Notes

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Preparation of Pure Isomers of Dinitropyrenes

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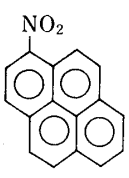
Isomers of dinitropyrenes (1,3-, 1,6-, and 1,8-dinitropyrenes) uncontaminated by the other isomers were prepared from the corresponding diaminopyrenes by oxidation, or nucleophilic substitution with nitrite after diazotization.

Keywords——dinitropyrene; 1,3-dinitropyrene; 1,6-dinitropyrene; 1,8-dinitropyrene; diaminopyrene; preparation of nitroarenes

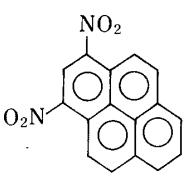
Dinitropyrenes are of interest as possible environmental mutagens.[1] These compounds exist in the environment as isomeric mixtures of 1,3-, 1,6-, and 1,8-dinitropyrenes. To evaluate the biological activities of the dinitropyrene isomers, it is necessary to prepare each isomer in pure form, uncontaminated by the other isomers. Nitration of pyrene under various conditions (*e.g.*, with a mixture of nitric acid and sulfuric acid, with nitric acid in acetic acid, with acetyl nitrate, with a mixture of silver nitrate and acetyl chloride in acetonitrile, or with dinitrogen tetroxide) yields 1,3-, 1,6-, and 1,8-dinitropyrenes in a ratio of about 1 : 2 : 2 together with various amounts of 1-nitropyrene.[2] However, separation of these isomers in preparative amounts is difficult because of the slight solubility of these compounds in light organic solvents and their similar polarity values. Rosenkranz *et al.* reported the preparation of 1,3-, 1,6-, and 1,8-dinitropyrenes by separation of a nitrated mixture of pyrene,[3] though the method is difficult to apply to large-scale preparation of each dinitropyrene isomer. Here we report two methods for the preparation of pure isomers of dinitropyrenes.

Our strategy was to derivatize the mixture of dinitropyrenes to an easily separable and soluble form, that is, a mixture of diaminopyrenes. After separation of the diaminopyrene mixture, pure 1,3-, 1,6-, and 1,8-diaminopyrenes were oxidized to the corresponding dinitropyrenes. The same compounds were also prepared by substitution of the amino group by nitrite after diazotization.

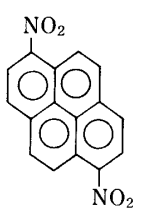
Nitration of pyrene with nitric acid in acetic acid was performed by the method of Vollmann *et al.*[4] The nitrated mixture was reduced with sodium hydrogen sulfide in ethanol to aminopyrenes,[4] which are quite soluble in methylene chloride and can be easily separated by the use of silica gel column chromatography with a mixture of *n*-hexane and methylene



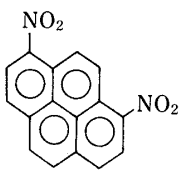
1-nitropyrene



1,3-dinitropyrene



1,6-dinitropyrene



1,8-dinitropyrene

chloride. During the purification of each aminopyrene, the use of protic solvents should be avoided (aminopyrenes were transformed to very polar brown substance(s) in protic solvents). The yields of the aminopyrenes from pyrene were 27% for 1-aminopyrene, 12% for 1,3-diaminopyrene, 22% for 1,6-diaminopyrene, and 17% for 1,8-diaminopyrene (total: 78%). Each pure aminopyrene isomer was oxidized in a mixture of acetonitrile and 30% aqueous hydrogen peroxide containing sodium tungstate. The yields of nitropyrene were 21% for 1-nitropyrene, 2% for 1,3-dinitropyrene, 8% for 1,6-dinitropyrene, and 2% for 1,8-dinitropyrene. The major products of the reaction were azoxy derivatives. This oxidation system is very useful for the preparation of nitroaromatics from the corresponding aromatic amines.[5]

Pure nitropyrene isomers were also prepared by substitution of the amino group of the separated aminopyrene isomers with nitrite after diazotization in the presence of cupric sulfate.[6] The yields of nitropyrenes were 6% for 1-nitropyrene, 1% for 1,3-dinitropyrene, 28% for 1,6-dinitropyrene and 11% for 1,8-dinitropyrene.

Dinitropyrene isomers thus obtained were recrystallized from a mixture of benzene and *n*-hexane to give brown needles. The purity of each nitropyrene isomer was checked by high performance liquid chromatography (Polygosil $_5$CN, $4.6\phi \times 250$ mm, 5% isopropanol in *n*-hexane). Contamination by the other isomers was undetectable (less than 0.05%).

In conclusion, each isomer of dinitropyrene was prepared in pure form by methods which consist of, i) reduction of the mixture of nitropyrene to a soluble, easily separable mixture of aminopyrenes, and ii) oxidation of aminopyrene to nitropyrene, or substitution of the amino group with nitrite after diazotization.

