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THERMAL REARRANGEMENT OF N-ALLYL ANHYDRO BASES OF QUINOLINES AND INDOLENINES[1]

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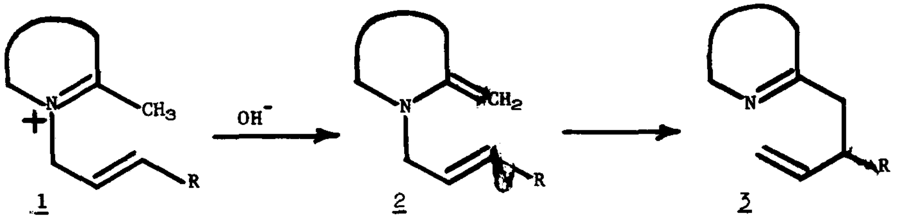
We report a new method, based on the recent discovery of the thermal rearrangement of allyl vinylamines to unsaturated imines[4], of introducing a specific allyl substituent onto a carbon attached to the C=N double bond of unsaturated nitrogen heterocycles.

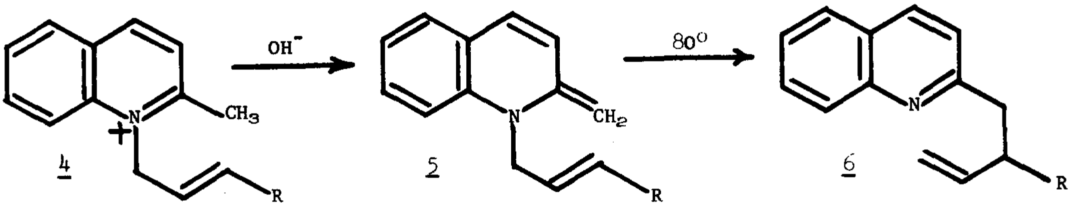
Quaternary salts (1) of unsaturated nitrogen heterocycles containing an alkyl group at the α-position are known[5] to be converted to anhydro bases (2) by the action of alkali; when the quaternizing substituent is allylic, the anhydro base contains an allyl vinylamine moiety which should be capable of Claisen rearrangement to products of structure (3). This reaction, which constitutes a method of alkylating at active carbon in the absence of the usual strongly basic alkylating conditions, has now been realized in the quinoline and indolenine series and appears capable of extension to isoquinolines, benzthiazoles, and related heterocycles.



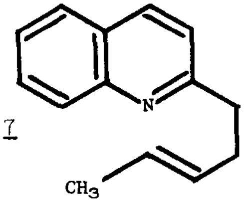
N-Crotyl quinaldinium bromide (4b), m.p. 182-184° (dec), was prepared by heating crotyl bromide with quinaldine in nitrobenzene[6] at 70°; the nmr spectrum showed that the crotyl group had not isomerized during reaction. This method of preparation failed for the cinnamyl salt

(4c), and consequently both it and the allyl salt (4a) were prepared by an alternate route involving quaternization of quinoline with allyl or cinnamyl iodide, addition of methyl Grignard reagent, and oxidation of the resulting dihydroquinoline with iodine[7]. The nmr spectra (Table 1) of 4a, m.p. 200-201° (dec), lit.[8] m.p. 196°, and 4c, m.p. 177-179° (dec), are consistent with their structures.

Each of the salts (4) was suspended in benzene and stirred with 1N NaOH for 10 minutes. The benzene layer containing anhydro base (5) was separated, dried, and refluxed under N_2 for 12-24 hr. The products (6) were isolated from the concentrate by preparative vpc[9]; their structures were confirmed by elemental analysis and infrared and nmr spectra. All three products had characteristic vinyl infrared bands at 1640, 990, and 910 cm^{-1} The structure of 6a was confirmed further by catalytic reduction to 2-n-butylquinoline, picrate m.p. 163°, lit.[10] m.p. 161.5-164°. Quinaldine was identified as a by-product in all three cases, in yields of 22-39 °/o. Rearrangement of 4b and 4c, salts with unsymmetrical allyl groups, showed the double bond inversion characteristic of concerted cyclic rearrangements. Accompanying 6b, however, was a low yield of 2-(3-pentenyl)-quinoline (7) formed by rearrangement without double bond migration. Yields and nmr spectra of the products are shown in Table 1.



