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ACID-CATALYZED OLIGOMERIZATION BETWEEN 4-(1-ETHYL-1-PROPENYL)MORPHOLINE AND BENZYLIDENEANILINES. SYNTHESIS OF 1,2,3,4,7a,8-HEXAHYDRO-4-AZA-s-INDACENE DERIVATIVES

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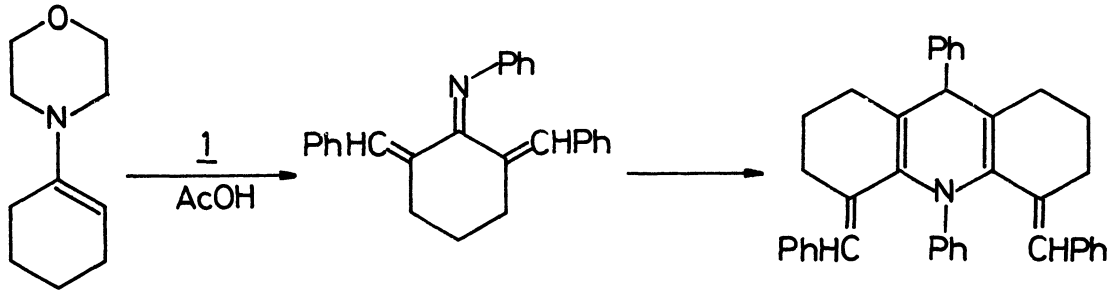
Reaction of 4-(1-ethyl-1-propenyl)morpholine with benzylideneanilines in acetic acid provided 1,2,4,6,7-pentaaryl-3,5,7a-trimethyl-1,2,3,4,7a,8-hexahydro-4-aza-s-indacene in decent yield. The reaction mechanism involving the conrotatory cyclization of an intermediate pentadienyl cation has been proposed.

The acid-catalyzed oligomerization reaction between pyrrole, a conjugated enamine, and an aldehyde in acetic acid or in propionic acid has been successfully utilized for the synthesis of porphyrin derivatives.[1] In a slightly modified systematic investigation, we have been interested in the reaction of enamines with Schiff bases, nitrogen-analog of aldehydes, in acetic acid to prepare compounds having unusual carbon skeletons which are extraordinarily hard to construct using available synthetic methodology.[2,3] Thus we previously reported that 4-(1-cyclohexenyl)morpholine undergoes rapid oligomerization with benzylideneaniline (1) in acetic acid to provide the decahydroacridine derivative (2) presumably via the conjugated imine (3).[3]

In order to test the versatility of the reaction as well as the appropriateness of the reaction mechanism, we used 4-(1-ethyl-1-propenyl)morpholine (4), an open-chain enamine, this time and obtained the tricyclic 1,2,3,4,7a,8-hexahydro-4-aza-s-indacene derivatives 5 as the main product. We wish to report here the preparation and structural identification of 5 and to briefly discuss the mechanism of this reaction.



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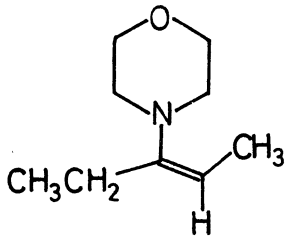
The reaction was carried out as follows. A solution of benzylideneaniline (1a)(11.44 g, 0.063 mol) in anhydrous acetic acid(100 ml) was dropwise added at room temperature to 4-(1-ethyl-1-propenyl)morpholine (4)(5.55 g, 0.035 mol) with magnetic stirring. After 12 hr stirring, the resulting yellow precipitates were collected by filtration and recrystallized from acetone-ethanol to give 1,2,4,6,7-pentaphenyl-3,5,7a-trimethyl-1,2,3,4,7a,8-hexahydro-4-aza-s-indacene (5a) (1.46 g, yield 15.9%) as yellow needles: mp 220°C, M^+=581($C_{44}H_{39}N$), Anal., Found(Calcd):C, 91.03(90.83); H, 6.98(6.76); N, 2.27(2.41). IR(KBr): 1645, 1640, 1242 cm^{-1}. UV(ethanol): λ_{max}(log ε); 373(3.08), 291 (4.12), 243(4.38) nm.

The corresponding reactions using 1b and 1c gave 5b(mp 164°C) and 5c(mp 160°C) in 13.8 and 15.3% yields, respectively.



