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Polycyclic N-Hetero Compounds. XII.[1] Reactions of Dihydroxynaphthalenes with Formamide or Trisformylaminomethane

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Syntheses of tetraazatriphenylenes (II, VI, VIII) from dihydroxynaphthalenes (I, V, VII) with formamide or trisformylaminomethane (Chart 1) are described. Reaction of ethyl 1,3-hydroxy-2-naphthoate (III) with trisformylaminomethane afforded II and N^2-(1,3-dihydroxy-2-naphthoyl)formamidine (IV). Ammonolysis of III with formamidine acetate gave IV.

In the previous paper,[3] it was reported that reactions of 1,3-cyclohexanedione and its dimer with formamide or trisformylaminomethane afforded some fused pyrimidines. The present paper describes the similar reactions for dihydroxynaphthalenes (tetralinediones) to obtain new type of tetraazatriphenylenes.

As shown in Chart 1, 1,3-dihydroxynaphthalene (tetraline-1,3-dione) (I), ethyl 1,3-dihydroxy-2-naphthoate (ethyl 1,3-dioxo-2-tetralinecarboxylate) (III), 2,3-dihydroxynaphthalene (tetraline-2,3-dione) (V), and 1,4-dihydroxynaphthalene (tetraline-1,4-dione) (VII) were used as starting materials.

The reaction of I with large excess of formamide under dry ammonia stream at 160—170° gave expectedly 1,3,5,7-tetraazatriphenylene (II) as colorless needles. The mass spectrum of II showed the parent peak at *m/e* 232 and fragments eliminated four hydrogen cyanide successively apeared at *m/e* 205, 178, 151, 124 as remarkable peaks. The nuclear magnetic resonance (NMR) spectral data of II are shown in Table I. Perkampus and Bluhm[4] reported that C^5-proton of 2,4-diazaphenanthrene resonanced at lower field *ca.* 0.5 ppm than C_5-proton of 1,3-diazaphenanthrene by the paramagnetic effect of nitrogen of 4-position in NMR. The lower field shift of C_4- and C_{12}-protons of II seems to be due to polycyclic aromatic system and additional paramagnetic effect of 1- and 5-nitrogen atoms. The ultraviolet (UV) spectrum of II showed complex curve above 300 nm. As the yield of II was low in the above method, condensation of I with trisformylaminomethane was attempted according to pyrimidine synthesis with carbonyl compounds and trisformylaminomethane by Bredereck, *et al.*[5] The yield of II in this method was better than the previous method, and the products from the above two method were identical with mixed mp, infrared (IR), NMR, and thin-layer chromatography (TLC).

Reaction of III with trisformylaminomethane afforded II (identical with the above product by mixed mp, IR, NMR, and TLC) and N^2-(1,3-dihydro-2-naphthoyl)formamidine(IV). Isolation of expected 4-hydroxy-1,3,5,7-tetraazatriphenylene failed. Formation of II suggested that at first I was formed by hydrolysis and decarboxylation of III and then condensed

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[1] Part XI: T. Koyama, T. Hirota, C. Basho, Y. Watanabe, Y. Kitauchi, Y. Satoh, S. Ohmori, and M. Yamato, *Chem. Pharm. Bull.* (Tokyo), 24, 1459 (1976).

[2] Location: *1-1, Tsushima-naka 1-chome, Okayama, 700, Japan.*

[3] T. Koyama, S. Fukuoka, T. Hirota, J. Maeyama, S. Ohmori, and M. Yamato, *Chem. Pharm. Bull.* (Tokyo), 24, 591 (1976).

[4] H.H. Perkampus and T. Bluhm, *Z. Naturforschung*, 27a, 310 (1960).

[5] H. Bredereck, R. Gompper, and B. Geiger, *Chem. Ber.*, 93, 1402 (1960).

