cooled, and neutralized with aq. 2 N HCl solution. The precipitate thereby formed was extracted with chloro form. The chloroform solution was dried over anhyd. Na_2SO_4 and evaporated to give crystals which were recrystallized from methanol affording 62 mg of VI.

Reaction of II with Benzoyl Chloride——i) To a mixture of 850 mg (5 mmol) of II and 690 mg (5 mmol) of powdered K_2CO_3 in 5 ml of chloroform, was added 840 mg (6 mmol) of benzoyl chloride dropwise during 15 minutes. The temperature of the reaction mixture was maintained below −5°. After stirred for 1 hr at room temperature, the reaction mixture was poured into cold water and the whole was extracted with chloroform. The chloroform solution was washed with water, dried over anhyd. Na_2SO_4. On removing chloroform, the residue was recrystallized from methanol to afford 240 mg of colorless needles (VII), mp 164—165° (dec.), *Anal.* Calcd. for $C_{14}H_{14}N_2O_4$: C, 61.31; H, 5.15; N, 10.21; Found: C, 61.29; H, 5.17; N, 10.28; UV. λ_{max}^{EtOH} nm (ε): 232 (18500), 297.5 (49600), λ_{min}^{EtOH} nm (ε): 247 (14900). IR(KBr) cm^{-1}: 3220, 1780, 1650—1670 (split), 1620 (–CONHOCO), δ_{CH} 1043—1060 (split), 993, 915. ii) To a solution of 850 mg (5 mmol) of II in 2 ml of pyridine, was added dropwise during 15 minutes 840 mg (6 mmol) of benzoyl chloride. The temperature of the reaction mixture was maintained below −5°. After stirring for 1 hr room temperature, the whole was further allowed to stand overnight. The reaction mixture was poured into ice-water and extracted with chloroform. The chloroform solution was washed with aq. 5% $NaHCO_3$ solution and then with water, dried over Na_2SO_4. After removal of chloroform, the residual oil was chromatographed on alumina column, The fractions eluted with chloroform afford a pale yellow solid, which was recrystallized from methanol giving 175 mg of colorless needles (VIII), mp 130—131° (dec.), *Anal.* Calcd. for $C_{14}H_{13}ClN_2O_3$: C, 57.44; H, 4.44; N, 9.57; Found: C, 57.67; H, 4.87; N, 9.17; UV. λ_{max}^{EtOH} nm (ε): 235 (7000), 312.5 (52100), 323 (sh) (49000); λ_{min}^{EtOH} nm (ε): 252.5 (5900) IR(KBr) cm^{-1}: 1770, 1252 (–O–CO–), δ_{CH} 1050, 1000, 898.

Hydrolysis of VII——A solution of VII (100 mg) in 1 ml of aq. 2 N NaOH solution was heated on a steam bath for 10 minutes. The reaction mixture was neutralized with aq. 2 N HCl solution and the whole was extracted with chloroform. The chloroform solution was dried over anhyd. Na_2SO_4 and concentrated to dryness, affording a crystalline mass. Recrystallization of this residue from methanol resulted with formation of 48 mg of colorless cubiform crystals (VI), mp 174° (dec.).

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Synthesis of Polycyclines. I. Diels-Alder Reaction of 5-Nitronaphthoquinone with Unsymmetrical Butadienes

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Diels-Alder reaction of 5-nitro-1,4-naphthoquinone (**1**) and unsymmetrical butadienes was carried out. Reaction of **1** and 2-methyl-1,3-butadiene gave 1,4,4a,9a-tetrahydro-2-methyl-5-nitro-anthraquinone (**2**) and its 3-methyl analogue (**3**) at the ratio of 9.2: 1. Reaction of **1** and 1,3-pentadiene gave 1,4,4a,9a-tetrahydro-1-methyl-8-nitroanthraquinone (**8**) and its 5-nitro analogue (**9**) at the ratio of 10: 7. Their structures have been determined by aromatization to methyl-nitroanthraquinones.

