Synthesis of the Chrysene Bay Region *anti*-Diolepoxide from Chrysene

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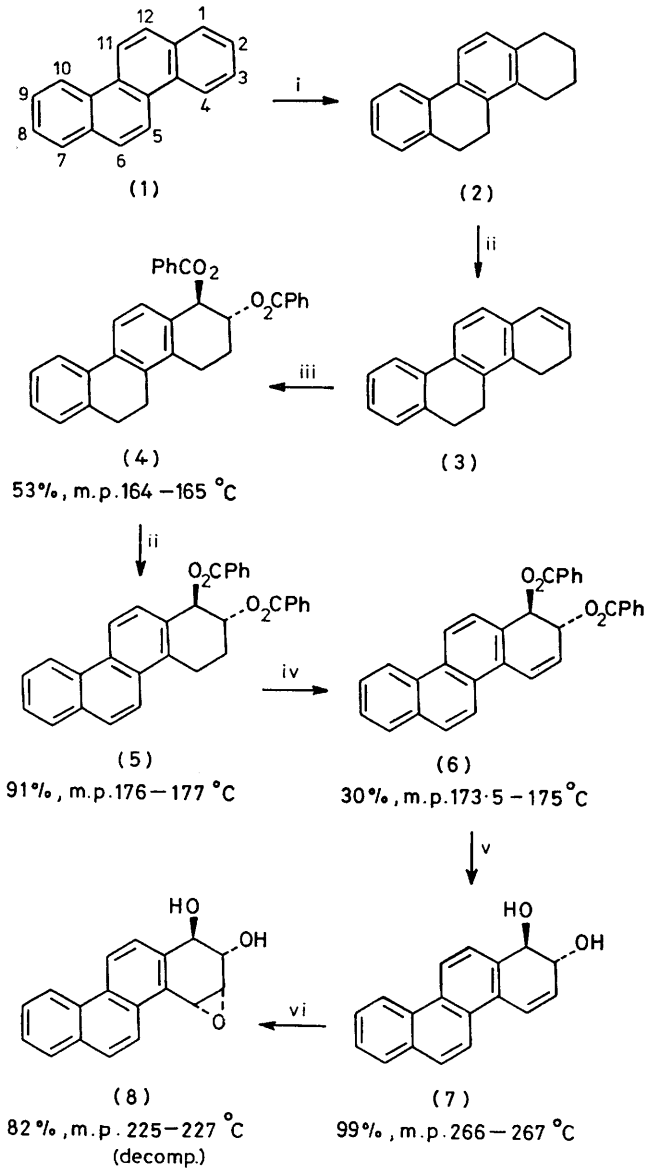
Summary The bay region *anti*-diolepoxide of chrysene (**8**) is conveniently synthesized from 3,4,5,6-tetrahydrochrysene obtained from chrysene in two steps.

RECENT research has implicated diolepoxide metabolites as the active forms of benzo[*a*]pyrene[1] and other carcinogenic hydrocarbons.[2] Although synthetic approaches to several of the isomeric *syn* and *anti* arene diolepoxides have been described,[1] these methods are dependent upon the availability of the appropriate dihydroarenes as synthetic intermediates. In the case of chrysene (**1**), the requisite 1,2- and 3,4-dihydro-(**1**) are available only *via* complex multistep synthesis† from phenanthrene and naphthalene, respectively. We now report the synthesis of the bay region *anti*-diolepoxide of chrysene (**8**) directly from the parent hydrocarbon.

