96–97°);[19] *p*-bromophenylferrocene, mp 121.5–123° (lit.[7] 122–123°).

1,1′-Bis(*p*-bromophenyl)ferrocene had mp 195–196°; ν_{max}^{Nujol} 1110 and 1000 absent (no unsubstituted ferrocene ring), 860–800 (*para*-disubstituted benzene ring) obscured by a strong complex band at 819 cm^{-1} (ferrocene out-of-plane C–H bending). *Anal.* Calcd for $C_{22}H_{16}Br_2Fe$: C, 53.27; H, 3.25; Br, 32.22; Fe, 11.26. Found: C, 53.16; H, 3.26; Br, 32.26; Fe, 11.65.

Reactions under Modified Conditions.—Summarized in Table II are reactions of ferrocene (FcH), phenylhydrazine, and anhydrous aluminum chloride employed in the molar ratios indicated. The reactions were performed based on the general method above, except for the modification specified.

TABLE II

Molar ratio	Modification	% of phenylferrocene, 1,1′-diphenylferrocene, recovd FcH
1:2:3	Powdered Zn (1 g-atom) present	29, 0, 65
1:2:3	Solvent: *n*-octane	26, 2, 60
1:1:2	Solvent: benzene	4, 0, 74
1:1:2	40-hr reflux	19, 0, 56
1:1:2	6-hr reflux	18, 0, 76
1:1:1	$AlBr_3$ replaced $AlCl_3$	18, 0, 67
1:1:2	$AlBr_3$ replaced $AlCl_3$	12, 0, 30

Attempted Reactions of Ferrocene with Hydrazines and Other Compounds.—Procedures were similar to those of the general method above. The following reactants were refluxed in *n*-heptane with ferrocene (FcH) and anhydrous aluminum chloride in the molar ratios (FcH:reactant:$AlCl_3$) indicated, with negative results except in the case of benzophenone phenylhydrazone which yielded 2% of phenylferrocene: aniline (1:1:2), N-nitrosoaniline (1:1:2), *p*-methoxyphenylhydrazine (1:2:3), *sym*-diphenylhydrazine (1:2:3), *unsym*-diphenylhydrazine (1:2:3), benzoylhydrazine (1:1:2), phenylhydrazine-*p*-sulfonic acid (1:2:3), 4-nitrophenylhydrazine (1:2:3), 2,4-dinitrophenylhydrazine (1:1:2), benzophenone phenylhydrazone (1:1:2), methylhydrazine (1:2:3), *t*-butylhydrazine (1:2:3).

m-Tolylhydrazine (1:2:3) yielded 1.5 g of orange needles upon elution of the chromatographic column with benzene and crystallization from *n*-heptane, mp 295° dec, ν_{max}^{Nujol} 1106 and 1003 (unsubstituted ferrocene ring) and 761 cm^{-1} (aromatic C–H?). *Anal.* Calcd for $C_{17}H_{16}Fe$ (*m*-tolylferrocene): C, 73.93; H, 5.84; Fe, 20.22. Found: C, 70.21; H, 3.21; Fe, 27.14.

1,5-Diphenylcarbazide (1:1:2) yielded 14% of 1,1′-(1,3-cyclopentylene)ferrocene, mp 138–139° from 30–60° petroleum ether (lit.[14] 140°), undepressed by admixture with an authentic sample.[14]

Attempted Reaction of Phenylferrocene with Phenylhydrazine.—Phenylferrocene (0.1 mole), phenylhydrazine, and anhydrous aluminum chloride (molar ratio, 1:2:3) were refluxed in *n*-heptane employing procedures similar to those of the general method above. No 1,1′-diphenylferrocene was detected upon election of the chromatographic column as above.

Attempted Reactions of Benzenoid Aromatics with Phenylhydrazine.—Using procedures based on the general method above, mesitylene and 1,3-dimethoxybenzene were refluxed, in place of ferrocene, with phenylhydrazine and anhydrous aluminum chloride in a 1:2:2 molar ratio. Benzene and anisole were refluxed with phenylhydrazine (0.2 mole) and aluminum chloride (0.3 mole), using excess of the aromatic compound as solvent in place of *n*-heptane. No biphenyl derivative was detected upon elution of the chromatographic columns with solvents as above, or with chloroform or methanol.

