Reactions of Conjugated Arylazocyclohexenes with Grignard Reagents. Part 2.[1] A New Stereospecific Route to 2-Alkyl- and 2-Aryl-cyclohexanones

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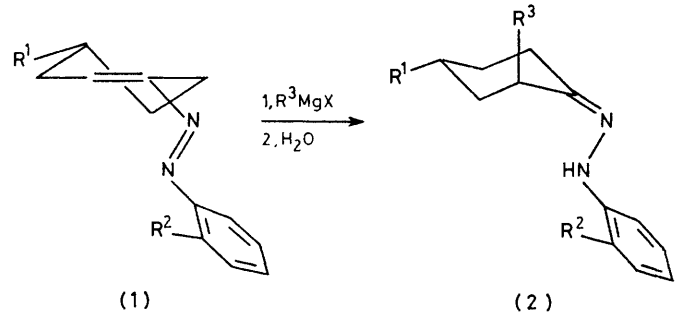
4-Methyl- and 4-t-butyl-1-arylazocyclohexenes react with aliphatic and aromatic Grignard reagents, to furnish, after oxidative hydrolysis of the intermediate arylhydrazones, 2-alkyl-4-methyl-, 2-aryl-4-methyl-, 2-alkyl-4-t-butyl-, and 2-aryl-4-t-butyl-cyclohexanones, with a *trans*-configuration. From the reactions with *o*-tolyl- and α-naphthyl-magnesium bromide only the *cis*-isomers were obtained. The structures of the products were determined by spectroscopic methods and by epimerization of the *trans*-cyclohexanones into the more stable *cis*-isomers.

In previous work we reported that the reactions of arylazocyclohexenes with methylmagnesium iodide and phenylmagnesium bromide yield *syn*-2-methyl- and *syn*-2-phenyl-cyclohexanone arylhydrazones, respectively, through a mechanism involving 1,4-addition of the Grignard reagent to the system $-N=N-C=C<$.[1] In this work we exploit this reaction as a general synthetic method for 2-alkyl- and 2-aryl-cyclohexanones.

2-Alkylcyclohexanones can be obtained *via* alkylation of cyclohexanone enamines followed by hydrolysis,[2,3] and in higher yields, through α-lithiation, alkylation, and hydrolysis of the *NN*-dimethylhydrazones.[4] In addition, arylation at the 2-position by the aryne reaction on cycloalkanones [5,6] and on the corresponding cycloalkanone enamines [6a,7] have been reported. Nevertheless this reaction presents some limitations, for

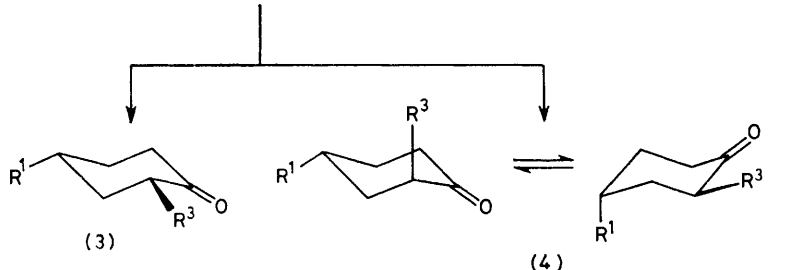


(1)

a; R^1 = Me, R^2 = OMe
b; R^1 = Bu^t, R^2 = OMe
c; R^1 = Me, R^2 = H
d; R^1 = Bu^t, R^2 = H

