SYNTHESIS OF N-ALKYL(ACYL)-1,2,3,4-TETRAHYDRO-4-METHYL-SPIRO[QUINOLINE-2-CYCLOHEXANES] AND THEIR CONVERSIONS

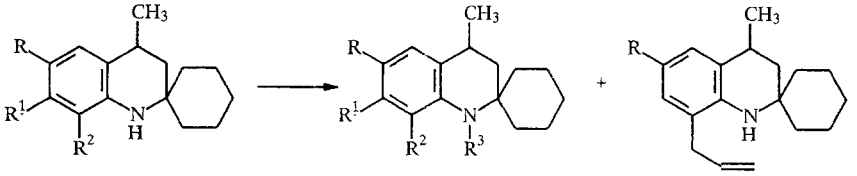
V. V. Kuznetsov, A. Pal'ma, A. É. Aliev, N. S. Prostakov, and A. V. Varlamov

The alkylation and acylation of 1,2,3,4-tetrahydro-4-methylspiro[quinoline-2-cyclohexane] and its bromo(methyl) derivatives substituted in the benzene ring, as well as 1,2,3,4-tetrahydro-4-methylspiro[benzo(h)quinoline-2-cyclohexane], were studied. It was established that the N-allyl derivatives of spiro[tetrahydroquinolinecyclohexanes] are converted to their 8-allyl-substituted analogs by the action of sulfuric acid, boron trifluoride etherate, and aluminum chloride. It was shown that the N-acyl-substituted spiro[tetrahydroquinolinecyclohexanes] are recyclized to spiro[indan-1-cyclohexanes] in phosphoric acid.

The synthesized and previously unknown N-alkyl- and N-acyl-substituted spiro[tetrahydroquinoline-2-cyclohexanes] are objects for the study of their biological activity. They also present interest as starting compounds for the synthesis of more complex compounds structurally close to the alkaloids. In performing the syntheses of these compounds, the stereochemical problem as to whether the introduction of acyl radicals at the nitrogen atom will influence the conformation of the spiro[tetrahydroquinoline-2-cyclohexanes] was resolved. It is known [1] that the N-acylation of ring-substituted piperidines is accompanied by the inversion of the piperidine ring.

The N-alkylation and N-acylation of 1,2,3,4-tetrahydro-4-methyl-, 1,2,3,4-tetrahydro-4,6-dimethyl-, 1,2,3,4-tetrahydro-4,8-dimethyl-, and 1,2,3,4-tetrahydro-6-bromo-4-methyl-spiro[quinoline-2-cyclohexanes] (I)-(IV) and 1,2,3,4-tetrahydro-4-methylspiro[benzo(h)quinoline-2-cyclohexane] (V), as well as the conversions of the N-allyl- and N-acyl-substituted compounds by acids, were studied in the present work.

The synthesis of the spiro compounds (I)-(V) is described in [2-4]. The alkylation of compound (I) was performed with methyl iodide, propargyl bromide, and allyl bromide in acetone, acetonitrile, or DMF in the presence of potassium carbonate, and the alkylation of the compounds (II) and (IV) was performed by allyl bromide in DMF in the presence of potassium carbonate. The 1,2,3,4-tetrahydro-1,4-dimethyl-, 1,2,3,4-tetrahydro-1-propargyl-4-methyl-, and 1,2,3,4-tetrahydro-1-allyl-4-methylspiro[quinoline-2-cyclohexanes] (VI)-(VIII) were obtained with the yield of 70-80% from the compound (I). Compound (VIII) was described in [5]. This compound was obtained by us in the yield of 85% by the treatment of compound (I), in DMF, with sodium hydride and then allyl bromide.



I, II, IV, V — VI - X, XIV — XI - XIII

I, VI—VIII, XI, XIV R = H; II, IX, XII R = CH_3; IV, X, XIII R = Br; I, II, IV, VI—X $R^1 = R^2 = H$; V, XIV $R^1 + R^2 =$ —CH=CH—CH=CH; VI $R^3 = CH_3$; VII $R^3 = CH_2—C{\equiv}CH$; VIII—X, XIV $R^3 = CH_2—CH{=}CH_2$

Russian University of the Friendship of Peoples, Moscow 117923. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 6, pp. 789-796, June, 1993. Original article submitted May 14, 1993.