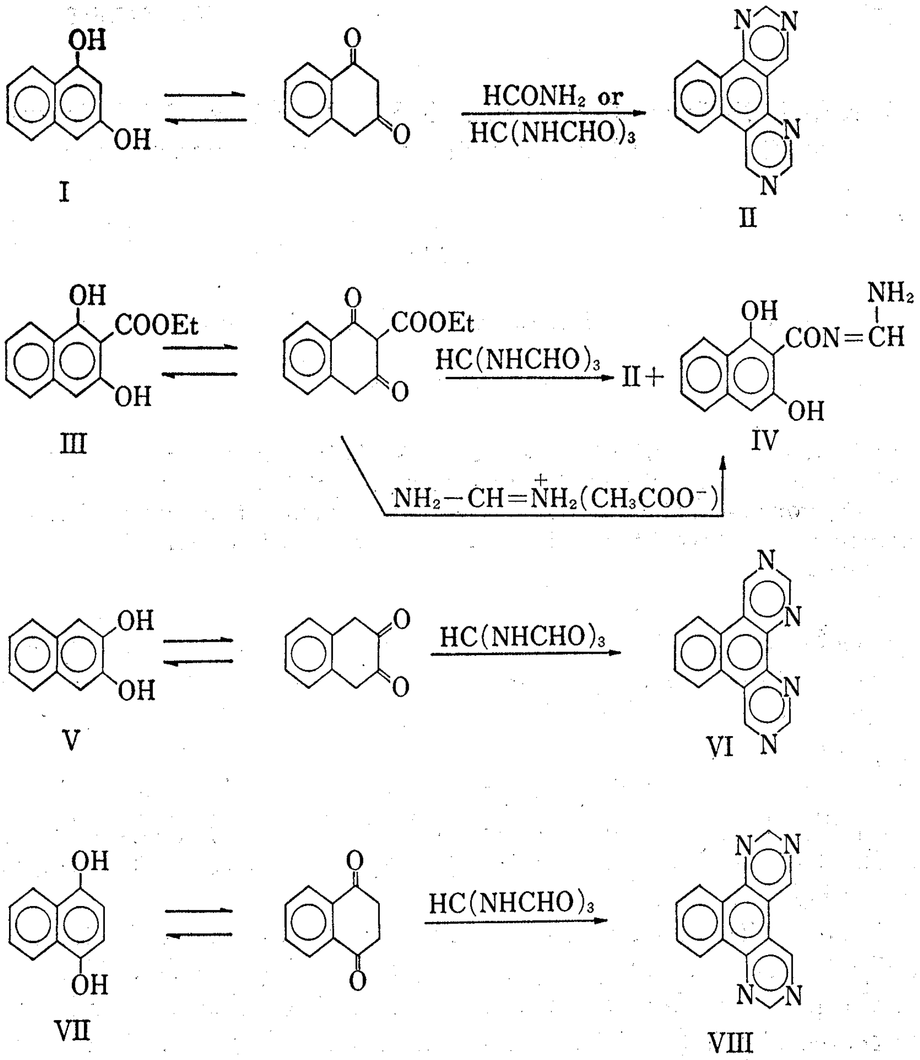
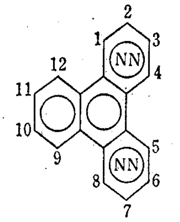


Chart 1

Table I. NMR Spectral Data of Tetraazatriphenylenes



Comps.	Protons 1	2	3	4	5	6	7	8	9	10	11	12
II	N	9.58 or 9.68	N	10.54	N	9.58 or 9.68	N	10.09	8.70	7.90	7.90	9.36
VI	10.12	N	9.67	N	N	9.67	N	10.12	8.72	7.85	7.85	8.72
VIII	N	9.58	N	10.05	10.05	N	9.58	N	9.32	7.98	7.98	9.32

All values are in δ units for $CDCl_3$ solution at 90 MHz (Hitachi Model R-22 spectrometer with tetramethylsilane as an internal standard.

All 1 to 8 protons are singlet and all 9 to 12 protons are multiplet.

with trisformylaminomethane to II. Bredereck, *et al.*,[6] reported that thermal decomposition of trisformylaminomethane gave formamidine, *etc.* Perhaps IV was yielded by ammonolysis of ester III with formamidine formed by thermal decomposition of trisformylaminomethane. Sure enough IV was obtained with good yield by treating III with formamidine acetate in the presence of precipitated calcium carbonate. The IR spectrum of IV in KBr disk showed O–H and N–H bands at 3450, 3320, 3270, and 3150 cm^{-1} and C=O band at 1640 cm^{-1}. The mass spectrum of IV showed the parent peak at m/e 230. The NMR spectrum of IV exhibited five aromatic protons at δ 7.20—8.15, four D_2O exchangeable protons at lower field, and vinyl proton between two nitrogen atoms at δ 8.70 as broad doublet doublet (J=15 Hz, 10 Hz) which was changed to broad singlet by few drops of D_2O.

Condensation of V with trisformylaminomethane afforded 1,3,10,12-tetraazatriphenylene (VI) as pale yellow needles. The mass spectrum of VI is similar to that of II and NMR spectral data of VI is shown in Table I.

Condensation of VII with trisformylaminomethane gave similarly 1,3,6,8-tetraazatriphenylene (VIII) as colorless feathers. Analytical data supported the structure of VIII.

Experimental

Melting points are uncorrected. NMR spectra were taken on a Hitachi Model R-22 spectrometer (90 MHz) with tetramethylsilane as an internal standard. Mass spectra were taken on a Shimadzu-LKB 9000 spectrometer with a direct inlet system. IR spectra were recorded with a DS-301 (JASCO) spectrometer in KBr disk. UV spectra were taken on a Hitachi EPS-2 spectrophotometer in 99% EtOH.

