A New Aziridine Synthesis from 2-Azido Alcohols and Tertiary Phosphines. Preparation of Phenanthrene 9,10-Imine

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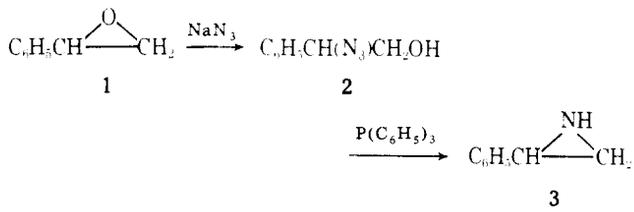
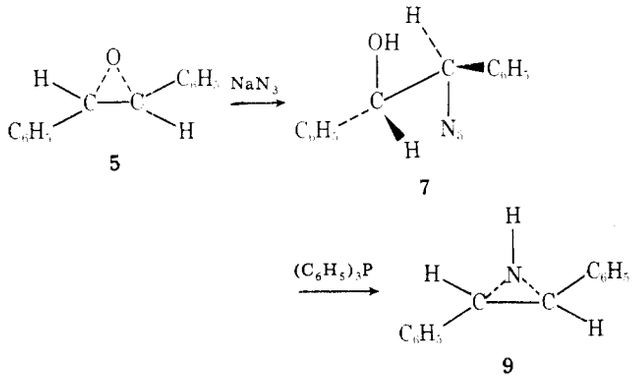
A new stereospecific synthesis of aziridines is described. It consists of the reaction of sodium azide with an oxirane, followed by treatment of the 2-azido alcohol formed with a tertiary phosphine. The method has been applied for the preparation of the first unsubstituted phenanthrene imine. The synthesis of 1a,9b-dihydrophenanthr[9,10-*b*]azirine proved to proceed via a phosphonium hydroxide intermediate which could be isolated under mild conditions. The unsubstituted arene imine proved to be thermally stable (up to 190 °C), but rearranges to 9-aminophenanthrene in the presence of hydrochloric acid.

In a recent paper,[3] we discussed a hypothesis concerning the intermediary of arene imines in chemical carcinogenesis and described the syntheses of several *N*-acetyl- and *N*-alkylphenanthrene imines. However, unsubstituted arene imines that are isoelectronic with the well-documented arene oxides[4] could not be obtained by the available methods.

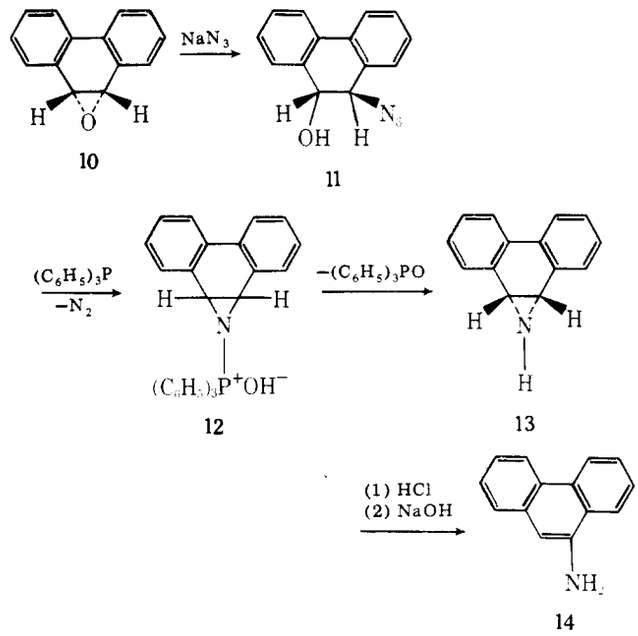
We now wish to report a new transformation of oxiranes to aziridines by which the first unsubstituted polycyclic arene imine has been synthesized. The process includes the reaction of epoxide with sodium azide followed by treatment of the 2-azido alcohol with a tertiary phosphine. 2-Phenylaziridine (**3**), e.g., was obtained in 72% yield simply by the addition of an ether solution of triphenylphosphine to 2-azido-2-phenylethanol (**2**).[5]



When *cis*- and *trans*-stilbene oxide (**4** and **5**) were converted into the corresponding *threo*- and *erythro*-2-azido-1,2-diphenylethanol (**6** and **7**)[6] followed by treatment with $(C_6H_5)_3P$, *cis*- and *trans*-2,3-diphenylaziridine (**8** and **9**) resulted in a highly selective fashion.