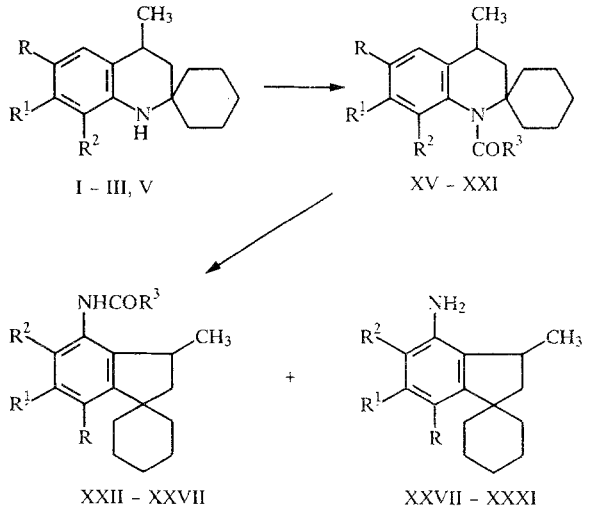
0009-3122/93/2906-0676$12.50

The allylation of the compounds (I), (II), and (IV) by allyl bromide in DMF afforded, besides the N-allyl-substituted spiro compounds (VIII)-(X), 1,2,3,4-tetrahydro-4-methyl-8-allyl-, 1,2,3,4-tetrahydro-4,6-dimethyl-8-allyl-, and 1,2,3,4-tetrahydro-6-bromo-4-methyl-8-allylspiro[quinoline-2-cyclohexane] (XI)-(XIII) with yields of 9-29%. The spiro compound (V) only gave the N-allyl-substituted derivative (XIV) under the same conditions.

The N-allyl-substituted spiro compound (VIII) is unchanged when heated in DMF in the presence of potassium carbonate. This provides the basis for the proposition that the 8-allyl-substituted spiro compounds (XI)-(XIII) are formed as the result of electrophilic substitution, and not by the rearrangement of the corresponding N-allyl derivatives. The ionization of allyl bromide probably occurs in DMF, which solvates cations specifically. The resulting allyl cation attacks both the nucleophilic atom of nitrogen and the aromatic ring.

The N-allyl-substituted compound (VIII) undergoes rearrangement to the 8-allyl-substituted compound (XI), the yield of which comprised 62-75%, in the presence of aluminum chloride, boron trifluoride etherate, and 2 N sulfuric acid. This method can be considered as a preparative method for the isolation of 8-allyl-substituted spiro[tetrahydroquinolinecyclohexanes].

The acylation of the spiro compounds (I)-(III) and (V) was performed with acetic anhydride, as well as chloroacetyl chloride and α-bromopropionyl chloride (bromide), in the presence of triethylamine. The yields of 53-94% were obtained for N-acetyl-, N-chloroacetyl-, and N-(α-bromopropionyl)-1,2,3,4-tetrahydro-4-methylspiro[quinoline-2-cyclohexane] (XV)-(XVII), N-acetyl-1,2,3,4-tetrahydro-4,6-dimethyl-, and N-acetyl-1,2,3,4-tetrahydro-4,8-dimethylspiro[quinoline-2-cyclohexane] (XVIII) and (XIX), as well as N-acetyl- and N-(α-bromopropionyl)-1,2,3,4-tetrahydro-4-methylspiro[benzo(h)quinoline-2-cyclohexane] (XX) and (XXI). The compound (XV) was previously obtained with the yield of 94%, and was described in [5].



XV—XVII, XIX—XXII, XXIV—XXVIII, XXX R = H; XVIII, XXIII, XXIV R = CH_3; XV—XIX, XXII—XXVI, XXVIII—XXX R^1 = H; XX, XXI, XXVII, XXXI $R^1 + R^2$ = CH=CH—CH=CH; XV—XVIII, XXII, XXIII, XXV, XXVI, XXVIII, XXIX R^2 = H; XIX, XXIV, XXX R^2 = CH_3; XV, XVIII—XX, XXII—XXIV, XXVII R^3 = CH_3; XVI, XXV R^3 = CH_2Cl; XVII, XXI, XXVI R^3 = $CHBrCH_3$

