

A NEW VARIATION OF THE PSCHORR SYNTHESIS

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[Manuscript received December 24, 1968]

Summary

A new variation of the Pschorr phenanthrene synthesis giving improved yields is described. In addition, the ester of the newly prepared by-product of this reaction, 2-iodo-4,5-dimethoxy- α -phenyleinnamic acid, cyclizes to the corresponding phenanthrene-9-carboxylic acid derivative on irradiation with ultraviolet light.

In connection with our work on the synthesis of phenanthroindolizidine derivatives¹ in order to correlate physiological activity² with chemical work relating to the *Tylophora* alkaloids,³ it was necessary to prepare derivatives of substituted phenanthrene-9-carboxylic acids. The commonly used Pschorr phenanthrene synthesis⁴ gave not only variable yields but yields which diminished considerably with an increase in the number of methoxyl substituents. The synthesis we envisaged was intended to proceed through 2-amino- α -phenyleinnamic acid to 2-iodo- α -phenyleinnamic acid by the Sandmeyer reaction, followed by cyclization by means of irradiation with ultraviolet light. Photocyclization of *ortho*-iodostilbenes has recently been discussed in a review⁵ and was used during the synthesis of aristolochic acid.⁶ The yields recorded in these experiments indicated a promising approach.

The reaction sequence followed the usual steps for the preparation of substituted 2-amino- α -phenyleinnamic acids.⁴ However, when replacement of the amino group by iodine was attempted by diazotization with isopentyl nitrite in acetone followed by addition of sodium iodide, only a small yield of the 2-iodo- α -phenyleinnamic acids could be isolated. The main product obtained was identified as the corresponding phenanthrene-9-carboxylic acid derivative, indicating that in acetone solution the diazonium salt in the presence of iodide underwent spontaneous cyclization to the phenanthrene ring. As this reaction is practically instantaneous, while decomposition of the diazonium salt with copper powder (as in the Pschorr synthesis) usually requires more than 10 hr, and as this reaction gives better overall yields, this variation provides an important new procedure. The yields achieved with the variously substituted compounds are listed in Table I.

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¹ Chauncy, B., Gellert, E., and Trivedi, K. N., *Aust. J. Chem.*, 1969, **22**, 427.

² Gellert, E., and Rudzats, R., *J. mednl Chem.*, 1964, **7**, 361.

³ Gellert, E., Govindachari, T. R., Lakshmikantham, M. V., Ragade, I. S., Rudzats, R., and Viswanathan, N., *J. chem. Soc.*, 1962, 1008; Govindachari, T. R., Pai, B. R., Prabhakar, S., and Savitri, T. S., *Tetrahedron*, 1965, **21**, 2573.

⁴ Leake, P. H., *Chem. Rev.*, 1956, **56**, 27.

⁵ Warrenner, R. N., and Bremner, J. B., *Rev. pure appl. Chem.*, 1966, **16**, 117.

⁶ Kupcham, S. N., and Wormser, H. C., *J. org. Chem.*, 1965, **30**, 3792.

2-Iodo- α -phenylcinnamic acid derivatives can be isolated from the reaction mixture both when the diazotization is carried out in acetone or in water. However, the yield of phenanthroic acid is less than 5% if the reaction is carried out in water. These 2-iodo- α -phenylcinnamic acids can, after esterification, be cyclized to the corresponding substituted phenanthrene-9-carboxylates by irradiation with ultraviolet light, thereby further increasing the overall yield of the phenanthrene derivative obtained by the variation described.