This process is thus particularly useful for epoxide to aziridine transformation in which an overall retention of configuration is required. Its greatest advantage is, however, its utility for the synthesis of unsubstituted arene imines. 1a,9b-Dihydrophenanthr[9,10-*b*]azirine (**13**) could be prepared by the reaction of triphenylphosphine with *trans*-10-azido-9,10-dihydrophenanthr-9-ol (**11**) [from phenanthrene 9,10-oxide (**10**) and NaN_3[7]]. When the phosphine was added to **11** below 20 °C, a labile phosphorus-containing compound,



$C_{32}H_{26}NOP$ (**12**), could be isolated. The ^1H NMR spectrum taken in $CDCl_3$ below 25 °C shows typical aziridine signals at δ 3.53 and 3.59[8] that suggest an aziridinylphosphonium structure **12** for this intermediate. At 30 °C the two peaks collapse into a sharp singlet at δ 3.56 that is characteristic for the phosphourus-free imine **13**.

The structure of **13** was established mainly on basis of elementary analysis and spectral data. An N–H absorption at 3180 cm^{-1} is observed in the IR spectrum. The ^1H NMR ($CDCl_3$) spectrum shows two equivalent aziridine protons that resonate at δ 3.56 and indicates that **13** does not exist to any detectable extent as an azepine derivative.[9] The principal fragment ions in the mass spectrum (see Experimental Section) are the molecular ion and the characteristic fragments of the 9,10-dihydrophenanthrene skeleton.[10]

The unsubstituted phenanthrene 9,10-imine proved to be thermally more stable than the reported *N*-acetyl,[11] *N*-tosyl,[6] and *N*-alkyl derivatives[3] and more than the analogous phenanthrene 9,10-oxide.[12] It can be heated up to 190 °C (above the melting point) without any significant change. Only above 210 °C does rapid ring opening take place, and a mixture of compounds that contains ca. 30% of 9-aminophenanthrene (**14**) is formed. Smooth transformation of **13** to **14** can, however, be accomplished upon brief reflux in aqueous hydrochloric acid followed by neutralization with base. Triphenylphosphine oxide also promotes the conversion of **13** into the aromatic amine above 80 °C, albeit not in quantitative yield. Under nitrosating conditions (isoamyl nitrite and triethylamine), **13**, like aliphatic aziridines,[13] is deaminated to

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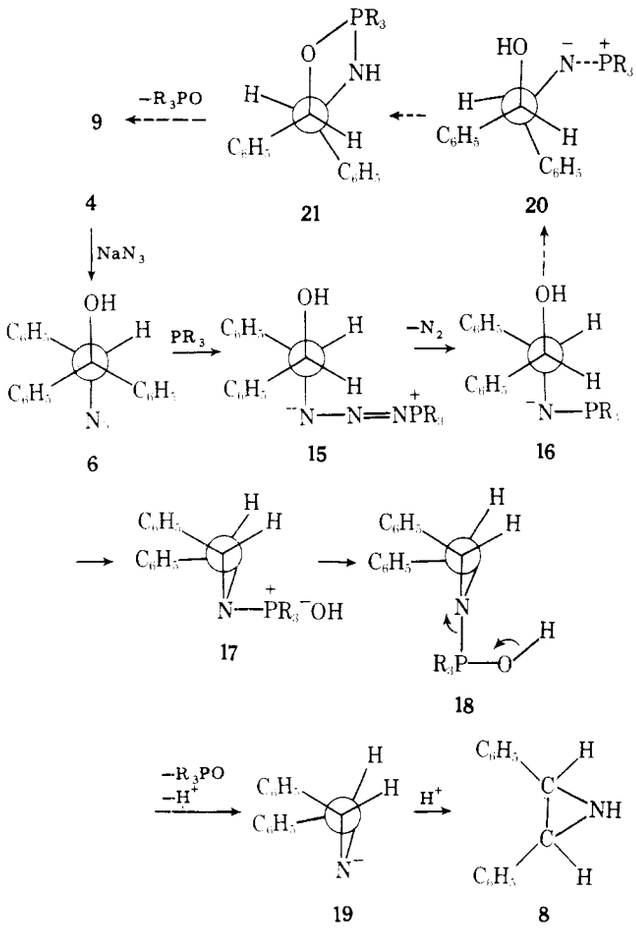
give phenanthrene. This latter experiment thus provides the linking step for a reaction cycle in which phenanthrene 9,10-oxide and phenanthrene imine can be interconverted.