The structure of the N-alkyl- and N-acyl-substituted spiro compounds (VI)-(XXI) was confirmed using PMR (Table 1) and mass spectrometry. The mass spectra contain peaks of the molecular ions corresponding with the empirical formulas. The chemical shifts and multiplicity of the signals in the PMR spectra are in good agreement with the disposition of the proton in their molecule. The hydrogen atoms of the methylene group of the allyl radical in the PMR spectra of the N-allyl-substituted compounds (VIII)-(X) are nonequivalent and appear in the form of two characteristic doublets (^2J = 18.8 Hz), each component of which is split into five lines due to the interaction with the protons of the vinyl fragment. The methylene protons of the propargyl radical in the N-substituted compound (VII) are also nonequivalent. In contrast, the protons of the methylene group of the allyl substituent in the PMR spectra of the 8-allyl-substituted compounds (XI)-(XIII) are equivalent and appear in the form of a doublet, each component of which is broadened on account of further interactions. According to the $^3J_{3,4}$ SSCCs, the compounds (VI)-(XXI) occur in the form of one conformer with the equatorial methyl group at $C_{(4)}$. Therefore, the acylation of the compounds (I)-(III) and (V) proceeds without the inversion of the tetrahydropyridine ring.

It is known that 1-acetyl-2,2-dimethyl-1,2,3,4-tetrahydroquinolines are converted to 4-acetylaminoindans by phosphoric or sulfuric acids [6]. Under these conditions, the N-acyl-substituted spiro[tetrahydroquinoline-2-cyclohexanes] (XV)-(XX)

TABLE 1. PMR Spectral Parameters of N-Alkyl- and N-Acyl-Substituted Spiro[tetrahydroquinoline-2-cyclohexanes] (VI)-(XXI)

Compound	δ, ppm (J, Hz)										
	3a-H	3e-H	4-H	5-H	6-H	7-H	8-H	4-CH_3	CH_2 cyclohexane	Ar—R	N—R
VI	1,10 (−13,0; 13,0)	2,37 (−13,0; 4,2)	2,70	6,53	—	7,19		1,36 (7,0)	1,45...1,84	—	2,80 —CH_3
VII	1,08 (−13,0; 13,0)	2,36 (−13,0; 5,0)	2,77	6,42	—		7,27	1,32 (7,0)	1,45....1,75	—	2,16 HC≡; 4,05 CH_2
VIII	1,27 (−13,0; 13,0)	2,38 (−13,0; 4,2)	2,83	7,15	6,63	7,04	6,53	1,33 (6,2)	1,44...1,90	—	3,85 CH_2; 5,00...5,23 CH_2=; 5,60...6,05 CH=
IX	1,20 (−13,0; 13,0)	2,35 (−13,0; 4,8)	2,78	6,93	—	6,89 (8,0)	6,43 (8,0)	1,30 (6,8)	1,41...2,00	2,22 CH_3	3,85 CH_2; 5,00...5,30 CH_2=; 5,68...6,13 CH=
X	1,33 (−13,0; 13,0)	2,35 (−13,0; 5,0)	2,77	7,15 (2,0)	—	7,07 (8,0)	6,35 (8,0)	1,35 (6,8)	1,41...1,91		3,85 CH_2; 5,00...5,30 CH_2=; 5,65...6,07 CH=
XI	1,34 (−12,4; 12,8)	1,83 (−12,4; 5,4)	2,90	7,08 (7,0)	6,60 (7,0)	6,88 (7,0)	—	1,30 (7,0)	1,43	3,28 CH_2; 5,00...5,26 CH_2=; 5,75...6,19 CH≡	4,05 H
XII	1,31 (−13,0; 12,8)	1,80 (−13,8; 6,0)	2,90	6,88	—	6,70	—	1,28 (6,8)	1,45	2,20 CH_3; 3,25 CH_2; 5,00...5,13 CH_2=; 5,72...6,18 CH=	3,93 H
XIII	1,28 (−13,0; 13,0)	1,80 (−13,0; 5,6)	2,93	7,13 (2,0)	—	6,95 (2,0)	—	1,28	1,43	3,23 CH_2; 5,00...5,18 CH_2=; 5,71...6,20 CH=	4,00 H
XIV	*	*	2,97	7,13...8,39 (5-H—10-H)				1,34 (7,0)	1,50...1,90	—	3,84 —CH_2; 4,75...5,17 CH_2=; 5,68...6,22 CH=
XV	0,95 (−13,1; 11,2)	2,33 (−13,1; 3,7)	2,69	6,94...7,16				1,33 (6,7)	1,18...3,03	—	2,01 CH_3
XVI	1,20**	2,38**	2,72	6,98...7,20				1,36	1,44...1,81	—	4,00 CH_2
XVII	1,35**	2,34**	2,66	7,12...7,16				1,37	1,42...1,64	—	1,69 CH_3; 4,52 CH
XVIII	1,00	2,30	2,70	6,80...7,00				1,32 (7,0)	1,47...1,85	2,30 CH_3	2,00 CH_3
XIX	0,91 (−12,5; 12,3)	2,32 (−12,5; 4,6)	2,65	7,08	7,14	7,05		1,32 (7,0)	1,11...1,90	2,27 CH_3	1,78 CH_3
XX	1,03 (−13,0; 13,0)	2,42 (−13,0; 5,0)	2,93	7,30...8,17 (5-H—10-H)				1,45 (7,0)	1,28...2,12	—	1,63 CH_3
XXI	1,20 (−12,8; 13,0)	2,48 (−12,8; 4,5)	3,08	7,31...7,95 (5-H—10-H)				1,43 (6,8)	1,05...2,25	—	1,60 CH_3; 4,05 CH