Reaction of 1,3-Dihydroxynaphthalene (I) with $HCONH_2$——To 20 ml of $HCONH_2$ heated at 140° for 0.5 hr under dry ammonia stream, 2.4 g of I in 20 ml of $HCONH_2$ was added dropwise during *ca.* 0.5 hr. After the addition was completed, the solution was heated at 160° for 10 hr. The resulting black solid mass in the reaction mixture was filtered off and $HCONH_2$ in the mother liquid was distilled off *in vacuo*. The dark brown viscous residue was suspended with H_2O and extracted with benzene, ether, and $CHCl_3$ successively each 10 hr. The organic layer was washed with sat. NaCl solution, dried over Na_2SO_4, and evaporated independently. The benzene and ether extracts were combined (same spots on TLC) and chromatographed over alumina with ether. After the elution of ether, the ether–$CHCl_3$ (2: 1) eluate was recrystallized from EtOH to 25 mg of 1,3,5,7-tetraazatriphenylene (II) as colorless needles, mp 243—245°. The $CHCl_3$ extract was fractionated with preparative TLC (Merck Kieselguhr PF_{254}, $CHCl_3$: ether=9: 1). The fraction of *Rf* value *ca.*0.8 was collected and recrystallized from EtOH to 10 mg of II as colorless needles, mp 243—245°, combined yield 35 mg (1%). *Anal.* Calcd. for $C_{14}H_8N_4$: C, 72.40; H, 3.47; N, 24.13. Found: C, 72.69; H, 3.52; N, 23.96. Mass Spectrum m/e: 232 (M^+), 205 (M^+-HCN), 178 (M^+-2HCN), 151 (M^+-3HCN), 124 (M^+-4HCN). The NMR spectral data are shown in Table I. UV λ_{max}^{EtOH} nm (log ε): 209 (4.35), 253 (4.60), 274 (4.21), 307 (3.67), 322 (3.54), 337 (3.41).

Reaction of I with $HC(NHCHO)_3$——A mixture of 2.40 g of I, 13.1 g of $HC(NHCHO)_3$, 7 ml of $HCONH_2$, and 1 g of *p*-toluenesulfonic acid was heated at 160—170° for 5 hr under stirring. After cooled, the reaction mixture was made alkaline with NH_4OH and extracted with $CHCl_3$. The $CHCl_3$ layer was washed with sat. NaCl solution, dried over Na_2SO_4, and evaporated. The residue was recrystallized from EtOH to 240 mg (7%) of II as colorless needles, mp 243—245°, identical with the specimen prepared from the above method with $HCONH_2$ (mixed mp, IR, NMR, and TLC).

Reaction of Ethyl 1,3-Dihydroxy-2-naphthoate (III) with $HC(NHCHO)_3$——A mixture of 3.48 g of III, 13.1 g of $HC(NHCHO)_3$, 7 ml of $HCONH_2$, and 1 g of *p*-toluenesulfonic acid was heated at 160—170° for 4 hr under stirring. After cooled, the reaction mixture was made alkaline with NH_4OH and extracted with $CHCl_3$ for 2 days. The $CHCl_3$ extract was washed with sat. NaCl solution, dried over Na_2SO_4, and evaporated. The residue was recrystallized from EtOH to 125 mg (3.6%) of II as colorless needles, mp 243—245°, identical with the above product (mixed mp, IR, NMR, and TLC). Condensing the mother liquid to *ca.* one-fifth, yellow needles were deposited. The crystals were recrystallized from benzene–EtOH (7: 1) to 210 mg (6.1%) of N^2-(1,3-dihydroxy-2-naphthoyl)formamidine (IV) as yellow feathers, mp above 300°, turn to red at *ca.* 240°. *Anal.* Calcd. for $C_{12}H_{10}O_3N_2$: C, 62.60; H, 4.38; N, 12.17. Found: C, 62.64; H, 4.36; N, 12.37. Mass Spectrum m/e: 230 (M^+). IR ν_{max}^{KBr} cm^{-1}: 3450, 3320, 3270, 3150 (O-H, N-H), 1640 (C=O). NMR (Me_2SO-d_6, δ): 7.40 (1H, singlet, 4-H), 7.25, 7.56 (each 1H, broad triplet, J=8 Hz, 6-H, 7-H), 7.94, 8.10 (each 1H, broad doublet, J=8 Hz, 5-H, 8-H), 8.70 (1H, broad double doublet, J=15 Hz, 10 Hz, N=CH–N, changed to broad

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[6] H. Bredereck, R. Gompper, H.G.V. Schuh, and G. Theilig, "Newer Methods of Preparative Organic Chemistry" Vol. III, ed. by W. Foerst, Academic Press Inc., New York and London, 1964, p. 241.

singlet with a few drops of D_2O), 8.24, 9.30, 10.55, 11.40 (each 1H, broad, 2-OH, NH_2, disappeared with D_2O exchange). UV λ_{max}^{EtOH} nm (log ε): 215 (4.50), 250 (4.64), 260 (4.58), 317 (4.18), 327 (4.21), 368 (4.18), 380 (4.27), 398 (4.05).