Since the separation of **13** from the accompanying triphenylphosphine oxide proved tedious and led to heavy losses of the desired product, we found it useful to employ tri-*n*-butylphosphine instead of triphenylphosphine for the transformation of **11** to **13**. The tri-*n*-butylphosphine oxide and the other impurities could be easily removed by washing with dry ether, leaving 72% of analytically pure imine.

The resemblance of the stereochemical course of the Staudinger reaction[14] of 2-iodoalkyl azides with tertiary phosphines[8] to that observed in our aziridine synthesis suggests similar features in the mechanisms of both processes. Thus, e.g., in the transformation of *cis*-stilbene oxide (**4**) to *cis*-2,3-diphenylaziridine (**8**), (±)-*threo*-azido alcohol **6** is assumed to add R_3P at the terminal nitrogen atom.[15] Loss of N_2 from **15** and intramolecular nucleophilic substitution in ylide **16** would then lead to the azyridinylphosphonium hydroxide **17**.



Elimination of triphenylphosphine oxide from **18** affords then *cis*-2,3-diphenylaziridine (**8**). Rotation of the C_1–C_2 bond of **16** to give conformer **20** followed by S_Ni ring closure would generate the precursor of *trans*-2,3-diphenylaziridine (**9**). Since no **9** is formed from **4**, the pathway leading to **21** must be ruled out.

Experimental Section

Melting points were taken on a Thomas-Hoover capillary melting point apparatus and are not corrected. Infrared and ultraviolet spectra were recorded on a Perkin-Elmer Model 157 and a Unicam SP-800 spectrophotometer, respectively. Proton magnetic resonance spectra were run using HA-100D and CFT-20 spectrometers. The latter instrument, equipped with a Fourier transformer, was also used for the recording of ^{13}C magnetic resonance spectra. Mass spectra were obtained with the aid of a Varian MAT-311 instrument at 70 eV.

2-Phenylaziridine (3). A solution of 8.15 g (50 mmol) of 2-azido-2-phenylethanol (**2**) [prepared in 85% yield from styrene oxide (**1**)[5]] and 13.10 g (50 mmol) of triphenylphosphine in 250 mL of dry ether was stirred at room temperature. Evolution of N_2 and precipitation of triphenylphosphine oxide started after 10 min. When gas evolution had ceased, the oxide was filtered off and the ether removed in vacuo. The residue was distilled at 75 °C (15 mm) to give 4.30 g (72%) of **3** that was identical with an authentic sample.[16]

