Syntheses of Benzo[5,6]cyclohept[1,2-*b*]indol-6-ones

Kameji Yamane and Kunihide Fujimori
Department of Chemistry, Faculty of Science, Shinshu University, Matsumoto

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The monoarylhydrazones(IIa—c) of benzocycloheptene-5,6-dione (I) underwent Fischer indolization to form 11,12-dihydrobenzo[5,6]cyclohept[1,2-*b*]indol-6-ones (IIIa—c). The treatment of IIIa—c with *N*-bromosuccinimide gave the benzoindolotropone derivatives (Va—c). Va, Vc, and VI afforded a dibromo compound (VII) on treatment with bromine in acetic acid.

Previous investigations in this area have dealt almost exclusively with syntheses of indolotropones[1] and indolotropolones.[2-4] The present paper will report on the syntheses of benzotropone derivatives fused with the indole ring.

Results and Discussion

When benzocycloheptene-5,6-dione (I) was treated in ethanol or acetic acid with an equivalent amount of phenylhydrazine, hydrochloride of *p*-tolylhydrazine, or *p*-bromophenylhydrazine, monoarylhydrazones (IIa—c) were obtained. IIa—c underwent Fischer indolization in acetic acid in the presence of zinc chloride or concd. hydrochloric acid to form 11,12-dihydrobenzo[5,6]cyclohept[1,2-*b*]indol-6-ones (IIIa—c). IIIa and IIIb were also prepared by the reaction of I with phenyl- or *p*-tolylhydrazine hydrochloride in acetic acid.

The dione (I) or monophenylhydrazone (IIa) gave IV, the phenylhydrazone of IIIa, on treatment with an excess of phenylhydrazine in acetic acid, but IIIa did not give the compound (IV). It can be presumed that bisphenylhydrazone was first formed, and that the Fischer indolization occurred smoothly under these conditions, although the bisphenylhydrazone could not be isloated.

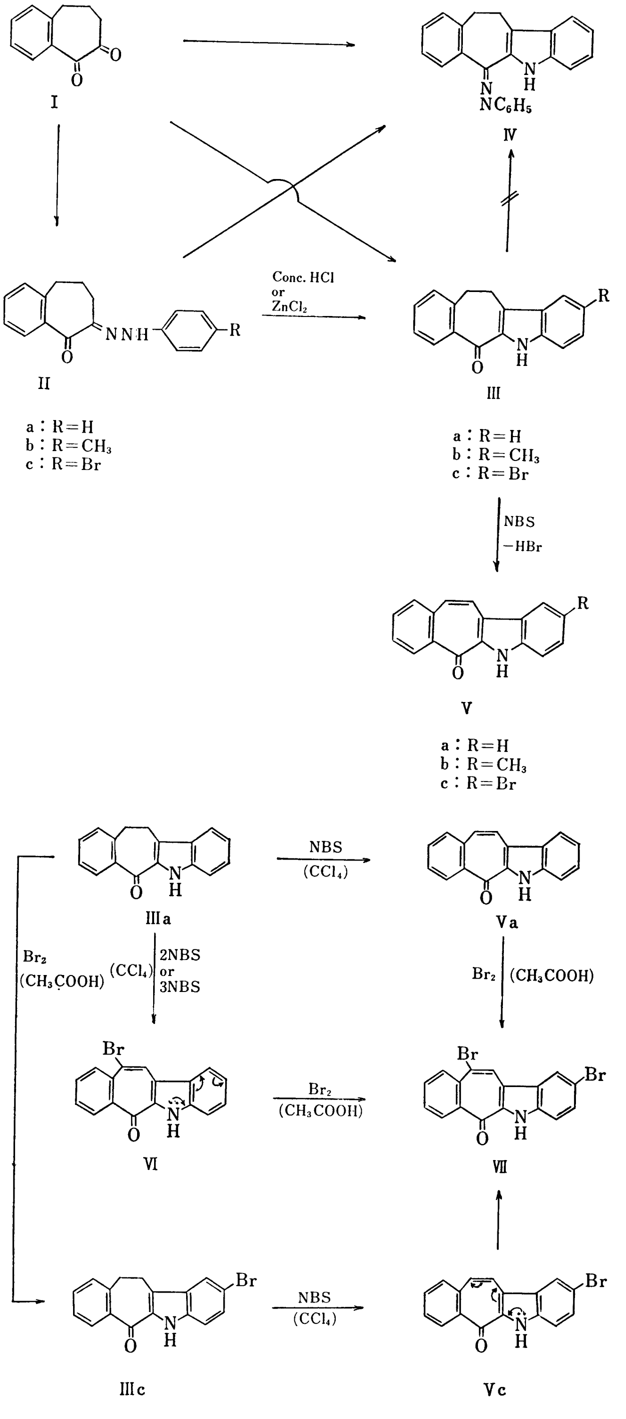
The treatment of IIIa—c with *N*-bromosuccinimide resulted in dehydrogenation, thus formed the benzoindolotropone derivatives (Va—c) in good yields; however, the treatment of IIIa with bromine in acetic acid gave the monobromo compound (IIIc). The reaction of IIIa with two or three molar equivalents of *N*-bromosuccinimide afforded the monobromo compound (VI), which is isomeric with Vc.