(2)

a; R^1 = Me, R^2 = OMe R^3 = Ph
b; R^1 = Bu^t, R^2 = OMe R^3 = Ph



(3)

a; R^1 = Me, R^3 = Ph
b; R^1 = Bu^t, R^3 = Ph
c; R^1 = Me, R^3 = *o*-tolyl
d; R^1 = Bu^t, R^3 = *o*-tolyl
e; R^1 = Me, R^3 = *m*-tolyl
f; R^1 = Bu^t, R^3 = *m*-tolyl
g; R^1 = Me, R^3 = *p*-tolyl
h; R^1 = Bu^t, R^3 = *p*-tolyl
i; R^1 = Me, R^3 = α-naphthyl
j; R^1 = Bu^t, R^3 = α-naphthyl
k; R^1 = Me, R^3 = β-naphthyl
l; R^1 = Bu^t, R^3 = β-naphthyl
m; R^1 = Bu^t, R^3 = Pr^i
n; R^1 = Bu^t, R^3 = cyclohexyl

(4)

(A)

a; R^1 = Bu^t, R^3 = Ph
b; R^1 = Bu^t, R^3 = *m*-tolyl
c; R^1 = Bu^t, R^3 = *p*-tolyl
d; R^1 = Bu^t, R^3 = β-naphthyl
e; R^1 = Bu^t, R^3 = Pr^i
f; R^1 = Bu^t, R^3 = cyclohexyl
g; R^1 = Me, R^3 = Ph
h; R^1 = Me, R^3 = *m*-tolyl
i; R^1 = Me, R^3 = *p*-tolyl
j; R^1 = Me, R^3 = β-naphthyl

(B)

Scheme

instance low yields [7] and, in the case of the benzyne reaction of *ortho*-substituted halogenobenzenes, formation of *meta*-substituted products only.[6]

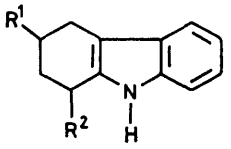
The reaction of 1-arylazocyclohexenes with a Grignard reagent and subsequent hydrolysis of the hydrazones, allowed us to synthesize in good yields (80—85%) a wide variety of both 2-alkyl- and 2-aryl-cyclohexanones, some of which are not obtainable by other routes.

The 1-phenylazocyclohexenes (1c—d) reacted with the following Grignard reagents: phenyl-, *o*-tolyl-, *m*-tolyl-, *p*-tolyl-, α-naphthyl-, β-naphthyl-, and cyclohexylmagnesium bromide and iso-propylmagnesium iodide. From the reaction mixtures of (1a and b) with phenylmagnesium bromide 2-phenyl-4-methylcyclohexanone *o*-methoxyphenylhydrazone (2a) and 2-phenyl-4-t-butylcyclohexanone *o*-methoxyphenylhydrazone (2b) were isolated, respectively. To these compounds, the *syn*-configuration, with the phenyl group axially oriented was assigned on the basis of their ^{1}H n.m.r. spectra. Compound (2a) shows a signal [δ 4.25 (W_H 7.50 Hz)] for the equatorially oriented benzylic proton and a doublet [δ 0.92 (J 5.25 Hz)] typical of the equatorial methyl group. Compound (2b) exhibits a signal [δ 4.25 (W_H 7.50 Hz)] for the equatorial benzylic proton. This is in accord with the previously reported mechanism [1] and with antiparallel attack of the incoming group at C-2 of the cycloaliphatic ring.

Hydrolysis of (2a) furnishes the ketones (3a) or (4g) and hydrolysis of (2b) gives the ketones (3b) or (4a), depending on the reaction conditions.

Since the presence of the *o*-methoxy group is not important to the reactivity of 1-arylazocyclohexenes (1),[1] we preferred to carry out the reactions of the above mentioned Grignard reagents on the more simple 1-phenylazocyclohexenes (1c and d). Moreover, owing to the instability of the hydrazones (2), which undergo autoxidation very easily,[1] these products were not isolated, but directly hydrolysed to the corresponding ketones.

Hydrolysis attempts in acidic medium were unsuccessful. For instance, treatment of hydrazones (2; R^1 = Bu^t, R^2 = H, R^3 = Ph) and (2; R^1 = Me, R^2 = H, R^3 = *o*-tolyl) with 20% sulphuric acid furnished *via* Fischer's indole cyclization only the carbazoles (5a and b) respectively.