(a) R = H
(b) R = CH_3
(c) R = C_6H_5



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The same type of rearrangement could be effected in a nonaromatic heterocycle, the indolenine system. N-Allyl-2,3,3-trimethylindoleninium iodide (8), m.p. 154-155° (dec), nmr ($CDCl_3$)

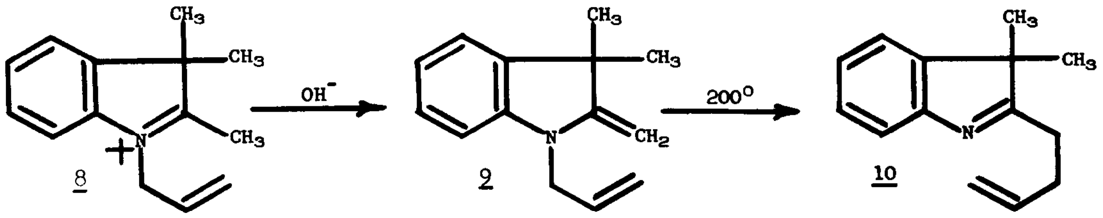
Table 1. NMR Spectra.

	$2\text{-}CH_3$	$N\text{-}CH_2\text{-}$	olefinic	aromatic	R
4a (D_2O)	3.11, s, 3H	5.6, m, 2H	4.7-6.6, m, 3H	7.8-9.5, m, 6H	---
4b (D_2O)	3.0, s, 3H	5.38, m, 2H	5.63, m, 2H	7.6-8.7, m, 6H	1.62, dd, 3H
4c ($CDCl_3$)	3.38, s, 3H	6.0, m, 2H	6.6, m, 2H	7.2-8.6, m, 11H	

	$2\text{-}CH_2\text{-}$	allylic	olefinic	quinoline	R	Yield
6a (CCl_4)	2.65, split t, 2H	3.05, dt, 2H	5.0-5.8, m, 3H	7.0-8.1, m, 6H	---	52.5 $^{o}/_{o}$
6b (CCl_4)	--- 2.9, m, 3H ------		4.8-5.8, m, 2H	7.0-8.1, m, 6H	1.08, d, J=7, 3H	56.7
6c (CCl_4)	2.58, m, 2H	3.31, m, 1H	4.6-6.4, m, 2H	6.8-8.2, m, 6H	7.18, s, 5H	38
7 (CCl_4)	2.5, m, 2H	2.9, m, 2H	5.4, m, 2H	7.0-8.1, m, 6H	1.4, m, 3H	8.4

[Values given in δ; s = singlet, d = doublet, t = triplet, m = multiplet]

δ1.68 (s, 6H, gem. dimethyl), 3.15 (s, 3H, 2-methyl, exchanges rapidly in D_2O), 5.0-6.5 (m, 5H, allyl), and 7.5-7.7 (m, 4H, aromatic), was prepared from the parent indolenine and allyl iodide at room temperature in the dark under N_2 for two days. Treatment with aqueous base gave the anhydro base (9), stable enough to be isolated; b.p. 74-76° (0.2 mm), nmr (CCl_4 under N_2) δ 1.33 (s, 6H, gem. dimethyl), 3.91 (s, 2H, 2-methylene), 4.1 (broad d with splitting, 2H, $N\text{-}CH_2$), 5-6 (m, 3H, vinyl), and 6.4-7.3 (m, 4H, aromatic). Compound 9 was more resistant to rearrangement than anhydro bases 5 and was recovered unchanged after 24 hr. at 134°. Heating at 200° for 24 hr, however, gave 95 $^{o}/_{o}$ of indolenine 10, nmr (neat) δ 0.68 (s, 6H, gem. dimethyl), 2.12 (m, 4H, $-CH_2CH_2-$), 4.6-5.8 (m, 3H, vinyl), and 6.6-7.3 (m, 4H, aromatic). Satisfactory analyses were obtained for 8 and 10.



Though rearrangement of anhydro base **9** requires a temperature similar to that at which Claisen rearrangement of most allyl vinyl ethers and allyl vinylamines occurs, the ease of rearrangement of anhydro bases **5** at 80° is striking. We attribute this to the regain of aromaticity in the heterocyclic ring in the conversion of **5** to **6**.

REFERENCES AND FOOTNOTES

1. This work was supported in part by research grant GP-3811 from the National Science Foundation, to whom we express our appreciation.
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3. Public Health Service Postdoctoral Fellow, 1967-1968; present address, Department of Chemistry, Louisiana State University, Baton Rouge, La., 70803.
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