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SYNTHESIS AND STRUCTURE OF 2-ARYL-2,4-DIMETHYL-1,2,3,4-TETRAHYDROQUINOLINES AND 1,3-DISUBSTITUTED INDENES

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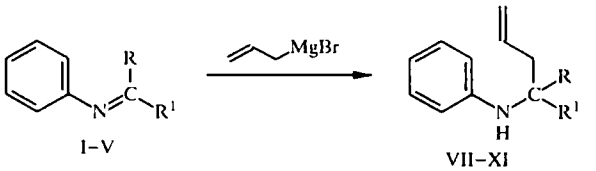
It has been shown that the intramolecular cyclization of N-(1-arylbutenyl)arylamines under acid catalysis conditions may proceed in two directions with the formation of 2-aryl-2,4-dimethyl-1,2,3,4-tetrahydroquinolines and 1,3 disubstituted indenes.

A method of synthesizing 2-alkyl(aryl)-4-methyl-1,2,3,4-tetrahydroquinolines was developed in our laboratory starting from aldimines obtained by the condensation of aniline (or substituted anilines) with aldehydes. On reacting these Schiff's bases with allylmagnesium bromide N-[1-alkyl(aryl)-3-butenyl]anilines are formed which are converted under conditions of intramolecular cyclization into tetrahydroquinolines [1-3].

Similar conversions of ketimines obtained from aniline (or a substituted aniline) and aliphatic-aromatic (or aromatic) ketones have not been studied previously.

The following compounds were used as starting Schiff's bases: N-(α-methylbenzylidene)- (I), N-[α-(4-[2,2]pyracyclophanyl)ethylidene)-(II),N-[4-methoxy(α-methyl)benzylidene]-(III),N-(1-phenyl-2-propylidene)-(IV),N-(α-phenylbenzylidene)-(V) anilines and N-(α-methylbenzylidene)-α-naphthylamine (VI).

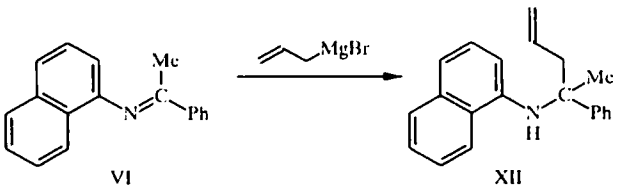
Compounds (I) and (III) were obtained as described in [4, 5]. The ketimines (II) and (IV)-(VI) were synthesized for the first time. On reacting ketimines (I)-(V) with allylmagnesium bromide the following previously unknown anilines were obtained in high yield: N-(1-methyl-1-phenyl-3-butenyl)- (VII), N-(1-methyl-1-(4-[2.2]paracyclophanyl)-3-butenyl)- (VIII), N-[1-methyl-1-(p-anisyl)-3-butenyl]- (IX), N-(1-methyl-1-benzyl-3-butenyl)- (X), and N-(1,1-diphenyl-3-butenyl)aniline (XI).



I–V VII–XI

I—IV, VII—X R = CH_3; V, XI R = R^1 = C_6H_5; I, VII R^1 = C_6H_5; II, VIII R^1 = 4-[2,2]paracyclophanyl; III, IX R^1 = $C_6H_4OCH_3$-p; IV, X R^1 = $CH_2C_6H_5$

The previously unknown N-(1-methyl-1-phenyl-3-butenyl)-α-naphthylamine (XII) was obtained similarly from N-(α-methylbenzylidene)-α-naphthylamine (VI). The characteristics and PMR spectra of compounds (II) and (IV)-(XII) are given in Tables 1 and 2.



