

A Novel Route to Condensed Polynuclear Systems; Reality and Illusion of Benzyne Intermediacy

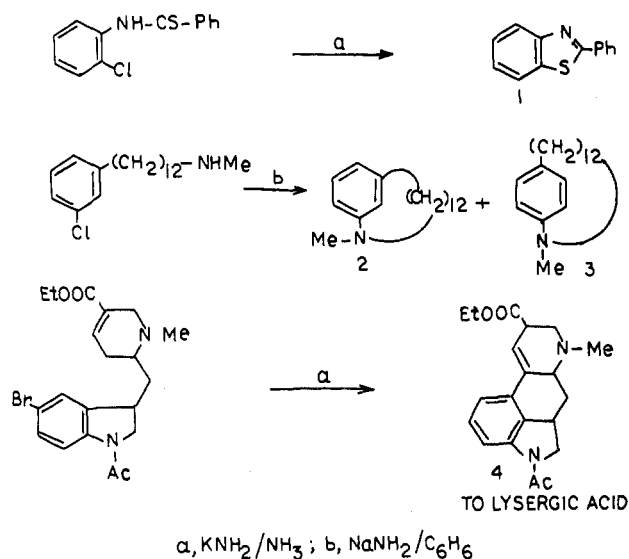
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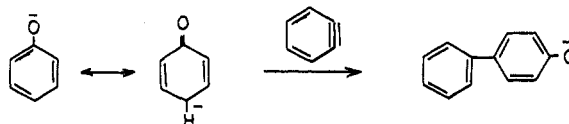
Construction of carbon-carbon bonds lies at the heart of organic chemistry, yet not many methods for linking aryl-carbon atoms are available.¹ Most of the known procedures involve generation of a conventional reactive intermediate on one ring for attack on the other. The present Account is concerned with the use of benzyne² for this purpose, primarily in intramolecular reactions leading to condensed polynuclear compounds.

Ever since the definitive work of Roberts³ and Wittig⁴ on benzyne⁵ there has been considerable effort to develop synthetically viable reactions emanating from these transitory species.⁶ Besides bidentate reactions, a variety of nucleophilic and electrophilic additions have been successfully carried out. If a nucleophile is located on a side chain attached to the generated benzyne, ring closure can occur to give a bicyclic system.⁷⁻⁹ The practical limitations of this synthetic principle, often called a benzyne cyclization, have been delineated by Bunnett.¹⁰ A few illustrative examples (1-4) are given.^{6,11-17}



For joining aryl groups, benzyne cyclization may seem inadequate as simple aromatic compounds do not function as effective nucleophiles toward this reactive intermediate. In fact some of its reactions can be carried out using solvents like benzene. However, appendage of a negatively charged atom to an aromatic

ring confers, on the ortho and para positions, sufficient nucleophilicity for reaction with benzyne. The C-



phenylation products formed in the Dow-phenol process, digestion of chlorobenzene with sodium hydroxide at 300 °C, probably arise in this manner.¹⁸⁻²⁰ Nitranions from aniline,²¹ pyrrole,²² and indole²³ are also known to display ambident reactivity toward benzyne. Hey and co-workers²⁴ were the first to utilize this reactivity pattern in an intramolecular reaction.

Reaction of compound 5 with excess potassium amide in liquid ammonia has been used²⁵⁻²⁷ for synthesis of aporphine (7), morphinandienone (8), and dibenz-

(1) R. L. Clough, P. Mison, and J. D. Roberts, *J. Org. Chem.*, **41**, 2252 (1976).

(2) Also commonly named as 1,2-dehydrobenzene or aryne.

(3) J. D. Roberts, H. E. Simmons Jr., L. A. Carlsmith, and C. W. Vaughan, *J. Am. Chem. Soc.*, **75**, 3290 (1953).

(4) G. Wittig, *Naturwissenschaften*, **30**, 696 (1942).

(5) For the structure, see J. W. Laing and R. S. Berry, *J. Am. Chem. Soc.*, **98**, 660 (1976).

(6) For a comprehensive review, see the monograph by R. W. Hoffmann, "Dehydrobenzene and Cycloalkynes", Academic Press, New York and London, 1967.

(7) G. Wittig and L. Pohmer, *Chem. Ber.*, **89**, 1334 (1956).

(8) R. Huisgen and H. König, *Angew. Chem.*, **69**, 248 (1957).

(9) J. F. Bunnett and B. F. Hrutford, *J. Am. Chem. Soc.*, **83**, 1691 (1961).

(10) J. F. Bunnett, T. Kato, R. R. Flynn, and J. A. Skorcz, *J. Org. Chem.*, **28**, 1 (1963).

(11) M. Julia, F. LeGoffic, J. Igolen, and M. Baillarge, *Tetrahedron Lett.*, 1569 (1969). For other examples in natural product synthesis, see ref 12-17.

