Benzocyclobutenes Part 8.[1] Geometrical Isomerism of Arylhydrazones of Benzocyclobutene-1,2-dione

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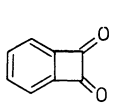
Synopsis. Four mono(arylhydrazone)s of benzocyclobutene-1,2-dione (BBD) have been prepared in which the aryl group is 2,4-dinitrophenyl, 4-bromophenyl, phenyl, and 4-nitrophenyl. The first three have been separated into their *E*- and *Z*-isomers whose configurations are assigned on the basis of spectra and R_f values. Improvements in the preparation of BBD from 1,2-dibromo-1,2-dihydrobenzocyclobutene are described.

During studies on reactions of 5,10-diazabenzo-*b*-biphenylene it was found that hydrolysis of this compound with hydrochloric acid in the presence of 2,4-dinitrophenylhydrazine gave the mono(2,4-dinitrophenylhydrazone) of benzocyclobutene-1,2-dione (BBD) (**1**) as a mixture of *E*- and *Z*-isomers.[2] BBD was known to give a bis(2,4-dinitrophenylhydrazone) but attempts to prepare mono-derivatives with hydrazine and tosylhydrazine had given the 1(2*H*)-phthalazinones **2** and **3** respectively.[3] We describe here an improved preparation of BBD and the preparation from it of four monoarylhydrazones also the separation of three of them into their geometrical isomers and the assignment of their configuration.

The monoarylhydrazones were made by treating BBD with one equivalent of the appropriate arylhydrazine. With each reagent a mixture of the *E*- and *Z*-isomers was obtained and those from 2,4-dinitrophenyl-, 4-bromophenyl-, and phenyl-hydrazine were separated by preparative TLC. The mixture of isomers from 4-nitrophenylhydrazine could not be separated. 4-Bromophenylhydrazine gave a variable yield of the 1(2*H*)-phthalazinone **4** (as well as the *E*- and *Z*-hydrazones) depending on the reaction conditions. The structure of the phthalazinone **4** follows from its analysis and its IR spectrum ($\nu_{C=O}$ 1660 and $\nu_{C=N}$ 1595 cm^{-1}; ν_{N-H} was absent) which agrees with that of the 2-tosyl-1(2*H*)-phthalazinone **3** ($\nu_{C=O}$ 1695 and $\nu_{C=N}$ 1600 cm^{-1}). Furthermore the NMR spectrum of compound **4** showed a singlet at δ 8.29 for the azomethine proton and the spectrum did not change when D_2O was added to the solvent, thus confirming the absence of an NH group.

Assignment of Configuration. Our assignments are based on the work of Nashima and co-workers[4] who studied the geometrical isomerism of the 2,4-dinitrophenylhydrazones of four esters of pyruvic acid. They found that in each pair of geometrical isomers the *Z*-isomer (having an intramolecular hydrogen bond between the imino hydrogen and the ester carbonyl group) has the higher R_f value, the longer wavelength of the absorption maximum in the UV/visible spectrum, and the lower C=O and N–H stretching frequencies in the IR spectrum. Our results, shown in the Table 1, are consistent with those of the Japanese workers. Unfortunately most of our compounds were too sparingly soluble in dichloromethane to observe the weak N–H stretching bands. The NMR spectra of each pair of isomers should provide confirmation of the assignments since the hydrogen bonded imine proton should resonate well downfield of the non-hydrogen bonded imine proton. This effect was found by Nashima and co-workers but we were unable to obtain information about the δ_{NH} values, except for compound **9**, because of the low solubility of the arylhydrazones in $CDCl_3$ and CD_3COCD_3. We did not try more polar solvents because they are known to favour interconversion of isomers.[5]

In the above discussion we have tacitly assumed that the *Z*-isomers **5**, **7**, and **9** contain intramolecular N–H···O hydrogen bonds. Scale drawings of these isomers (based on the crystal structure of BBD[6]) show that the relevant N to O distance is about 3.3 Å which is just within the limits for an N–H···O bond (2.6—3.3 Å).[7] However the angle subtended by the atoms N, H, and O can be 134° to 123° depending on the values (from 109° to 120°) chosen for the NNH angle.