VI XII

Characteristic signals were present in the PMR spectra of compounds (VII)-(XII) for the olefinic protons of the allyl fragment, viz. a multiplet at 4.9-5.5 ppm (2H) assigned to the terminal vinyl group, a multiplet at 5.5 ppm (2H) assigned to

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TABLE 1. Physicochemical Characteristics of Compounds (II) and (IV)-(XIX)

Compound	Empirical formula	Found N, % / Calculated N, %	R_f *	mp, °C	M^+	IR spectrum, ν, cm^{-1}	Yield, %
II	$C_{24}H_{23}N$	4,31 / 4,36	0,75	56...58	325	1653 (CN)	75,5
IV	$C_{15}H_{15}N$	—	0,56	Oil †	209	1651	60
V	$C_{19}H_{15}N$	—	0,56	115...116	257	1649	36
VI	$C_{18}H_{15}N$	—	0,68	74...76	245	1650	35
VII	$C_{17}H_{19}N$	5,90 / 5,83	0,75	38...40	237	3400 (NH)	90
VIII	$C_{27}H_{29}N$	3,87 / 3,81	0,63	Oil	367	3413	52,5
IX	$C_{18}H_{21}NO$	5,24 / 5,22	0,77	Oil	267	3405	84
X	$C_{18}H_{21}N$	5,57 / 5,59	0,58	Oil	251	3415	51
XI	$C_{22}H_{21}N$	4,68 / 4,57	0,62	70...71	299	3420	67
XII	$C_{21}H_{21}N$	4,87 / 4,88	0,73	66...68	287	3410	82
XIII	$C_{17}H_{19}N$	5,9 / 5,91	0,77	Oil	237	3380	10
XIV	$C_{18}H_{21}N$	5,57 / 5,51	0,60	Oil	251	3415	10
XV	$C_{21}H_{21}N$	4,87 / 4,90	0,68	Oil	287	3415	15
XVI	$C_{27}H_{29}N$	3,81 / 3,78	0,73	Oil	367	3440	15
XVII	$C_{21}H_{22}$	—	0,73	173...175	274	—	30
XVIII	$C_{11}H_{13}O$	—	0,81	Oil	161	—	30
XIX	$C_{16}H_{14}$	—	0,80	Oil	206	—	15

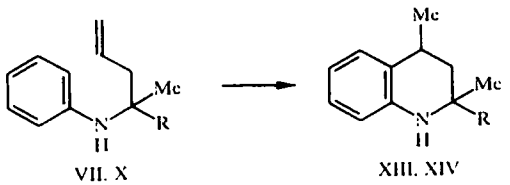
*Eluent was heptane–ethyl acetate, 3:1.

†bp 170-175°C (9 mm Hg).

the terminal vinyl group, a multiplet at 5.5-6.2 ppm (1H) for the methine proton interacting with the protons of the CH_2 group. The signal for the latter was at 2.0-2.9 ppm and is the AB portion of an ABMXY spin system with a difference in chemical shifts of the A and B protons varying within the limits 0.05-0.3 ppm and with characteristic values for the coupling constants J_{AB} = 14 Hz, ^3J = 7.0 Hz.

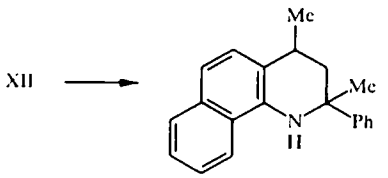
The ^{13}C NMR spectra also confirmed the structure of compounds (VII)-(XII). The signals of the spectrum of compound (IX) characterizing the alkenyl fragment may be cited as an example: $C_{(1)}$ 119.15 (CH_2), $C_{(2)}$ 133.7 (CH), $C_{(3)}$ 48.96 (CH_2), $C_{(4)}$ 57.16 (C quat.), $C_{(5')}$ 25.66 (CH_3). Bands for the stretching vibrations of the C=N bond at 1650-1680 were absent from the IR spectra of these compounds and a band was observed for the stretching vibrations of the NH bond at 3400-3415 cm^{-1}.

A complex mixture of substances was formed on heating (60-70°C) compounds (VII), (X), and (XII) in chloroform in the presence of concentrated sulfuric acid from which the following were isolated: 2,4-dimethyl-2-phenyl-1,2,3,4-tetrahydroquinoline (XIII), 2-benzyl-2,4-dimethyl-1,2,3,4-tetrahydroquinoline (XIV), and 2,4-dimethyl-2-phenyl-benzo[h]-1,2,3,4-tetrahydroquinoline (XV) respectively.