(12) M. F. Semmelhack, B. P. Chong, R. D. Stauffer, T. D. Rogerson, A. Chong, and L. D. Jones, *J. Am. Chem. Soc.*, **97**, 2507 (1975).

(13) N. Ueda, T. Kokuyama, and T. Sakan, *Bull. Chem. Soc. Jpn.*, **39**, 2012 (1966).

(14) F. Benington and R. D. Morin, *J. Org. Chem.*, **32**, 1050 (1967).

(15) T. Kametani and K. Ogasawara, *J. Chem. Soc. C*, 2208 (1967).

(16) S. V. Kessar, R. Randhawa, and S. S. Gandhi, *Tetrahedron Lett.*, 2923 (1973).

(17) T. Kametani, K. Fukumoto, and T. Nakano, *J. Heterocycl. Chem.*, **9**, 1363 (1972).

(18) W. J. Hale and E. C. Britton, *Ind. Eng. Chem.*, **20**, 114 (1928).

(19) A. Luttringhaus and D. Ambros, *Chem. Ber.*, **89**, 463 (1956).

(20) R. Huisgen and J. Sauer, *Angew. Chem.*, **72**, 91 (1960).

(21) R. E. Wright and F. W. Bergstrom, *J. Org. Chem.*, **1**, 179 (1936).

(22) G. Wittig and B. Reichel, *Chem. Ber.*, **96**, 2851 (1963).

(23) M. E. Kuehne and T. Kitagawa, *J. Org. Chem.*, **29**, 1270 (1964).

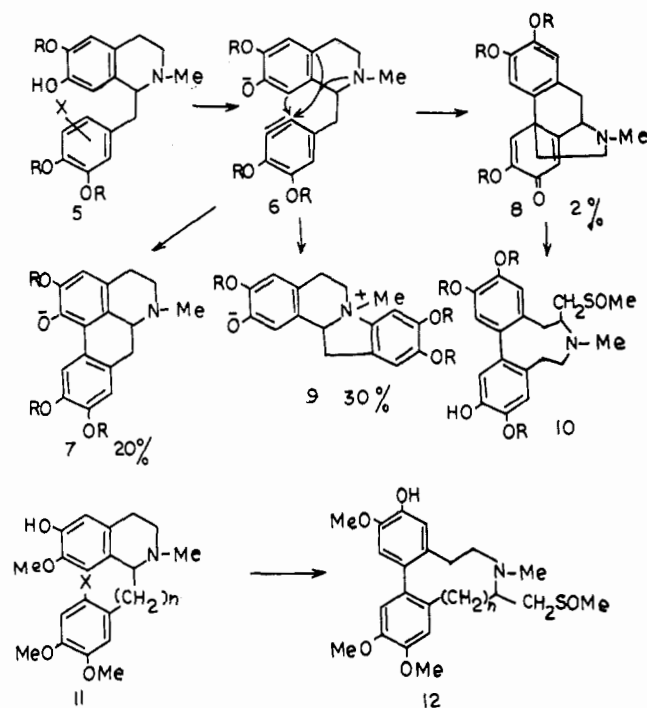
(24) D. H. Hey, J. A. Leonard, and C. W. Rees, *J. Chem. Soc.*, 5266 (1963).

(25) S. V. Kessar, S. Batra, and S. S. Gandhi, *Indian J. Chem.*, **8**, 468 (1970); S. V. Kessar, R. Randhawa, and S. S. Gandhi, *Tetrahedron Lett.*, 2923 (1973); S. V. Kessar, S. Batra, U. K. Nadir, and S. S. Gandhi, *Indian J. Chem.*, **13**, 1109 (1975).

(26) T. Kametani, S. Shibuya, K. Kigasawa, M. Hiiragi, and O. Kusama, *J. Chem. Soc. C*, 2712 (1971); T. Kametani, K. Fukumoto, and T. Nakano, *Tetrahedron*, **28**, 4667 (1972).

(27) M. S. Gibson, G. W. Prenton, and J. M. Walthew, *J. Chem. Soc. C*, 2234 (1970); I. Ahmad and M. S. Gibson, *Can. J. Chem.*, **53**, 3660 (1975).

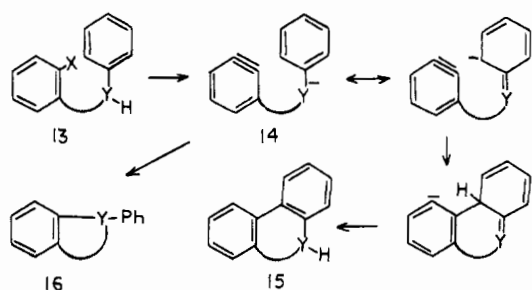
Satinder Vir Kessar was born at Hoshiarpur, India, in 1932. He studied chemistry at the honors school of Panjab University, to which he returned as a Lecturer after obtaining a Ph.D. degree working with M. C. Kloetzel at University of Southern California. He is Professor of Organic Chemistry and is a Fellow of the Indian Science Academy. His research interests lie in the areas of synthetic organic chemistry, reaction mechanisms, and photochemistry.



indolizine (9) alkaloids. Recently formation of di-benzoazonine and azecine ring systems on treatment of substrates like 5 and 11 with NaH/Me₂SO has been reported.²⁸ It seems that under these conditions the dienones suffer further attack by methylsulfinyl carbanions.