TABLE I
YIELDS OF PRODUCTS

Acetone solvent used for diazotization, except with the tetramethoxy compound (DMF)

Substituents in 2-Amino- α -phenyl- cinnamic Acid	Isopentyl Nitrite (ml)	20% aq. H ₂ SO ₄ (ml)	Substituents in Phenanthrene-9- carboxylic Acid	Yield of 9- Carboxylic Acid Derivative	Yield by Pschorr Method
Nil ^a	1.0	2.0	Nil	70%	93%
4,5-(OMe) ₂ ^b	0.9	1.8	2,3-(OMe) ₂	72	55
4,5,4'-(OMe) ₃ ^c	1.0	0.2 ^f	2,3,6-(OMe) ₃	60	55
4,5,3',4'-(OMe) ₄ ^d	1.0	0.2 ^f	2,3,5,6- and 2,3,6,7-(OMe) ₄	45	25
4,5-(OMe) ₂ ,4'-Me ^e	1.0	1.8	2,3-(OMe) ₂ ,6-Me	55	—
2'-Me ^f	1.0	1.3	8-Me	65	65

^a Hey, D. H., and Osbond, J. M., *J. chem. Soc.*, 1949, 3164. ^b Pschorr, R., and Buckow, W., *Ber. dt. chem. Ges.*, 1900, **33**, 1829. ^c Bradsher, C. K., and Berger, H., *J. Am. chem. Soc.*, 1958, **80**, 930. ^d Govindachari, T. R., Lakshmikantham, M. V., Nagarajan, K., and Pai, B. R., *Tetrahedron*, 1958, **4**, 311. ^e Chauncy, B., and Gellert, E., unpublished data. ^f Pschorr, R., and Hofman, R., *Ber. dt. chem. Ges.*, 1906, **39**, 3110. [†] Conc. H₂SO₄ used instead of 20% aqueous H₂SO₄.

EXPERIMENTAL

Microanalyses were carried out by Dr E. Challen, School of Chemistry, University of New South Wales, Kensington, N.S.W. Ultraviolet irradiation was carried out using an internally mounted Hanovia photochemical reactor. The procedure followed in all preparations was identical with the one described in the example below.

2,3-Dimethoxyphenanthrene-9-carboxylic Acid

2-Amino-4,5-dimethoxy- α -phenylcinnamic acid (1 g, 3.3 mmole; prepared according to Pschorr⁷) was dissolved in acetone (100 ml) and 20% sulphuric acid (1.8 ml) added. The white suspension of the hydrogen sulphate was diazotized between 5 and 10° with 0.9 ml of isopentyl nitrite; stirring was continued for 1 hr. Solid sodium iodide (2 g) was then added to the solution and, after evolution of gas ceased, the mixture was poured into hot water. On cooling, the precipitated solid was filtered off, dried, and recrystallized from alcohol to yield 700 mg (72%) of 2,3-dimethoxyphenanthrene-9-carboxylic acid, m.p. 272° (lit.⁷ 272°). The mother liquors were concentrated and a small amount of water added. On standing, a further 0.15 g of needles separated, which after recrystallization twice from toluene (charcoal), then from ethyl acetate, yielded 0.10 g of 2-iodo-4,5-dimethoxy- α -phenylcinnamic acid, m.p. 223–224° (Found: C, 50.0; H, 4.0. C₁₇H₁₅IO₄ requires C, 49.8; H, 3.7%).

The *methyl ester*, prepared from the acid by treatment with diazomethane, melted at 125–126° after crystallization from methanol–water (Found: C, 50.9; H, 4.0. C₁₈H₁₇IO₄ requires C, 51.0; H, 4.0%).

⁷ Pschorr, R., and Buckow, W., *Ber. dt. chem. Ges.*, 1900, **33**, 1829.

On irradiation with ultraviolet light at room temperature, the ester (0.10 g in 200 ml cyclohexane) was converted into methyl 2,3-dimethoxyphenanthrene-9-carboxylate, m.p. 136–137° (lit.⁸ 137°), in 61% yield in 3 hr. The progress of the reaction was followed semiquantitatively by the intensity of the strong absorption band at 262 m μ (log ϵ 4.6).

ACKNOWLEDGMENTS

The authors gratefully acknowledge the financial support provided for this work by the Australian Research Grants Committee. They also wish to thank Mr W. Liao for his assistance.

⁸ Cook, J. W., Loudon, J. D., and Razdan, R. K., *J. chem. Soc.*, 1954, 4234.