In preliminary experiments, hydrogenation of (**1**) over 10% Pd–C catalyst[3] at low pressure (45 lb in^{-2}) was shown to afford 5,6-dihydro-(**1**), while similar reaction over PtO_2 gave 1,2,3,4-tetrahydro-(**1**) along with several minor hydroaromatic products. Hydrogenation of (**1**) over a mixed Pd–C–PtO_2‡ catalyst under similar conditions cleanly furnished 1,2,3,4,5,6-hexahydrochrysene (**2**), m.p. 112·5—113·5 °C. Partial dehydrogenation of 1,2,3,4-tetrahydro-(**1**) through bromination–dehydrobromination[4] with *N*-bromosuccinimide (NBS) and 1,5-diazabicyclo[4.3.0]non-5-ene (DBN) furnished 1,2-dihydro-(**1**) in low yield. In contrast, partial dehydrogenation of (**2**) with dichlorodicyanobenzoquinone (DDQ) in refluxing benzene[4,5] took place regiospecifically in the alternative molecular region to provide 3,4,5,6-tetrahydrochrysene (**3**).

Transformation of (**3**) into (**8**) was accomplished through the reaction sequence depicted in the Scheme. The experimental procedures employed were patterned after those utilized for related syntheses described in previous papers[6] and in a review article.[1] The ^{1}H n.m.r. spectra of all compounds were in complete agreement with the structural assignments (Table). In particular, the H-4 protons of (**6**)—(**8**) exhibited the downfield shift characteristic of bay region protons as a consequence of interaction with the adjacent H-5 proton. In further confirmation of the isomeric structural assignments, the u.v. spectrum of (**7**) matched that reported[7] for the 1,2-dihydrodiol which differed distinctively from that of the 3,4-dihydrodiol.



SCHEME. i, Pt–Pd, H_2; ii, DDQ; iii, $PhCO_2Ag$, I_2; iv, NBS, DBN; v, NaOMe; vi, *m*-chloroperbenzoic acid.

† Conventional synthesis of 1,2-dihydrochrysene (W. E. Bachmann and W. S. Struve, *J. Org. Chem.*, 1939, **4**, 456) involves Friedel-Crafts succinoylation of phenanthrene, separation of the resulting isomeric keto-acids, Clemmensen or Wolff-Kishner reduction, acid-catalysed cyclization (two isomers possible), reduction of the desired isomeric ketone to the alcohol, and dehydration.

‡ All new compounds gave satisfactory microanalyses for C and H within ±0·3%. ^{1}H N.m.r. spectra of all compounds were consistent with the assigned structures.

TABLE. ^{1}H N.m.r. spectra of compounds (4)—(8) (δ relative to Me_4Si).[a]

Compound	H-1	H-2	H-3	H-4
(4)[b]	6·57 (d) $J_{1,2} = 6·5$	5·37—5·78 (m)	2·16—2·53 (d)	2·63—3·12 (m)
(5)[b]	6·71 (d) $J_{1,2} = 5·0$	5·45—5·83 (m)	2·37—2·70 (m)	3·29—3·66 (m)
(6)[b]	6·85 (d) $J_{1,2} = 7·5$; $J_{2,3} = 3·5$; $J_{3,4} = 10$	6·17 (dd)	6·38 (dd)	c
(7)[d]	4·92 (d) $J_{1,2} = 10·5$; $J_{2,3} = 2$; $J_{3,4} = 10$; $J_{2,4} = 2$	4·41 (ddd)	6·20 (dd)	7·30 (dd)
(8)[d]	4·63 (dd) $J_{1,2} = 8$; $J_{2,3} = ca.\ 2$; $J_{3,4} = 4$; $J_{11,12} = 10$	3·90 (dd)	3·76 (dd)	4·99 (d)

[a] Aromatic protons in the appropriate ratio were detected in the aromatic region. The H-5 and H-6 benzylic protons of (4) had δ 2·77(s). Coupling constants are in Hz. [b] Solvent $CDCl_3$. [c] In the aromatic region. [d] Solvent $(CD_3)_2CO$ + $(CD_3)_2SO$ + 1 drop of D_2O.

Preliminary experiments indicate (8) to be an effective inhibitor of φX 174 DNA viral replication.[8] The 1,2-dihydrodiol (7) is reported[9] to be highly mutagenic towards *S. typhimurium* bacterial cells in the presence of hepatic microsomes.

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