Attempted Preparation of *o*-Tolylferrocene from *o*-Tolyldiazonium Fluoroborate in the Presence of Zinc.—The method was based on the published procedure[7] except that powdered zinc (1 g-atom) was added to the methylene chloride solution of ferrocene (0.1 mole) prior to addition of the dry diazonium fluoroborate (0.1 mole) over 1 hr with cooling (water bath). After stirring of the mixture 2 hr at room temperature, no *o*-tolylferrocene was detected *via* chromatography on alumina, and ferrocene was recovered nearly quantitatively.

Registry No.—Aluminum chloride, 7446700; ferrocene, 102545; 1,1′-bis(*p*-bromophenyl)ferrocene, 12155-929; *m*-tolylferrocene, 12344364.

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[19] α-Naphthylferrocene, mp 93–95°, and β-naphthylferrocene, mp 137–142°, have been reported by K. Schlögl and H. Egger, *Monatsh.*, **94**, 1054 (1963); *Chem. Abstr.*, **60**, 13269*h* (1964).

The Selectivity of Benzyne. A New Approach Using the Reaction of Benzyne with Ambident[1] Nucleophiles

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In an attempt to find the optimum conditions for the reaction of bromobenzene with potassium anilide we varied the solvent as well as the ratio of aniline to potassium anilide. The results are summarized in Table I. As expected, we observed the well-known[2] increase in yield as the amount of free amine in the reaction mixture was increased. Most remarkable, however, was the observation that a dramatic change in product *composition* takes place as the ratio of aniline/anilide is changed. In each of the three solvents examined there was at least a tenfold increase in the carbon to nitrogen phenylation ratio (C/N) when an excess of aniline was present in the reaction mixture.

In order to subject this interesting phenomenon to a more systematic and quantitative examination we needed a reaction system in which higher and more consistent yields could be obtained. Reaction in dimethyl sulfoxide at 25° provided such data. As can be seen in Table II, 4-aminobiphenyl was now found as a product, in addition to 2-aminobiphenyl, diphenylamine, and small amounts of triphenylamine.

Discussion

An interesting question concerning the reactivity of benzyne is the degree of its selectivity among various nucleophiles. For example, it has been reported[3] that 9,10-phenanthryne in ether solution reacts with equal speed with piperidine and with lithium piperidide. On the other hand, benzyne generated in ethanol by the decomposition of benzothiadiazole dioxide was found to react with LiCl, LiBr, and LiI at relative rates of 1:8:65.[4]

It appeared to us that our data enable us to obtain an estimate of the relative rates of the reaction of benzyne[5] with aniline and with potassium anilide by a

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(1) N. Kornblum, R. A. Smiley, R. K. Blackwood, and D. C. Iffland, *J. Amer. Chem. Soc.*, **77**, 6269 (1955).

(2) R. Huisgen and J. Sauer, *Chem. Ber.*, **92**, 192 (1959).

(3) W. Mack and R. Huisgen, *ibid.*, **93**, 608 (1960).

(4) G. Wittig and R. W. Hoffman, *ibid.*, **95**, 2729 (1962).

(5) (a) J. D. Roberts and F. Scardiglia [*J. Org. Chem.*, **23**, 629 (1958)] have shown that this reaction goes by way of a benzyne intermediate. They found that bromobenzene and potassium anilide in aniline as solvent gave a 60% yield of diphenylamine. They did not wish to investigate possible primary amine products. Using their reaction conditions we obtained a 50% yield of diphenylamine and a 5% yield of 2-aminobiphenyl. (b) Further evidence that this type of reaction proceeds by way of a benzyne intermediate in dimethyl sulfoxide solution as well can be found in the work of D. J. Cram, B. Rickborn, and G. R. Knox, *J. Amer. Chem. Soc.*, **82**, 6412 (1960).

TABLE I

THE REACTION OF BROMOBENZENE WITH POTASSIUM ANILIDE AND ANILINE IN BENZENE, DIETHYL ETHER, AND 2,2′-DIMETHOXYDIETHYL ETHER (1-4-1).