Keywords——Diels-Alder reaction; teterahydro-anthraquinone; butadiene; 1,4-naphthoquinone; aromatization

Although there are many reports on the Diels-Alder reaction of symmetrical naphthoquinones and butadienes, relatively a few has been reported on the reaction of unsymmetrical naphthoquinones and butadienes.[2)] As the basic study for the synthesis of linear polycyclines,

1) Location: *3-1 Tanabe-dori, Mizuho-ku, Nagoya 467, Japan.*
2) L.W. Butz and A.W. Rytina, "Organic Reactions," Vol. 5. ed. by R. Adams, John Wiley and Sons, Inc., New York, 1949, pp. 136—192.

we tried some Diels-Alder reaction of 5-nitro-1,4-naphthoquinone (**1**) with unsymmetrical butadienes *i.e.* 2-methyl-1,3-butadiene and 1,3-pentadiene.

Diels-Alder cyclization of **1** with 2-methyl-1,3-butadiene gave two adducts of mp 145—147° (**2**) and 141—143° (**3**). **2** and **3** gave same empirical formula and molecular ion peak at *m/e* 271 in the mass (MS) spectra. The infrared (IR) and nuclear magnetic resonance (NMR) spectra suported the structures of the expected adducts. The structural assignment of these adducts **2** and **3** were made on aromatization to anthraquinone derivatives. Air oxidation of **2** in alcoholic alkaline solution gave methyl-nitroanthraquinone (mp 266°), whose structure was verified by the obvious synthesis starting with 3-nitrophthalic anhydride (**6**). Toluoylation of **6** by the method of Chase *et al.*[3] gave 3-nitro-2-*p*-toluoylbenzoic acid

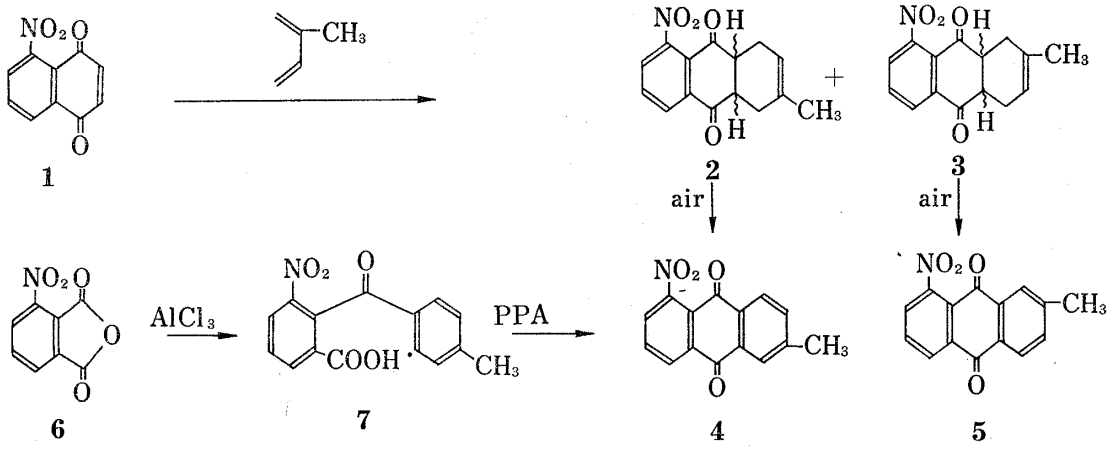

Chart 1

(**7**), which was cyclized in polyphosphoric acid (PPA) to give 2-methyl-5-nitroanthraquinone (**4**). This compound (**4**) was found to be identical with the above aromatized compound in mp, IR and NMR spectra. Thus the adduct **2** was characterized to be 1,4,4a,9a-tetrahydro-2-methyl-5-nitroanthraquinone. Another adduct **3** was then aromatized in the same way to give methyl-nitroanthraquinone (mp 240—242°) which was undoubtedly 3-methyl-5-nitroanthraquinone (**5**). Accordingly the adduct **3** must be 1,4,4a,9a-tetrahydro-3-methyl-5-nitroanthraquinone. The ratio of the production of the regioisomers 2:3 was 9.2:1.

