Some Benzonorbornadiene Derivatives[1)]

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Bicyclo [2, 2, 1] heptane and the compounds with this skeleton have received wide attention in the past few years. They have been employed so often as a suitable model for developing modern organic theory because of their special fixed stereochemistry and because of the high strain of the ring system. Of particular interest are the demonstration of anchimeric assistance or homoconjugation in solvolytic displacement reactions,[2)] and that of trans-annular interaction between the double bond and the carbonyl group of dehydronorcamphor.[3)] Along with these developments in the theoretical field, remarkable progress was made in the syntheses of bridged ring compounds. Particularly, the success of the syntheses of norbornane derivatives condensed with an aromatic nucleus have opened a new area of organic chemistry. Norbornadiene I prepared by the Diels-Alder reaction of cyclopentadiene and acetylene[4)] is commercially available now,

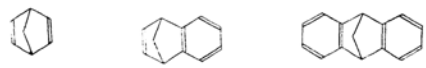
1) Some of the results of this paper have appeared in preliminary form: H. Tanida, *J. Am. Chem. Soc.*, **85**, 1703 (1963).

2) S. Winstein and C. Ordronneau, ibid., **82**, 2084 (1960) and references therein.

3) R. C. Cookson and N. S. Wariyar, *J. Chem. Soc.*, **1956**, 2302.

4) J. Hyman, E. Freireich and R. E. Lidov, U. S. Pat. 2875256; *Chem. Abstr.*, 53, 13082 (1959).

benzonorbornadiene II is easily obtained by the cycloaddition of benzyne to cyclopentadiene,[5] and dibenzobicyclo[2, 2, 1]heptadiene III can be prepared by the condensation of norbornadiene with butadiene, followed by dehydrogenation.[6] They may be likened to a series of benzene, naphthalene and anthracene.



I II III

One of our chief objectives in investigating the chemistry of these systems has been to gain some insight into the nature of the homobenzylic conjugation.[1] Toward this end, we have studied the cycloaddition of substituted benzynes in the preparation of β-substituted benzonorbonadiens. This paper describes a convenient and steady method for the generation of benzynes, which carry several kinds of substituents, by the development of Wittig's procedure.[5] Furthermore, we would like to demonstrate that Wittig's procedure is very often more convenient than the decomposition of the zwitterionic diazonium salts of anthranilic acid derivatives,[7] a method which has recently been advocated, for use in syntheses.

Results and Discussion

One of the conditions necessary for the cycloaddition of benzynes generated via metal aromatics is the fragmentation of suitably ortho-substituted di-halobenzenes under an aprotic solvent. According to the Huisgen addition-elimination mechanism[8] for the formation of benzynes, the Wittig process is assumed to be composed of two steps, the metallation and the subsequent elimination of metal halogenide. Huisgen proposed that the rate-determining step was generally in the metalation reaction and that the rate of the elimination of halogen anions was in the order of iodine > bromine > chlorine ≫ fluorine. Several kinds of *o*-dihalobenzene have been prepared on the basis of the above discussions.

4-Bromo-3-iodoanisole IV, prepared from 6-bromo-*m*-anisidine V,[9] was proved to be a good source for the generation of 4-methoxybenzyne. Racemic 4'-methoxybenzonorbornadiene VI was obtained in a 40% yield by the reaction of IV with cyclopentadiene and magnesium. 3-Bromo-4-flourotoluene VII was prepared from 2-bromo-*p*-toluidine by the Schiemann reaction, and its cycloaddition to cyclopentadiene was satisfactorily carried out, yielding 4'-methylbenzonorbornadiene VIII in a 54% yield. The benzyne reaction of 2-bromo-4-chloroflourobenzene IX, obtained by the Schiemann reaction of 2-bromo-4-chloroaniline, proceeded successfully with cyclopentadiene by the elimination of bromine and fluorine, giving 4'-4-chlorobenzonorbornadiene X in a 55.6% yield. The position of the substituents on the benzene nucleus of the benzonorbornadienes obtained was unequivocally established by the conversion into the 2-substituted naphthalenes through the route of benzoyloxylation at the 7-position, hydrolysis and the Oppennauer oxidation.[1,10]