*The signals are superimposed by signals of the cyclohexane protons.

**The SSCC could not be measured due to the superimposition of the signals.

TABLE 2. PMR Spectral Parameters of Spiro[indan-1-cyclohexanes] (XXII)-(XXXI)

Compound	δ, ppm (J, Hz)										
	2-H	2'-H	3-H	5-H	6-H	7-H	3-CH_3	NH or NH_2	R—C=O	CH_2 cyclohexane	CH_3Ar
XXII	1,75 (−13,0; 5,0)	2,56 (−13,0; 8,7)	3,30	7,78 (7,93)	7,19 (7,93; 7,78)	6,96 (7,80)	1,29 (7,20)	9,60; 9,68	2,17 CH_3	0,98...1,90	—
XXIII	1,81 (−13,0; 4,0)	*	3,20	7,56 (8,09)	6,90 (8,00)	—	1,22 (6,7)	6,90	2,18 CH_3	1,40...2,29	2,44
XXIV	1,73 (−13,7; 5,0)	2,28 (−13,7; 8,5)	3,25	—	7,08 (7,13; 7,20)	7,00 (7,06; 7,20)	1,23 (6,7)	6,82; 6,78	2,24 CH_3; 2,25 CH_3	1,26...1,80	2,21
XXV	1,83 (−13,7; 4,2)	2,28 (−13,7; 8,8)	3,35	7,81 (7,6); 7,78 (7,6)	7,23	7,01	1,35 (6,7)	8,24; 8,38	4,23 CH_2Cl; 4,24 CH_2Cl	1,42...1,75	—
XXVI	1,75 (−13,0; 4,1)	2,30 (−13,0; 8,2)	3,33	7,82 (7,93)	7,16 (7,93)	6,94 (7,93; 1,07)	1,24 (7,0)	8,25	2,0 CH_3; 4,63 CHBr	1,30...1,75	—
XXVII	*	2,50 (−12,8; 5,0)	3,48	7,30...8,05 (5-H—9-H)			1,25 (7,0)	7,13	2,30 CH_3	1,25...2,0	—
XXVIII	1,7 (−13,2; 4,2)	2,17 (−13,2; 8,0)	3,21	6,50 (7,28; 1,1)	7,00 (7,20; 0,80)	6,63 (7,20; 1,00)	1,25 (6,8)	3,42	—	1,31...1,70	—
XXIX	1,90 (−13,4; 4,0)	2,27 (−13,4; 5,8)	3,10	6,41 (7,10)	6,77 (7,10)	—	1,25 (6,7)	3,39	—	1,38...1,75	2,36
XXX	1,8 (−13,0; 4,0)	2,20 (−13,0; 8,2)	3,18	—	6,93 (7,20)	6,53 (7,20)	1,25 (7,2)	3,48	—	1,38...1,68	2,10
XXXI	1,85 (−13,8; 4,9)	2,30 (−14,0; 8,0)	3,37	7,08...7,88 (5-H—9-H)			1,38 (7,0)	**	—	1,18...1,73	—

*It is superimposed by signals of the cyclohexane protons.