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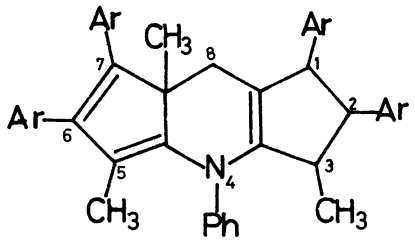
PhN=CH–Ar (1)

1a Ar=C_6H_5

b Ar=p-Cl-C_6H_4

c Ar=p-Br-C_6H_4



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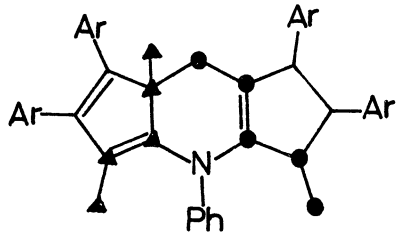
The structure of 5a was identified as follows. The molecular formula was found to be $C_{44}H_{39}N$ by elemental analysis and its mass spectrum. As shown in Table 1, the ^{1}H-NMR spectrum showed three methyl, one methylene, three methyne and five phenyl groups. The ^{13}C-NMR spectrum also shown in the the Table was most consistent with the presence of three C=C double bonds in addition to the five phenyl groups. These necessarily required a tricyclic structure with three tetrasubstituted C=C double bonds. Considering that two molecules of the enamine and four molecules of 1a participated in the reaction as shown by its molecular formula, it was expected that the most reasonable tricyclic structure should be the one presented by 6. Off-resonance decoupling of the ^{13}C-NMR spectrum and homonuclear spin-decoupling of the ^{1}H-NMR spectrum were most consistent with the carbon skeleton proposed. Thus the connectivity pattern between C-1, -2 and -3 was unequivocally established by irradiating H-1, -2 and -3. The location of the three olefinic double bonds was also supported by its UV spectrum which showed a strong absorption due to the conjugated dienamine moiety at 243 nm. All other structural informations can be reasonably explained by structure 5.



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Symbols, ● and ▲, indicate the carbon skeleton originated from the enamine (4).