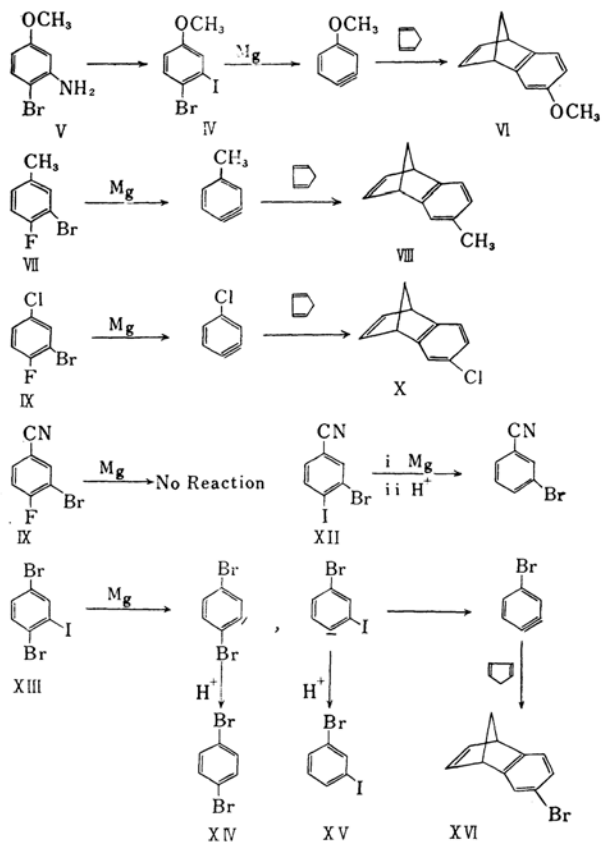


Chart. 1

5) G. Wittig and E. Knauss, *Chem. Ber.*, **91**, 895 (1958).
6) W. R. Vaughan and M. Yoshimine, *J. Org. Chem.*, **22**, 7 (1957).
7) M. Stiles and R. G. Miller, *J. Am. Chem. Soc.*, **82**, 3802 (1960); M. Stiles, R. G. Miller and U. Burckhardt, ibid., **85**, 1792 (1963); R. G. Miller and M. Stiles, ibid., **85**, 1798 (1963); L. Friedman and F. M. Logullo, ibid., **85**, 1549 (1963).
8) R. Huisgen and J. Sauer, *Angew. Chem.*, **72**, 91 (1960); R. Huisgen, in H. Zeiss, "Organometallic Chemistry," Reinhold Publishing Co., New York, N. Y. (1960), p. 36 and references thereon.
9) V was prepared in the following way: *p*-Anisidine—(nitration)→2-nitro-*p*-anisidine—(Sandmeyer)→4-bromo-3-nitroanisole—(Fe+HCl)→6-bromo-*m*-anisidine.
10) H. Tanida and T. Tsuji, *Chem. & Ind.*, **1963**, 211.

Attempts to generate cyanobenzyne, which is interesting in view of the fact that the benzyl has a strongly electronegative group, failed when either 3-bromo-4-fluorobenzonitrile XI or 3-bromo-4-iodobenzonitrile XII was used.[11] Compound XI did not react with magnesium in tetrahydrofuran. The reaction of XII with magnesium afforded 3-bromobenzonitrile as an isolable product, while no reaction with lithium occurred.

Of particular interest was the reaction of 2, 5-dibromo-1-iodobenzene XIII with cyclopentadiene and magnesium. Gas chromatography of the product, which had been distilled under reduced pressure, indicated the existence of seven compounds. The residue not distillated presumably consisted of high molecular substances. The identities of the main four compounds, *p*-dibromobenzene XIV, 3-bromoiodobenzene XV, the desired 4'-bromobenzonorbornadiene XVI and benzonorbornadiene XVII, were confirmed by retention time analysis in gas chromatography. The estimation of their relative yields was carried out on the basis of the peak area, as Table II shows. Furthermore, XIV, XVI and XVII were isolated and identified by mixed melting point determination and by a comparison of the infrared spectra. The formation of XVII is probably due to the further reaction of XVI with magnesium. No evidence of the formation of *o*-bromoiodobenzene was obtained. This fact may imply that the rate of formation of phenyl anion was enhanced by ortho halogen.[12] The percentage of the benzyne formation would be more than the total yield of XVI and XVII because of the polymerization of benzynes.

