A Novel Azocine Synthesis

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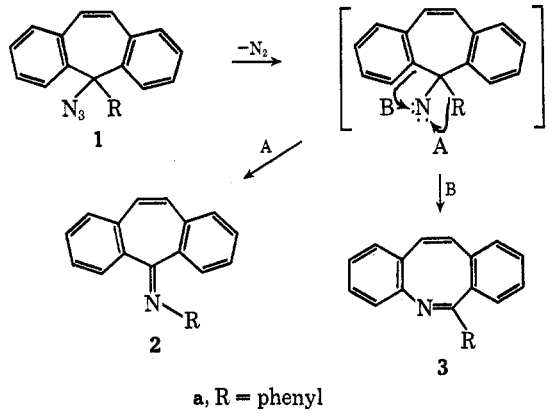
Photochemical decomposition of 5-phenyl- and 5-(1-naphthyl)-5-azido-5*H*-dibenzo[*a*,*d*]cycloheptene has been found to cause ring expansion to the 6-substituted dibenz[*b*,*f*]azocine system. Hydrolysis of the azocines gives the expected amino ketones. Reduction of 6-phenyldibenz[*b*,*f*]azocine with potassium in liquid ammonia leads to a bicyclic reduction product in addition to a dihydro- and a tetrahydroazocine.

We wish to report a synthesis of the dibenz[*b*,*f*]azocine ring system (**3**) by ring expansion of a cycloheptatriene (**1**). This method complements the two recently reported syntheses[1,2] of the parent azocine ring. When azide **1a** is photolyzed in methylene chloride solution, nitrogen is smoothly evolved and two isomers are formed. The major product is imine **2a** (58%), formed by

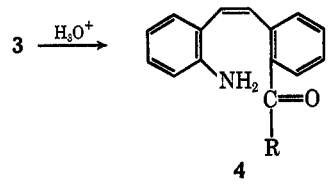


a, R = phenyl
b, R = hydrogen
c, R = 1-naphthyl

phenyl migration to the nitrene nitrogen atom (path A). This material is the same as that obtained by pyrolysis[3] of the azide. The minor isomer (24%) is 6-phenyldibenz[*b*,*f*]azocine (**3a**), formed by migration of one of the other aryl groups attached to C-5 (path B).

Photolysis of unsubstituted azide **1b** gives imine **2b** (26%) as the only identifiable product. It readily affords the corresponding ketone upon hydrolysis. Upon irradiation of the naphthyl-substituted compound **1c**, imine **2c** and azocine **3c** are obtained in yields of 46 and 14%, respectively. The similar photochemical behavior of the phenyl- and naphthyl-substituted azides contrasts markedly with their thermal decomposition.[3] The naphthyl-substituted azide undergoes ring contraction exclusively to 9-(1-naphthyl)anthracene, whereas the phenyl-substituted azide yields mainly imine **2a** along with a small amount of 9-phenylanthracene. No anthracenes were detected in any of the photolysis experiments, nor were the azocines formed in the thermal decomposition.

While the spectral properties of the two azocines **3a** and **3c** agree with the ring structures, they do not define the molecules unambiguously (see Experimental Section). Supporting chemical evidence was obtained by hydrolysis of the azocines to the expected amino ketones **4a** and **4c**.

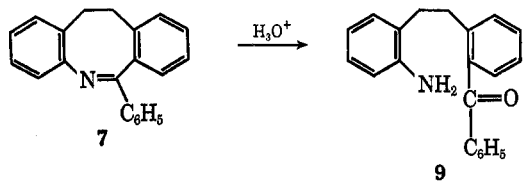


Conversion of compound **3a** to its dianion with potassium and subsequent protonation with water also provided evidence for the azocine structure. When 1 molar equiv of the azocine **3a** was allowed to react with 2 atomic equiv of potassium, amine **6** (45%) and unchanged starting material were isolated. When the ratio of potassium to azocine **3a** was 3:1, two new products were produced in addition to amine **6** (45%). Dihydroazocine **7** was obtained in 8% and tetrahydroazocine **8** in 10% yield (Scheme I).