Diels-Alder reaction of **1** with 1,3-pentadiene, a regioisomer of 2-methyl-1,3-butadiene, gave two adducts of mp 117—118° (**8**) and 111—113° (**9**). The analytical and IR and NMR spectral data were consistent with the structure of the expected tetrahydro-nitroanthraquinones. Thus it is obvious that these are regioisomer each other. In order to

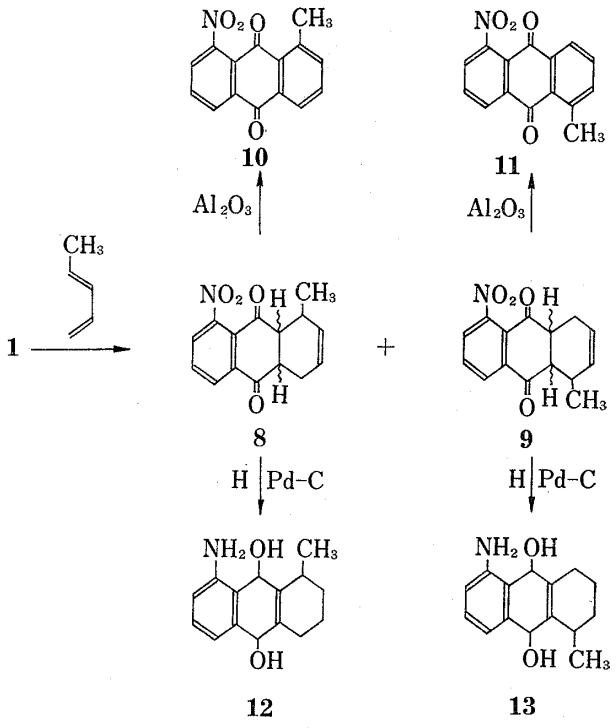

Chart 2

3) B.H. Chase and D.H. Hey, *J. Chem. Soc.*, **1952**, 553.

comfirm the structure of the regioisomer, **8** and **9** were subjected to aromatization in the same manner as for **2** and **3**. But the reaction failed to effect aromatization, giving only unidentified amorphous powder. Then alminium oxide was used for the reaction to give smoothly expected anthraquinone derivatives (**10**, **11**). 1-Methyl-8-nitroanthraquinone (**10**) has mp 258—260° which agreed well with that given by Gudzenko[4] (mp 258—259°). Similarly 1-methyl-5-nitroanthraquinone (**11**) has mp 254—255°, which agreed with that given by the same author[4] (mp 254—256°). Thus the adduct **8** was characterized to be 1,4,4a,9a-tetrahydro-1-methyl-8-nitroanthraquinone, and the adduct **9** to be 1,4,4a,9a-tetrahydro-1-methyl-5-nitroanthraquinone. The ratio of the production of the regioisomers 8: 9 was 10: 7.

When adduct **8** was catalytically hydrogenated in the presence of palladium on charcoal, 5 moles of hydrogen were absorbed to give 1-amino-5,6,7,8,9,10-hexahydro-9,10-dihydroxy-8-methylanthracene (**12**). In the similar catalytic hydrogenation, adduct **9** gave the corresponding 1-amino-5,6,7,8,9,10-hexahydro-9,10-dihydroxy-5-methylanthracene (**13**).

Experimental

Melting points were measured on a Yanagimoto melting point apparatus and uncorrected. IR spectra were taken on a Nihon Bunko IR–G spectrophotometer. NMR spectra were measured on a Jeol JNM–NH–100 spectrometer using tetramethylsilane as an internal standard. MS spectra were measured with a Hitachi M-52 Mass spectrometer.

1,4,4a,9a-Tetrahydro-2-methyl-5-nitroanthraquinone (2) and 1,4,4a,9a-Tetrahydro-3-methyl-5-nitroanthraquinone (3)——A mixture of 12.18 g of 5-nitro-1,4-naphthoquinone (**1**) and 8.18 g of 2-methyl-1,3-butadiene in 300 ml of anhyd. EtOH was stirred for 5 hr at 40°. After cooling, the crystals which appeared were filtered and recrystallized from ether to give 9.2 g (56.6%) of 1,4,4a,9a-tetrahydro-2-methyl-5-nitroanthraquinone (**2**), colorless needles, mp 145—147°. *Anal.* Calcd. for $C_{15}H_{13}NO_4$: C, 66.41; H, 4.83; N, 5.16. Found: C, 66.56; H, 4.83; N, 5.38. IR ν_{max}^{KBr} cm^{-1}: 2902 (C–H), 1698 (C=O), 1530, 1365 (NO_2). NMR-($CDCl_3$) δ: 5.41 (1H, m, –CH=), 3.48 (2H, m, >CH–CH<), 3.32 (4H, m, 2 × methylene H), 1.70 (3H, s, CH_3).