The bromination of Va in acetic acid gave the dibromo compound (VII), which was also prepared by the reaction of Vc or VI with bromine in acetic acid.

Furthermore, the *N*-benzyl derivative was obtained by the reaction of IIIa with benzyl chloride.

The ultraviolet spectra of Va—c and VI were more complex than those of IIIa—c.

The infrared spectra of Va—c and VI showed olefinic C–H stretching absorption at 3100—3000 cm^{-1}. In contrast with IIIa—c, Va—c, and VI indicated the absence of paraffinic C–H stretching absorption bands in the 3000—2800 cm^{-1} region. The N–H and C=O stretching absorption bands of Va—c and VI appeared



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[1] T. Nozoe, Y. Kitahara, and J. Shin, unpublished works.

[2] M. Mühlstädt and W. Treibs, *Ann.*, **608**, 38 (1957).

[3] T. Nozoe, H. Horino, and T. Toda, *Tetrahedron Lett.*, **1967**, 5349.

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in regions about 60—65 cm^{-1} and 60—62 cm^{-1} lower than those of IIIa—c respectively. It can, therefore, be concluded that Va—c and VI are the dehydro products of IIIa—c.

As Va—c and VI were only slightly soluble in common organic solvents, the NMR spectra could not be measured. In the NMR spectra of III, four methylene protons appeared as a singlet at τ 6.7.

Experimental

All the melting points were determined in a liquid bath and are uncorrected. The IR spectra were run as KBr tablets on a Hitachi Model EPI-G spectrophotometer. The UV absorption spectra were measured in ethanol on a Hitachi spectrophotometer Model 124. The NMR measurements were carried out on a JEOL Model JNM-4H-100 spectrometer in deuterochloroform as the solvent, with tetramethylsilane as the internal standard.

Benzocycloheptene-5,6-dione Monophenylhydrazone (IIa). *a)* A mixture of I (0.5 g) and phenylhydrazine (0.3 g) in ethanol (6 m*l*) was refluxed for 2 hr on a water bath. After cooling, the separated crystalline material was collected and recrystallized from ethanol as orange needles (0.3 g, 39%); mp 111—112°C. Found: C, 77.24; H, 6.11; N, 10.61%. Calcd for $C_{17}H_{16}ON_2$: C, 77.24; H, 6.14; N, 10.60%.

b) The reaction of I with an equivalent amount of phenylhydrazine in acetic acid afforded orange needles, mp 111°C, which are also obtained when using 2.5 molar amounts of phenylhydrazine in *n*-butyl alcohol; these needles showed no depression in mp on mixed fusion with monophenylhydrazone (IIa).