Solvent[b]	Concn of starting materials, mol/l. C_6H_5Br	C_6H_5NHK	$C_6H_5NH_2$	Yield, % Diphenylamine[a]	2-Aminobiphenyl	C/N (ratio of carbon to nitrogen phenylation)
Benzene	0.13	1.30	0.00	0.50	0.21	0.42
Benzene	1.00	1.00	1.00	6.50	0.29	0.045
Diethyl ether	0.13	1.30	0.00	0.04	0.08	2.0
Diethyl ether	1.00	1.00	9.00	1.94	0.19	0.09
1-4-1[b]	0.24	1.46	0.00	21.9	8.8	0.40
1-4-1	1.25	1.25	11.2	56.2	2.49	0.044

[a] The yield of diphenylamine includes some triphenylamine which was obtained in varying amounts, from zero to 4.5%. [b] The reaction temperature was 25° in diethyl ether and at the reflux temperature of the other two solvents.

TABLE II

STARTING MATERIALS AND PRODUCTS IN THE REACTION OF 0.031 *M* BROMOBENZENE WITH POTASSIUM ANILIDE AND ANILINE IN DIMETHYL SULFOXIDE AT 25°

Initial concn of potassium anilide and aniline, mol/l. C_6H_5NHK	$C_6H_5NH_2$	Yield of products, % 4-Amino-biphenyl	2-Amino-biphenyl	Diphenyl-amine[a]
0.031	0.82	0.0[b]	0.13	54
0.20	1.28	4.1	5.9	48
0.20	0.82	3.8	4.5	45
0.20	0.20	4.0	4.1	50
0.20	0.00	5.7	4.8	54

[a] The yield of diphenylamine includes some triphenylamine which was obtained in varying amounts, from zero to 4%. [b] Less than 0.01%.

new and interesting method. Furthermore we can obtain such a rate comparison for this pair of nucleophiles with respect to the formation of three products (Scheme I). An examination of the kinetic scheme for the formation of 2- and 4-aminobiphenyl from the reaction of benzyne with $C_6H_5NH_2$ or with C_6H_5NHK yields the expression[6]

SCHEME I

$$C_6H_4 \left\{ \begin{array}{l} \left.\begin{array}{l} \xrightarrow[k_{H_2}]{+C_6H_5NH_2} \\ \xrightarrow[k_{K_2}]{+C_6H_5NHK} \end{array}\right\} \text{2-aminobiphenyl} \\ \left.\begin{array}{l} \xrightarrow[k_{H_4}]{+C_6H_5NH_2} \\ \xrightarrow[k_{K_4}]{+C_6H_5NHK} \end{array}\right\} \text{4-aminobiphenyl} \\ \left.\begin{array}{l} \xrightarrow[k_{HN}]{+C_6H_5NH_2} \\ \xrightarrow[k_{KN}]{+C_6H_5NHK} \end{array}\right\} \text{diphenylamine} \end{array}\right.$$

$$\frac{\text{yield of 2-aminobiphenyl}}{\text{yield of 4-aminobiphenyl}} = \frac{k_{K_2}[C_6H_5NHK] + k_{H_2}[C_6H_5NH_2]}{k_{K_4}[C_6H_5NHK] + k_{H_4}[C_6H_5NH_2]}$$

The result of the first reaction in Table II indicates that $k_{H_4} = 0$, therefore

$$\frac{\text{yield of 2-aminobiphenyl}}{\text{yield of 4-aminobiphenyl}} = \frac{k_{K_2}}{k_{K_4}} + \frac{k_{H_2}[C_6H_5NH_2]}{k_{K_4}[C_6H_5NHK]}$$

In Table III are listed the variations in product ratios as a function of the variation of the initial aniline–anilide ratio. A plot of the 2-aminobiphenyl/4-aminobiphenyl yield ratio *vs.* $[C_6H_5NH_2]/[C_6H_5NHK]$ yielded[7] a straight line whose slope and intercept gave $k_{K_2}/k_{K_4} = 0.90$, $k_{H_2}/k_{K_4} = 0.064$ and therefore $k_{K_2}/k_{H_2} = 14.0$.

