

Synthesis of Juncunone: An Unusual Dihydrophenanthrene from *Juncus roemerianus*

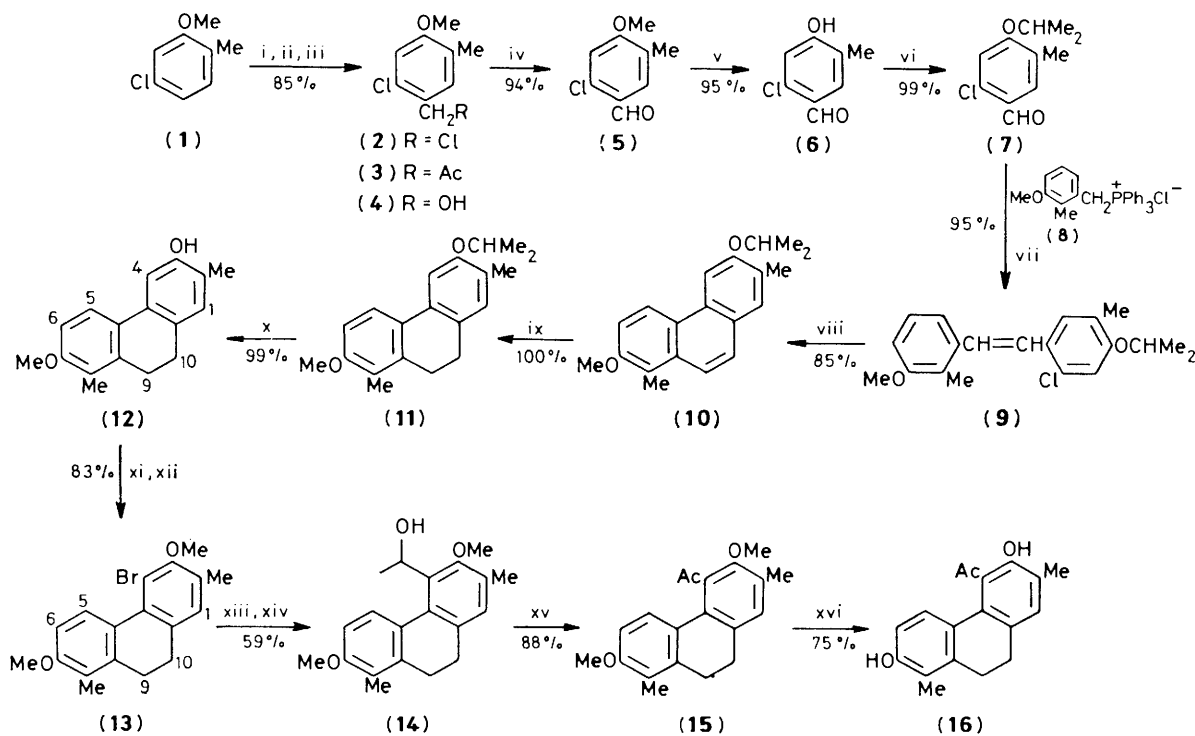
Christopher F. Carvalho and Melvyn V. Sargent*

Department of Organic Chemistry, University of Western Australia, Nedlands, W.A. 6009, Australia

An efficient synthesis of the biogenetically unusual 9,10-dihydrophenanthrene, juncunone, is reported; the key step involves ring-closure of a (*Z*)-2-chlorostilbene to a phenanthrene by an intramolecular homolytic substitution induced by activated magnesium.

Reports that extracts of the marsh grass, *Juncus roemerianus*,¹ have shown activity against leukaemia have resulted in several

syntheses² of the vinyl-9,10-dihydrophenanthrenes isolated from this source. We now report an efficient synthesis, provid-



Scheme 1. i, HCl, aq. HCHO, Et₂O, ZnCl₂, NaCl, 25 °C, 12 h; ii, NaAc, *N,N*-dimethylformamide (DMF), 80 °C, 17 h; iii, NaOH, aq. MeOH, 0 °C, 1.5 h; iv, MnO₂, boiling PhH, 12 h; v, BBr₃, CH₂Cl₂, -10 to 25 °C, 13 h; vi, Me₂CHI, DMF, K₂CO₃, 55 °C, 72 h; vii, LiOMe, DMF, 90 °C, 3 h; viii, activated Mg, boiling tetrahydrofuran, 12 h; ix, 10% Pd/C, EtAc, 25 °C, 144 h; x, BCl₃, CH₂Cl₂, -10 °C, 3 h; xi, Br₂, CH₂Cl₂, 25 °C; xii, MeI, DMF, K₂CO₃; xiii, BuLi, Et₂O, -10 °C, 5 min; xiv, MeCHO; xv, pyridinium chlorochromate, CH₂Cl₂, 25 °C, 3 h; xvi, BBr₃, CH₂Cl₂, -10 °C, 1 h.