Experimental

Aminopyrenes——Pyrene (10 g) was dissolved in CH_3COOH (100 ml) and the solution was heated to 90 °C. HNO_3 (7.5 ml) was added slowly, and the mixture was heated at 90 °C for 30 min, then cooled. The resulting yellow precipitates were collected by filtration (a mixture of nitropyrenes, 13.5 g). Nitropyrenes thus obtained were dissolved in EtOH (100 ml) and aqueous NaSH (42 g/100 ml H_2O) was added to the solution. The mixture was heated at reflux for 3 h, then H_2O (100 ml) was added and the whole was allowed to cool. The resulting crystals were collected by filtration (10.9 g of aminopyrenes). The crystals were dissolved in a minimum amount of CH_2Cl_2 and the solution was subjected to silica gel column chromatography (1 kg of Wakogel C-200, eluted with CH_2Cl_2). Each fraction was checked by silica gel thin layer chromatography (Silica gel 60/Kieselguhr F_{254}; solvent, 10% AcOEt in CH_2Cl_2; *Rf* values were 0.9 for 1-aminopyrene, 0.6 for 1,6-diaminopyrene, 0.4 for 1,3-diaminopyrene, and 0.3 for 1,8-diaminopyrene). 1-Aminopyrene (2.8 g, 27%), 1,6-diaminopyrene (2.6 g, 22%), 1,3-diaminopyrene (1.4 g, 12%), and 1,8-diaminopyrene (1.9 g, 17%) were eluted in that order. Each aminopyrene isomer was recrystallized from AcOEt to give pale yellow needles. The structure of 1,6-diaminopyrene was confirmed by X-ray analysis.[7] 1-aminopyrene: mp 118—119 °C. *Anal.* Calcd for $C_{16}H_{11}N$: C, 88.45; H, 5.08; N, 6.46. Found: C, 88.45; H, 5.10; N, 6.45.

1,3-Diaminopyrene: mp 184—186 °C. *Anal.* Calcd for $C_{16}H_{12}N_2$: C, 82.73; H, 5.21; N, 12.06. Found: C, 82.55; H, 5.23; N, 12.20.

1,6-Diaminopyrene: mp 234—235 °C. *Anal.* Found: C, 82.56; H, 5.36; N, 11.94.

1,8-Diaminopyrene: mp 177—179 °C. *Anal.* Found: C, 82.56; H, 5.28; N, 12.16.

Dinitropyrenes——(A) Aminopyrene (100 mg) was dissolved in CH_3CN (200 ml) and 30% aqueous H_2O_2 (100 ml) containing Na_2WO_4–$2H_2O$ (200 mg) was added. After two weeks at room temperature, H_2O (500 ml) was added to the mixture and the whole was extracted with CH_2Cl_2. Then 10% Pd–C (100 mg) was added to the organic layer to decompose H_2O_2, and the mixture was filtered. The filtrate was evaporated and the residue was extracted with a large volume of CH_2Cl_2. The CH_2Cl_2 solution was concentrated and the residue was subjected to silica gel column chromatography (150 g of Wakogel C-200, eluted with a mixture of benzene and *n*-C_6H_{14} (2 : 1 v/v)).

(B) Aminopyrene (500 mg) was suspended in dilute HCl (pH 3, 400 ml) and vigorously stirred. To this suspension, $NaNO_2$ (5 g) and $CuSO_4$–$5H_2O$ (15 g) were added, and the whole was stirred at room temperature for 20 h. Then, the mixture was extracted with a large volume of CH_2Cl_2 and the extract was concentrated by evaporation. The residue was subjected to silica gel column chromatography (250 g of Wakogel C-200, eluted with a mixture of benzene and *n*-C_6H_{14} (2 : 1 v/v)). The yellow nitropyrene fraction was evaporated and the residue was recrystallized from a mixture of benzene and MeOH to give light brown needles.

1-Nitropyrene: mp 156 °C. Proton nuclear magnetic resonance (^{1}H-NMR) (DMSO-d_6) δ: 8.15—8.80 (m). Infrared (IR) (KBr): 1590, 1500, 1330, 1310, 880, 840, 820, 700 cm^{-1}. *Anal.* Calcd for $C_{16}H_9NO_2$: C, 77.72; H, 3.67;

N, 5.67. Found: C, 77.89; H, 3.68; N, 5.35.

1,3-Dinitropyrene: mp 274—276 °C. ^{1}H-NMR (DMSO-d_6) δ: 8.2—8.8 (m, 7H), 9.32 (s, 1H). IR (KBr): 1590, 1500, 1350, 1340, 1295, 1215, 890, 880, 840, 825 cm^{-1}. *Anal.* Calcd for $C_{16}H_8N_2O_4$: C, 65.76; H, 2.76; N, 9.58. Found: C, 65.68; H, 2.67; N, 9.29.

1,6-Dinitropyrene: mp >300 °C. ^{1}H-NMR (DMSO-d_6) δ: 8.63 (d, J=9 Hz, 2H), 8.65 (d, J=8 Hz, 2H), 8.83 (d, J=9 Hz, 2H), 8.84 (d, J=8 Hz, 2H). IR (KBr): 1590, 1510, 1340, 1310, 845, 815 cm^{-1}. *Anal.* Found: C, 65.72; H, 2.66; N, 9.30.

1,8-Dinitropyrene: mp >300 °C. ^{1}H-NMR (DMSO-d_6) δ: 8.58 (s, 2H), 8.67 (d, J=8 Hz, 2H), 8.88 (d, J=8 Hz, 2H), 8.94 (s, 2H). IR (KBr): 1600, 1500, 1340, 1180, 860, 820, 790, 700 cm^{-1}. *Anal.* Found: C, 66.01; H, 2.73; N, 9.47.

Each isolated nitropyrene was analyzed by high performance liquid chromatography (Polygosil $_5$CN, 4.6ϕ × 250 mm, 5% iso-PrOH in n-C_6H_{14}, 1.0 ml/min, detected by absorption measurement at 400 nm). Retention times: 5.2 min for 1-nitropyrene, 6.9 min for 1,3-dinitropyrene, 8.3 min for 1,6-dinitropyrene, and 9.1 min for 1,8-dinitropyrene. The chromatogram showed that each isomer was pure (less than 0.05% of the other isomers).

References and Notes

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