An Aryne Pathway in the Decomposition of Diazotized 2,5-Di-*t*-butylaniline[1]

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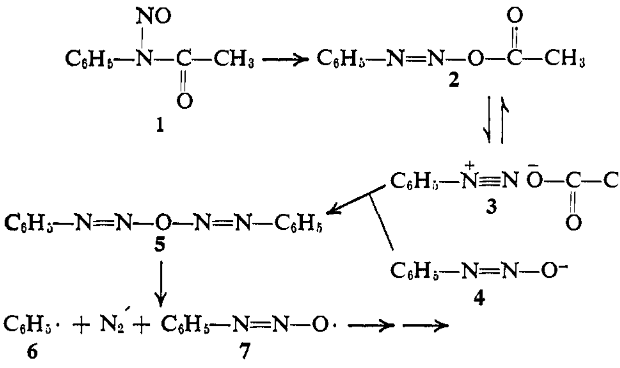
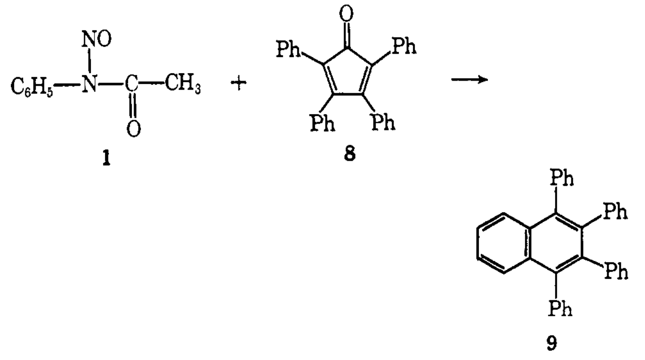
Abstract: An arynoid adduct **19** can be obtained when 2,5-di-*t*-butylaniline (**16**) is diazotized in the presence of furan. In order to decide whether aryne **18** is an intermediate in the decomposition, experiments were undertaken with aniline-d_2 as substrate. Mass spectral isotope analyses as well as product yields were used as evidence for possible mechanisms. A partitioning isotope effect was detected, with adduct **19** decreasing in yield with **16**-d_2 as substrate. Apparent reduction of aryne to arene was observed, particularly in control experiments when furan was omitted as a trap. A consistent reaction scheme including aryne **18** is presented.

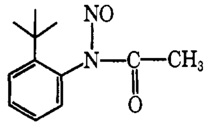
The decomposition reactions of aromatic diazo species in aprotic media present a broad range of possibilities. The Ruchardt scheme,[3] with its set of ionic, radical, and covalent diazo species, successfully accounts for the formation of phenyl radicals *via* the thermolysis of N-nitroso-N-phenylamides (**1**). The postulated decomposition scheme depicted in Chart I also

Chart I



explains the nonappearance of carboxyl radical products and instead the formation of products requiring carboxylate ion. However, this scheme does not account for the arynelike behavior of the decomposition of N-nitrosoanilides in the presence of tetracyclone **8**.[4] The remarkable isolation of an aryne product **9** is not due to an unusual reaction of phenyl radical. Apparently, tetracyclone "intercepts" the radical precursor or causes the diazo species to decompose *via* a different pathway. That there is another pathway available to simple nitrosamides was previously shown by Cadogan[5] in the decomposition of *o*-*t*-butyl-N-nitrosoacetanilide (**10**). No radical products were detected while the isolation of triptycene **11** (when anthracene was included in the reaction) and the isomeric acetates **12** and **13** strongly suggested an aryne intermediate **14**. The authors proposed a concerted elimination of a proton, molecular nitrogen, and acetate from the *cis*-diazoacetate **15** as the aryne-forming step. That a phenyl radical derived from a nitrosoamide decomposition might be a precursor for aryne has been suggested by Kampmeier as an explanation for reactions of *o*-iodo-N-nitrosoacetanilide.[6] Also, there are apparent ionic eliminations that form arynes when carboxylic,[7] sul-





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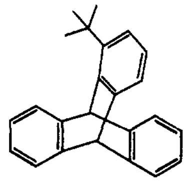

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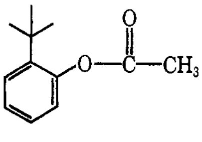

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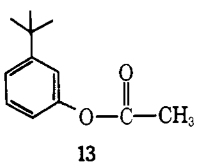

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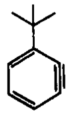

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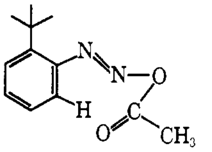

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[1] (a) Parts of this work have been previously reported, R. W. Franck and K. Yanagi, *Tetrahedron Lett.*, 2905 (1966); R. W. Franck and K. Yanagi, Abstracts, 155th National Meeting of the American Chemical Society, San Francisco, Calif., April 1968, No. P188. (b) We thank the National Science Foundation (Grants GP 5160 and 7754) for support of this work.