The formation of considerable amounts of XIV and XV suggests that the metalation reaction took place without the subsequent elimination. The above experiments of XII gave an analogous result. Contrary to Huisgen's popular mechanism, Zieger and Wittig[13] recently reported that, in the case of the reaction of 3-chloro-4-dimethylaminophenylsulfone XVIII with *n*-butyllithium and furan, XVIII was metalated very rapidly and completely at a low temperature such as −80°C, but that the elimination of lithium chloride proceeded at a measurable rate, giving a k_1 value of 0.094~0.064 min^{-1} at 0°C. Therefore, we think that Huisgen's discussions and Wittig's finding are probably valid in terms of their own experiments and, that which step, metalation or elimination, is the rate-determining step depends primarily upon the particular case. The benzyne formation will substantially be a two-step reaction.

The ultraviolet spectra data, listed in Table I, exhibits the transannular interaction of the double bond and the benzene ring in the benzonorbornadiene derivatives prepared here. It is interesting to note the absorption maximum[14] around 230~240 mμ, which may correspond to the π-π^* band of the styrene derivatives. The spectral data and electronic structures of these compounds will be discussed in detail later.

TABLE I. UV SPECTRA OF BENZONORBORNADIENE DERIVATIVES

λ_{max} in mμ, log ε in parentheses, solvent is cyclohexane, except for the 4'-bromo compound in *n*-hexane.

Substituent	λ_{max}				
None	216	231	262	269	277
	(4.00)	(3.06)	(2.66)	(2.76)	(2.72)
4'-CH_3		238	267	273	281
		(3.13)	(2.79)	(2.90)	(2.91)
4'-CH_3O		249		284	290
		(3.35)		(3.26)	(3.23)
4'-Cl	214	241	269	276	284
	(4.23)	(3.28)	(2.83)	(2.92)	(2.90)
4'-Br		242	267	275	284
		(3.38)	(2.86)	(2.89)	(2.82)

Experimental[15]

4-Bromo-3-iodoanisole.—Into a mixture of 20.2 g. (0.10 mol.) of 6-bromo-*m*-anisidine,[16] 47 ml. of concentrated hydrochloric acid and 31 g. of cracked ice, a solution of 7.6 g. (0.11 mol.) of sodium nitrite in 31 ml. of water at 0~3°C was slowly stirred over a ten-minute period. Stirring was kept up for additional fifteen minutes. The deep orange solution which resulted was filtered, slowly stirred at approximately 10°C into a solution of 57 g. (0.344 mol.) of potassium iodide in 187 ml. of water, and left to stand overnight at room temperature. The violet oil which separated was extracted with ether, wahed with 10% aqueous sodium hydroxide, water and 5% aqueous sodium bisulfite, and then dried over anhydrous sodium sulfate. After the removal of the solvent, the residue was distilled at 124~126°C (2 mmHg) to give 15.9 g. of the expected product as a yellow oil, in a 60% yield; n_D^{26} 1.6493.

11) XI (m. p. 57~58°C) was prepared in the following way: VII→3-bromo-4-fluorobenzaldehyde (b. p. 120°C) (21 mmHg), n_D^{24} 1.5795→the oxime (m. p. 104~104.5°C)→XI. XII (m. p. 137~138.5°C) was prepared from 3-amino-4-iodobenzonitrile by the Sandmeyer reaction.

12) Cf. J. Hine and P. B. Langford, *J. Org. Chem.*, **27**, 4149 (1962) and references therein.

13) H. Zieger and G. Wittig, *J. Org. Chem.*, **27**, 3270 (1962).

14) No maximum was observed in benzobicyclo[2, 2, 2]-octadiene, according to a private communication from Dr. K. Kitahonoki. Cf. K. Kitahonoki and Y. Takano, *Tetrahedron Letters*, **24**, 1597 (1963).

15) All melting points and boiling points are uncorrected.

16) H. H. Hodgson and R. J. H. Dyson, *J. Chem. Soc.*, 1935, 946.

Found: C, 27.09; H, 1.99; Br, 25.25. Calcd. for C_7H_6OBrI: C, 26.86; H, 1.93 Br, 25.55%.

3-Bromo-4-fluorotoluene (VII).—B. p. 186°C; n_D^{25} 1.5281. Found: C, 44.70; H, 3.27. Calcd. for C_7H_6BrF: C, 44.47; H. 3.20%.