ing sufficient material for biological testing, of the biogenetically unusual acetyl-9,10-dihydrophenanthrene, juncunone (**16**), a minor constituent of *J. roemerianus*.³ This synthesis also illustrates the general applicability of the ring-closure of (*Z*)-2-chlorostilbenes to phenanthrenes, induced by activated magnesium,⁴ which we believe involves intramolecular homolytic substitution.⁵

The aldehyde (**5**), † m.p. 106.5–107.5 °C, was readily available by chloromethylation⁶ (see Scheme 1) of the chloro-*O*-methyl-*o*-cresol (**1**).⁷ Subjection of the resultant chloromethyl compound (**2**), m.p. 21–22 °C, to displacement by acetate furnished the acetoxymethyl compound (**3**), m.p. 28–30 °C, and thence by hydrolysis the hydroxymethyl compound (**4**), m.p. 81.5–82.5 °C. Oxidation then afforded the aldehyde (**5**) which on demethylation gave the phenol (**6**), m.p. 178–179.5 °C, and thence by isopropylation the ether (**7**), m.p. 43–45 °C. Wittig reaction of the last-mentioned compound by the *in situ* method with the readily available phosphonium salt (**8**)⁵ gave the stilbene (**9**) as a 2:1 mixture of (*Z*)- [b.p. 120 °C (kugelrohr) at 0.05 mmHg, λ_{max} 278 nm] and (*E*)-isomers (m.p. 85–86 °C, λ_{max} 300 nm).

Reaction of the 2-chlorostilbene (**9**) [75% (*Z*)-isomer] with activated magnesium gave the phenanthrene (**10**) [85% based on (*Z*)-stilbene], m.p. 118–119 °C, which on catalytic reduction smoothly gave the 9,10-dihydrophenanthrene (**11**), m.p. 98.5–99.5 °C. Deisopropylation was achieved with boron trichloride and the resultant phenol (**12**), m.p. 198–199 °C, furnished on bromination only one product, isolated as its

methyl ether (**13**), m.p. 113.5–114 °C. The position of bromination was convincingly demonstrated by the marked n.m.r. spectral downfield shift (0.68 p.p.m.) of the 5-proton on going from the phenol (**12**) to the bromo-compound (**13**). Bromine-lithium exchange and subsequent reaction with acetaldehyde gave the secondary alcohol (**14**), m.p. 151.5–152.5 °C, which on oxidation gave di-*O*-methyljuncunone (**15**), m.p. 133.5–134 °C. This on demethylation afforded juncunone (**16**), m.p. 191–192 °C, identical with the natural product by all the usual criteria.

We thank Professor D. H. Miles for carrying out the comparison between synthetic and natural juncunone, and the Australian Research Grants Committee for financial support.

Received, 17th August 1982; Com. 992

References

- D. H. Miles, J. Bhattacharyya, N. V. Mody, J. L. Atwood, S. Black, and P. A. Hedin, *J. Am. Chem. Soc.*, 1977, **99**, 618; J. Bhattacharyya and D. H. Miles, *Tetrahedron Lett.*, 1977, 2749; J. Bhattacharyya, *Experientia*, 1980, **36**, 27.
- A. S. Kende and D. P. Curran, *J. Am. Chem. Soc.*, 1979, **101**, 1857; E. McDonald and R. T. Martin, *Tetrahedron Lett.*, 1978, 4723; A. L. Cossey, M. J. Gunter, and L. N. Mander, *ibid.*, 1980, 3309; A. G. Schulz and M. Shen, *ibid.*, 1981, 1775.
- D. H. Miles, S. Randle, R. Shakir, and J. L. Atwood, *J. Org. Chem.*, 1981, **46**, 2813.
- R. D. Rieke and S. E. Bales, *J. Am. Chem. Soc.*, 1974, **96**, 1775.
- C. Brown, B. J. Sikkil, C. F. Carvalho, and M. V. Sargent, *J. Chem. Soc., Perkin Trans. 1*, 1982, in the press.
- Cf. K. Kraft, *Chem. Ber.*, 1951, **84**, 150.
- H. E. Ungnade and E. F. Orwoll, *J. Am. Chem. Soc.*, 1943, **65**, 1736.

† All new compounds gave satisfactory microanalytical data and exhibited spectroscopic properties in accord with the assigned structures.