VII, X XIII, XIV

VII, XIII R = Ph; X, XIV R = CH_2–Ph

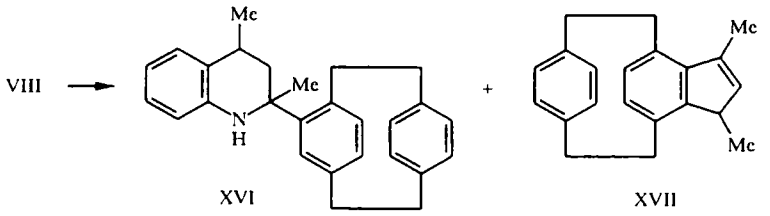


XV

The spectral characteristics of compounds (XIII)-(XV) are given in Table 3. It was established on the basis of PMR spectral data on the substituted tetrahydroquinoline (XIII) that it was formed as two isomers (ratio 3:1) with different dispositions of the methyl and phenyl groups at position 2. The piperidine ring has a halfchair conformation in both isomers and the methyl group at position 4 has an equatorial orientation. This is indicated by the size of the coupling constants of the 4-H proton, viz. $J_{3a,4c}$ = 11.0 Hz, $J_{3a,4c}$ = 5.8 Hz (3.05 ppm) in the predominant isomer and $J_{3a,4a}$ = 12.6 Hz, $J_{3a,4e}$ = 4.6 Hz (2.37 ppm) in the minor isomer. The orientation of the substituent at position 4 was established by investigating the nuclear Overhauser effect (NOE) [6]. On saturating the signal of the 2-CH_3 group of the predominant isomer, an NOE was observed on the protons of the 4a-H and 3e-H (1.97 ppm), but in the minor isomer only on the 3a-H proton (1.76 ppm). This indicates that the predominant isomer has a cis (2e-Ph, 4e-Me) configuration and the minor isomer a trans (2a-Ph, 4e-Me) configuration.

It was established chromatographically that aniline was present in the reaction products on heating compounds (VII) and (X) and α-naphthylamine (15%) was isolated from the reaction mixture in the case of compound (XII). The formation of these aromatic amines is probably linked with a different direction for the cyclization mechanism.

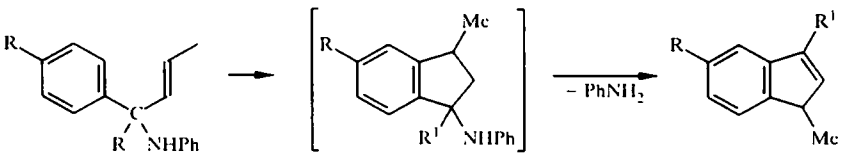
This suggestion was confirmed on cyclizing N-(1-methyl-1-(4-[2,2]paracyclophanyl)-3-butenyl)aniline (VIII). In this case two substances were isolated from the reaction mixture, viz. 2,4-dimethyl-2-(4-[2.2]paracyclophanyl)-1,2,3,4-tetrahydroquinoline (XVI) and 4,5-(1,3-dimethylcyclopenteno) [2,2]paracyclophane (XVII). It was established chromatographically that aniline was also present in the reaction products, which was probably split off when forming the indene (XVII).



XVI XVII

The structure of the indene derivative (XVII) was confirmed spectrally. Two signals were present in its PMR spectrum for methyl groups at 1.66 ppm, d, J = 7.1 Hz (1-CH_3) and 1.86 ppm, d, J = 1.1 Hz (3-CH_3) and a signal for the olefinic 2-H proton at 5.0 ppm (narrow multiplet). The signal for the 1-H proton overlapped with the multiplet of the methylenic protons of the paracylophane (2.7-3.5 ppm) and was detected at 3.15 ppm on uncoupling from the methyl group in position 1. The protons of the aromatic rings of the paracyclophane rings formed a multiplet at 6.0-6.65 ppm.