[2] On leave from The Research Institute for Science and Industry, Kyushu University, Fukuoka, Japan.

[3] (a) C. Ruchardt and B. Freudenberg, *Tetrahedron Lett.*, 3623 (1964); (b) G. R. Chalfont and M. S. Perkins, *J. Amer. Chem. Soc.*, **89**, 3055 (1967).

[4] D. L. Brydon, J. I. G. Cadogan, D. M. Smith, and J. B. Thomson, *Chem. Commun.*, 727 (1967).

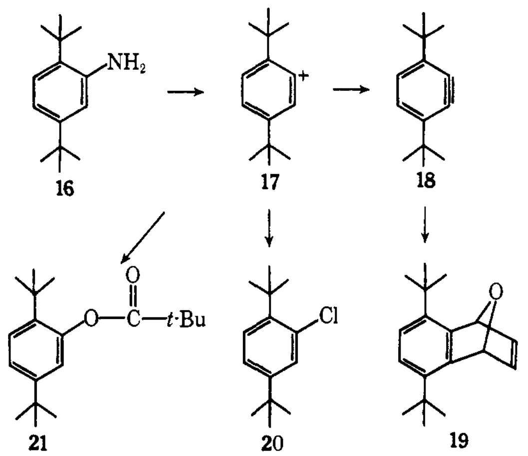
[5] J. I. G. Cadogan and P. G. Hibbert, *Proc. Chem. Soc.*, 338 (1964).

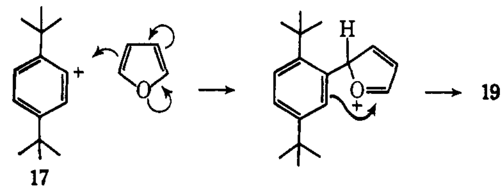
[6] (a) J. A. Kampmeier and A. B. Rubin, *Tetrahedron Lett.*, 2853 (1966); (b) D. L. Brydon and J. I. G. Cadogan, *Chem. Commun.*, 744 (1966).

[7] (a) M. Stiles, R. G. Miller, and U. Burckhardt, *J. Amer. Chem.*

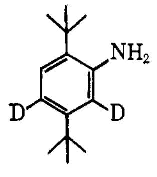
finic,[8] and boronic[9] acid functions are *ortho* to diazonium species generated in nonaqueous media.

Our study of the aprotic decomposition of diazo species began when insurmountable difficulties were encountered in the conventional aqueous preparation of the diazonium compound of 2,5-di-*t*-butylaniline (**16**) as precursor to the phenylhydrazine desired for a different study.[10] When aprotic techniques also failed to yield a stable diazonium compound, we searched for an aryne intermediate **18** by conducting a diazotization in the presence of furan, whereupon the adduct **19** was obtained.[11] The diazotizations were catalyzed with 1 equiv of carboxylic acid using butyl nitrite as the diazotization reagent in methylene chloride as solvent. The reaction mixtures were separated by silica gel chromatography affording adduct **19**, chlorobenzene **20**, and ester **21**. The best yields of adduct and lowest yield of ester were obtained using pivalic acid as catalyst.[1a] Thus a scheme incorporating aryne **18** which arose from a partitioning of an intermediate carbonium ion **17** between substitution and elimination pathways was proposed.[12] However, a proof of the intermediacy of a symmetrical species was lacking and the "benzyne" adduct could have arisen *via* a two-step sequence. The scheme envisions electrophilic attack of carbonium ion on furan followed by attack of the generated furocarbonium ion on the benzene ring.[13] A possible product arising from this pathway would be a 2-arylfuran coming from proton ejection from the farocarbonium ion. We have no evidence for this compound, but this is negative proof. In summary, the available evidence, from all sources, for the possibility of elimination of a proton adjacent to a diazo species (or electron-deficient aromatic carbon) to form aryne was reasonable but not compelling.