A Novel Benzyne Cyclization: the Concept

For some time we have been interested in exploring benzyne cyclization with aromatic rings rendered reactive by a feature built into the system. This type of reaction can have a wide synthetic scope as the need of an extraneous activating function is obviated. A generalized case may be represented by the cyclization of 13, where Y is an atom, like C, N, P, Si, capable of

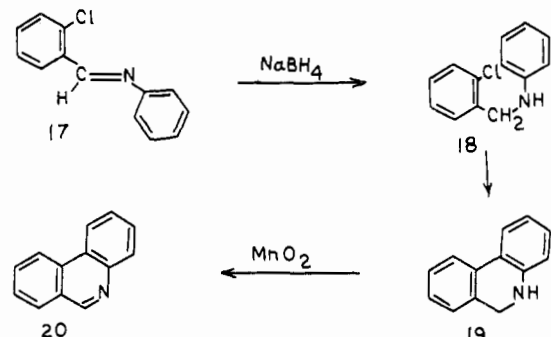


supporting a negative charge for activating the attached ring. If, on treatment of 13 with a strong base, anion formation at Y is rapid, then the generated benzyne (14) can be expected to ring-close to 15. However, diversion to 16 may also occur. Length of the bridge between the two rings of the reactant, bond angles, electronegativity, and the size of Y orbitals can be critical factors in this context.

Phenanthridine Synthesis

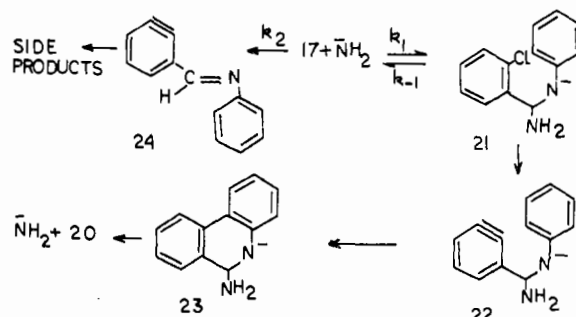
To test the workability of the above model when Y is a nitrogen atom, the chloro amine 18 was treated (1

(28) S. Kano, T. Ogawa, T. Yokomatsu, E. Komiyama, and S. Shibuya, *Tetrahedron Lett.*, 1063 (1974).



h) with KNH₂ (6 mol) in liquid ammonia. On workup, the cyclized product 19 was isolated in an almost quantitative yield.²⁹ It could be readily aromatized to 20. An efficient route to the widely prevalent phenanthridine ring system was thus at hand.

Even though the overall yield of 20 from 17 was very satisfactory, the sequence entails two redundant steps—reduction and oxidation. Synthetic economy requires direct progression from 17 to 20. This objective may seem impractical since anils are known to have a trans structure. Further, the cis-trans conversion rate³⁰ is too slow to allow inversion during the short lifetime of a benzyne intermediate. Nevertheless, the desired reaction could proceed through the adduct 21 as shown.



Addition of amide ions across azomethine linkage is well precedented;³¹ only it needed to be sufficiently fast.

Treatment of the chloro anil 17 with KNH₂/NH₃ gave phenanthridine (20) cleanly.³² In fact the yield (>90%) was beyond expectation for a complex multistep sequence. Obviously, wasteful benzyne (24) generation is minimal, perhaps due to extremely rapid adduct formation and favorable equilibrium position^{33,34} ($k_1 \gg k_2$ and k_{-1}).

Mechanism of Phenanthridine Cyclization

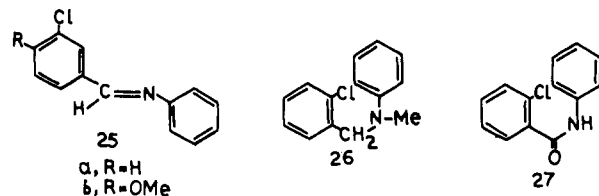
It was desirable to confirm if the mechanism of this cyclization was in accord with the rationale of its development. An alternate simple nucleophilic displacement mechanism seemed untenable as subjecting the reactant 18 to a base which would generate its nitranion, but not the benzyne, caused no change.³⁵

(29) S. V. Kessar, R. Gopal, and M. Singh, *Tetrahedron Lett.*, 71 (1969).
 (30) E. Fischer and Y. Frei, *J. Chem. Phys.*, 27, 808 (1957); G. Wettermark, J. Weinstein, J. Sousa, and L. Dogliotti, *J. Phys. Chem.*, 69, 1584 (1965).