The structure of compound **6** is supported by its nmr spectrum, which has the correct ratio of aromatic, aliphatic, and amine protons (13:3:1) and an ABX pattern for the aliphatic protons (see Experimental Section).

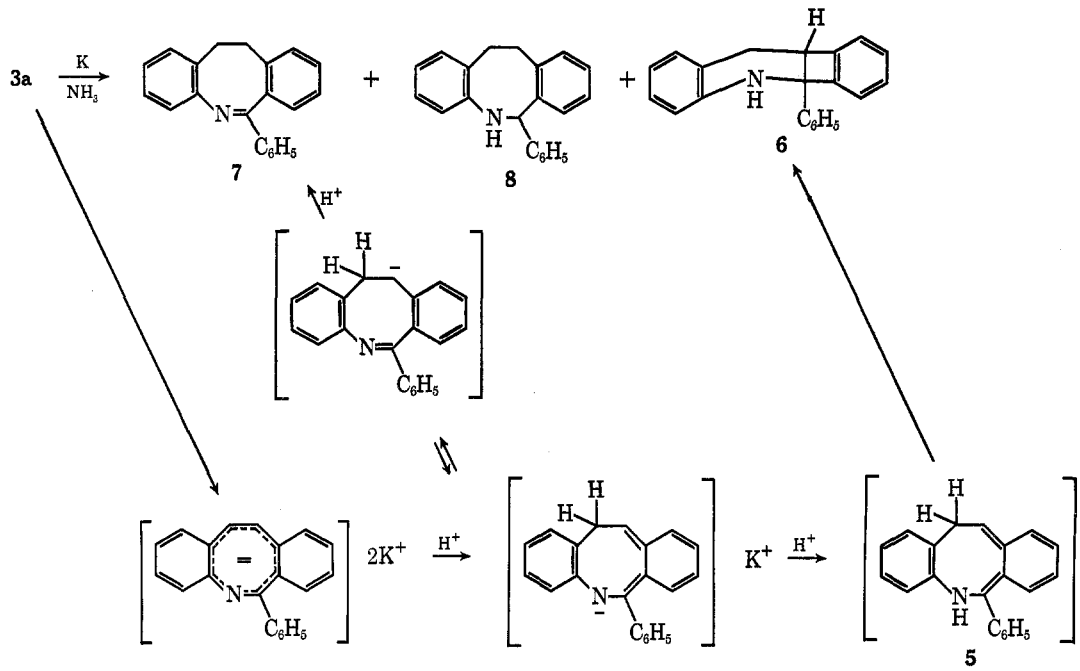
Formation of amine **6** can be explained by stepwise protonation of the dianion on carbon, then on nitrogen to give intermediate **5**, which would be expected to aromatize by valence isomerization to the observed product. Valence isomerizations of this type are well established in cyclooctatetraene reactions. The bicyclic system formed here is noteworthy when compared with the reduction products obtained by Paquette, *et al.*,[4] from the simple azocine ring; only isomeric monocyclic dihydroazocines were produced.

The structure of dihydroazocine **7** is in agreement with its spectral properties (absence of NH) and its hydrolysis to amino ketone **9**. Formation of **7** is readily explained by double protonation of the dianion on carbon. The tetrahydroazocine **8**, whose structure is proposed on the basis of its spectral properties (see Experimental Section), probably forms during the protonation step *via* anion interchange.



(1) L. A. Paquette and T. Kakihana, *J. Amer. Chem. Soc.*, **90**, 3897 (1968).
(2) J. A. Elix, W. S. Wilson, and R. N. Warrener, *Tetrahedron Lett.*, 1837 1970).
(3) J. J. Looker, *J. Org. Chem.*, **36**, 1045 (1971).
(4) L. A. Paquette, T. Kakihana, and J. F. Hansen, *Tetrahedron Lett.*, 529 (1970).