(5)

a; R^1 = Bu^t, R^2 = Ph
b; R^1 = Me, R^2 = *o*-tolyl

The carbazole structure of compounds (5a and b) was assigned on the basis of elemental and spectral analysis. This structure is in agreement with that one of the cyclization products of 2-phenylcyclohexanone phenylhydrazone.[8]

Further attempts to hydrolyse the hydrazones (2) by acetic acid or hydrochloric acid gave no carbonyl compounds. On the contrary, hydrolysis of the same products by 10% nitric acid furnished in high yield a mixture of the *cis*-2,4-disubstituted-cyclohexanones (3) together with a little of the *trans*-isomers (4). When R^3 is *o*-tolyl or α-naphthyl the *cis*-isomer was obtained uniquely.

These results, which seem in contrast with the stereochemistry postulated for the hydrazones (2), are due to the fact that, under the acidic conditions of hydrolysis, epimerization at C-2 of the cyclohexanone ring also occurs. In fact, under non-epimerizing hydrolytic conditions, using aqueous sodium periodate at pH 7 and 20—25 °C,[4] the *trans*-isomers (4) were obtained exclusively. This behaviour confirms the stereochemistry of the hydrazones (2) with respect to the orientation of R^1 and R^3, according with the reaction mechanism previously shown.[1] However also under these conditions, the hydrazones (2) where R^3 is *o*-tolyl or α-naphthyl, still furnished only the *cis*-2,4-disubstituted cyclohexanones. It is reasonable to assume that in these cases, owing to the steric bulk of the incoming group, parallel attack through a twist-boat conformation is favoured over the antiparallel one.

Further investigations concerned with the Grignard reaction mechanism of 1-phenylazocyclohexenes, where the incoming substituent is forced to enter by parallel attack, are in progress.

The structure of the *cis*-cyclohexanones (3) and of the *trans*-isomers (4) were established both by ^{1}H n.m.r. spectral analysis and by base-catalysed equilibration of the *trans*-derivatives into the more stable *cis*-isomers.

The *trans*-isomers (4a—f) have the expected rigid conformation (A). By comparison of the ^{1}H n.m.r. spectra of the *trans*-compounds (4g—j) with those of the corresponding *cis*-isomers (3a,e, g, k), it appears that in the former the signal for 2-H is somewhat different from that of the corresponding proton in the *cis*-isomers and it is similar to that of the corresponding *trans*-derivatives (4a—d). Moreover 4-Me of compounds (4g—j) exhibits ^{1}H n.m.r. spectral features (J 6.0—6.1 Hz), which are intermediate between those of an axial and an equatorial methyl group.[9] This leads us to suppose that in the case of the *trans*-2-aryl-4-methyl cyclohexanones (4) an equilibrium between conformations (A) and (B) is possible. Conformational analysis of these products is in progress.

EXPERIMENTAL

^{1}H N.m.r. spectra were recorded with a JEOL JNM 60 HL spectrometer (Me_4Si as internal standard) and i.r. spectra with a Perkin-Elmer 257 spectrophotometer. U.v. spectra were determined for solutions in 95% ethanol with a Perkin-Elmer 124 spectrophotometer. Analytical t.l.c. plates were coated with silica gel G(Merck). Arylazocyclohexenes were purified by column chromatography on

alumina (Merck) (elution with light petroleum). Grignard reactions were carried out in anhydrous ether with stirring, at room temperature, under dry oxygen-free nitrogen. Cyclohexanones were isolated and purified by chromatographic columns on extra pure silica gel (Merck; 70—230 mesh ASTM) (elution with benzene). Light petroleum refers to the fraction of b.p. 40—70 °C. Solutions were dried over sodium sulphate. All evaporations were carried out with a rotary evaporator under vacuum.