TABLE III

PRODUCT RATIOS AS A FUNCTION OF INITIAL CONCENTRATIONS OF ANILINE AND POTASSIUM ANILIDE

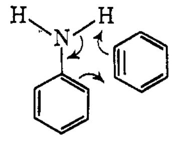
$[C_6H_5NH_2]/[C_6H_5NHK]$	2-Aminobiphenyl/ 4-aminobiphenyl	Diphenylamine/ 4-aminobiphenyl
26.4	>13	>5400
6.4	1.44	12.9
4.1	1.19	12.0
1.0	1.02	12.5
0.0	0.84	9.54

Analogous considerations yield the expression

$$\frac{\text{yield of diphenylamine}}{\text{yield of 4-aminobiphenyl}} = \frac{k_{KN}}{k_{K_4}} + \frac{k_{HN}[C_6H_5NH_2]}{k_{K_4}[C_6H_5NHK]}$$

Here the scatter of the data was such as to enable us merely to obtain $k_{KN}/k_{K_4} \geqq 9.6$, $k_{HN}/k_{K_4} \leqq 0.041$, and therefore $k_{KN}/k_{HN} \geqq 234$. Converting the above rate ratios into relative rates by setting $k_{H_2} = 1.0$ we then have $k_{H_4} = 0.0$, $k_{K_4} = 15.6$, $k_{H_2} = 1.0$, $k_{K_2} = 14.0$, $k_{HN} \leq 0.64$, $k_{KN} \geqq 150$.

Thus the largest difference in the nucleophilicities of $C_6H_5NH_2$ and C_6H_5NHK is found in the formation of 4-aminobiphenyl and the smallest in the formation of 2-aminobiphenyl. We can consider two factors which determine this difference. (1) The greater inherent nucleophilicity of the much more basic C_6H_5NHK. (2) The fact that the transition state for nucleophilic attack of aniline on benzyne involves charge separation (assuming a two-step process, (a) attack by the nucleophile, (b) protonation of the phenide ion), whereas nucleophilic attack by potassium anilide does not. Since factor 1 remains constant for the three processes, factor 2 must be invoked in explaining the dramatic differences in the nucleophilic



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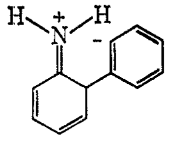
[6] This equation holds rigorously only if the ratio $[C_6H_5NHK]/[C_6H_5NH_2]$ remains constant. As can be seen in Table II an excess of $C_6H_5NH_2$ and C_6H_5NHK was used to keep this ratio as constant as possible.

[7] Since each mole of C_6H_5Br converted into products consumes 2 mol of C_6H_5NHK and produces 1 mol of $C_6H_5NH_2$ the value of $[C_6H_5NH_2]/[C_6H_5NHK]$ does not remain exactly constant during the course of the reaction. For the purpose of calculation the value of $[C_6H_5NH_2]/[C_6H_5NHK]$ at half-reaction was used.

rate ratios for the three processes. In the formation of 2-aminobiphenyl from $C_6H_5NH_2$ and C_6H_4 a six-membered ring transition state is conceivable which would involve nucleophilic attack and protonation in one step, avoiding charge separation. In the formation of diphenylamine a four-membered ring transition state of this type is possible. In the formation of 4-aminobiphenyl no such cyclic transition state is possible. The fact that attack of the benzyne by $C_6H_5NH_2$ competes best with attack by C_6H_5NHK in the case of 2-aminobiphenyl formation and not at all in the case of 4-aminobiphenyl formation suggests that such a one-step cyclic process for the nucleophilic attack and protonation of benzyne by an amine is very probable.[8] Alternately, in a two-step process, the reaction of $C_6H_5NH_2$ and C_6H_4 to form 2-aminobiphenyl would lead to a charged intermediate having little charge separation, whereas the intermediate for 4-aminobiphenyl formation would involve a great deal of charge separation. This may account for the fact that no 4-aminobiphenyl at all could be found in the three much less polar solvents where such charge separation would be particularly energetically unfavorable.



It is of great interest that such simple changes in the steric and electrostatic nature of the transition states can so radically alter the degree of selectivity of benzyne between a pair of nucleophiles.

Experimental Section

Materials.—Aniline (Baker & Adamson) was dried over KOH and distilled from zinc dust. Bromobenzene (Baker) was dried over calcium sulfate and distilled. Dimethyl sulfoxide (Fisher Reagent) was dried over calcium hydride and distilled, ethyl ether and 1-4-1 were distilled from sodium wire.