Only substituted indenes were isolated on cyclizing the phenylalkenylamines (IX) and (XI), viz. 1,3-dimethyl-5-methoxyindene (XVIII) (30% yield) and 1-methyl-3-phenyl-indene (XIX) respectively. It follows that in these cases cyclization occurred not at the aniline fragment but onto the aryl substituent of the butenyl group.



IX, XI XVIII, XIX

IX, XVIII R = OMe, R^1 = Me; XI, XIX R = H, R^1 = Ph

Signals were observed in the PMR spectrum of substituted indene (XVIII) for the 1-H proton at 3.5 ppm (br.q), the 2-H proton at 6.1 ppm (br.s), three signals for methyl groups at 1.4 (J = 7.4 Hz, 1-CH_3), 2.2 (s, 3-CH_3), and 3.9 (s, 5-OCH_3), and three signals for the aromatic protons at 7.40 (d, J = 2.2 Hz, 4-H), 6.87 (d.d, J = 8.2, 2.2 Hz, 6-H), and 7.20

TABLE 2. Parameters of the PMR Spectra of Compounds (II)-(XII)*

Compound	Chemical shift, δ, ppm
II †	2.15 (3H, s, CH_3); 2.70-3.30 (7H, m, CH_2-PCP); 3.73 (1H, m, CH_2-PCP); 6.30-7.0 (7H, m, ArH-PCP); three groups of signals 6.88 (2H, d, J = 8.3 Hz), 7.12 (1H, t, J = 8.0 Hz), and 7.42 (2H, t, J = 7.7 Hz, N-ArH)
III	2.10 (3H, s, CH_3); 3.70 (3H, s, OCH_3); 7.7 (2H) and 6.70 (2H) (two d, splitting 9.0 Hz, O-ArH); 6.4-7.2 (5H, m, =N-ArH)
IV	2.17 (3H, s, CH_3); 3.54 and 3.86 (2H, type AB spectrum, J_{AB} = 13.8 Hz, CH_2-Ar); 6.70-7.60 (10H, m, ArH)
V	6.75-7.80 (m, ArH)
VI	2.17 (3H, s, CH_3); 6.86-8.13 (12H, m, ArH)
VII	1.70 (3H, s, CH_3); 2.62 (2H, m, CH_2); 4.1 (1H, br s, NH); 5.08-5.12 (2H, m, $=CH_2$); 5.70 (1H, m, =CH); three groups of signals 6.33 (2H, d), 6.62 (1H, t), and 7.0 (2H, t, J = 8 Hz, N-ArH); 7.30-7.50 (5H, m, ArH)
VIII	1.68 (3H, s, CH_3); 2.30-2.60 (2H, m, CH_2); 2.90-3.30 (7H, m, CH_2-PCP + NH); 3.90 (1H, m, CH_2-PCP); 5.05 (2H, m, $=CH_2$); 5.50 1H, m, =CH); 6.30-7.10 (12H, m, ArH)
IX	1.75, (3H, s, CH_3); 2.70 (2H, m, CH_2); 3.90 (3H, s, OCH_3); 4.2 (1H, br s, NH); 5.20-5.30 (2H, m, $=CH_2$); 5.57 (1H, m, =CH); 7.0 (2H) and 7.50 (2H) (two d, J = 8.8 Hz, O-ArH); three groups of signals 6.47 (2H, d, J = 8.2 Hz), 6.72 (1H, t, J = 7.7 Hz), and 7.12 (2H, d d, J = 7.7 8.2 Hz, N-ArH)
X	1.58 (3H, s, CH_3); 2.60-2.95 (2H, m, CH_2); 3.24 and 3.43 (2H, type AB spectrum, J_{AB} = 14 Hz, CH_2Ar); 3.80 (1H, br s, NH); 5.40-5.55 (2H, m, $=CH_2$); 6.25 (1H, m, =CH); 7.00-7.71 (10H, m, ArH)
XI	3.42 (2H, m, CH_2); 4.51 (1H, s, NH); 5.2 (2H, m, $=CH_2$); 5.68 (1H, m, =CH); 6.52-7.73 (15H, m, ArH)
XII	1.97 (3H, m, CH_3); 2.89 (2H, m, CH_2); 5.20 (1H, br s, NH); 5.42 (2H, m, $=CH_2$); 6.22 (1H, m, =CH); 7.12-8.09 (12H, m, ArH)