(±)-*threo*-2-Azido-1,2-diphenylethanol (6). A mixture of 3.92 g (20 mmol) of *cis*-stilbene oxide (**4**) and 4.48 g (70 mmol) of NaN_3 in 60 mL of 50% aqueous acetone was refluxed for 3 h, The solvent was evaporated in vacuo and the residue extracted with $CHCl_3$. The organic solution was washed with water, dried ($MgSO_4$), and concentrated. Distillation of the residue afforded 3.70 g (77%) of **6** as a pale yellow oil: bp 122 °C (0.15 mm); IR 2118 (N_3), 3434 (OH) cm^{-1}; UV λ_{max} (log ϵ) (EtOH) 226 (3.21), 247 (2.87), 252 (2.89), 258 (2.88), 264 nm (2.76); ^1H NMR ($CDCl_3$) δ 3.10 (brd s, 1), 4.45 and 4.69 (AB pattern, 2, J_{AB} = 7.5 Hz), 7.20 (m, 10); MS *m/e* (relative intensity) 211 ($M^+ \cdot - N_2$, 0.4), 197 (1.1), 196 (1.1), 195 (1.1), 180 (1.1), 179 (1.4), 178 (1.7), 167 (2.9), 165 (2.3), 152 (1.4), 135 (4.6), 107 (100), 105 (31.4), 104 (25.7), 79 (78.6), 77 (68.6), 51 (27.7). Anal. Calcd for $C_{14}H_{13}N_3O$: C, 70.3; H, 5.4. Found: C, 70.2; H, 5.7.

***cis*-2,3-Diphenylaziridine (8).** A solution of 0.84 g (3.5 mmol) of **6** and 0.92 g (3.5 mmol) of triphenylphosphine in 25 mL of dry ether was refluxed for 1 h. Ether (50 mL) was added, and the mixture was allowed to stand overnight at 5 °C to allow complete precipitation of the triphenylphosphine oxide. Column chromatography on silica gel yielded 0.53 g (77%) of **8** that was identical with an authentic sample obtained by the method of Hassner et al.[17]

(±)-*erythro*-2-Azido-1,2-diphenylethanol (7). As for **6**, 3.92 g of **5** was reacted with 4.48 g of sodium azide. However, prolonged reflux was necessary as the last traces of *trans*-stilbene oxide (TLC test) disappeared only after 48 h. The azido alcohol was obtained in 88% yield (2.12 g), bp 158 °C (0.8 mm). On standing, **7** solidified to give colorless crystals of mp 60–61 °C: IR (Nujol) 2108 (N_3), 3430 (OH) cm^{-1}; UV λ_{max} (log ϵ) (EtOH) 226 (3.20), 252 (2.79), 258 (2.82), 264 (2.73), 268 nm (2.60); ^1H NMR ($CDCl_3$) δ 2.11 (brd s, 1), 4.63 and 4.76 (AB pattern, 2, J_{AB} = 8 Hz), 7.15 (m, 10); MS *m/e* (relative intensity) 211 ($M^+ \cdot - N_2$, 0.4), 197 (3.6), 196 (2.6), 195 (2.8), 165 (4.8), 152 (2.5), 107 (100), 106 (26.7), 105 (51.0), 104 (37.9), 79 (49.5), 77 (63.1), 51 (24.3). Anal. Calcd for $C_{14}H_{13}N_3O$: C, 70.3; H, 5.4. Found: C, 70.3; H, 5.7.

***trans*-2,3-Diphenylaziridine (9)** was obtained in 68% yield by the manner described for **3**. (Slight heating was required.) The colorless product of mp 45–46 °C proved to be identical with a sample prepared according to Heine et al.[18]

***trans*-10-Azido-9,10-dihydrophenanthr-9-ol (11)** was obtained in quantitative yield when the method of Shudo and Okamoto[6] was modified as follows. A solution of 20 g (0.31 mol) of sodium azide in 500 mL of acetone, 250 mL of water, and 0.5 mL of concentrated sulfuric acid was stirred at room temperature for 10 min. Phenanthrene oxide (**10**) (0.97 g, 5 mmol) was added, and stirring was continued for 48 h. The acetone was removed in vacuo and the organic residue taken in CH_2Cl_2. Evaporation of the solvent afforded 1.18 g of **11** with the same melting point and IR spectrum as reported[6]: ^1H NMR ($CDCl_3$) δ 1.26 (s, 1), 4.68 and 4.77 (AB pattern, 2, J_{AB} = 8 Hz), 7.2–8.4 (m, 8); ^{13}C NMR (Me_2SO-d_6) δ 135.98, 133.16, 132.55, 131.47, 128.03, 127.81 (12 C, aromatic), 74.96 (1 C, CHOH), 68.73 (1 C, CHN_3); MS *m/e* (relative intensity) 237 ($M^+ \cdot$, 9.2), 209 (7.5), 208 (10), 180 (100), 165 (12.1), 152 (20.4).