*Benzocycloheptene-5,6-dione Mono-*p*-tolylhydrazone (IIb).* A mixture of I, *p*-tolylhydrazine hydrochloride, and sodium acetate in ethanol was treated by a method similar to that described above. Orange needles (44%); mp 160—161°C. Found: C, 77.39; H, 6.42; N, 10.08%. Calcd for $C_{18}H_{18}ON_2$: C, 77.68; H, 6.51; N, 10.06%.

*Benzocycloheptene-5,6-dione Mono-*p*-bromophenylhydrazone (IIc).* This was obtained by a method similar to that used for IIb; it was recrystallized from ethanol to give orange yellow needles (54%); mp 160—161°C. Found: C, 59.68; H, 4.38; N, 8.19%. Calcd for $C_{17}H_{15}ON_2Br$: C, 59.48; H, 4.41; N, 8.16%.

*11,12-Dihydrobenzo[5,6]cyclohept[1,2-*b*]indol-6-one (IIIa).* *a)* To a solution of IIa (0.5 g) in acetic acid (15 m*l*) we added zinc chloride (0.4 g) or concd. hydrochloric acid (a few m*l*); the mixture was then refluxed for 4 hr in an oil bath. After cooling, the reaction mixture was diluted with water, and the resulting material was collected and recrystallized from ethanol to give yellow needles (0.45 g, 96%); mp 185—186°C. IR(KBr): ν NH 3305 cm^{-1}, ν conjugated C=O 1612 cm^{-1}, 1586 cm^{-1}. UV: λ_{max} (EtOH): 253 mμ (log ε 4.15), 338 mμ (log ε 4.32). NMR (in $CDCl_3$): τ 1.8—3.0 (multiplet, 8H), τ 6.74 (singlet, 4H). Found: C, 82.58; H, 5.31; N, 5.99%. Calcd for $C_{17}H_{13}ON$: C, 82.57; H, 5.30; N, 5.67%.

b) A suspension of I (0.5 g) and phenylhydrazine hydrochloride (0.5 g) in acetic acid (5 m*l*) was refluxed for 3 hr in an oil bath. After cooling, the reaction mixture was diluted with water, and the resulting material was collected and recrystallized from ethanol to give yellow needles (0.43 g, 61%); mp 185—186°C.

*2-Methyl-11,12-dihydrobenzo[5,6]cyclohept[1,2-*b*]indol-6-one (IIIb).* *a)* A mixture of IIb (0.12 g), zinc chloride (0.4 g), and acetic acid (6 m*l*) was treated as in IIIa a). Yellow needles (0.09 g, 82%); mp 174—176°C.

b) A mixture of I (0.5 g), *p*-tolylhydrazine hydrochloride (0.46 g), and acetic acid (5 m*l*) was treated as in IIIa. Yellow needles (0.47 g, 63%); mp 174—175°C. IR(KBr): ν NH 3306 cm^{-1}, ν conjugated C=O 1611 cm^{-1}, 1590 cm^{-1}. UV: λ_{max} (EtOH): 254 mμ (log ε 4.18), 345 mμ (log ε 4.37). NMR (in $CDCl_3$) τ 1.8—3.0 (multiplet, 7H), τ 6.76 (singlet, 4H), τ 7.53 (singlet, 3H). Found: C, 82.75; H, 5.70; N, 5.48%. Calcd for $C_{18}H_{15}ON$: C, 83.05; H, 5.82; N, 5.38%.