**It could not be measured.

TABLE 3. Characteristics of Spiro[indan-1-cyclohexanes] (XXII)-(XXXI)

Compound	Empirical formula	mp, °C (from heptane)	R_f (heptane–ethyl acetate)	IR spectrum, ν, cm^{-1}	M^+ found	M^+ calculated	Yield, %
XXII	$C_{15}H_{21}NO$	146...148	0,45 (5 : 2)	1670 (C=O); 3300 (NH)	257	257	42,5
XXIII	$C_{16}H_{23}NO$	125...127	0,42 (1 : 1)	1672 (C=O); 3270 (NH)	271	271	66,9
XXIV	$C_{16}H_{23}NO$	160...162	0,59 (1 : 1)	1670 (C=O); 3300 (NH)	271	271	47,0
XXV	$C_{17}H_{22}ClNO$	99...101	0,50 (5 : 1)	1685 (C=O); 3280 (NH); 3420 (NH)	291*	291*	62,5
XXVI	$C_{18}H_{24}BrNO$	174...176	0,52 (2 : 1)	1670 (C=O); 3280 (NH)	350	350	16,6
XXVII	$C_{21}H_{25}N$	194...196	0,37 (1 : 1)	1675 (C=O); 3268 (NH)	307	307	34,4
XXVIII	$C_{15}H_{21}N$	—	0,81 (1 : 1)	3430 (NH); 3470 (NH)	215	215	13,3
XXIX	$C_{16}H_{23}N$	—	0,32 (5 : 1)	3460 (NH); 3470 (NH)	229	229	20,0
XXX	$C_{16}H_{23}N$	—	0,35 (5 : 1)	3390 (NH); 3475 (NH)	229	229	21,7
XXXI	$C_{18}H_{21}N$	—	0,80 (5 : 1)	3400 (NH); 3480 (NH)	265	265	9,5

*Calculated for the isotope ^{35}Cl.

undergo cyclization to spiro[indan-1-cyclohexanes]. The compounds (XV), (XVIII), and (XIX) afford 4-acetylamino-3-methyl-, 4-acetylamino-3,7-dimethyl-, and 4-acetylamino-3,5-dimethyl-spiro[indan-1-cyclohexane] (XXII)-(XXIV) correspondingly in yields of 43-67%; the compounds (XVI) and (XVII) yielded 4-chloroacetylamino- and 4-(α-bromopropionylamino)-3-methylspiro[indan-1-cyclohexane] (XXV) and (XXVI), and the benzo-ring-closed spiro compound (XX) yielded 4-acetylamino-3-methylspiro[benz(f)indan-1-cyclohexane] (XXVII). Besides the acylamino-substituted compounds (XXII)-(XXVII), the N-unsubstituted spiro compounds (I)-(III), (V), and 4-aminospiro[indan-1-cyclohexane] (XXVIII)-(XXXI) were isolated from the reaction mixture in all cases. These compounds, which are not acylated at the nitrogen, are probably formed as a result of hydrolysis of the N-acyl-substituted spiro[tetrahydroquinolinecyclohexanes] (XV)-(XX) and the products of recyclization (XXII)-(XXVII) under the conditions of the reaction. The compound (XXVI) was also obtained by the acylation of the amine (XXVIII) with α-bromopropionyl bromide.

The N-methyl-substituted spiro[tetrahydroquinolinecyclohexane] (VI) does not undergo recyclization in the presence of polyphosphoric acid; this is in agreement with the data of the work [6]. Therefore, the recyclization of the compounds (XV)-(XX) commences with the protonation of the carbonyl oxygen. The breaking of the $N-C_2$ bond then occurs with the formation of the tertiary carbocation. This is followed by the closing of the five-membered ring as the result of electrophilic attack of the phenylene fragment.

The structure of the compounds (XXII)-(XXXI) was confirmed using spectral data. The mass spectra contain peaks of molecular ions corresponding with their empirical formulas. The IR spectra of the 4-acylamino-substituted spiro[indancyclohexanes] (XXII)-(XXVII) are characterized by the presence of intense bands of the stretching vibrations of the NH and CO groups at 3270-3300 and 1670-1672 cm^{-1}, and the spectra of the 4-amino-substituted compounds (XXVIII)-(XXXI) are characterized by the presence of two NH bands in the region of 3390-3475 cm^{-1}.