(31) H. H. Strain, *J. Am. Chem. Soc.*, 50, 2218 (1928).
 (32) S. V. Kessar and M. Singh, *Tetrahedron Lett.*, 1155 (1969).
 (33) The kinetic requirements necessary for the success of such a reaction have been discussed; see ref 34.
 (34) S. V. Kessar, M. Singh, R. Chander, D. Pal, and U. K. Nadir, *Tetrahedron Lett.*, 467 (1971).

(35) S. V. Kessar, R. Gopal, and M. Singh, *Tetrahedron*, 29, 167 (1973). An intramolecular electron transfer, followed by loss of halide and ring closure, is untenable on the same grounds.

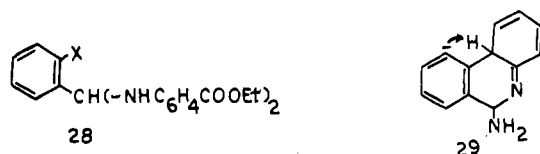
Positive support for the intermediacy of benzyne came from successful³⁵ cyclization of the meta chloro anils **25a** (70%) and **25b** (90%).



Dependence of this cyclization on the nature of the aromatic ring activation was probed through reactions of the amine **26** and the anilide **27**. In neither case could any cyclic products be isolated.³⁵ Formation of a nitranion is not feasible in **26**, while in the anion from **27** the charge on nitrogen is largely shared on the carbonyl side. Thus it seems that strong anionic activation of the aromatic ring is essential for success. It may be pointed out that in the direct cyclization of anils the postulated intermediate **21** is not only free of the initial steric constraint but also has the requisite ring activation. Additional support for its formation was sought through the following experiments.

A mixture of benzylideneaniline, sodium amide, and ammonia was brought together and sealed under vacuum in an NMR tube at liquid nitrogen temperature. The tube was allowed to warm up to -40°C and immediately placed in the spectrometer probe maintained at this temperature.³⁵ Successive scanning showed rapid disappearance of the anil and formation of a product, giving signals characteristic of the protons of a phenyl ring attached to a nitranion.³⁶

Condensation of certain aromatic amines with *o*-chlorobenzaldehyde is known to afford stable bis adducts which resemble intermediate **21** and should behave similarly under the cyclization conditions. Treatment of **28** with KNH_2/NH_3 indeed furnished³⁵



the expected phenanthridine, along with *p*-carbethoxyaniline. Similar results³⁷ were obtained with the dicondensation product derived from 4-aminopyridine. Thus it was possible to simulate the path proposed for cyclization of halo anils ($17 \rightarrow 21 \rightarrow 20$)—an aromatic amine being added and expelled across the carbon nitrogen double bond.

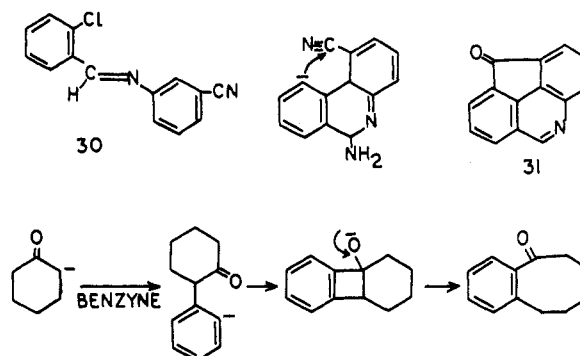
In the proposed cyclization mechanism, the immediate product of nucleophilic attack on benzyne in the intermediate **22** would be the carbanion **29**. Of interest was to find out if the isomerization of **29** to **23** involved proton transfer intramolecularly or through the solvent. Reaction of the Schiff base from 2,4,6-trideuterioaniline and *o*-chlorobenzaldehyde with KNH_2/NH_3 afforded³⁵ 2,4-dideuteriophenanthridine, showing that the intramolecular process does not operate under these conditions.

(36) T. Birchall and W. L. Lolly, *J. Am. Chem. Soc.*, **88**, 5439 (1966); R. Waack, M. A. Doran, E. B. Baker, and G. A. Olah, *ibid.*, **88**, 1272 (1966).
 (37) S. V. Kessar and G. S. Joshi, *Tetrahedron*, **29**, 419 (1973).

Scope of the Phenanthridine Synthesis

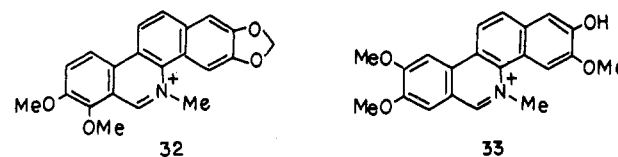
Phenanthridines bearing alkyl, alkoxy, dimethylamino, carboxyl, carbonyl, and chloro groups can be obtained in good yields³⁸ by this method. Presence of a nitro function is deleterious, and free hydroxy groups also depress formation of the desired product. Phenanthridines bearing substituents at position 6 can be obtained, in moderate yields, through anils derived from *o*-chlorophenyl ketones.³⁸