SCHEME I



Experimental Section[5]

Photolysis of 5-Phenyl-5-azido-5*H*-dibenzo[*a*,*d*]cycloheptene (1a).—A solution of 8.15 g (0.026 mol) of azide[3] **1a** in 1 l. of methylene chloride was treated with a stream of dry nitrogen passed through a gas dispersion tube for 15 min and irradiated for 6 hr with a 450-W Hanovia lamp through a Corex filter. The solvent was removed, the residue dissolved in 60 ml of ligroin (bp 63–75°), and the insoluble material (0.13 g) removed by filtration. The filtrate was concentrated to 20 ml and left for 3 hr. The solid that separated was collected and recrystallized from methylcyclohexane, 3.75 g, mp 122–123°. This material has spectral properties which are identical with those of imine **2a**, obtained by pyrolysis[3] of azide **1a**.

The filtrate was chromatographed on Florisil. Benzene–ligroin (1:1) eluted 0.40 g (5%) of azide **1a** followed by 6-phenyldibenz[*b*,*f*]azocine (**3a**), which slowly crystallized from ligroin, mp 94–95°. Methylene chloride eluted additional imine **2a**, 0.50 g (total yield 4.25 g, 58%).

Azocine **3a** was best purified by precipitation of the hydrochloride salt from ether. This salt was suspended in ether and stirred with aqueous sodium bicarbonate until it disappeared. Concentration of the dried ether layer gave 1.75 g (24%) of azocine **3a**, mp 117–119°. When the form melting at 94–95° was dissolved in ethanol and seeded with the higher melting form, it melted at 118–119°: uv max (EtOH) 236 nm (log ϵ 4.40), 328 (3.30); ir (KBr) 1630 cm^{-1} (C=N); nmr ($CDCl_3$) τ 2.17–2.35 (m, 2, aromatic), 2.5–2.9 (m, 11, aromatic), 3.17 (s, 2, olefinic); mass spectrum *m*/*e* 281.

Anal. Calcd for $C_{21}H_{15}N$: C, 89.6; H, 5.4; N, 5.0. Found: C, 89.4; H, 5.5; N, 5.0.

Hydrolysis of 6-Phenyldibenz[*b*,*f*]azocine (3a).—A mixture of 1.2 g (0.0043 mol) of azocine **3a**, 15 ml of 1,2-dimethoxyethane, and 1 ml of 18% hydrochloric acid was heated at reflux for 45 min and concentrated. The residue was treated with aqueous sodium bicarbonate and the organic material extracted into benzene. The solution was chromatographed on Florisil. Benzene eluted 0.40 g (33%) of unchanged starting material. Ethyl acetate gave an oil which crystallized from ethanol giving 0.50 g (39%) of amino ketone **4a**: mp 91–92°; ir (KBr) 1640 (C=O), 1620 (C=C), 3250 and 3500 cm^{-1} (NH_2); nmr ($CDCl_3$) τ 6.38 (s, 2, NH_2) (exchanges with D_2O), 2.0–3.6 (m, 15, aromatic and olefinic); mass spectrum *m*/*e* 200.

Anal. Calcd for $C_{21}H_{17}NO$: C, 84.3; H, 5.7; N, 4.7. Found: C, 84.1; H, 5.9; N, 4.9.

(5) The various spectra were recorded on Varian Associates Model T-60 (nmr; compound **6** was recorded on a Bruker Model B-90C) with TMS, Perkin-Elmer Model 137 (ir), and Perkin-Elmer Model 202 (uv) instruments. Melting points are uncorrected.