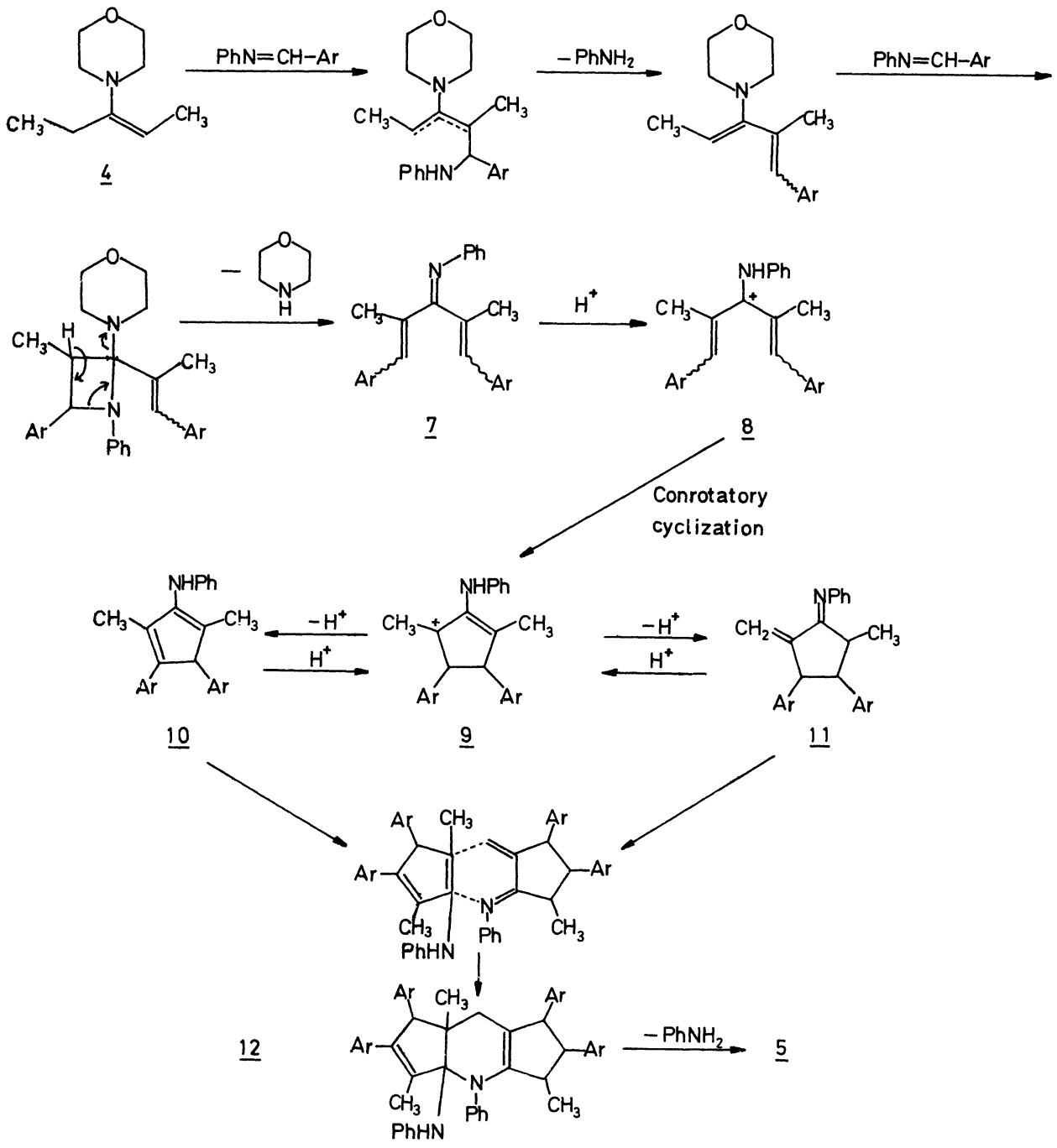
This structure was further rationalized by the formation mechanism of 5a outlined in the scheme. The key intermediate of this mechanistic sequence is the conjugated symmetrical imine (7) arising from one enamine and two benzylideneaniline molecules. The formation of 7 can be explained by Michael-type addition, deamination, [2+2] cycloaddition and deamination as previously proposed for the formation of 3 from the cyclohexanone enamine and 1.[3] The protonated open-chain conjugated imine (8) can then undergo conrotatory ring closure to afford cyclopentenyl cation 9. The cyclization of such a pentadienyl cation should be thermally allowed process[4] and a few examples have been known.[5] The cation 9 can lose one proton to give either the conjugated imine (10) or the substituted cyclopentadiene (11). The thermally allowed [4+2] cycloaddition between 10 and 11 should readily produce the tricyclic compound 12 which would undergo deamination to provide the final product 5. It may be worthwhile to note that the open-chain 7 underwent cyclization in the presence of acetic acid, whereas the sterically rigid conjugated imine 3 did not take the same route under analogous conditions.[3]

Although the yields of the 4-aza-indacene derivatives (5) are by no means spectacular, it is now clear that reactions of enamines with benzylideneanilines in acetic acid provide compounds having various carbon skeletons which are otherwise hard to access. Further investigations are now in progress.

Table 1. NMR spectral data of 1,2,4,6,7-pentaphenyl-3,5,7a-trimethyl-1,2,3,4,7a,8-hexahydro-4-aza-s-indacene (5a)

^{1}H-NMR				^{13}C-NMR		
δ[a]	Area	Appearance (J, in Hz)	Assignments	δ[a]	Appearance[b]	Assignments
0.49	3	d(J=8)	3-CH_3	11.7	q	3-CH_3
1.14	3	s	7a-CH_3	14.5	q	7a-CH_3
1.36	3	s	5-CH_3	21.5	q	5-CH_3
2.01 2.52	2	d(J=16) d(J=16)	8-CH_2	30.6	t	C-8
3.20	1	bm	3-CH	41.6	d	C-3
3.58	1	t(J=9)	2-CH	49.0	s	C-7a
4.26	1	d(J=9)	1-CH	54.0	d	C-2
7.0-7.4	25	m	Aromatic protons	57.8	d	C-1
				108.1-142.8		36 sp^2 Carbons

[a]Measured in $CDCl_3$ with TMS as internal standard.
[b]Splitting pattern determined by off-resonance decoupling.



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