Cyclization of Schiff bases from meta-substituted anilines affords a mixture of two phenanthridines corresponding to benzyne attack on either side. However, the anil **30** gave, besides the expected 3-



cyanophenanthridine, the tetracyclic ketone **31**. Apparently reaction of the initially formed phenyl carbanion with the proximate cyano group effectively competes with protonation. Interesting intermolecular benzyne reactions entailing a similar addition to a carbonyl function have been reported recently.³⁹

Cyclization of the Schiff bases from naphthylamines proceeds well provided ether is used as a cosolvent with ammonia. This procedure constitutes a very practical route to benzophenanthridine alkaloids,⁴⁰ especially of the chlerythrine (**32**) type. It has been used by Stermitz



and co-workers⁴¹ to synthesize fagaronine (**33**) and many other benzo[*c*]phenanthridine derivatives of interest in cancer chemotherapy.

Some pentacyclic compounds can be obtained through an interesting "double" benzyne cyclization. For example, reaction of the anil **34** with KNH_2/NH_3 gives **35** in one step.⁴²

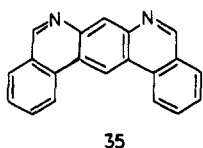
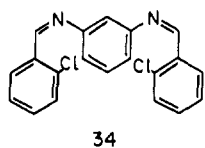
(38) S. V. Kessar, D. Pal, and M. Singh, *Tetrahedron*, **29**, 177 (1973).

(39) M. Essiz, G. Coudert, G. Guillaumet, and P. Caubere, *Tetrahedron Lett.*, 3185 (1976).

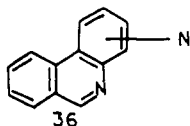
(40) S. V. Kessar, M. Singh, and P. Balakrishnan, *Indian J. Chem.*, **12**, 323 (1974). It may be noted that stilbene-type photocyclization of anils is successful only in concentrated sulfuric acid. Even then the yields are poor, and workup is cumbersome. It fails altogether for alkaloid synthesis; S. F. Dyke, M. Sainsbury, and B. J. Moon, *Tetrahedron*, **24**, 1467 (1968); S. V. Kessar, G. Singh, and P. Balakrishnan, *Tetrahedron Lett.*, 2269 (1974).

(41) J. P. Gillespie, L. G. Amros, and F. R. Stermitz, *J. Org. Chem.*, **39**, 3239 (1974); F. R. Stermitz, J. Gillespie, L. G. Amros, R. Romero, T. A. Stermitz, K. A. Larson, S. Earl, and J. E. Ogg, *J. Med. Chem.*, **18**, 708 (1975).

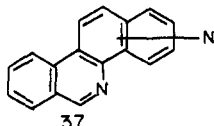
(42) Unpublished results from this laboratory.



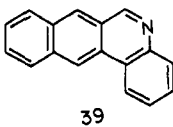
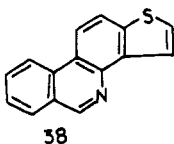
Schiff bases derived from pyridyl and other heterocyclic amines undergo benzene cyclization readily. A few ring systems synthesized in this manner are shown (36–38). Some of these constitute valuable interme-



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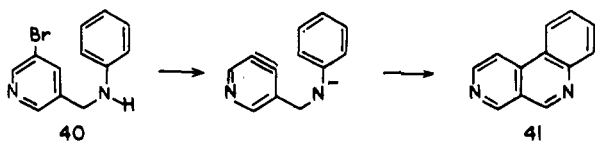


(N AT POSITION 1, 2, 4, 11 OR 12)



diates for drugs⁴³ and aza analogues of steroidal hormones.^{44–46} Furthermore, cyclizations proceeding through 1,2- and 2,3-naphthynes are also successful.^{42,47} For example, 39 can be readily obtained from the anil of 3-chloro-2-naphthaldehyde. In these syntheses sometimes the overall yield was better if the Schiff base was reduced prior to KNH_2/NH_3 treatment.

Turning to heterarynes, it is known that certain problems which are only marginal in benzyne chemistry assume greater proportions⁴⁸ with these reactive intermediates. However, treatment of 40 with KNH_2/NH_3



followed by aromatization gave the diazaphenanthrene 41 smoothly.⁴⁹ The high cyclization yield (90%) confirmed the expectation⁴⁸ that with a 3-halogenated pyridine elimination would occur primarily on the desired side and incursion of addition–elimination processes would be minimal. Synthesis of 41 had been achieved earlier by a much longer route.⁵⁰

A similar pyridyne cyclization reaction constitutes the key step in synthesis⁴⁹ of the alkaloid perlolidine (45). It may be noted that here complete selectivity in successive replacement of the three bromine atoms (43 to 44) could be achieved by using reactants of increasing basic strength.

(43) S. S. Berg and V. Petrow, *J. Chem. Soc.*, 3713 (1952).

(44) S. V. Kessar, Manmohan Singh, Pawan Jit, Gurdev Singh, and A. K. Lumb, *Tetrahedron Lett.*, 471 (1971).