Photolysis of 5-Azido-5*H*-dibenzo[*a*,*d*]cycloheptene (1b).—A solution of 8.0 g (0.034 mol) of azide[3] **1b** in 1 l. of methylene chloride was irradiated in the same manner as azide **1a**. The residue was dissolved in 60 ml of 1,2-dimethoxyethane and left overnight. The yellow solid was collected, 1.5 g, mp 165–170°. All attempts to purify this material, reduce it with hydrogen or potassium in liquid ammonia, or hydrolyze it with acid were unsuccessful. It has only aromatic and/or olefinic protons (nmr CF_3CO_2H) and a molecular weight of 205 (mass spectrum). The filtrate was treated with hydrogen chloride and the precipitate collected, mp 150–170° dec. When heated in water the solid gave 2.5 g (36%) of 5*H*-dibenzo[*a*,*d*]cyclohepten-5-one, mp 87–88° (mixture melting point not depressed).

Photolysis of 5-(1-Naphthyl)-5-azido-5*H*-dibenzo[*a*,*d*]cycloheptene (1c).—Photolysis of 8.0 g (0.022 mol) of azide[3] **1c** as described for azide **1a** left an oil which, upon dissolving in 140 ml of ethanol, gave 3.35 g (46%) of imine **2c**: mp 168–169°; ir (KBr) 1610 and 1620 cm^{-1} (C=C and C=N); nmr ($CDCl_3$) τ 2.0–4.2 (aromatic and olefinic); mass spectrum *m*/*e* 331.

Anal. Calcd for $C_{25}H_{17}N$: C, 90.5; H, 5.2; N, 4.2. Found: C, 90.6; H, 5.6; N, 4.3.

When 1 g of this imine was allowed to stand 15 min in a mixture of 20 ml of 1,2-dimethoxyethane and 1 ml of 18% HCl, 0.50 g (81%) of 5*H*-dibenzo[*a*,*d*]cyclohepten-5-one was obtained from the oil left upon removal of the solvent.

The ethanol filtrate from isolation of imine **2c** was concentrated and chromatographed on Florisil. Elution with benzene–ligroin (1:9) gave 0.45 g (6%) of azide **1c**. Ethyl acetate eluted a mixture of imine **2c** and azocine **3c** which could not be separated by chromatography. This solid was dissolved in 100 ml of 1,2-dimethoxyethane containing 2 ml of concentrated hydrochloric acid and left for 30 min. The solid that separated was collected, suspended in a mixture of benzene and aqueous sodium bicarbonate, and stirred until the solid disappeared. The benzene solution, upon drying and concentration, gave solid azocine **3c** which was recrystallized from ethanol: 0.90 g (14%); mp 157–158°; uv max (EtOH) 216 nm (log ϵ 4.86), 290 (3.95); ir (KBr) 1640 cm^{-1} (C=N); nmr ($CDCl_3$) τ 0.93–1.13 (m, 1, aromatic), 2.0–3.1 (m, 16, aromatic); mass spectrum *m*/*e* 331.

Anal. Calcd for $C_{25}H_{17}N$: C, 90.5; H, 5.2; N, 4.2. Found: C, 90.2; H, 5.2; N, 4.4.

Hydrolysis of 6-(1-Naphthyl)dibenz[*b*,*f*]azocine (3c).—A mixture of 0.50 g (0.0015 mol) of azocine **3c**, 50 ml of 1,2-dimethoxyethane, and 1 ml of 18% hydrochloric acid was heated at reflux for 2 hr. The solvent was removed, and the residue was treated with saturated sodium bicarbonate and extracted with benzene. The extract was chromatographed on Florisil. Elution with benzene gave 0.10 g (20%) of unchanged azocine. A mixture of 10% ethyl acetate in benzene gave 0.36 g (73%) of amino ketone

4c, which would not crystallize: ir (neat) 3300 (NH_2), 3400 (NH_2), 1650 (C=O), and 1630 cm^{-1} (C=C); nmr ($CDCl_3$) τ 1.4–3.6 (m, 17, aromatic and olefinic), 2.52 (s, 2, NH_2, exchanges with D_2O); mass spectrum *m/e* 349. The oil was dissolved in ether and treated with hydrogen chloride gas to prepare the hydrochloride salt, mp 182° dec (depends upon rate of heating).