*Chemical shifts and coupling constants were calculated as first order in all cases except for the AB spin system.

†Here and subsequently the abbreviation PCP is used to designate the paracyclophane fragment.

ppm (d, J = 8.2 Hz, 7-H). Signals were present in the ^{13}C NMR spectrum for three methyl groups at 12.95, 16.56, and 55.4 ppm, five groups for CH at 43.5, 109.4, 111.3, 119.2, and 134.0 ppm, and four quaternary carbon atoms at 137.6, 138.4, 151.7, and 158.1 ppm. It may be suggested that the intermediate stage of this reaction is the formation of a substituted indane, elimination of a molecule of aniline from which leads to the thermodynamically more favored indene system.

It has therefore been shown that the electrophilic cyclization of arylalkenylamines may occur in two directions with the formation of tetrahydroquinolines or indenes.

EXPERIMENTAL

The PMR spectra of compounds were drawn on Bruker spectrometers with operating frequencies of 200 and 30 MHz in $CDCl_3$. The IR spectra were drawn on a Specord IR 75 instrument. Mass spectra were obtained on an MX 1303 instrument. A check on the progress of reactions and the homogeneity of the compounds obtained was effected by TLC on Silufol UV 254 plates.

Ketimines (I)-(VI). A solution of amine (0.01 mole) and ketone (0.01 mole) in absolute toluene (30 ml) with catalytic quantities of glacial acetic acid was boiled with a Dean and Stark separator for 24-30 h. At the end of the reaction, the solvent was distilled off. The ketimine was isolated from the residue by vacuum distillation or by fractional crystallization.

Arylalkenylamines (VII)-(XII). The appropriate ketimine (I)-(VI) (0.03 mole) was added gradually to a solution of allylmagnesium bromide prepared from magnesium (0.12 mole) and allyl bromide (0.06 mole) in absolute ether (100 ml) and the mixture boiled for 3 h. The mixture was decomposed with saturated ammonium chloride solution. The ether layer was separated, the aqueous layer extracted with ether (3 × 50 ml), and the combined ether solution dried over $MgSO_4$. The ether

