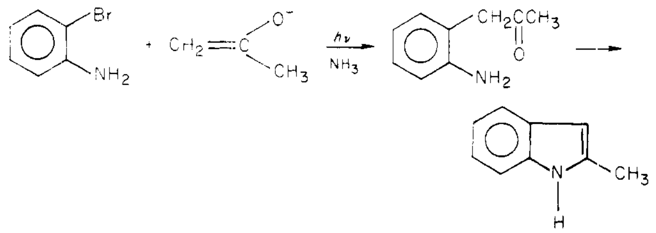
Table I. Indole Syntheses by Photostimulated Reactions of *o*-Haloanilines with Ketone Enolate Ions in Ammonia

expt no.	aniline deriv	enolate ion from	irradn time, h	% X^- release	indole deriv formed (% yield)
1	2-bromo-	acetone	2	98	2-methyl- (93)
2	2-bromo-3-methyl-	acetone	4	86	2,4-dimethyl- (80)
3	2-bromo-4-methyl-	acetone	2	98	2,5-dimethyl- (88)
4	2-bromo-5-methyl-	acetone	2	90	2,6-dimethyl- (82)
5	2-chloro-5-phenyl-	acetone	12	98	2-methyl-6-phenyl- (88)
6	2-chloro-5-methoxy-	acetone	10.5	53	2-methyl-6-methoxy- (42)
7	2-chloro-5-carboxy-	acetone	12	95	2-methyl-6-carboxy- (89)
8	2-bromo-*N*-methyl-	acetone	3	97	1,2-dimethyl- (79)
9	2-bromo-	3-methyl-2-butanone	4	97	2-isopropyl- (84[a])
10	2-bromo-	3,3-dimethyl-2-butanone	3	97	2-*tert*-butyl (94)
11	2-bromo-	cyclohexanone	4	97	1,2,3,4-tetrahydrocarbazole (14)
12	2-bromo-4-methyl-	3-pentanone	2	98	3,5-dimethyl-2-ethyl- (73)
13	2-chloro-3-aza[b]	acetone	10.5	60	4-aza-2-methyl- (45)

[a] Approximately 6 mg (ca. 0.05%) of 2,3,3-trimethylindolenine was also obtained. [b] 3-Amino-2-chloropyridine.

Scheme I. An Indole Synthesis



erality for the synthesis. It should be noted that enolate ions from various ketones can be employed and that only in the case of cyclohexanone enolate (experiment 11) is there an indication of a serious side reaction, possibly hydrogen atom abstraction from the β-carbon.[6] We call attention to the facts that 2-bromo-*N*-methylaniline with acetone enolate affords 1,2-dimethylindole in good yield (experiment 8) and that 3-amino-2-chloropyridine with acetone enolate gives 2-methyl-4-azaindole (experiment 13).

An interesting limitation lies in the fact that 2,4-dihaloanilines show very low reactivity. Thus in reactions with acetone enolate ion, 2,4-dibromoaniline released only 11% of bromide ion during 2-h irradiation under our usual reaction conditions, which involve 1 equiv of excess potassium *tert*-butoxide (*t*-BuOK) in the medium, and only 28% of bromide without excess *t*-BuOK. Likewise, 2-iodo-4-chloroaniline under the usual conditions released only 9% of iodide ion and 1% of chloride ion during 1.5 h of irradiation. We postulate that the second halogen increases the acidity of the aniline[7] sufficiently so that a large fraction of it exists as its unreactive conjugate base under our usual conditions. The fact that more bromide release occurred from 2,4-dibromoaniline in the absence of excess *t*-BuOK is consistent with this view.

We foresee wide applicability for this synthesis and for analogous transformations.

After these experiments had been completed and a draft of this communication had been written, we learned of the work of Beugelmans and Roussi,[8] who have independently discovered this principle of indole synthesis and who have reported four examples of it.

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Supplementary Material Available: Experimental procedures and evidence for assignment of product structures (5 pages). Ordering information is given on any current masthead page.

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[6] J. F. Wolfe, M. P. Moon, M. C. Sleevi, J. F. Bunnett, and R. R. Bard, *J. Org. Chem.*, **43**, 1019 (1978).

[7] Cf. F. G. Bordwell, D. Algrim, and N. R. Vanier, *J. Org. Chem.*, **42**, 1817 (1977).

[8] R. Beugelmans and G. Roussi, *J. Chem. Soc., Chem. Commun.*, 950 (1979).