(45) S. V. Kessar, P. S. Pahwa, Paramjit Singh, Pawan Jit, and Y. P. Gupta, *Indian J. Chem.*, in press.

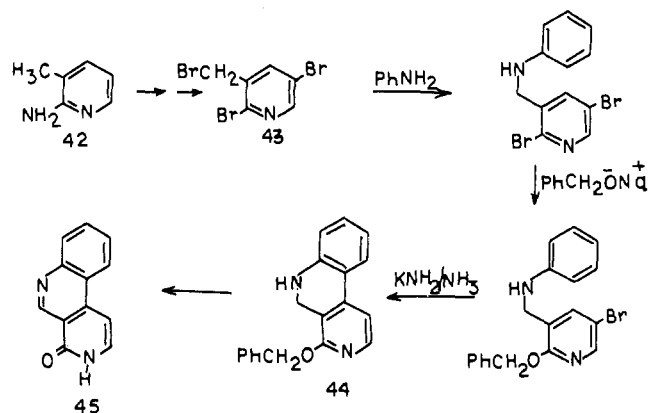
(46) S. V. Kessar, N. Parkash, and G. S. Joshi, *J. Chem. Soc., Perkin Trans. 1*, 1158 (1973).

(47) S. V. Kessar, B. S. Dhillon, and G. S. Joshi, *Indian J. Chem.*, 11, 624 (1973).

(48) T. Kauffmann and R. Wirthwein, *Angew. Chem., Int. Ed. Engl.*, 10, 20 (1971). For an interesting ring-opening–closure reaction of quinoline halides, see G. M. Sanders, M. Van Dijk, and H. J. Hertog, *Recl. Trav. Chim. Pays-Bas*, 93, 198 (1974).

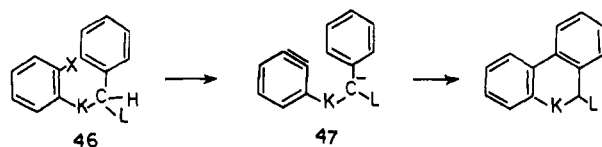
(49) S. V. Kessar, Y. P. Gupta, P. S. Pahwa, and Paramjit Singh, *Tetrahedron Lett.*, 3207 (1976).

(50) M. A. Akhtar and J. A. D. Jeffreys, *Tetrahedron Lett.*, 3329 (1970).



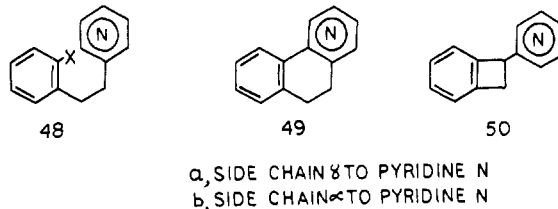
Benzyne Cyclization with Carbanion-Activated Aromatic Rings

It was of interest to find out if the cyclization concept outlined earlier is also applicable when Y–H of 13 is a suitable carbon acid. Accordingly, reactions expected to proceed through intermediates like 47 were inves-



tigated. It is evident that moieties K and/or L should stabilize the carbanion, to ensure its rapid generation, but not to the extent that sufficient ring activation does not ensue. In view of the success with substituted anilines a $\text{p}K_a$ value in the same range, ~ 27 on the McEwen scale,⁵¹ was considered desirable for the carbon acid (46) to be cyclized. On the basis of literature data,⁵² it was hoped that the correct balance would be struck somewhere in the series 46 ($\text{K} = \text{S}, \text{SO}, \text{SO}_2, \text{L} = \text{H}; \text{K} = \text{O}, \text{L} = \text{H}; \text{K} = \text{CH}_2, \text{L} = \text{C}_6\text{H}_5$). However, reaction of these compounds with KNH_2/NH_3 gave complex mixtures having no major nonbasic components.⁴²

Since carbanions can be generated readily from picolines, cyclization of 48a with KNH_2/NH_3 was attempted. In this case the benzoquinoline 49a (15%) and benzocyclobutene 50a (37%) were isolated, along with some amination material.⁵³ Similarly the α -pyridyl compound 48b gave 49b and 50b. Thus, intramolecular reaction of benzyne with an aromatic ring activated by an appended carbanion was finally achieved, albeit in modest yield. Failure of cyclization with 46 and isolation of substantial quantities of



four-membered ring compounds from 48, in contrast to almost exclusive phenanthridine formation with 18,

(51) W. K. McEwen, *J. Am. Chem. Soc.*, 58, 1124 (1936).

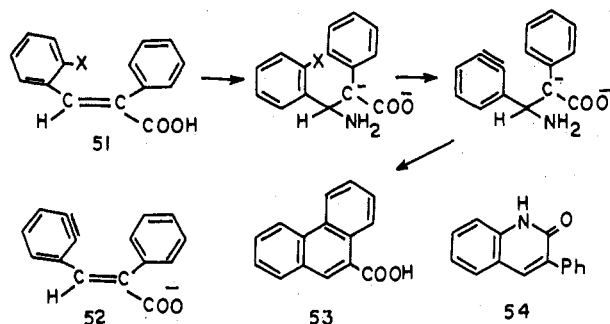
(52) F. G. Bordwell, R. H. Imes, and E. C. Steiner, *J. Am. Chem. Soc.*, 89, 3905 (1967).