Sample Run.—A mixture of potassium anilide and aniline (prepared from 4.75 g (0.510 mol) of aniline and 0.391 g (0.010 mol) of potassium) was dissolved in 50 ml of dimethyl sulfoxide. To this stirred solution was added 0.244 g (0.00155 mol) of bromobenzene and the solution left to stand at 25° under an atmosphere of nitrogen for 18 hr. The solution was then diluted with water and extracted with benzene. The benzene phase was washed thoroughly with water and then extracted with 3 *N* HCl. The organic phase, containing diphenylamine and triphenylamine, was then dried, an internal standard was added, and the mixture subjected to vpc analysis at 210° on a 5-ft long steel column packed with 20% SF-96 on 60/80 firebrick. The above aqueous HCl phase was neutralized with 10 *N* NaOH and extracted with ether. The ether phase, containing 2-aminobiphenyl and 4-aminobiphenyl, was then dried and analyzed by vpc as above. Samples of all four products were collected from the vpc and their infrared spectra determined. The spectrum of each compound was found to be identical with that of an authentic sample.

Registry No.—Benzyne, 462-80-6; bromobenzene, 108-86-1; potassium anilide, 19642-99-0; aniline, 62-53-3.

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[8] A four-membered cyclic process of this type was proposed by Mack and Huisgen.[5] On the other hand, J. F. Bunnett, D. A. R. Happer, M. Patsch, C. Pyun, and H. Takayama [*J. Amer. Chem. Soc.*, **88**, 5250 (1966)] have good evidence for a stepwise addition of methanol to 4-chlorobenzyne in methanol solution.

Transannular Oxide Formation. Bicyclo[3.2.1] *vs.* Bicyclo[2.2.2] Systems

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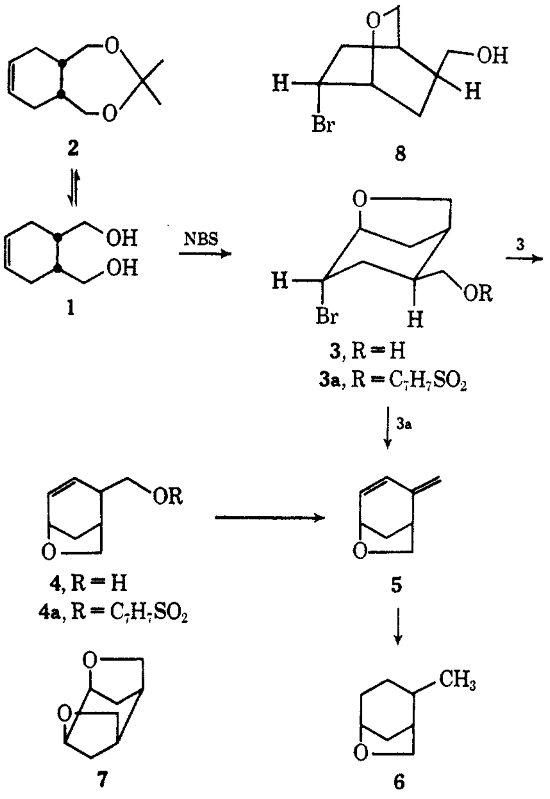
The relatively greater apparent stability of six-membered *vs.* five-membered oxide rings as evidenced, for example, by the preferred pyranose ring system in sugars as well as the formation of six-membered cyclic ketals in certain bicyclic systems[1] doubtlessly reflects the consequences of optimized conformational effects. In this connection it was of interest to us to determine the course of transannular oxide formation wherein competition exists for the formation of a bicyclo[3.2.1] or a bicyclo[2.2.2] product.

Treatment of the symmetrical system, *cis*-1,2-bishydroxymethylcyclohex-4-ene (1), with N-bromsuccinimide in aqueous *t*-butyl alcohol afforded a good yield of essentially a single bromoxide which proved to have the bicyclo[3.2.1] structure **3**[2] (Scheme I). The structure of **3** was established by conversion in essentially quantitative yield to a crystalline tosylate derivative **3a**, mp 80–81°; the latter, in turn, on treatment with

Scheme I



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[1] R. E. Beyler and L. H. Sarett, *J. Amer. Chem. Soc.*, **74**, 1406 (1952).

[2] Recently G. M. Brown, P. Dubrueil, and E. P. Denvers [*Can. J. Chem.*, **46**, 1849 (1968)] observed a similiar transannular oxide formation during epoxidation of a derived cyclohexene. The use of NBS in *t*-butyl alcohol for the formation of five-membered ring oxides has been previously reported. See, *e.g.*, F. W. Bollinger and N. L. Wendler, *Chem. Ind.* (London), 441 (1960); J. F. Bagl, P. F. Morand, and R. Gaudry, *J. Org. Chem.*, **28**, 1207 (1963).