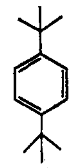
Thus experiments with 2,5-di-*t*-butylaniline (**16**) and 2,5-di-*t*-butyl-4,6-dideuterioaniline (**16**-d_2) (prepared by acid-catalyzed exchange of **16** with D_2O) in the presence and absence of furan were undertaken. Our purpose was to examine the product distribution for an isotope effect which would suggest the partitioning of an ion between substitution and elimination pathways.[11,14] In experiments with furan absent we hoped to find products attributable to other trapping reactions of benzyne. Also, the deuterium content of all products was to be examined for indications of an intermediate that had lost an *o*-deuterium as well as nitrogen.



16-d_2

Results and Discussion

All diazotizations were carried out under identical conditions except for the presence or absence of 2 equiv of furan. The analytical method for determining product yields was vapor phase chromatography using benzophenone as an internal standard. The analysis of the reaction mixtures revealed the presence of di-*t*-butylbenzene (**22**) as a product in addition to the previously identified adduct **19**, chloro compound **20**, and ester **21**. In our original column chromatography procedure,[1] the hydrocarbon was eluted with chlorobenzene **20**. Evaporative distillation and recrystallization techniques used to purify the latter low-melting compound resulted in our not detecting the volatile hydrocarbon. The product yields of the four kinds of diazotizations are tabulated in Table I. The two results that are certainly outside experimental error and that require explanation are the isotope effect in adduct **19** formation from aniline-d_2 and the replacement of adduct **19** with reduced hydrocarbon when furan is absent. The former observation is consistent with an elimination step involving the deuterium, the elimination being slower than with protium, thus less benzyne formation resulting from the diazotization reaction. The decrease in adduct **19** can also be explained by the alternate two-step scheme where the final aromatiza-



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Soc., **85**, 1792 (1963); (b) L. Friedman and F. M. Logullo, *ibid.*, **85**, 1549 (1963); (c) D. F. Lindow and L. Friedman, Abstracts, 151st National Meeting of American Chemical Society, Pittsburgh, Pa., April 1966, No. O-111. This last report describes some products of nonbenzyne decomposition of benzenediazonium-2-carboxylate.

[8] G. Wittig and R. W. Hoffman, *Chem. Ber.*, **95**, 2718 (1962).

[9] L. Verbit, J. S. Levy, H. Rabitz, and W. Kwalwasser, *Tetrahedron Lett.*, 1053 (1966).

[10] R. W. Franck and E. P. Reilly, Fordham University, unpublished results.

[11] R. W. Franck and K. Yanagi, *J. Org. Chem.*, 33, 811 (1968). The chemistry of **19** and related compounds is described.

[12] Except for ester **21**, the products could arise from radical intermediates *via* homolytic atom transfer.[3,5] It is not our intention to rule out the possibility of a partitioning of the diazo species between radical and ionic electron-deficient species. Our concern is whether either a proton or a hydrogen atom is lost to afford an aryne.

[13] Electrophilic attack at the α carbon in furans is the preferred course: P. Bosshard and C. H. Eugster, *Advan. Heterocyclic Chem.*, 7, 396 (1966).

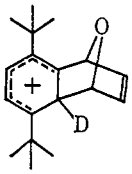
[14] (a) P. Myhre and M. Beug, *J. Amer. Chem. Soc.*, **88**, 1569 (1966); (b) R. W. Franck and K. Yanagi, *Tetrahedron Lett.*, 1789 (1967).

Table I. Product Yields (%) of Diazotizations[a]

Reactants	19	20	21	22
16, furan	23	19	22	15
16, no furan[b]	. .	20	28	34
16-d_2, furan	11	17	25	16
16-d_2, no furan[b]	. .	23	26	28

[a] The yields are the average of two experiments (except for the **16**-d_2, no furan run), and the reproducibility was close to the systematic error (paper cutting and weighing) in determining each yield (±1.4%). [b] There may be a solvent effect in the change from 95% CH_2Cl_2-5% furan to 100% CH_2Cl_2. Compensation for this effect cannot be made by addition of 5% tetrahydrofuran because ethers serve as hydride donors, affecting reduction yields, as shown by trial experiments using tetrahydrofuran and monoglyme as solvents.

tion step could be retarded by an isotope effect. The ring closure might then reverse and other processes would occur.



The increased yield of hydrocarbon **22** when furan is absent can also be rationalized in two ways. If the diazotization does produce benzyne, then this benzyne, in the absence of furan, must be reduced.