(53) S. V. Kessar, U. K. Nadir, Paramjit Singh, and Y. P. Gupta, *Tetrahedron*, in press.

show that many subtle factors affect the course of this reaction.

Cyclization of Halogenated α -Phenylcinnamic Acids

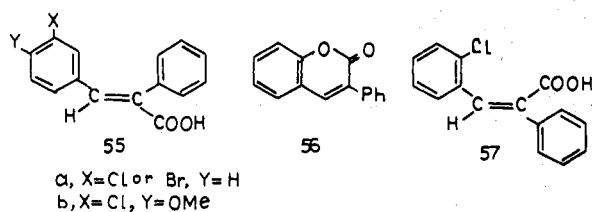
In quest of further examples where an aromatic ring attached to a carbon atom undergoes a benzyne cyclization, reaction of *trans*-*o*-chloro- α -phenylcinnamic acid (**51**) with KNH_2/NH_3 was studied. The pre-



sumption was that NH_2^- addition to the double bond would afford a dianion⁵⁴ capable of cyclizing like the adducts from Schiff bases. Alternately, a reaction between the generated benzyne and the aromatic ring could occur due to sheer proximity (**52**).

Treatment of the chloro acid **51** with KNH_2 (10 mol) in liquid ammonia gave⁵⁵ 9-phenanthrenecarboxylic acid (**53**, 52%) along with a small quantity of 3-phenylcarbostyryl (**54**). The balance of the material was accounted for by amination products. This procedure is also useful for synthesis of some substituted phenanthrenes.⁵⁶

Although this cyclization had been devised assuming benzyne intermediacy and the reaction conditions used were typical, yet the usual tests were undertaken as a matter of routine. Normal cyclization was observed with the bromo analogue of **51**, while the fluoro compound failed to react as expected. However, treatment of the meta halogenated *trans* acid **55a** with $\text{KNH}_2/$



NH_3 led to little phenanthrene formation. The only nonbasic material isolated from this reaction turned out to be the coumarin **56** (~40%). Similar results were obtained with the methoxy acid **55b**. Matters took a still more mysterious turn when it was found that reaction of the ortho halogenated *cis* acid **57** furnished phenanthrenecarboxylic acid (**53**, 26%) and carbostyryl (**54**, 30%), but no coumarin.³⁴

(54) Carboxylate groups stabilize adjoining carbanions, and generation of a dianion from phenylacetic acid under these conditions is known: C. R. Hauser and W. J. Chambers, *J. Am. Chem. Soc.*, **78**, 4942 (1956).

(55) S. V. Kessar, R. Sood, U. K. Nadir, and Manmohan Singh, *J. Chem. Soc., Chem. Commun.*, 316 (1969).

(56) U. K. Nadir, Ph.D. Thesis, Panjab University, Chandigarh, India, 1974.

Mechanism of Cyclization of Halogenated α -Phenylcinnamic Acids

The formation of **56** from **55** and of **53** from **57** constitutes a "trans cyclization"³³ which must involve a rotation around the double bond at some stage or the other. This rotation may be envisaged to occur through reversibly formed amide ion adducts or vinylic anions. However, experimental evidence⁵⁶ inveighed against these possibilities, and involvement of inverting radical anions ($58 \rightleftharpoons 59$) was considered. Generation of radical



anions on exposure of certain aromatic substrates to strong bases and nucleophiles has been postulated, although the nature of the electron-transfer reagents is not always clear.⁵⁷ Further, it is known that in stilbene-type radical anions both rotation around the double bond⁵⁸ and electron exchange with the neutral substrate are fast,⁵⁹ so that *cis*-*trans* isomerization can occur through a chain process.⁶⁰

As ESR experiments to detect radical ions under the conditions used for isomerization were unsuccessful in our hands, indirect chemical evidence was sought. It was argued that if these species are generated, then the chloro acid **60** should lose⁶¹ its halogen on contact with



KNH_2/NH_3 , even though 1,2-benzyne formation is not possible. The actual experiment⁶² gave insight into the mechanism of isomerization as well as that of cyclization, since along with halogen loss from **60** formation of the cyclic acid **61** (45%) was observed. Thereby, it could be surmised that cyclization of ortho-halogenated α -phenylcinnamic acids to phenanthrenes is not benzyne mediated and, perhaps, phenyl radicals are involved in it. Moreover, it seems that in the case of meta-halogenated acids (**55a,b**) radical anions serve as vehicles for isomerization but halide loss does not occur through them.⁶³ In these substrates further reaction probably proceeds via benzyne intermediates which can

(57) J. K. Kim and J. F. Bunnett, *J. Am. Chem. Soc.*, **92**, 7463 (1970); J. A. Zoltewicz, T. M. Oestreich, and A. A. Sale, *ibid.*, **97**, 5889 (1975). Criteria for electron transfer from nucleophiles and their possible role in *cis*-*trans* isomerization have been discussed: H. O. House and P. D. Weeks, *J. Am. Chem. Soc.*, **97**, 2770 (1975).