Anal. Calcd for $C_{25}H_{20}ClNO$: C, 77.8; H, 5.2; N, 3.6; Cl, 9.2. Found: C, 77.5; H, 5.3; N, 3.7; Cl, 8.9.

Reduction of 6-Phenyldibenz[*b*,*f*]azocine. A.—To 50 ml of liquid ammonia at −78° under nitrogen was added 2.0 g (0.0071 mol) of azocine **3a**. The mixture was stirred while 0.78 g (0.020 g-atom) of potassium was added in small pieces over a 15-min period. The dark suspension was stirred 15 min longer and the solvent was distilled using a water bath at room temperature. The residue was suspended in 100 ml of ether and water was added dropwise. The ether layer was washed well with water and concentrated, and the resulting oil was chromatographed on Florisil. Benzene eluted three solids and ethyl acetate, a residual oil.

The first solid was recrystallized from ethanol and gave 0.90 g (45%) of amine **6**: mp 116–117°; ir (KBr) 3400 cm^{-1} (NH); nmr ($CDCl_3$) τ 2.7–3.5 (m, 13, aromatic), 5.6 (broad s, 1, exchangeable with D_2O, NH), 6.48 H_A, 6.82 H_B, 6.10 H_X (3, aliphatic H, ABX system, J_{AB} = 15.9, J_{AX} = 8.0, J_{BX} = 1.5 Hz, actually on the border between ABX and ABC); mass spectrum *m/e* 283.

Anal. Calcd for $C_{21}H_{17}N$: C, 89.0; H, 6.1; N, 4.9. Found: C, 89.2; H, 6.1; N, 4.7.

The second solid was recrystallized from ethanol and gave 0.20 g (10%) of tetrahydroazocine **8**: mp 105–106°; ir (KBr) 3400 cm^{-1} (NH); nmr ($CDCl_3$) τ 6.2–7.0 (m, 5, NH and ethane protons; one is exchangeable with D_2O), 4.18 (s, 1, methine), 2.4–3.0 (m, 14, aromatic); mass spectrum *m/e* 385.

Anal. Calcd for $C_{21}H_{19}N$: C, 88.4; H, 6.7; N, 4.9. Found: C, 88.4; H, 6.7; N, 4.7.

The third solid was recrystallized from ethanol and afforded 0.15 g (8%) of dihydroazocine **7**: mp 94–95°; ir (KBr) 1620 cm^{-1} (C=N); nmr ($CDCl_3$) τ 6.5-7.5 (m, 4, aliphatic methylenes), 2.1–3.3 (m, 13, aromatic); mass spectrum *m/e* 283.

Anal. Calcd for $C_{21}H_{17}N$: C, 89.0; H, 6.1; N, 4.9. Found: C, 89.0; H, 6.3; N, 4.8.

B.—To 50 ml of liquid ammonia at −78° under nitrogen was added 0.70 g (0.0025 mol) of azocine **3a** followed by 0.196 g (0.0050 g-atom) of potassium in small pieces over 10 min with stirring. After stirring had been continued for 15 min, the solvent was removed by a water bath. The solid was treated with 50 ml of ether, and water was carefully added dropwise. The ether layer was separated, washed well with water, and concentrated. The oil was dissolved in benzene and chromatographed on Florisil. The first fraction contained 0.32 g (45%) of amine **6**, mp 115–116°, after recrystallization from ethanol. The second fraction gave 0.15 g (14%) of starting material, mp 116–118°. The nmr spectra of the crude materials showed no trace of either the dihydroazocine **7** or the tetrahydro compound **8**.

Hydrolysis of 11,12-Dihydro-6-phenyldibenz[*b*,*f*]azocine (7).—A solution of 0.10 g (0.00035 mol) of imine **7** in 20 ml of 1,2-dimethoxyethane was treated with 1 ml of water and 1 ml of concentrated hydrochloric acid and heated at reflux for 30 min. The solvent was removed in a stream of nitrogen and the residue treated with benzene and aqueous sodium bicarbonate solution. The organic layer was chromatographed on Florisil. The amino ketone **9** was eluted with 10% ethyl acetate–benzene and obtained as a noncrystallizable oil: ir (KBr) 3400 and 3500 (NH_2) and 1660 cm^{-1} (C=O); nmr ($CDCl_3$) τ 7.06 (s, 4, aliphatic), 6.09 (s, 2, NH_2, exchanges with D_2O), 2.0–3.4 (m, 13, aromatic); mass spectrum *m/e* 301.