(1a,9b-Dihydrophenanthr[9,10-*b*]azirin-1-yl)triphenylphosphonium Hydroxide (12). To a stirred solution of 2.62 g (10 mmol) of triphenylphosphine in 50 mL dry ether was added 2.37 g (10 mmol) of **11**. After 10 min at 18 °C, evolution of nitrogen started. Stirring was continued for 20 min further. The solution was concentrated in vacuo (below 15 °C) to a volume of 10 mL. The colorless phosphonium hydroxide (3.95 g, 84%) was filtered off and washed with 20 mL of *cold* ether: ^1H NMR ($CDCl_3$, 20 °C) δ 3.52 (brd s, 1), 3.58 (brd s, 1), 7.10–8.07 (m, 23). At 31 °C, the spectrum was identical with that of equimolar amounts of **13** and triphenylphospine oxide. MS *m/e* (relative intensity) 454 ($C_{32}H_{25}NP^+ \cdot$, 3.2), 278 [$(C_6H_5)_3PO^+ \cdot$, 31], 262 [$(C_6H_5)_3P^+ \cdot$, 7.7), 198 (7.1), 196 (9.0), 193 ($13^+ \cdot$, 100), 182 (11.6), 177 (13.5), 165 (60.6), 152 (11.0), 50 (42.6). At 25 eV, $M^+ \cdot$ of the phosphorane of *m/e* 471 (0.7) was observed. Anal. Calcd for $C_{32}H_{26}NOP$: C, 81.5; H, 5.5; N, 3.0; P, 6.6. Found: C, 81.5; H, 5.7; N, 3.3; P, 6.2.

1a,9b-Dihydrophenanthr[9,10-*b*]azirine (13). A. Under an N_2 atmosphere and external cooling (ice water), there was added with vigorous stirring 3.1 g (15.3 mmol) of tri-*n*-butylphosphine to 3.40 g (14.3 mmol) of **11**. After the exothermic reaction had ceased, the

mixture was cooled to 0 °C and washed four times with 15 mL of dry ether to yield 2.0 g (72%) of colorless crystals: mp 163–164 °C (from benzene–cyclohexane); IR (Nujol) 3180 cm^{-1} (N-H); UV λ_{max} (log ϵ) ($CHCl_3$) 273 (4.12), 277 (4.15), 281 (4.17), 288 (4.02), 294 (3.90), 305 nm (3.59); ^1H NMR ($CDCl_3$) δ 3.56 (s, 2), 7.2–8.3 (m, 8); ^{13}C NMR ($CDCl_3$) δ 136.22, 134.53, 133.68, 132.54, 130.98, 127.76 (12 C, aromatic) 41.88 (2 C, CHNH); MS (relative intensity) *m/e* 193 (M^+, 100), 192 (11.6), 178 (34.0), 176 (9.6), 165 (74.0), 152 (6.4), 151 (3.6), 150 (3.2), 139 (6.4), 127 (5.2), 89 (5.2), 76 (6.0). Anal. Calcd for $C_{14}H_{11}N$: C, 87.0; H, 5.7; N, 7.3. Found: C, 87.3; H, 5.9; N, 7.0.

B. A solution of 0.942 g (2 mmol) of **12** in 100 mL of CH_2Cl_2 was refluxed for 15 min. The solvent was distilled, and most of the triphenylphosphine oxide was removed by extraction with ether (3 × 25 mL). The residue was dissolved in 2 mL of CH_2Cl_2 and purified by two dimensional PLC on alumina (5:1 hexane–ether eluent). In the best run we obtained 0.234 g of **13** (85% purity). Further purification by PLC and by recrystallization was associated with significant losses.