4-Alkyl-1-arylazo-cyclohexenes (1a—d).—These compounds were synthesized by Brodka's method [10] from 2-bromo-4-methyl-[11] and 2-bromo-4-t-butyl-cyclohexanone [12] chloride (200 ml). The organic layer was washed until neutral, dried, and evaporated. From the solid residue, biphenyl was eliminated by washing with light petroleum, under cooling. The crude product (2a and b) was obtained in quantitative yield. Analytical and spectral data are reported in Table 1.

cis-2,4-*Disubstituted Cyclohexanones* (3a—n).—The 1-phenylazocyclohexenes (1c) (0.03 mol) and (1d) (0.03 mol) reacted with the Grignard reagents under the conditions and the molar ratios reported for (2a and b). After hydrolysis with aqueous 20% ammonium chloride (200 ml), the organic layer was washed and evaporated. The residue was

TABLE 1

Analytical and spectral data of arylazocyclohexenes (1a—d) and *syn*-arylhydrazones (2a and b)

Compound	M.p. (°C)	Formula	Found (%) C	H	N	Required (%) C	H	N	$\lambda_{max.}$ [a] nm	$\nu_{max.}$ [b] cm^{-1}	δ($CDCl_3$)
(1a)	78 (from light petroleum)	$C_{14}H_{18}N_2O$	73.15	7.95	11.95	73.0	7.9	12.15	428		7.60—6.80 (5 H, m, ArH and vinyl H), 3.95 (3 H, s, OCH_3), 2.90—1.20 (7 H, m, aliphatic ring H), 1.05 (3 H, d, *J* 5.25 Hz, CH_3)
(1b)	56 (from ethanol)	$C_{17}H_{24}N_2O$	74.9	9.1	10.3	74.95	8.9	10.3	434		7.80—6.50 (4 H, m, ArH), 6.25—6.05 (1 H, m, W_H 4.5 Hz, vinyl H), 3.75 (3 H, s, OCH_3), 3.00—1.20 (7 H, m, aliphatic ring H), 0.90 [9 H, s, $C(CH_3)_3$]
(1c)	71—73 (from light petroleum)	$C_{13}H_{16}N_2$	77.7	8.1	14.3	77.95	8.05	14.0	427		7.90—7.20 (5 H, m, ArH), 7.00—6.85 (1 H, m, W_H 9.45 Hz, vinyl H), 3.00—1.20 (7 H, m, aliphatic ring H), 1.05 (3 H, d, *J* 5.40 Hz, CH_3)
(1d)	61—62 (from light petroleum)	$C_{16}H_{22}N_2$	79.2	9.1	11.4	79.3	9.15	11.55	427		7.90—7.20 (5 H, m, ArH), 7.12—6.82 (1 H, m, W_H 9.45 Hz, vinyl H), 3.10—1.20 (7 H, m, aliphatic ring H), 0.93 [9 H, s, $C(CH_3)_3$]
(2a)	88—90 (from ethanol)	$C_{20}H_{24}N_2O$	77.6	7.9	8.95	77.9	7.85	9.1		3 360 [c]	7.80—6.60 (10 H, m, ArH and NH), 4.25 (1 H, m, W_H 7.50 Hz, C*H*Ph), 3.70 (3 H, s, OCH_3), 2.90—1.15 (7 H, m, aliphatic ring H), 0.92 (3 H, d, *J* 5.25 Hz, CH_3)
(2b)	117—120 (from ethanol)	$C_{23}H_{30}N_2O$	78.8	8.35	8.1	78.8	8.65	8.0		3 360 [c]	7.80—6.55 (10 H, m, ArH and NH), 4.25 (1 H, m, W_H 7.50 Hz, C*H*Ph), 3.60 (3 H, s, OCH_3), 2.90—1.10 (7 H, m, aliphatic ring H), 0.85 [9 H, s, $C(CH_3)_3$]

[a] N=N band (n–π^*). [b] NH stretch. [c] Nujol.