The ethereal mother liquor was condensed to give 1,4,4a,9a-tetrahydro-3-methyl-5-nitroanthraquinone (**3**) as the second crystals, colorless needles, mp 141—143°. Yield, 1.0 g (6.2%). *Anal.* Calcd. for $C_{15}H_{13}NO_4$: C, 66.41; H, 4.83; N, 5.16. Found: C, 66.29; H, 4.81; N, 5.10. IR ν_{max}^{KBr} cm^{-1}: 2867 (C–H), 1695 (C=O), 1523, 1348 (NO_2). NMR($CDCl_3$) δ: 5.43 (1H, m, =CH–), 3.48 (2H, m, >CH–CH<), 2.36 (4H, m, 2 × methylene H), 1.65 (3H, s, CH_3).

2-Methyl-5-nitroanthraquinone (4) a) Aromatization of 1,4,4a,9a-tetrahydro-2-methyl-5-nitroanthraquinone (2)——A solution of 4 g of **2** in 600 ml of alcoholic 0.4% NaOH was aerated for 24 hr. The precipitate was filtered and crystallized from benzene to give 3.2 g (81.2%) of yellow needles, mp 266°. *Anal.* Calcd. for $C_{15}H_9NO_4$: C, 67.41; H, 3.39; N, 5.24. Found: C, 67.33; H, 3.28; N, 5.03. IR ν_{max}^{KBr} cm^{-1}: 1675 (C=O), 1538, 1325 (NO_2). MS *m/e*: 267 (M^+).

b) Cyclization of 3-Nitro-2-*p*-toluoylbenzoic Acid (7)——A mixture of 0.4 g of **7**[3] and 10 g of PPA was heated at 145° for 4 hr under stirring. The mixture was poured into 90 ml of ice water and extracted with benzene. The benzene extract was extracted with 10% $NaHCO_3$ solution. After acidification with conc. HCl, the solution was extracted with benzene and evaporated to dryness. The residue was crystallized from benzene to give 0.19 g (50.7%) of yellow needles, mp 260—263°. This compound was found to be identical with the sample obtained above method a) in IR and NMR spectra and analytical data.

3-Methyl-5-nitroanthraquinone (5)——This compound was prepared from 1 g of **3** and 150 ml of 0.4% alcoholic NaOH in the same manner as for (4)–a). Yield, 0.7 g (71.1%), mp 240—242°. *Anal.* Calcd. for $C_{15}H_9NO_4$: C, 67.41; H, 3.39; N, 5.24. Found: C, 67.48; H, 3.49; N, 5.37. IR ν_{max}^{KBr} cm^{-1}: 1663 (C=O), 1524, 1353 (NO_2). MS *m/e* 267 (M^+).

3-Nitro-2-*p*-toluoylbenzoic Acid (7)[3]——To a stirred solution of 6 g of 3-nitrophthalic anhydride in 80 ml of anhyd. toluene was added 9 g of $AlCl_3$ in 20 ml of anhyd. toluene gradually. The mixture was heated at 60° for 1 hr. 100 g of ice and 5 ml of conc. HCl was added to the mixture and the solvent was removed by steam distillation. The solid was filtered and extracted with saturated $NaHCO_3$. The extract was acidified with conc. HCl and the solid which appeared was crystallized from benzene to give 3.6 g (40.6%) of light yellow prisms, mp 215° (lit.[3] 219.5—220.5°).

1,4,4a,9a-Tetrahydro-1-methyl-8-nitroanthraquinone (8) and 1,4,4a,9a-Tetrahydro-1-methyl-5-nitroanthraquinone (9)——A mixture of 16.2 g of 5-nitro-1,4-naphthoquinone (**1**) and 10.98 g of 1,3-pentadiene in 300 ml of anhyd. EtOH was stirred for 5 hr at 50°. After cooling, the crystals which appeared were filtered. Repeated fractional crystallizations of the crystals from ether gave **8**, as colorless prisms, mp 117—

4) V.I. Gudzenko, *Zh. Organ. Khim.*, **1** (9), 1653 (1965) [*C.A.*, **64**, 667*d* (1966)].