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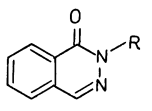
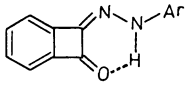
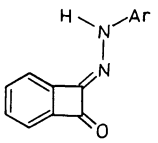


(2) R = H
(3) R = 4-$MeC_6H_4SO_2$-
(4) R = 4-BrC_6H_4-





(5) Ar = 2,4-dinitrophenyl (6)
(7) Ar = 4-bromophenyl (8)
(9) Ar = phenyl (10)

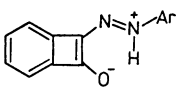


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Table 1. Physical properties of (*Z*)- and (*E*)-mono(arylhydrazone)s

Compound	R_f value (CH_2Cl_2/silica gel)	λ_{max}/nm (CH_2Cl_2)	$\nu_{C=O}$/cm^{-1} (CH_2Cl_2)
5	0.35	418	1768
6	0.30	382	1793
7	0.70	434	1760
8	0.50	407	1787
9	0.70	432	1760
10	0.50	408	1782

According to Speakman[7] when the angle NHO becomes less than 140° "genuine hydrogen bonding must become minimal." Nevertheless the physical properties of isomers **5**, **7**, and **9**, compared with those of isomers **6**, **8**, **10**, do suggest intramolecular hydrogen bonding. The actual bond angles in these *Z*-isomers may be more favourable than the scale drawings suggest. Furthermore there is the possibility that the canonical form **11** makes a small but significant contribution which would strengthen the hydrogen bond.

Experimental

IR and UV spectra were measured as solutions in dichloromethane. Some of the UV spectra are qualitative because of the sparing solubility of the arylhydrazones in this solvent. The ^{1}H NMR spectra were recorded on a Varian HA-100 spectrometer. Petroleum refers to light petroleum (bp 60—80 °C). TLC was carried out on silica gel M. F. C. (Hopkin and Williams). The product compositions were estimated from the size of spots on TLC and are therefore very approximate.

Improved Preparation of Benzocyclobutene-1,2-dione. 1,2-Dibromo-1,2-dihydrobenzocyclobutene[8] was freed from iodine-containing impurities by keeping a solution of it (100 g) and bromine (20 g) in carbon tetrachloride (600 ml) for 24 h, preferably in sunlight. The solution was then washed with aqueous sodium hydrogensulfite, dried and distilled in vacuo. A solution of the purified dibromide (20 g) in carbon tetrachloride (300 ml) was irradiated by two 200-W tungsten-filament light bulbs placed under the flask: the heat from the bulbs kept the liquid boiling. Bromine (27.2 g) was added dropwise during 2 h and heating/irradiation was continued for 16 h more. The solvent and excess of bromine were removed under reduced pressure. The residual solid (32.5 g) was recrystallized from petroleum and gave 1,1,2,2-tetrabromo-1,2-dihydrobenzocyclobutene (28.9 g, 90%), mp 118—119 °C (lit,[9] mp 117—118 °C, yield 65%). The tetrabromide was hydrolysed to BBD as previously described.[9]

Benzocyclobutenedione Mono(2,4-dinitrophenylhydrazone). BBD (34 mg) was added to a warm solution of 2,4-dinitrophenylhydrazine (50 mg) in 5 M HCl (5 ml) and the mixture was warmed on a water bath at 60—70 °C for 30 min. The mixture was cooled and the mixture of *E*- and *Z*-isomers (70 mg, 89%) was collected, mp 228—240 °C (the previously recorded[2] mp 249—250 °C was an error). TLC using CH_2Cl_2 showed that the mixture contained roughly equal amounts of both isomers which were separated by preparative TLC (CH_2Cl_2–petroleum, 3:2). The band with the higher R_f value gave the (*Z*)-dinitrophenylhydrazone **5** as an orange solid, mp 235—240 °C; IR 1768 and 1713 cm^{-1}; UV λ_{max} (qualitative) 236, 258 sh, 400, and 418 nm. Found: M$^+$, 312.050. Calcd for $C_{14}H_8N_4O_5$: M, 312.049. The band with the lower R_f value gave the (*E*)-dinitrophenylhydrazone **6** as orange crystals, mp 238—239 °C; IR 1793, 1713, 1615, and 1600 cm^{-1}; UV λ_{max} 236 (log ε 3.96), 256 sh (3.86), and 382 (4.08) nm. Found: M$^+$, 312.050.