by reaction with *o*-methoxyphenylhydrazine [(1a and b)] and with phenylhydrazine [(1c and d)]. The bromo-derivative (0.02 mol) was heated in pyridine (0.02 mol) at 100 °C for 4.5 min [(1a and c)] or for 8 min [(1b and d)]. The mixture was cooled at room temperature, added to anhydrous THF (3 ml); and poured with stirring into a solution of arylhydrazine (0.02 mol) in anhydrous THF (20 ml) cooled at 0 °C. Stirring was continued for 3 h. The products were obtained in 65—80% yield. Analytical and spectral data are reported in Table 1.

trans-4-Alkyl-1-phenylcyclohexanone syn-o-*Methoxyphenylhydrazones* (2a and b).—A solution of azoalkene (1a and b) (0.03 mol) in anhydrous ether (25 ml) was added dropwise with stirring to an ethereal solution (35 ml) of PhMgBr [from PhBr (0.06 mol) and Mg (0.06 g atom)]. The mixture was stirred at room temperature for 3 h. The mixture was hydrolysed with aqueous 20% ammonium dissolved in benzene and hydrolysed with aqueous 10% nitric acid (250 ml) with stirring at room temperature for 3 h. The organic layer was washed until neutral, dried, and concentrated. Column chromatography of the solution afforded the *cis*-2,4-disubstituted cyclohexanones (3a,[5a] b,[5a] e—h, and k—n) together with a little amount of the corresponding *trans*-isomers. The *cis*-products (3c, d, i, and j) were obtained free of the *trans*-isomers. In each case good yields (80—85%) were obtained.

Under the same hydrolysis conditions the hydrazones (2a) (0.005 mol) and (2b) (0.005 mol) dissolved in benzene (50 ml) and treated with aqueous 10% nitric acid (85 ml) furnished the *cis*-cyclohexanone (3a and b) respectively contaminated by a little of the *trans*-isomers. Analytical and spectral data are reported in Table 2.

trans-2,4-*Disubstituted Cyclohexanones* (4a—j).—The Grignard reactions were performed as described above. The

TABLE 2

Analytical and spectral data of *cis*-2,4-disubstituted-cyclohexanones (3c—n)