Nitrogen Analogues of *o*-Xylylenes

Summary: The gas-phase pyrolysis of *o*-hydroxymethylanilines provides simple, one-step syntheses of acridines, acridones, and quinoline derivatives. The ease with which nitrogen analogues of *o*-xylylenes are formed during pyrolysis suggests that the methodology currently used in the synthetic applications of benzocyclobutenes can be employed with these azo-*o*-xylylenes to yield a variety of heterocycles and polycyclic amines.

Sir: The generation of benzocyclobutenes by gas-phase pyrolysis of *o*-(chloromethyl)toluenes,[1-3] and their valence tautomerization to *o*-xylylenes, has proved to be a generally useful method for syntheses of novel molecules of theoretical interest[4-8] and for syntheses of natural products.[9,10] Recently we have described the application of this method to the corresponding oxygen and sulfur analogues of the *o*-xylylenes,[11] and we now report that the extension of these methods to the nitrogen analogues provides simple, convenient syntheses for a variety of acridines, acridones, and quinolines.

An outstanding example from the literature of a nitrogen analogue of benzocyclobutene and its valence tautomerization to an *o*-xylylene analogue is the report of Burgess

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[8] Neuschwander, B.; Boekelheide, V. *Isr. J. Chem.*, in press.

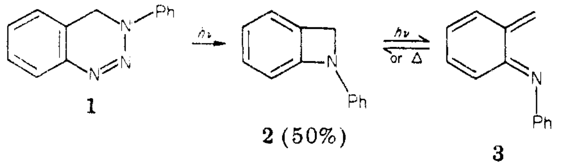
[9] Oppolzer, W. *Synthesis* **1978**, 793.

[10] Kametani, T. *Acc. Chem. Res.* **1976**, *9*, 319.

[11] Mao, Y.-l.; Boekelheide, V. *Proc. Natl. Acad. Sci. U.S.A.*, in press.

0022-3263/80/1945-1547$01.00/0

and McCullagh that 3-phenyl-4*H*-benzo-1,2,3-triazene (1) is converted photochemically to *N*-phenylbenzoazetine (2).[12] Thermal or photochemical excitation of 2 effects valence tautomerization to the *o*-xylylene derivative 3, as shown by trapping experiments.[12]



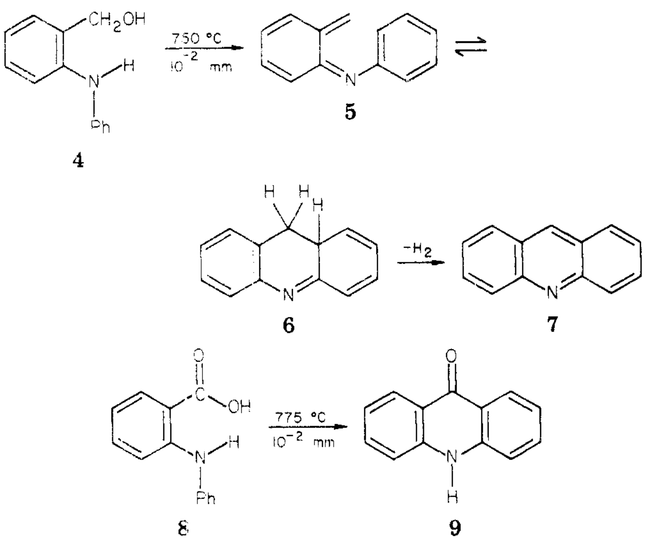
1

2 (50%)

3

In an attempt to provide a more convenient synthesis of *N*-phenylbenzoazetine, *N*-phenyl-*o*-(hydroxymethyl)aniline (4)[13] was subjected to gas-phase pyrolysis at 750 °C.[14] Under these conditions the product isolated in 64% yield was acridine (7). As a rationalization for the formation of acridine, one can presume that 4 undergoes elimination of water to give 5 which, after cyclization to 6, eliminates hydrogen thermally to yield acridine.[15] If so, use of an ortho-substituted aniline at a higher oxidation state would avoid the dehydrogenation step and might result in an even better yield. This proved to be true. When *N*-phenylanthranilic acid (8) was subjected to gas-phase pyrolysis at 775 °C, acridone (9) was isolated in 87% yield. Since the substitution patterns of the aromatic rings in 4 and 8 can be easily varied, the gas-phase pyrolysis of such substituted anilines offers a one-step, high-yield method of synthesis for both acridines and acridones.