2-Bromo-4-chlorofluorobenzene (IX).—B. p. 90°C (30 mmHg); n_D^{19} 1.5549. Found: C, 34.51; H, 1.58. Calcd. for C_6H_3BrClF: C, 34.41; H. 1.44%. were prepared from the corresponding amino compounds by the Schiemann procedure of Roe.[17]

4'-Methoxybenzonorbornadiene (VI).—A three-necked flask, equipped with a stirrer, a pressure-compensated dropping funnel, a gas inlet tube, and a reflux condenser with a Drierite tube, was charged with 4.1 g. (0.158 mol.) of magnesium turning and flushed with dry nitrogen for 30 min. to remove the air completely. In the dropping funnel there was then placed a solution of 44 g. (0.141 mol.) of 4-bromo-3-iodoanisole and 9.5 g. (0.143 mol.) of fresh-distilled cyclopentadiene in 240 ml. of anhydrous tetrahydrofuran. A part of the solution from the funnel was dropped to cover the magnesium and heated to boiling. When a vigorous reaction commenced, the stirrer was started and the remaining main part of the solution was added at such a rate that the temperature in the flask was kept at 60~65°C (this took about 50 min.), after which the mixture was refluxed gently for 30 min. After removal of the solvent under slightly reduced pressure, the residue was poured into a mixture of a saturated aqueous solution of ammonium chloride and 300 ml. of ether. The ether layer was separated, washed repeatedly with 5% aqueous sodium bisulfite and water, and dried over sodium sulfate. The ether extracts were distilled under reduced pressure to obtain 9.7 g. (40%) of a colorless oil at b. p. 99~100°C (4 mmHg). The oil contained a small amount of impurity, presumably 4-bromoanisole. Elution chromatography by Florisil, hexane and benzene gave completely pure 4'-methoxybenzonorbornadiene (n_D^{23} 1.5642) after of 4-bromoanisole had been eluted as a forerun. Found: C, 84.03; H, 7.16; O, 9.11. Calcd. for $C_{12}H_{12}O$: C, 83.69; H, 7.02; O, 9.29%.

4'-Methylbenzonorbornadiene (VIII).—By means of the above procedure, 42 g. of VII, 14.7 g. of cyclopentadiene and 6 g. of magnesium turning in 270 ml. of dry tetrahydrofuran, 18.6 g. (53.6%) of VIII as a colorless oil was obtained; b. p. 110~112°C (22mm Hg); n_D^{24} 1.5541.

Found: C, 93.09; H, 6.77, Calcd. for $C_{21}H_{18}$: C, 93.29; H,6.71%.

4'-Chlorobenzonorbornadiene (X)—It was prepared from XI, cyclopentadiene and magnesium in the same manner as the above. It is a colorless oil with a boiling point of 112~112.5°C (10 mmHg); n_D^{21} 1.5763. The yield was 55.6%.

Found: C, 74.44; H, 5.20; Cl, 20.25. Calcd. for $C_{11}H_9Cl$; C, 74.79; H, 5.14; Cl, 20.07%.

The Reaction of 2, 5-Dibromo-1-iodobenzene (XIII) with Magnesium and Cyclopentadiene.—With 75 g. of XIII, 16.5 g. of cyclopentadiene and 6.05 g. of magnesium turning in 300 ml. of tetrahydrofuran, the above procedure was carried out. The ether extracts were distilled up to 132°C (10 mmHg) to obtain 26.4 g. of a mixture of oil and crystals. The composition of the distillate was investigated by gas chromatography. The components and the relative yields are shown in Table II. 4'-Bromobenzonorbornadiene (XVI), fractionated by preparative gas chromatography, has a b. p. of 127 ~129°C (10 mmHg); n_D^{29} 1.5910.

Found: C, 59.96; H. 4.24. Calcd. for $C_{11}H_9Br$: C, 59.76; H, 4.10%.

Table II. The components of the reaction product of 2, 5-dibromo-1-iodobenzene with magnesium and cyclopentadiene

1	Benzonorbornadiene	25.4%
2	*p*-Dibromobenzene	28.6%
3	3-Bromoiodobenzene	6.6%
4	x(unidentified)	1.6%
5	4'-Bromobenzonorbornadiene	21.1%
6	y(unidentified)	4.9%
7	z(unidentified)	11.8%

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17) A. Roe, "Organic Reactions," Vol. V, John Wiley and Sons, Inc., New York, N. Y. (1949), p. 193.