The PMR spectra (Table 2) of the compounds (XXII)-(XXXI) have the signals of the protons of the 3-CH_3 (doublet), the 2-CH_2 group (two doublets of doublets), the 3-H protons (sextet), and the cyclohexane ring in the high field part. In the aromatic spectral region of the PMR for the compounds (XXII), (XXV), (XXVI), and (XXVIII), there are three characteristic signals of the three interacting protons 5-H, 6-H, and 7-H, and each of the spectra of (XXIII) and (XXIX), and (XXIV) and (XXX) contains two doublets of interacting protons, which are 6-H and 5-H, or 6-H and 7-H correspondingly. The low-field shift of the 5-H proton in the PMR spectra of the 4-acylamino-substituted (XXII), (XXIII), (XXV), and (XXVI) by comparison with the corresponding 4-amino-substituted compounds is caused by the anisotropic effect of the carbonyl group. The two signals

of the amide NHCO proton in the spectra of the compounds (XXII), (XXIV), and (XXV) show that they are isolated in the form of two geometrical isomers according to the disposition of the substituents in relation to the N−C=O bond [7].

EXPERIMENTAL

The IR spectra were recorded on the UR-20 spectrophotometer using tablets with KBr. The PMR spectra were obtained on Bruker WP-80 and WM-400 instruments in $CDCl_3$; the internal standard was TMS. Mass spectra were measured on the MX 1303 and LKB-9000 instruments fitted with a system for the direct input of the sample at the ion source with the ionizing voltage of 70 eV. The column chromatography utilized Al_2O_3 of the Brockmann 2 grade. The TLC utilized plates with a fixed layer of Al_2O_3 and silica gel of the Alufol and Silufol UV-254 types, and $MgSO_4$ was utilized as a drying agent for the extracts.

The analytical data for C, H, and N correspond with the calculated data.

1,2,3,4-Tetrahydro-1,4-dimethylspiro[quinoline-2-cyclohexane] (VI) ($C_{16}H_{23}N$). The mixture of 3 g (14 mmoles) of compound (I), 3.9 g (27.5 mmoles) of methyl iodide, and 4.0 g (28.9 mmoles) of potassium carbonate in 50 ml of abs. acetone is boiled for 8 h with the monitoring by TLC. The mixture is filtered, and the acetone is distilled off. The residue is treated with a solution of sodium carbonate prior to the extraction with ether (50 × 3 ml) and the drying. The residue remaining after the distillation of the ether is chromatographed on a column 40 × 1 cm with heptane as the eluent. Compound (VI) is obtained with the yield of 2.4 g (70%) as colorless crystals with the mp 31-32°C (from petroleum ether) and the R_f 0.72 (Silufol, the 5:2 mixture of heptane−ethyl acetate).

1,2,3,4-Tetrahydro-4-methyl-1-propargylspiro[quinoline-2-cyclohexane] (VII) ($C_{18}H_{23}N$). The mixture of 2.15 g (10 mmoles) of compound (I), 6.0 g (50 mmoles) of propargyl bromide, 3.0 g (21.7 mmoles) of potassium carbonate, 5 ml of acetonitrile, and 1 ml of water is heated for 6 h at 40-45°C. The mixture is acidified with 18% hydrochloric acid and extracted with ether. The acidic solution is made alkaline with sodium carbonate, and the nitrogen-containing reaction products are extracted with ether (50 × 3 ml) and dried. The residue remaining after the distillation of the ether is chromatographed on a column 60 × 2 cm with heptane as the eluent. Compound (VII) is obtained with the yield of 2.0 g (79%) as a colorless liquid with the R_f 0.70 (Silufol, the 5:2 mixture of heptane−ethyl acetate) and the IR spectrum characterized at 2100 (C≡C), and 3300 (HC≡) cm^{-1}.

1,2,3,4-Tetrahydro-4-methyl-1-allyl- and 1,2,3,4-Tetrahydro-4-methyl-8-allylspiro[quinoline-2-cyclohexanes] (VIII) ($C_{18}H_{25}N$) and (XI) ($C_{18}H_{25}N$). A. The mixture of 2.4 g (11 mmoles) of compound (I), 1.9 g (16 mmoles) of allyl bromide, and 3.5 g (25.3 mmoles) of potassium carbonate in 40 ml of abs. acetone is boiled for 7 h. The mixture is filtered, and the residue remaining after the distillation of the acetone from the filtrate is chromatographed on a column 60 × 1.5 cm with heptane as the eluent. Compound (VIII) is obtained with the yield of 2.05 g (72%) as a colorless liquid with the R_f 0.70 (Silufol, the 5:2 mixture of heptane−ethyl acetate).