Compound	M.p. (°C)	Formula	Found (%) C	Found (%) H	Required (%) C	Required (%) H	$\nu_{max.}$ [a] cm^{-1}	δ($CDCl_3$)
(3c)	75—76 (from methanol)	$C_{14}H_{18}O$	83.0	8.85	83.1	8.95	1 710 [b]	7.12 (4 H, s, ArH), 4.00—3.62 (1 H, m, W_H 13.50 Hz, C*H*Ar), 2.70—1.20 (7 H, m, aliphatic ring H), 2.17 (3 H, s, CH_3Ar), 1.05 (3 H, d, *J* 5.40 Hz, CH_3)
(3d)	75—76 (from methanol)	$C_{17}H_{24}O$	83.7	9.8	83.55	9.9	1 710 [b]	7.15 (4 H, s, ArH), 4.00—3.60 (1 H, m, W_H 12.80 Hz, CHAr), 2.70—1.50 (7 H, m, aliphatic ring H), 2.19 (3 H, s, CH_3), 0.95 [9 H, s, $C(CH_3)_3$]
(3e)	Oil	$C_{14}H_{18}O$	82.8	9.15	83.1	8.95	1 710 [c]	7.30—6.80 (4 H, m, ArH), 3.85—3.35 (1 H, m, W_H 14.25 Hz, CHAr), 2.70—1.40 (7 H, m, aliphatic ring H), 2.35 (3 H, s, CH_3Ar), 1.05 (3 H, d, *J* 5.25 Hz, CH_3)
(3f)	Oil	$C_{17}H_{24}O$	83.2	9.75	83.55	9.9	1 710 [c]	7.35—6.75 (4 H, m, ArH), 3.80—3.35 (1 H, m, W_H 14.85 Hz, CHAr), 2.65—1.10 (7 H, m, aliphatic ring H), 2.33 (3 H, s, CH_3), 0.95 [9 H, s, $C(CH_3)_3$]
(3g)	Oil	$C_{14}H_{18}O$	82.85	9.25	83.1	8.95	1 715 [c]	7.30—6.85 (4 H, m, ArH), 3.85—3.35 (1 H, m, W_H 14.20 Hz, CHAr), 2.65—1.30 (7 H, m, aliphatic ring H), 2.30 (3 H, s, CH_3Ar), 1.03 (3 H, d, *J* 5.40 Hz, CH_3)
(3h)	96—97 (from methanol)	$C_{17}H_{24}O$	83.75	10.0	83.55	9.9	1 705 [b]	7.30—6.85 (4 H, m, ArH). 3.80—3.30 (1 H, m, W_H 16.20 Hz, CHAr), 2.70—1.40 (7 H, m, aliphatic ring H), 2.30 (3 H, s, CH_3), 0.93 [9 H, s, $C(CH_3)_3$]
(3i)	114—115 (from methanol)	$C_{17}H_{18}O$	85.4	7.35	85.65	7.6	1 710 [b]	8.05—7.10 (7 H, m, ArH), 4.60—4.15 (1 H, m, W_H 11.47 Hz, CHAr), 2.85—1.35 (7 H, m, aliphatic ring H), 1.05 (3 H, d, *J* 5.40 Hz, CH_3)
(3j)	70—72 (from methanol)	$C_{20}H_{24}O$	85.75	8.8	85.65	8.65	1 710 [b]	7.90—7.10 (7 H, m, ArH), 4.50—4.10 (1 H, m, W_H 16.20 Hz, CHAr), 2.75—1.35 (7 H, m, aliphatic ring H), 0.95 [9 H, s, $C(CH_3)_3$]
(3k)	76—77 (from ethanol)	$C_{17}H_{18}O$	85.4	7.85	85.65	7.6	1 700 [b]	8.10—7.10 (7 H, m, ArH), 4.15—3.60 (1 H, m, W_H 14.85 Hz, CHAr), 2.80—1.40 (7 H, m, aliphatic ring H), 1.05 (3 H, d, *J* 5.40 Hz, CH_3)
(3l)	127—128 (from light petroleum)	$C_{20}H_{24}O$	85.8	8.8	85.65	8.65	1 710 [b]	7.95—7.10 (7 H, m, ArH), 3.90—3.50 (1 H, m, W_H 14.85 Hz, CHAr), 2.65—1.45 (7 H, m, aliphatic ring H), 0.92 [9 H, s, $C(CH_3)_3$]
(3m)	Oil	$C_{13}H_{24}O$	79.2	12.1	79.55	12.3	1 700 [c]	2.60—1.30 (15 H, m), 0.90 [9 H, s, $C(CH_3)_3$]
(3n)	50—52 (from methanol)	$C_{16}H_{28}O$	81.4	11.7	81.3	11.95	1 710 [b]	2.55—1.15 (19 H, m, aliphatic ring H), 0.90 [9 H, s, $C(CH_3)_3$]

[a] C=O stretch. [b] Nujol. [c] Liquid film.

TABLE 3

Analytical and spectral data of *trans*-2,4-disubstituted cyclohexanones (4b—j)