(58) C. S. Johnson Jr. and R. Chang, *J. Chem. Phys.*, **43**, 3183 (1965); J. W. Hupp, J. A. Ferguson, and D. G. Whitten, *J. Org. Chem.*, **37**, 1485 (1972).

(59) R. Chang and C. S. Johnson, *J. Chem. Phys.*, **46**, 2314 (1967).

(60) Under strongly reducing conditions further electron addition predominates; cf. G. Levin, T. A. Ward, and M. Szwarc, *J. Am. Chem. Soc.*, **96**, 271 (1974); P. R. Singh and Ramesh Kumar, *Indian J. Chem.*, **11**, 692 (1973).

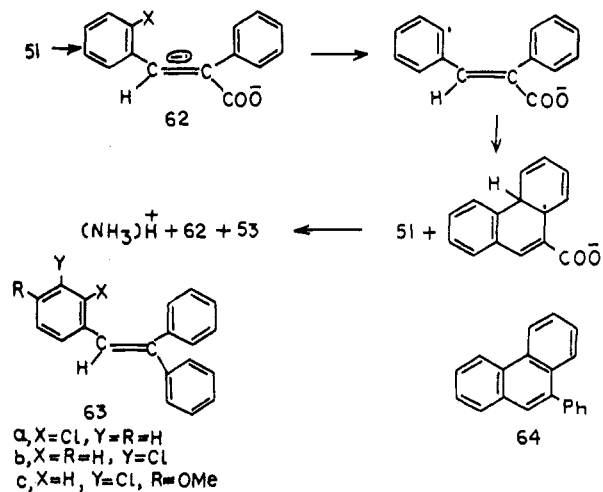
(61) Halogen loss from benzoic radical dianions is known to be very fast in liquid ammonia: A. R. Buick, T. J. Kemp, G. T. Neal, and T. J. Stone, *J. Chem. Soc. A*, 1609 (1969).

(62) S. V. Kessar, Suchita Narula, S. S. Gandhi, and U. K. Nadir, *Tetrahedron Lett.*, 2905 (1974).

(63) In stilbene-type ion radicals, the calculated electron density at the ortho position is far greater than that at the meta positions [J. C. Schug, *J. Chem. Phys.*, **37**, 330 (1962)], and so is the observed rate of halide ion loss from it [J. G. Smith and I. Ho, *J. Org. Chem.*, **38**, 4240 (1973)]. This trend can be predicted on the basis of simple valence bond structures also.

cyclize to coumarin but do not react with an unactivated aromatic ring even when located on the same side of a double bond. This would explain the perplexing dichotomy in product formation from the ortho and meta series.

It may be pointed out that phenanthrenecarboxylic acid formation can be a chain process with the following propagation cycle.⁶⁴



(64) Features reminiscent of the now well-established $\text{S}_{\text{RN}}1$ mechanism for aromatic substitution: J. K. Kim and J. F. Bunnett, *J. Am. Chem. Soc.*, **92**, 7463 (1970); R. G. Scamehorn and J. F. Bunnett, *J. Org. Chem.*, **42**, 1449 (1977).

If the above proposals are valid, substrates similar to **51** and capable of accepting electrons from KNH_2/NH_3 , presumably because of a low-lying LUMO, should also cyclize under these conditions. Reaction of the stilbene **63a** indeed gives **64** in excellent yield.⁶⁵ Further, in the reaction of meta compounds (**63b** and **63c**) halogen is lost promptly,⁴² but no phenanthrene formation is observed, as expected on the basis of the inactivity of benzynes toward phenyl rings lacking anionic activation.

Conclusions

Benzyne cyclization with aromatic rings activated by an adjoining nitranion built into the reacting system is a useful method for obtaining a variety of polynuclear compounds. Although extension to carbanion-promoted cyclizations has not been as successful, this synthetic principle admits of many variations which need to be explored. From a mechanistic point of view, interaction of strong nucleophiles and bases with aryl halides is a fascinating area deserving more attention.

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(65) Some of the earlier reported base-initiated cyclizations may be proceeding through radical anions: D. Y. Curtin and R. P. Quirk, *Tetrahedron*, **24**, 5791 (1968); C. L. Hewett, *J. Chem. Soc.*, 1286 (1938); N. Campbell and D. H. Reid, *J. Chem. Soc.*, 3281 (1952); N. P. Buu-Hoi, O. P. Roussel, and P. Jacquignon, *J. Chem. Soc., Perkin Trans. 1*, 234 (1972).