The oil was dissolved in ether, and hydrogen chloride was passed in until separation of the hydrochloride was complete. The oil crystallized and was collected: 0.080 g (68%); mp 165° dec; ir (KBr) 2850 (NH_3^+) and 1660 cm^{-1} (C=O).

Anal. Calcd for $C_{21}H_{20}ClNO$: C, 74.6; H, 6.0; Cl, 10.5; N, 4.1. Found: C, 74.3; H, 6.0; Cl, 10.2; N, 4.0.

Registry No.—**2a**, 27971-66-0; **2c**, 30319-08-5; **3a**, 30319-09-6; **3c**, 30319-10-9; **4a**, 30319-11-0; **4c**, 30319-12-1; **4c** HCl, 30319-13-2; **6**, 30319-14-3; **7**, 30319-15-4; **8**, 30319-16-5; **9**, 19947-17-2; **9** HCl, 19947-18-3.

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The Synthesis and Metalation of Some Phenalenothiophenes and a Fused Benzo Derivative

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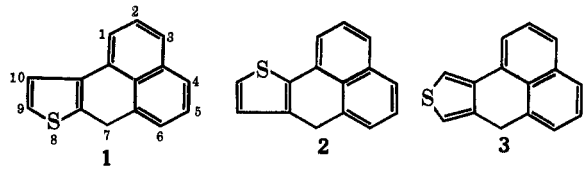
Three phenalenothiophenes (**1**, **2**, and **3**) have been synthesized by unambiguous methods from the corresponding phenalenothiophenones **4**, **5**, and **6**. Reaction of 4,9-dioxo-4,9-dihydronaphtho[2,3-*b*]thiophene with glycerol, sulfuric acid, and iron leads to the formation of a mixture of **4** and **5** in contrast to the claim in the literature[4] that only **4** was produced in this reaction. Fusion of 2-(1-naphthoyl)thiophene with an aluminum chloride–sodium chloride–potassium chloride mixture has been shown to produce **4** together with a very small amount of a high-melting dimeric product in contrast to the claim[4] that **5** was the product of this reaction. Metalation of **2** and **3** was shown to occur exclusively at the methylene bridge, the site of metalation being identified by methylation or by deuterium exchange. A benzo derivative of **3**, namely 4*H*-benzo[1,10]phenanthro[3,4-*c*]-thiophene, was synthesized and likewise shown to undergo metalation exclusively at the methylene bridge.

Three isomeric 7*H*-phenalenothiophenes[2] are possible, *viz.* 7*H*-phenaleno[2,1-*b*]thiophene (**1**), 7*H*-phenaleno[1,2-*b*]thiophene (**2**), and 7*H*-phenaleno[1,2-*c*]-thiophene (**3**). The existence of any of these has not been reported in the literature. This paper describes the synthesis of these compounds and discusses their metalative reactions with *n*-butyllithium.



A logical synthetic route to **1**, **2**, and **3** appeared to lie in reducing the corresponding 7*H*-phenalenothiophenones **4**, **5**, and **6**. The literature contains a few references to the preparation of **4** and **5**. Scholl[3] reported the synthesis of a phenalenothiophenone, mp 210°, in low yield, formulated as **4**, by dehydrogenation of

(1) Abstracted from the M.S. Thesis of G. E. Paulovicks, West Virginia University, 1970.

(2) We are indebted to Dr. Kurt L. Loening of Chemical Abstracts Service for information pertaining to the naming of this system.

(3) R. Scholl and C. Seer, *Justus Liebigs Ann. Chem.*, **394**, 111 (1912).