Compound	M.p. (°C)	Formula	Found (%) C	Found (%) H	Required (%) C	Required (%) H	$\nu_{max.}$ [a] cm^{-1}	δ($CDCl_3$)
(4b)	Oil	$C_{17}H_{24}O$	83.3	10.0	83.55	9.9	1 705 [b]	7.20—6.80 (4 H, m, ArH), 3.80—3.50 (1 H, m, W_H 8.10 Hz, C*H*Ar), 2.65—1.10 (7 H, m, aliphatic ring H), 2.30 (3 H, s, CH_3), 0.95 [9 H, s, $C(CH_3)_3$]
(4c)	Oil	$C_{17}H_{24}O$	83.3	9.75	83.55	9.9	1 705 [b]	7.40—7.10 (4 H, m, ArH), 3.90—3.50 (1 H, m, W_H 9.45 Hz, C*H*Ar), 2.80—1.50 (7 H, m, aliphatic ring H), 2.37 (3 H, s, CH_3), 1.00 [9 H, s, $(C(CH_3)_3$]
(4d)	Oil	$C_{20}H_{24}O$	85.55	8.4	85.65	8.65	1 700 [b]	7.90—7.15 (7 H, m, ArH), 4.10—3.80 (1 H, m, 9.45 Hz, C*H*Ar), 2.80—1.10 (7 H, m, aliphatic ring H), 1.00 [9 H, s, $C(CH_3)_3$]
(4e)	Oil	$C_{13}H_{24}O$	79.25	12.35	79.55	12.3	1 700 [b]	3.10—1.20 (15 H, m), 0.97 [9 H, s, $C(CH_3)_3$]
(4f)	Oil	$C_{16}H_{28}O$	80.9	12.15	81.3	11.95	1 710 [b]	2.50—1.05 (19 H, m, aliphatic ring H), 0.93 [9 H, s, $C(CH_3)_3$]
(4h)	Oil	$C_{14}H_{18}O$	82.95	8.9	83.1	8.95	1 710 [b]	7.40—6.80 (4 H, m, ArH), 3.85—3.50 (1 H, m, W_H 9.45 Hz, C*H*Ar), 2.60—1.40 (7 H, m, aliphatic ring H), 2.30 (3 H, s, CH_3Ar), 1.10 (3 H, d, *J* 6.10 Hz, CH_3)
(4i)	Oil	$C_{14}H_{18}O$	82.95	8.7	83.1	8.95	1 710 [b]	7.15 (4 H, s, ArH), 3.85—3.55 (1 H, m, W_H 9.00 Hz, CHAr), 2.60—1.30 (7 H, m, aliphatic ring H), 2.33 (3 H, s, CH_3Ar), 1.10 (3 H, d, *J* 6.00 Hz, CH_3)
(4j)	Oil	$C_{17}H_{18}O$	85.35	7.75	85.65	7.6	1 700 [b]	7.90—7.20 (7 H, m, ArH), 4.05—3.70 (1 H, m, W_H 10.12 Hz, CHAr), 2.75—1.50 (7 H, m, aliphatic ring H), 1.15 (3 H, d, *J* 6.07 Hz, CH_3)

[a] C=O stretch. [b] Liquid film.

organic layer, obtained after hydrolysis with aqueous 20% ammonium chloride, was evaporated and the residue was dissolved in methanol (50 ml). To this solution pH 7 1.0N-phosphate buffer (15 ml) and then a solution of sodium periodate (1.2 g) in water (25 ml) were added at 20—25 °C with stirring.

TABLE 4

Analytical and spectral data of 3-alkyl-1-aryl-1,2,3,4-tetrahydrocarbazoles (5a and b)

Compound	M.p. (°C)	Formula	Found (%) C	H	N	Required (%) C	H	N	$\nu_{max.}$ [a]/ cm^{-1}	δ(CDCl$_3$)
(5a)	158—160 (from light petroleum)	$C_{22}H_{25}N$	87.15	8.15	4.7	87.1	8.3	4.6	3 380 [b]	7.50—6.70 (10 H, m, ArH and NH), 4.20—4.00 (1 H, m, W_H 8.10 Hz C*H*Ph), 2.90—1.40 (5 H, m, aliphatic ring H), 0.85 [9 H, s, C(CH$_3$)$_3$]
(5b)	155—157 (from ethanol)	$C_{20}H_{21}N$	86.9	7.8	5.3	87.25	7.7	5.1	3 410 [b]	7.45—6.45 (9 H, m, ArH and NH), 4.40—4.15 (1 H, m, W_H 8.10 Hz C*H*Ar), 3.20—1.50 (5 H, m, aliphatic ring H), 2.40 (3 H, s, CH$_3$Ar), 1.05 (3 H, d, *J* 5.00 Hz, CH$_3$)

[a] NH stretch. [b] Nujol.