TABLE 3. Parameters of the PMR Spectra of Compounds (XIII)-(XIX)*

Compound	Chemical shift, δ, ppm, coupling constant J, Hz
cis-XIII	1.27 (3H, d, J = 6.5 Hz, 4-CH_3); 1.60 (3H, s, 2-CH_3); 1.97 (1H, d d, J = 13.0, 5.8 Hz, 3e-H); 1.83 (1H, d d, J = 13.0, 11.0 Hz, 3a-H); 3.05 (1H, m, 4-H), 4.3 (1H, br s, NH); 6.53 (1H, d d, J = 8.1, 1.3 Hz, 8-H); 6.58 (t d, J = 7.4, 1.2 Hz, 6-H); 7.08 (1H, t, 7-H); 7.23 (1H, d, 5-H); three groups of signals 7.26 (1H, t), 7.37 (2H, t), and 7.58 (2H, t, ArH)
trans-XIII	1.29 (3H, d, J = 6.5 Hz, 4-CH_3); 1.55 (3H, s, 2-CH_3); 1.76 (1H, t, J = 12.5 Hz, 3a-H); 2.25 (1H, d d, J = 12.4, 4.6 Hz, 3e-H); 2.37 (1H, m, 4-H); 3.7 (1H, br s, NH); 6.58 (1H, d d, J = 8.4, 1.2 Hz, 8-H); 6.70 (1H, t d, J = 7.4, 1.2 Hz, 6-H); he remaining signals in the aromatic region were overlapped by the signals of the predominant isomer cis-(XIII)
XIV	1.32 (3H, s, 2-CH_3); 1.55 (3H, d, J = 6.6 Hz, 4-CH_3)' 2.02 (1H, d d, J = 12.9, 5.5 Hz, 3e-H, 1.75 (1H, br t, J = 12.6 Hz, 3a-H); 2.93 and 2.98 (type AB spectrum, J = -13.0 Hz, CH_2-Ar); 3.12 (1H, m, 4-H); 3.7 (1H, br s, NH); 6.64 (1H, d d, J = 7.9, 1.3 Hz, 8-H); 6.88 (1H, t d, J = 7.4, 1.3 Hz, 6-H); 7.19 (1H, t, J = 7.6 Hz, 7-H); 7.38 (1H, d d, J = 7.6, 1.2 Hz, 5-H); 7.6-7.7 (5H, m, ArH)
XV	1.29 (3H, d, J = 6.8 Hz, 4-CH_3); 1.70 (3H, s, 2-CH_3); 1.96 (1H, d d, J = -13.1, 10.2 Hz, 3a-H); 2.12 (1H, d d, -13.1, 6.0 Hz, 3e-H); 3.24 (1H, m, 4-H); 4.7 (1H, br s, NH); 7.2-7.9 (12H, m, ArH)
XVI	1.30 (3H, s, 2-CH_3); 1.65 (3H, d, J = 7.0 Hz, 4-CH_3); 1 90-3.80 (11H, m, overlapping signals of 3-H, 4-H, and CH_2-PCP); 3.90 (1H, br s, NH); 6.2-7.4 (11H, m, ArH)
XVII	1.66 (3H, d, J = 7.1 Hz, 1-CH_3); 1.86 (3H, d, J = 1.1 Hz, 3-CH_3); 2.70-3.60 (9H, m, 1-H + CH_2-PCP); 5.0 (1H, narrow m, 2-H); 6.60-6.70 (6H, m, ArH)
XVIII	1.39 (3H, d, J = 7.4 Hz, 1-CH_3); 2.2 (3H, br s, 3-CH_3); 3.5 (1H, br q, 1-H); 3.9 (3H, s, OCH_3); 6.1 (1H, br s, 2-H); 6.93 (1H, d d, J = 8.2, 2.2 Hz, 6-H), 7.10 (1H, d, J = 2.2 Hz, 4-H); 7.27 (1H, d, J = 8.2 Hz, 7-H)
XIX	1.42 (3H, d, J = 7.0 Hz, 1-CH_3); 3.62 (1H, br q, J = 7.0 Hz, 1-H); 6.55 (1H, d, J = 1.1 Hz, 2-H); 7.00-7.90 (1H, m, ArH)

*See footnote to Table 2.

was evaporated and the reaction product isolated chromatographically on a column of Al_2O_3 (h = 20 cm, d = 2 cm, eluent hexane). The characteristics of compounds (VII)-(XII) are given in Tables 1 and 2.

Substituted 1,2,3,4-Tetrahydroquinoline (XIII)-(XVI) and Substituted Indenes (XVII)-(XIX). A mixture of the appropriate arylalkenylamine (VII)-(XII) dissolved in $CHCl_3$ (10 ml) and H_2SO_4 (monohydrate) (5 ml) was heated at 60°C for 3-4 h. The mixture was poured onto ice and decomposed with aqueous ammonia solution to pH 8-9. The solution was extracted with chloroform (3 × 20 ml). After distilling off the solvent, the residue was separated chromatographically on a column of Al_2O_3 (h = 20, d = 2 cm, eluent was hexane–ethyl acetate 30:1). The characteristics of compounds (XIII)-(XIX) are given in Tables 1 and 3.

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