118°, yield, 10.0 g (46.2%), and **9**, as colorless prisms, mp 111—113°, yield, 7.0 g (32.4%). **8**: *Anal.* Calcd. for $C_{15}H_{13}NO_4$: C, 66.41; H, 4.83; N, 5.16. Found: C, 66.33; H, 4.79; N, 4.95. IR ν_{max}^{KBr} cm^{-1}: 1690 (C=O), 1541, 1380 (NO_2). NMR ($CDCl_3$) δ: 5.70 (2H, broad s, ethylene H), 3.60 (2H, m, >CH-CH<), 1.05 (3H, d, CH_3). MS *m/e*: 271 (M^+). **9**: *Anal.* Calcd. for $C_{15}H_{13}NO_4$: C, 66.41; H, 4.83; N, 5.16. Found: C, 66.48; H, 4.77; N, 4.87. IR ν_{max}^{KBr} cm^{-1}: 1708 (C=O), 1535, 1380 (NO_2). NMR ($CDCl_3$) δ: 5.75 (2H, broad s, ethylene H), 3.60 (2H, m, >CH-CH<), 2.72 (3H, m, methyiene H and CH_3-C<u>H</u><), 0.83 (3H, d, CH_3). MS *m/e*: 271 (M^+).

1-Methyl-8-nitroanthraquinone (**10**)——A mixture of 500 mg of **8** and 500 mg of Al_2O_3 in 40 ml of hexane was heated at 100° for 2 hr. The mixture was filtered and the filtrate was evaporated to dryness. The residue was dissolved in benzene and purified through column chromatography on Al_2O_3 to give 280 mg (56.8%) of yellow needles, mp 258—260° (lit.[4] 258—259°). IR ν_{max}^{KBr} cm^{-1}: 1673 (C=O), 1545, 1332 (NO_2). MS *m/e*: 267 (M^+).

1-Methyl-5-nitroanthraquinone (**11**)——A mixture of 100 mg of **9** and 100 mg of Al_2O_3 in 20 ml of hexane was heated at 100° for 1.5 hr. The mixture was filtered and the filtrate was evaporated to dryness. The residue was dissolved in benzene and chromatographed on Al_2O_3. The eluate was evaporated and the residue was crystallized from benzene to give 80 mg (81.2%) of yellow needles, mp 254—256° (lit.[4] 254—256°). IR ν_{max}^{KBr} cm^{-1}: 1670 (C=O), 1535, 1330 (NO_2). MS *m/e* 267 (M^+).

1-Amino-5,6,7,8,9,10-hexahydro-9,10-dihydroxy-8-methylanthracene (**12**)——A solution of 542 mg of **8** in 120 ml of EtOH was hydrogenated over 0.1 g of 5% palladium on charcoal at atmospheric pressure for 5 hr during which time 225 ml (5 mol) of hydrogen was absorbed. The catalyst was filtered and the filtrate was evaporated under reduced pressure. The residue was crystallized from petroleum ether (bp 40—70°) to give 280 mg (57.1%) of colorless needles, mp 205°. *Anal.* Calcd. for $C_{15}H_{19}NO_2$: C, 73.44; H, 7.81; N, 5.71. Found: C, 73.50; H, 7.69; N, 5.53. IR ν_{max}^{KBr} cm^{-1}: 3377, 3277 (NH_2), 2917 (C-H). NMR($CDCl_3$) δ: 5.10 (1H, m, CH_3-C<u>H</u><), 1.54 (3H, broad s, CH_3). MS *m/e*: 245 (M^+).

1-Amino-5,6,7,8,9,10-hexahydro-9,10-dihydroxy-5-methylanthracene (**13**)——A solution of 542 mg of **9** in 100 ml of EtOH was hydrogenated over 0.1 g of 5% palladium on charcoal at atmospheric pressure for 3 hr during which time 230 ml (*ca.* 5 mol) of hydrogen was absorbed. The catalyst was filtered and the filtrate was evaporated under reduced pressure. The residue was crystallized from hexane to give 320 mg (65.3%) of colorless needles, mp 190—191°. *Anal.* Calcd. for $C_{15}H_{19}NO_2$: C, 73.44; H, 7.81; N, 5.71. Found: C, 73.64; H, 7.75; N, 5.55. IR ν_{max}^{KBr} cm^{-1}: 3437, 3338 (NH_2), 2927 (C-H). NMR($CDCl_3$) δ: 5.20 (2H, broad m, NH_2), 5.02 (1H, m, CH_3-C<u>H</u><), 1.11 (3H, d, CH_3). MS *m/e*: 245 (M^+).

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