Completion of the hydrolysis (usually 3—4 h) was determined by t.l.c. analysis. The sodium iodate precipitate was filtered off and the mixture was diluted with water and extracted with chloroform. After drying, concentration, and purification by column chromatography the extracts afforded the *trans*-2,4-disubstituted cyclohexanones (4a,[5a] b—f, g,[5a] and h—j) as the only products in 80—85% yield.

From (2a) (0.005 mol) and (2b) (0.005 mol) oxidative hydrolysis under the same conditions also afforded (4g and a), respectively in quantitative yield. Analytical and spectral data are reported in Table 3.

Equilibration of the trans-2,4-*Disubstituted Cyclohexanones* (4a—j) *into the* cis-*Isomers* (3a, b, e—h, and k—n).—To a solution of the *trans*-isomer (0.002 mol) in a mixture of methanol (10 ml) and water (5 ml), pyrrolidine (2—3 drops) was added. After heating under reflux for 30 min a mixture of *cis*- and *trans*-2,4-disubstituted cyclohexanone in a *ca.* 9 : 1 ratio (t.l.c.) was obtained.

3-*Alkyl*-1-*aryl*-1,2,3,4-*tetrahydrocarbazoles* (5a *and* b).—Compound (5a) was prepared from (1d) (0.03 mol) and phenylmagnesium bromide and (5b) from (1c) (0.03 mol) and *o*-tolylmagnesium bromide under the conditions and molar ratios reported above for (2a and b). After hydrolysis with aqueous 20% ammonium chloride, the organic layer was evaporated and the residue dissolved in benzene (150 ml) was treated with aqueous 20% sulphuric acid (250 ml) at room temperature with stirring for 3—4 h. The organic layer was separated, washed, dried, and evaporated and furnished a solid residue (5a and b) in good yield. Analytical and spectral data are reported in Table 4.

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REFERENCES

[1] S. Bozzini, S. Gratton, A. Risaliti, A. Stener, M. Calligaris, and G. Nardin, *J.C.S. Perkin I*, 1977, 1377.
[2] A. G. Cook, 'Enamines: Synthesis, Structure, and Reactions,' Dekker, New York and London 1969.
[3] S. Karady, M. Lenfant, and R. E. Wolff, *Bull. Soc. chim. France*, 1965, 2472.
[4] E. J. Corey and D. Enders, *Tetrahedron Letters*, 1976, 3.
[5] (*a*) P. Caubere, M. S. Mourad, and G. Guillaumet, *Tetrahedron*, 1973, **29**, 1843; (*b*) P. Caubere, G. Guillaumet, and M. S. Mourad, *Bull. Soc. chim. France*, 1973, 3493.
[6] (*a*) T. Kametani, S. Noguchi, I. Agata, T. Aono, K. Kigasawa, M. Hiiragi, T. Hayasaka, and O. Kusama, *J. Chem. Soc.* (*C*), 1971, 1047; (*b*) T. Kametani, K. Kigasawa, M. Hiiragi, T. Hayasaka, and O. Kusama, *ibid.*, p. 1051.
[7] M. E. Kuehne, *J. Amer. Chem. Soc.*, 1962, **84**, 837.
[8] B. Robinson, *Chem. Rev.*, 1963, **63** 373.
[9] F. Johnson and N. A. Starkowsky, *Tetrahedron Letters*, 1962, 1173.
[10] S. Brodka and H. Simon, *Chem. Ber.*, 1969, **102**, 3647.
[11] R. Belcher, W. Hoyle, and T. S. West, *J. Chem. Soc.*, 1958, 2743.
[12] N. L. Allinger and J. Allinger, *J. Amer. Chem. Soc.*, 1958, **80**, 5476.