These results suggested that, if properly substituted anilines were chosen, a similar cyclization–aromatization sequence would yield quinoline derivatives. To test this idea a series of spirooxazine derivatives, 10–13, were prepared by boiling a solution of the appropriate carbonyl compound, 4, and a catalytic amount of *p*-toluenesulfonic acid in benzene with continuous removal of water. The properties of each of the spirooxazines and the yield obtained in their formation are summarized below.[16]



4

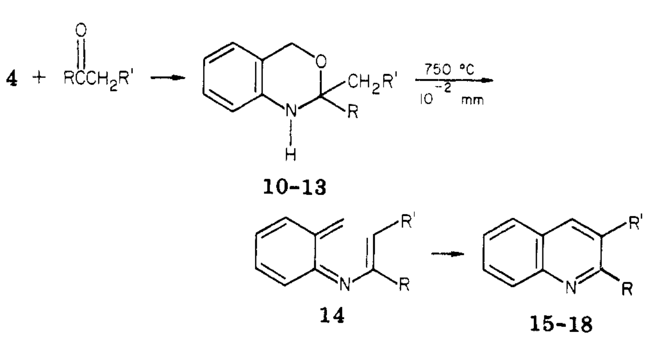
5

6

7

8

9



10–13

14

15–18

compd	R	R'	mp, °C	% yield
10	$-(CH_2)_3-$		49-51	98
11	$-(CH_2)_4-$		51-52	92
12	CH_3	H	53-55	90
13	H	CH_3	oil	89
15[17]	$-(CH_2)_3-$			36
16[18]	$-(CH_2)_4-$			42
17[19]	CH_3	H		29
18[20]	H	CH_3		32

The gas-phase pyrolyses of the spirooxazines 10–13 presumably involves first a ring opening with loss of water to give the corresponding *o*-xylylene derivatives 14 which, on cyclization and thermal elimination of hydrogen, then lead to the quinoline derivatives.[21]

The significant conclusion from these observations is that gas-phase pyrolyses of *o*-(hydroxymethyl)anilines provide a simple, convenient method for producing nitrogen analogues of *o*-xylylenes. When a multiple bond is also generated adjacent to the nitrogen, cyclization and formation of aromatic heterocycles occurs. However, in view of the considerable body of information on converting benzocyclobutenes to natural products,[9,10] a promising application for the generation of nitrogen analogues of *o*-xylylenes should be their intramolecular Diels–Alder cyclization to give polycyclic products.

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[14] The pyrolyses described in this communication were carried out by subliming the reactant at 10^{-2} mm slowly into an empty quartz tube (2.5 cm × 30 cm) held in the hot zone of a furnace and collecting the exit gases with a condenser cooled to -80 °C. See ref 1-3 for descriptions of other experimental designs for similar vapor-phase pyrolyses.

[15] Similar cyclization–aromatization sequences have been suggested: Ao, M. S.; Burgess, E. M. *J. Am. Chem. Soc.* **1971**, *93*, 5298. Jacqmin, G.; Nasielski, J.; Billy, G.; Remy, M. *Tetrahedron Lett.* **1973**, 3655.

[16] All new compounds and all of the pyrolysis products have been fully characterized and their spectral data, elemental composition, and/or high-resolution mass spectra are in accord with their assigned structures. In particular the infrared spectra of 10–13 showed in each case an absorption band in the region of 3340–3450 cm^{-1}, corresponding to an >N–H stretching vibration, and no absorption in the region of 1630–1690 cm^{-1}, indicating the absence of an imine function. Thus, these products are assigned the spirooxazine structures 10–13 rather than the alternate structures of hydroxymethyl imines.

[17] Mp 59–60 °C [lit. mp 60–61 °C (Beer, R. J. S.; Broadhurst, T.; Robertson, A. *J. Chem. Soc.* **1953**, 2440)].

[18] Mp 53–54 °C [lit. mp 54.5 °C (Perkin, W. H., Jr.; Sedgewick, W. G. *J. Chem. Soc.* **1924**, *125*, 2446)].

[19] Methiodide of 17, mp 193.5–194.5 °C [lit. mp 195 °C (Mills, W. H.; Harris, J. E. G.; Lambourne, H. *J. Chem. Soc.* **1921**, *119*, 1297)].

[20] Methiodide of 18, mp 218.0–219.5 °C [lit. mp 221 °C (Doebner, O.; Miller, W. V. *Ber. Dtsch. Chem. Ges.* **1885**, *18*, 1640)].

[21] The conditions for conducting the gas-phase pyrolyses for forming quinolines have not been studied intensively and quite probably the yields of quinolines produced in these reactions can be improved markedly by careful attention to the design of apparatus and the various parameters involved.