Conversion of 13 into 9-Aminophenanthrene (14). A mixture of 50 mg of the previous imine and 2 mL of 15% aqueous HCl was refluxed for 10 min. After cooling, 5 mL of benzene was added and the acid was neutralized with NaOH. The organic layer was dried and concentrated. The residue proved to be pure **14**, which was identical with an authentic sample prepared according to Schmidt and Heinle.[19]

Deamination of 13. A mixture of 0.97 g (5 mmol) of **13**, 6.4 g (50 mmol) of isoamyl nitrite, and 1.5 mL of triethylamine was stirred for 45 min at room temperature. Extraction with benzene and column chromatography on alumina afforded 0.63 g (71%) of phenanthrene.

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Registry No.—**2**, 67364-41-9; **3**, 1499-00-9; **4**, 1689-71-0; **5**, 1439-07-2; **6**, 67464-42-0; **7**, 67464-43-1; **8**, 1605-06-7; **9**, 25125-72-8; **10**, 585-08-0; **11**, 53581-32-1; **12** (uncharged), 67464-44-2; **12** (charged), 67464-45-3; **13**, 67464-46-4; **14**, 947-73-9.

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2-Chloroacrylonitrile as a Cyclodipolarophile in 1,3-Cycloadditions. 3-Cyanopyrroles

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The reaction of 2-chloroacrylonitrile with *N*-acyl-α-amino acids in acetic anhydride gave 3-cyanopyrroles, through an oxazolium 5-oxide (**2**) intermediate, with an overall yield of about 70%. Representative 3-cyanopyrroles, 7-cyano-2,3-dihydro-1*H*-pyrrolizines, and 1-cyano-5,6,7,8-tetrahydroindolizines were synthesized. Regiospecificity was achieved in some cases.

The 1,3-cycloaddition of oxazolium 5-oxides (**2**) with dipolarophiles has recently been utilized in the synthesis of a variety of heterocyclic systems,[1–3] the reaction pathway involving a cycloaddition to an azomethine ylide to give a N-bridged intermediate that loses carbon dioxide and forms a heterocycle.[4] This note describes the reaction between oxazolium 5-oxides and 2-chloroacrylonitrile to give 3-cyanopyrrole derivatives in a single pot operation starting from α-amino acids or their *N*-acyl derivatives.

The overall reaction is represented by the following sequence: N-acylation of the amino acid (**1**), oxazolium 5-oxide (**2**) formation, 1,3-cycloaddition to give a N-bridged intermediate (**3**), carbon dioxide elimination to give an unstable chlorocyanopyrroline (**4**), and elimination of hydrochloric acid[5] to give a 3-cyanopyrrole (**5**). When a cyclic α-amino acid (proline or pipecolic acid) was used, the corresponding 7-cyano-2,3-dihydro-1*H*-pyrrolizines (**14** and **15**) or 1-cyano-5,6,7,8-tetrahydroindolizines (**16** and **18**) were obtained.

This reaction can be carried out using aromatic, halogenated, or aprotic solvents or an excess of acetic anhydride at temperatures ranging between 20 and 100 °C. It represents a useful synthetic route to 3-cyanopyrroles with the same substituents in positions 2 and 5 (**6** and **12**) or when the reaction is regiospecific, giving only one isomer, as in the cycloaddition to the azomethine ylide system derived from *N*-formyl-*C*-phenylglycine, *N*-acylproline, or *N*-acylpipecolic acid (compounds **9** and **14–21**). As expected, a mixture of pyrroles is obtained when the reaction is not regiospecific, as with L-leucine, which gives compounds **7** and **8**. The same mixture of pyrroles **10** and **11** is obtained starting from either DL-α-phenylglycine or *N*-benzoylalanine. From this mixture, compound **11** was isolated. Both mixtures were hydrolyzed to the corresponding mixture of acids, which were decarboxylated to a single pyrrole **13**.

The presence of a substituent in position 4 in the oxazolium 5-oxide intermediate **2** seems to be necessary since no reaction was obtained with *N*-formylglycine, *N*-acetylglycine, or hippuric acid under experimental conditions described for the preparation of **9**. The oxazolone derived from hippuric acid (**2**; R = C_6H_5, R_1 = H) was isolated and does not react with 2-chloroacrylonitrile in the conditions described in this note. Anyhow, the desired compound **9** could be obtained using

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