Reaction of III with Formamidine Acetate——To a solution of 1.16 g of III in 100 ml of dioxane, 5.3 g of formamidine acetate in H_2O as little as possible and 6 g of fine powdered $CaCO_3$ were added. The mixture was stirred at room temperature for 5 days and the insoluble solid was filtered off. The mother liquor was evaporated to dryness under reduced pressure at 35—40°. The resulting mass was digested with cyclohexane–*n*-hexane (5: 1) to recover unreactive III (750 mg). The insoluble residue was dissolved in $CHCl_3$–ether (1: 1), treated with a little silica gel, and the solvent was evaporated. The residue was recrystallized from benzene–EtOH (7: 1) to 70 mg (18%) of IV as yellow needles, mp above 300°, identical with the above product (IR, NMR, and TLC).

Reaction of 2,3-Dihydroxynaphthalene (V) with $HC(NHCHO)_3$——A mixture of 5.3 g of V, 29 g of $HC(NHCHO)_3$, 14 ml of $HCONH_2$, and 1.5 g of *p*-toluenesulfonic acid was heated at 160—170° for 6.5 hr under stirring. After allowed to stand overnight, the reaction mixture was made alkaline with NaOH, and extracted with $CHCl_3$. The $CHCl_3$ layer was washed with H_2O, dried over Na_2SO_4, and evaporated. The benzene-insoluble fraction of the residue at room temperature was recrystallized from CH_2Cl_2 to light violet plates which were observed four spots on TLC with a main spot of *Rf* value *ca.* 0.5 (Wako gel B5-FM, acetone: CH_2Cl_2: EtOH = 5: 4: 1). A small part of the crystals was fractionated with preparative TLC (Merck, Kieselguhr PF_{254}, acetone: CH_2Cl_2: EtOH = 5: 11: 1). The fraction of *Rf* value *ca.* 0.6 which had dark blue fluorescence with PAN-UV lamp was collected and recrystallized from CH_2Cl_2 to 34 mg of 1,3,10,12-tetraazatriphenylene (VI) as pale yellow needles, mp 278—280°. The EtOH-insoluble fraction of the residual part of the crystals was recrystallized from $CHCl_3$–benzene (1: 1), inoculated with the above crystals VI and allowed to stand 3 days, to give 391 mg of VI as pale yellow needles, mp 277—280°, total yield 425 mg (5.5%). *Anal.* Calcd. for $C_{14}H_8N_4$: C, 72.40; H, 3.47; N, 24.13. Found: C, 72.46; H, 3.40; N, 24.28. Mass Spectrum *m/e*: 232 (M^+), 205 (M^+-HCN), 178 (M^+-2HCN), 151 (M^+-3HCN), 124 (M^+-4HCN). The NMR spectral data of VI are shown in Table I. UV λ_{max}^{EtOH} nm (log ε): 220 (4.18), 253 (4.18), 260 (4.16), 325 (3.62).

Reaction of 1,4-Dihydroxynaphthalene (VII) with $HC(NHCHO)_3$——A mixture of 2.4 g of VII, 13.1 g of $HC(NHCHO)_3$, 7 ml of $HCONH_2$, and 1 g of *p*-toluenesulfonic acid was heated at 160—170° for 8.5 hr under stirring. After allowed to stand overnight, the reaction mixture was made alkaline with NaOH and extracted with benzene for 24 hr. The benzene extract was dried over Na_2SO_4 and evaporated. The residue was recrystallized from EtOH to 36 mg (1%) of 1,3,6,8-tetraazatriphenylene (VIII) as colorless feathers, mp 236—238°. *Anal.* Calcd. for $C_{14}H_8N_4$: C, 72.40; H, 3.47; N, 24.13. Found: C, 72.60; H, 3.39; N, 24.25. Mass Spectrum *m/e*: 232 (M^+), 205 (M^+-HCN), 178 (M^+-2HCN), 151 (M^+-3HCN), 124 (M^+-4HCN). UV λ_{max}^{EtOH} nm (log ε): 250 (4.45), 280 (3.80), 324 (3.47), 338 (3.55).

The low yields of above reactions were due to resinifing of the reaction mixtures by heating and troublesome isolating of the pure samples.

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