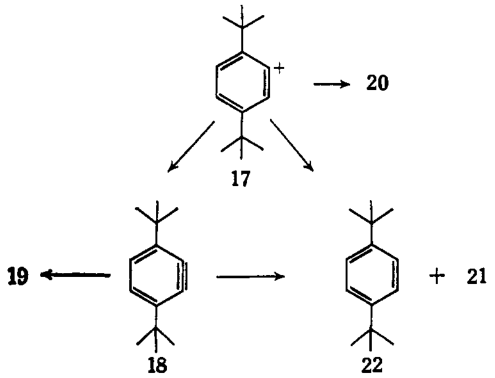
Alternately, the two-step mechanism for adduct formation would require a reactive species, which when not attacking furan, must attack a hydride (or hydrogen atom) source.

The two reduction pathways discussed require different predictions about isotope distribution. Benzyne formation and subsequent reduction would require loss of one of the two deuteriums of the starting aniline, while the direct reduction of an electrophilic carbon would require the retention of both deuteriums in hydrocarbon **22**. Thus, the products from the reactions with deuterated substrate **16** were collected (vpc) and were submitted to mass spectral analysis.[15] The isotopic compositions of the products, corrected for the natural abundance of C_{13}, O_{18}, and Cl_{37}, are recorded in Table II. Examination of the deuterium content of the products obtained when furan was present and adduct was formed suggest that 90% of the reduction product **22** has resulted from a direct substitution reaction, with only a 9% decrease in d_2 species, as compared with chloro compound **20**[16] the product with the highest d_2 content. However, in the reduction product **22** from the reaction performed in the absence of furan, there is a d_1 species that corresponds to the reduction of benzyne. The amount of d_1 agrees well with the apparent increase in yield of hydrocarbon **22**, from 16 to 28% in the presence and absence of furan, the original 16% being mainly d_2 and the additional 12% being d_1. This result strongly suggests that the proton α to the diazonium salt is being removed. To a lesser extent, α proton removal and benzyne intermediacy is indicated in the formation of ester when furan is not present during the decomposition of the diazonium salt. Although these protons could be lost by an exchange process that is not benzynoid (*e.g.*, prior to nitrogen loss) the three degrees of deuterium loss observed in the three substitution products would require three different diazo species with three rates of exchange, each species reacting in a specific pathway. The most rapidly exchanging diazo species in the absence of furan, affording exchanged hydrocarbon, must not exchange at all when furan is present so that an isotope effect in the cyclization can be detected. A simpler hypothesis requires one intermediate, an electron-deficient species that can react *via* hydride transfer to give hydrocarbon **22** and chloride transfer to give **20**, further that it can be attacked by carboxylate to give ester **21**, and lastly that it can lose a proton to give aryne **18**. Then the aryne can be trapped in a conventional way by furan, or it can be reduced.[17]

Table II. Isotopic Composition of Diazotization Products

	% deuterium in products from **16**-d_2 and furan			
	19	20	21	22
d_0	2.8	Trace	Trace	1.5
d_1	88.8	5.1	6.2	12.8
d_2	8.4	94.0	92.0	84.9
d_3	0.0	0.8	1.8	0.6
d_4	0.0	0.0	0.0	0.2
	% deuterium in products from **16**-d_2, no furan			
d_0	. . .	Trace	Trace	2.8
d_1	. . .	3.7	17.6	45.9
d_2	. . .	95.6	81.1	50.1
d_3	. . .	0.7	1.3	0.9
d_4	. . .	0.0	0.0	0.3

The question of the reducing agent in the above reaction scheme was tested by repeating a diazotization in CD_2Cl_2 as reaction solvent. The hydrocarbon was isolated by vpc and it was shown by mass spectral analysis to have an isotopic content of d_0 87.1%, d_1 11.1%, d_2 1.8%. Unless this experiment is the detection of a large isotope effect in the transfer of deuteride *vs.* hydride, it seems that methylene chloride is not the reducing agent causing formation of hydrocarbon **22**. Thus a test was made of the possibility that the alcohol arising from the butyl nitrite, was serving as the reducing agent. An experiment was run with the



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(15) Mass spectra obtained by Morgan-Schaffer Corp., Montreal, Quebec.