*2-Bromo-11,12-dihydrobenzo[5,6]cyclohept[1,2-*b*]indol-6-one (IIIc).* *a)* A mixture of IIc (0.3 g), zinc chloride (0.6 g), and acetic acid (10 m*l*) was treated by a method similar to that described above. Light yellow needles from ethanol (0.25 g, 86%); mp<230°C. UV: λ_{max} (EtOH): 257 mμ (log ε 4.06), 336 mμ (log ε 4.32). IR(KBr): νNH 3310 cm^{-1}, ν conjugated C=O 1613 cm^{-1}, 1585 cm^{-1}. Found: C, 62.59; H, 3.67; N, 4.11%. Calcd for $C_{17}H_{12}ONBr$: C, 62.59; H, 3.71; N, 4.30%.

b) Into a solution of IIIa (0.2 g) in acetic acid (35 m*l*), bromine (0.16 g) in acetic acid (5 m*l*) was stirred; the mixture was then stirred for 3 hr at room temperature. The separated material was collected by filtration and recrystallized from acetic aicd as yellow micro needles (0.23 g, 88%); mp>230°C. The needles were found to be identical with the product which was obtained by Method a).

Phenylhydrazone of IIIa (IV). *a)* A mixture of I (0.5 g) and phenylhydrazine (1.25 g) in acetic acid (10 m*l*) was refluxed for 4 hr. After cooling, the separated material was recrystallized from ethanol as yellow micro needles (0.43 g, 44%); mp 237—238°C. IR(KBr): νNH 3390 cm^{-1}, 3340 cm^{-1}. Found: C, 81.87; H, 5.62; N, 12.66%. Calcd for $C_{23}H_{19}N_3$: C, 81.87; H, 5.68; N, 12.45%.

b) A mixture of IIa (0.2 g) and phenylhydrazine (0.12 g) in acetitic acid (6 m*l*) was refluxed for 3 hr. After cooling, the separated material was recrystallized from ethanol as yellow micro needles (0.14 g, 54%); mp 237—238°C. Their mp was not depressed on admixture with IV, which was obtained by Method a).

*Benzo[5,6]cyclohept[1,2-*b*]indol-6-one (Va).* To a solution of IIIa (0.3 g) in carbon tetrachloride (30 m*l*), NBS (0.22 g) and benzoyl peroxide (0.06 g) were added; then the mixture was refluxed for 3 hr on a water bath. After cooling, the separated material was collected by filtration. The treatment of this with a small amount of chloroform gave an insoluble material which was then recrystallized from acetic acid as yellow micro needles (0.3 g, *ca.* 100%); mp >270°C. IR(KBr): νNH 3243 cm^{-1}, ν conjugated C=O 1581 cm^{-1} (medium), 1558 cm^{-1} (strong), 1533 cm^{-1} (shoulder). UV: λ_{max} (EtOH): 233 mμ (log ε 4.41), 295 mμ (log ε 4.53), 327 mμ (log ε 4.29). Found: C, 83.55; H, 4.34; N, 5.85%. Calcd for $C_{17}H_{11}ON$: C, 83.24; H, 4.52; N, 5.71%.

*2-Methylbenzo[5,6]cyclohept[1,2-*b*]indol-6-one (Vb).* A mixture of IIIb (0.15 g), NBS (0.10 g), benzoyl peroxide (0.06 g), and carbon tetrachloride (30 m*l*) was treated as in the case of Va. Yellow needles from chloroform (0.11 g, 81%); mp>270°C. IR(KBr): νNH 3251 cm^{-1}, ν conjugated C=O 1582 cm^{-1} (medium), 1550 cm^{-1} (strong), 1532 cm^{-1} (shoulder). UV: λ_{max} (EtOH): 235 mμ (log ε 4.46), 296 mμ (log ε 4.56), 336 mμ (log ε 4.36). Found: C, 83.38; H, 4.96; N, 5.40%. Calcd for $C_{18}H_{13}ON$: C, 83.37; H, 5.05; N, 5.40%.