Benzocyclobutenedione Mono(4-bromophenylhydrazone). BBD (34 mg) was added to a warm solution of 4-bromophenylhydrazine hydrochloride (54 mg) in 4 M HCl (10 ml) and the mixture was warmed on a water bath at 60—70 °C for 30 min. Next day the solid (51 mg) was collected. The mixture was separated into three components by preparative TLC (elution with CH_2Cl_2). The band with the highest R_f value (0.7) gave the (*Z*)-4-bromophenylhydrazone **7** as a yellow-orange solid, mp 205—206 °C; IR 1760, 1595, and 1070 cm^{-1}; UV λ_{max} (qualitative), 259, 295 sh, 315 sh, 339, and 434 nm. Found: M$^+$, 301.985 and 299.988. Calcd for $C_{14}H_9BrN_2O$: M, 301.987 and 299.987. The band with R_f value 0.5 gave the (*E*)-4-bromophenylhydrazone **8** as yellow-orange crystals, mp 219—220 °C (from ethanol) as major product; IR 1787 and 1570 cm^{-1}; UV λ_{max} 258 (log ε 4.26), 342 (4.10), and 407 (4.12) nm. Found: C, 56.1; H, 3.1; N, 9.4%. Calcd for $C_{14}H_9BrN_2O$: C, 55.8; H, 3.0; N, 9.3%. The band with the lowest R_f value (0.3) gave 2-(4-bromophenyl)-1(2*H*)-phthalazinone **4**, mp 168—169 °C; IR (Nujol) 1657 and 1595 cm^{-1}; UV λ_{max} 236 (log ε 4.42), 270 (3.89), and 303 (3.97) nm; NMR ($CDCl_3$) δ 8.50 (m, H-8), 8.29 (s, H-4), 7.83 (m, H-5,6,7), and 7.62 (s, H-2′,3′,5′,6′). Found: C, 55.6; H, 3.1; N, 9.1%. Calcd for $C_{14}H_9BrN_2O$: C, 55.8; H, 3.0; N, 9.3%. The ratio of *E*- to *Z*-isomer was always about 7 : 1 but the yield of phalazinone increased from about 20 to about 40% when the mixture was heated for longer times.

Benzocyclobutenedione Mono(4-nitrophenylhydrazone). This was made in the same way as the mono(2,4-dinitrophenylhydrazone). The crude product (78% yield) was freed from impurities by soxhlet extraction with acetone to give the mono(4-nitrophenylhydrazone) as yellow crystals, mp 265—266 °C; IR (Nujol) 3360, 3080, 1766, and 1747 cm^{-1}. Found: C, 62.9; H, 3.4; N, 15.7%. Calcd for $C_{14}H_9N_3O_3$: C, 62.9; H, 3.4; N, 15.8%. TLC (CH_2Cl_2) showed two yellow spots very close together but it was impossible to separate the *E*- and *Z*-isomers by preparative TLC.

Benzocyclobutenedione Mono(phenylhydrazone). BBD (67 mg) in hot ethanol (1 ml) was added to a solution of phenylhydrazine hydrochloride (73 mg) and sodium acetate (100 mg) in hot water (2 ml), and the mixture warmed on a water bath at 50—60 °C for 2 h. After cooling, the orange-yellow solid (59 mg) was collected. Examination by TLC (CH_2Cl_2) showed one major component (yellow spot, R_f 0.50) with a small component (orange spot, R_f 0.70) in the ratio of about 9 : 1. Recrystallization from ethanol gave the (*E*)-phenylhydrazone **10** as yellow needles, mp 180—183 °C; IR 1782, 1600, and 1042 cm^{-1} (in Nujol N–H stretch at 3310 cm^{-1}); UV λ_{max} 228 (log ε 4.10), 249 (4.09), 290 (3.79), 332 (4.01), and 408 (3.91) nm. Found: C, 75.5; H, 4.3; N, 12.3%. Calcd for $C_{14}H_{10}N_2O$: C, 75.7; H, 4.5; N, 12.6%.

Refluxing a solution of the crude (*E*)-phenylhydrazone (73 mg) in acetic acid (2 ml) increased the amount of orange component (R_f 0.70) in the mixture. Evaporation of the solution followed by preparative TLC (elution with CH_2Cl_2) gave the (*Z*)-phenylhydrazone **9** (20 mg) as red crystals, mp 122—135 °C which recrystallized above 140° to give a mixture of *E*- and *Z*-isomers (confirmed by TLC)as yellow needles, mp 170—178 °C; IR 3350, 3050 (br), 1760, and 1600 cm^{-1}; UV λ_{max} 252 (log ε 4.01), 258 (4.02), 293 (3.88), 334 (4.20), and 432 (4.05) nm; NMR ($CDCl_3$) δ 9.20 (br s, N–H), 7.9—6.7 (m, Ar–H′ s). Found: N, 12.6%. Calcd for $C_{14}H_{10}N_2O$: N, 12.6%.

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