(16) The chloro compound 20 is used as the standard for isotopic composition, because amine **16** undergoes intermolecular exchange in the sample introduction process to afford d_0 0.9%, d_1 12.2%, d_2 80.5%, d_3 5.4%, d_4 1.1%, that is a total of 1.94 deuteriums in **16** compared to 1.96 deuteriums in **20**.

(17) Precedent for the reduction of benzyne is given by R. W. Hoffman, "Dehydrobenzene and Cycloalkynes," Academic Press Inc., New York, N. Y., 1967, pp 194–196.

prior equilibration of the butyl nitrite with 2 equiv of perdeuterioethanol. The hydrocarbon **22** isolated had an isotopic content of d_0 43.7%, d_1 43.1%, d_2 13.2%. The calculated isotopic composition of **22** if 50% arises *via* reduction of the benzyne and 50% is due to reduction of the "carbonium ion" (these proportions deduced from the yield and isotopic data on **22** in the tables) is d_0 41.6%, d_1 45.6%, d_2 12.8%. If the reduction was due only to the "carbonium ion," the predicted composition of **22** would be d_0 42.4%, d_1 57.6%, d_2 0.0%.[18]

A sample of chloro compound **20** isolated from the reaction mixture was not isotopically enriched. These results showing some incorporation of two deuteriums, the incorporation not explainable by exchange of the starting amine **16**, are consistent with the benzyne hypothesis. The final test of our postulated scheme, including the reduction of benzyne, awaits an alternate, unambiguous route to the di-*t*-butylbenzyne **18** so that its behavior in the presence of alcohols can be examined.

Experimental Section[19]

Diazotization of 2,5-Di-*t*-butylaniline with Butyl Nitrite in the Presence of Furan. A solution of 500 mg (2.44 mmol) of 2,5-di-*t*-butylaniline[20] and 248 mg (2.44 mmol) of pivalic acid in 5 ml of methylene chloride was added to a refluxing solution of 276 mg (2.68 mmol) of butyl nitrite[21] and 497 mg (7.30 mmol) of furan in 5 ml of methylene chloride. The addition took 15 min and instantaneous gas evolution was observed with each drop. The solution was refluxed an additional 40 min whereupon it was cooled and washed with 30 ml of saturated aqueous sodium bicarbonate. The methylene chloride was then dried with sodium sulfate, the solvent was evaporated (*in vacuo*), and the residue was chromatographed on 50 g of silica gel. Hexane elution afforded a mixture of 2,5-di-*t*-butylchlorobenzene (**20**) and 2,5-di-*t*-butylbenzene (**22**).[20,22] The chloro compound was purified by dissolving the mixture in methanol and allowing the chloro compound to crystallize overnight with refrigerator cooling. Recrystallization from methanol afforded pure chloro compound, mp 28.5° (lit. mp 32°). By careful chromatography with small hexane fractions, pure di-*t*-butylbenzene, mp 77°, could be obtained from the later fractions. Hexane–benzene elution afforded 2,5-di-*t*-butylphenyl pivalate (**21**) initially as a liquid. Evaporative distillation and crystallization from methanol afforded 168 mg (11%) of pure ester, mp 67–67.5°, ir $\lambda_{\max}$ (CS_2) 5.69 μ.

Anal. Calcd for $C_{19}H_{30}O_2$: C, 78.6; H, 10.4. Found: C, 78.6; H, 10.5.

Further elution with benzene afforded crude 5,8-di-*t*-butyl-1,4-dihydronaphthalene 1,4-endoxide (**19**). Evaporative distillation of the oily solid followed by recrystallization from pentane afforded 226 mg (19%) of pure adduct: mp 115–116°; ir $\lambda_{\max}$ (CS_2) 13.95 μ; nmr (CCl_4), δ 1.30 (s) (*t*-butyl), 5.95 (m) (H_1, H_4), 6.77 (s) (H_6, H_7), 6.87 (m) (H_2, H_3).

Anal. Calcd for $C_{18}H_{24}O$: C, 84.3; H, 9.4. Found: C, 84.4; H, 9.5.