*2-Bromobenzo[5,6]cyclohept[1,2-*b*]indol-6-one (Vc).* This was prepared from IIIc (0.2 g), NBS (0.13 g), benzoyl peroxide (0.04 g), and carbon tetrachloride (40 m*l*) by a method similar to that used for Vb. Yellow micro needles (0.18 g, 90%); mp >270°C. IR(KBr): νNH 3262 cm^{-1}, ν conjugated C=O 1575 cm^{-1} (medium), 1555 cm^{-1} (strong), 1533 cm^{-1}

(weak). UV: λ_{max} (EtOH): 252 mμ (log ε 4.40), 284 mμ (log ε 4.57), 328 mμ (log ε 4.38). Found: C, 63.33; H, 3.03; N, 4.30%. Calcd for $C_{17}H_{10}ONBr$: C, 62.98; H, 3.11; N, 4.32%.

Bromo Compound (VI). To a solution of IIIa (0.2 g) in carbon tetrachloride (20 m*l*), NBS (0.30 g) and benzoyl peroxide (0.06 g) were added, and then the mixture was refluxed for 3 hr on a water bath. After cooling, the separated material was collected by filtration. This was dissolved in chloroform and purified by passing through a silica gel column. The eluate gave yellow needles (0.12 g, 46%); mp >270°C. IR(KBr): νNH 3254 cm^{-1}, ν conjugated C=O 1581 cm^{-1} (shoulder), 1559 cm^{-1} (strong), 1551 cm^{-1} (shoulder). UV: λ_{max} (EtOH): 237 mμ (log ε 4.34), 299 mμ (log ε 4.43), 332 mμ (log ε 4.31). Found: C, 62.99; H, 2.94; N, 4.16%. Calcd for $C_{17}H_{10}ONBr$: C, 62.98; H, 3.11; N, 4.32%.

Dibromo Compound (VII). *a)* Into a solution of Va (0.1 g) in acetic acid (25 m*l*), bromine (0.15 g) in acetic acid (5 m*l*) was stirred, and then the mixture was stirred for 3 hr at room temperature. The separated material was collected by filtration and recystallized from acetic acid as yellow micro needles (0.14 g, 85%); mp >270°C. IR(KBr): νNH 3249 cm^{-1}, ν conjugated C=O 1601 cm^{-1} (weak), 1571 cm^{-1} (shoulder), 1560 cm^{-1} (strong), 1541 cm^{-1} (shoulder). Found: C, 50.76; H, 2.25; N, 3.67%. Calcd for $C_{17}H_9ONBr_2$: C, 50.76; H, 2.25; N, 3.48%.

b) This was prepared from VI (0.1 g) and bromine (0.1 g) in acetic acid (160 m*l*) by a method similar to that used for VII a). Yellow micro needles (0.1 g, 83%); mp >270°C. This showed an infrared spectrum identical with that of VII a).

c) A mixture of Vc (0.05 g), bromine (0.05 g), and acetic acid (150 m*l*) was treated as in the case of VII a). Yellow micro needles (0.06 g, *ca.* 100%); mp >270°C. This showed an infrared spectrum identical with that of VII a).

N-*Benzyl Derivative (VIII).* A mixture of IIa (0.15 g) and potassium (0.02 g) in dry toluene (10 m*l*) was stirred for 10 hr at room temperature. The unreacted potassium was filtered off. Benzyl chloride (0.10 g) was added to the filtrate, and the mixture was refluxed for 3 hr in an oil bath. After the reaction mixture had then cooled, we added water to it. After the insoluble material had been removed by filtration, the toluene layer was dried and the solvent was evaporated. The residue was dissolved in benzene and purified by passing it through an alumina column. Yellow needles from ethanol (trace); mp 131—131.5°C. IR(KBr): ν conjugated C=O 1618 cm^{-1} (strong), 1588 cm^{-1} (medium). Found: C, 85.59; H, 5.76; N, 4.00%. Calcd for $C_{22}H_{19}ON$: C, 85.43; H, 5.68; N, 4.15%.

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