from the National Cancer Institute, of the National Institutes of Health, Public Health Service.

(2) C. T. Bahner, E. S. Pace and R. Prevost, This Journal, **73**, 3407 (1951).

(3) K. Loew, *Ber.*, **36**, 1666 (1903).

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(6) M. Nencki, *Ber.*, **27**, 1977 (1894).

(7) O. Bialon, *ibid.*, **35**, 2786 (1902).

(8) A. P. Phillips and J. G. Murphy, *J. Org. Chem.*, **16**, 954 (1951).

(9) Analyses by Galbraith Laboratories, Knoxville, Tennessee.

(10) Order Document 3620 from American Documentation Institute, 1719 N Street, N.W., Washington 6, D. C., remitting $1.00 for microfilm (images 1 inch high on standard 35 mm. motion picture film) or $1.00 for photocopies (6 × 8 inches) readable without optical aid.

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The Electrolytic Reduction of Homocystine at a Controlled Reference Potential

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The reduction of homocystine to homocysteine has previously been accomplished with tin and hydrochloric acid and by the action of sodium and liquid ammonia on the S-benzyl derivative.[2] As we are primarily interested in the application of electrolytic methods to the preparation of organic compounds, the preparation of homocysteine from homocystine by electrolytic reduction at a controlled reference potential was investigated. It was found that when the reduction was performed in a basic medium at a reference potential of −1.79 volts *vs.* a standard calomel electrode an almost quantitative yield of homocysteine, as determined titrimetrically, was obtained. However, because of the extreme ease with which homocysteine undergoes oxidation it was possible to isolate only 52.5% of the desired product.

Experimental

The electrolysis cell was a 1500-ml. beaker with a side arm extending to the base of the beaker through which was sealed a piece of platinum wire. This served as a contact for the mercury cathode which had an area of 95.03 sq. cm. In the beaker was placed a stirrer, thermometer, a standard calomel electrode which touched the mercury cathode surface, and an alundum membrane (fine porosity) 160 mm. high by 50 mm. diameter which served as an anode chamber. The anode consisted of a piece of platinum 10 cm. by 10 cm. Surrounding the cell was a cooling bath. The apparatus used for performing the reduction was the same as previously described.[3]

The catholyte was a solution of 94 g. of homocystine in 700 ml. of 1.25 *N* sodium hydroxide. The anolyte was a 1.25 *N* sodium hydroxide solution. At a reference potential *vs.* a standard calomel electrode of −1.79 volts the initial current density was 0.059 ampere per sq. cm. After four hours during which the temperature was maintained at 30–35° the current reached a plateau of 0.014 ampere per sq. cm. Iodimetric titration of the catholyte at this point indicated that there was a 100% reduction of the homocystine. The catholyte was cooled to 15°, rapidly adjusted

(1) Ciba Research Laboratories, Summit, New Jersey.

(2) B. Riegel and V. du Vigneaud, *J. Biol. Chem.*, **112**, 149 (1935).

(3) M. J. Allen, *Anal. Chem.*, **22**, 804 (1950); *Proc. Electrochem. Soc.*, Oct. (1951).