Diazotizations of Deuterium-Labeled and Unlabeled 2,5-Di-*t*-butylaniline in the Presence and Absence of Furan. A. 2,5-Di-*t*-butyl-4,6-dideuterioaniline. A mixture of 1.5 g (7.3 mmol) of 2,5-di-*t*-butylaniline, 0.73 g (1.0 mmol) of 96% sulfuric acid-d_2, 19.1 g (955 mmol) of 99.7% D_2O, and 9 ml of dioxane was refluxed for 48 hr. The cooled solution was made alkaline with 10% aqueous sodium hydroxide. The organic product was extracted with ether. The ether was dried with sodium sulfate and evaporated. The residue was evaporatively distilled and recrystallized from hexane to yield 875 mg of material (58% yield): mp 104°, ir λ_{max} (CS_2) 2.89 and 2.99 μ; nmr (CCl_4), δ 1.25 (s) and 1.35 (s) (*t*-butyls), 3.54 (s) (NH_2), 7.04 (s) (H_3).

B. Methylene Chloride. A 300-ml portion of commercial methylene chloride was washed with 200 ml of 5% aqueous sodium bicarbonate and with two 200-ml portions of distilled water. It was dried with sodium sulfate and then fractionally distilled to afford 230 ml of methylene chloride, bp 41°.

C. Furan. Commercial furan was dried with molecular sieves and distilled, bp 31.5–32°.

D. Diazotizations. A methylene chloride solution (5 ml) of 500 mg (2.44 mmol) of 2,5-di-*t*-butylaniline or 505 mg (2.44 mmol) of 2,5-di-*t*-butyl-4,6-dideuterioaniline and 248 mg (2.44 mmol) of pivalic acid was added to 5 ml of a refluxing methylene chloride solution containing 276 mg (2.68 mmol) of butyl nitrite. In trapping experiments the solution also contained 497 mg (7.30 mmol) of furan. Addition was complete in 15 min and refluxing was continued for an additional 40 min. The solvent was carefully removed at room temperature on a rotary evaporator; then 2 ml of benzene was added and this solution was used for the vpc analysis of the products using benzophenone as an internal standard. The analytical conditions used were a 0.25-in. SE 30 column (6 ft) at 200°. The order of elution was hydrocarbon **22**, chloro compound **20**, starting aniline **16**, benzophenone, ester **21**, and adduct **19**. Peak areas were determined by cutting and weighing, with a precision of 1.4%.

Diazotization with Methylene Chloride-d_2 as Solvent. A methylene chloride-d_2 solution (3.5 ml, Merck Sharpe and Dohme, Canada) of 350 mg (1.70 mmol) of 2,5-di-*t*-butylaniline and 174 mg (1.70 mmol) of pivalic acid was added to a refluxing solution of 193 mg (1.86 mmol) of butyl nitrite in 3.5 ml of methylene chloride-d_2. Addition was complete in 10 min and the refluxing was continued for 40 min. The deuterated solvent was recovered by distillation; benzene was added to the residue. The benzene solution was washed with sodium bicarbonate, dried with sodium sulfate, and used for the isolation of hydrocarbon **22** by vpc.

Diazotization with Added Perdeuterioethanol. A solution of 315 mg (1.54 mmol) of 2,5-di-*t*-butylaniline and 157 mg (1.54 mmol) of pivalic acid in 5 ml of methylene chloride was added to a refluxing solution of 180 mg (1.75 mmol) of butyl nitrite and 210 mg (3.10 mmol) of perdeuterioethanol (Stohler Isotopes) in 5 ml of methylene chloride. Addition was complete in 30 min and refluxing was continued for 30 min. The solvents were removed on a rotary evaporator. The residue was taken up in benzene and the hydrocarbon **22** and the chloro compound **20** were collected from the vpc.

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(18) The calculations for isotope composition are based on the relative amounts of CHOH (21.6%), CHOD (14.4%), CDOH (38.4%), and CDOD (25.6%) present in the reaction mixture. Also included is a correction for the 11% reduction of "carbonium ion" by methylene chloride. Further, there is an assumption that carbinyl hydrogen is the reducing agent for "ion," while the molecule of hydrogen transferred to the benzyne is derived from carbinyl and hydroxyl.

(19) Infrared spectra were obtained with a Perkin-Elmer 137 instrument. Nmr spectra were determined with a Varian A-60 spectrometer using TMS as an internal standard δ 0.00. Analyses were performed by Spang Microanalytical Laboratory, Ann Arbor, Mich.

(20) P. D. Bartlett, M. Roha, and R. M. Stiles, *J. Amer. Chem. Soc.*, 76, 2349 (1954).

(21) W. A. Noyes, "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1943, p 108.

(22) L. M. Stock and H. C. Brown, *J. Amer. Chem. Soc.*, **81**, 5165 (1959).