B. To the solution of 3.2 g (15 mmoles) of compound (I) in 40 ml of abs. DMF at 0°C is added, in portions, 0.7 g (29 mmoles) of sodium hydride. The mixture is stirred for 1 h at 20°C prior to the addition of 8.9 g (74 mmoles) of allyl bromide. After 5 h, 40 ml of water are added, and the mixture is extracted with ethyl acetate and dried. The residue remaining after the distillation of the ethyl acetate is chromatographed. Compound (VIII) is isolated with the yield of 1.8 g [80% based on the reacted (I)], and the initial compound (I) is isolated with the yield of 1.3 g.

C. The mixture of 2.0 g (9.3 mmoles) of the spiro compound (I), 1.9 g (16 mmoles) of allyl bromide, and 3 g (21.7 mmoles) of potassium carbonate in 30 ml of DMF is boiled for 4 h. The mixture is cooled and poured into 50 ml of water prior to the extraction with ether (50 × 3 ml) and the drying. The residue remaining after the distillation of the ether is chromatographed on a column 40 × 1.5 cm with the 25:1 mixture of heptane−chloroform as the eluent. There follows the sequential isolation of 1.4 g (75%) of compound (VIII) and 0.28 g (15%) of compound (XI) as a yellow liquid with the R_f 0.63 (Silufol, the 5:2 mixture of heptane−ethyl acetate) and the IR spectrum characterized at 3425 cm^{-1} (NH). At the end, 0.4 g of the initial compound (I) is isolated.

D. Compound (VIII) (2.3 g, 9 mmoles) in 4 ml of boron trifluoride etherate is boiled for 3 h. The mixture is cooled and poured into 20 ml of water prior to the alkalization with sodium carbonate solution, the extraction with ether, and the drying. The residue remaining after the distillation of the ether is chromatographed. The compound (XI) is obtained with the yield of 1.45 g (63%).

E. The mixture of 1.7 g (6.6 mmoles) of compound (VIII) and 2.67 g (20 mmoles) of aluminum chloride is heated for 1 h at 110-115°C. The mixture is cooled prior to the addition of ice and the alkalinization with 10% sodium carbonate solution.

The mixture is extracted with chloroform (50 × 2 ml) and dried. After the distillation of the chloroform, the chromatography of the residue leads to the isolation of 1.22 g (71.8%) of the compound (XI).

F. The solution of 0.4 g (1.9 mmoles) of compound (VIII) in 10 ml of 2 N sulfuric acid is heated for 3 days at 70-80°C. After the treatment of the reaction mass, as described in "E," compound (XI) is obtained with the yield of 0.3 g (75%).

1,2,3,4-Tetrahydro-4,6-dimethyl-1-allyl- and 1,2,3,4-Tetrahydro-4,6-dimethyl-8-allylspiro[quinoline-2-cyclohexanes] (IX) ($C_{19}H_{27}N$) and (XII) ($C_{19}H_{27}N$). Using the method described above in "C," 1.6 g (6.9 mmoles) of compound (II), 1.1 g (9.2 mmoles) of allyl bromide, and 2.5 g (18.1 mmoles) of potassium carbonate in 30 ml of DMF lead to the isolation of 0.86 g (61%) of compound (IX) as a yellowish liquid with the R_f 0.86 (Silufol, the 6:1 mixture of heptane–ethyl acetate) as well as 0.4 g (28.4%) of compound (XII) as a brown liquid with the R_f 0.83 (Silufol, the 6:1 mixture of heptane–ethyl acetate) with the IR spectrum characterized at 3418 cm^{-1} (NH). Moreover, 0.4 g more of the initial compound (II) is isolated.

1,2,3,4-Tetrahydro-1-allyl- and 6-Bromo-4-methyl-8-allyl-spiro[quinoline-2-cyclohexanes] (X) ($C_{18}H_{24}BrN$) and (XIII) ($C_{18}H_{24}BrN$). Using the method described in "C," 4.0 g (13.6 mmoles) of compound (IV), 2.44 g (20 mmoles) of allyl bromide, and 5.0 g (36.2 mmoles) of potassium carbonate in 50 ml of DMF lead to the isolation of 2.2 g (64%) of compound (X) as a yellowish liquid with the R_f 0.76 (Silufol, the 5:1 mixture of heptane–ethyl acetate). Also isolated, besides compound (X), is 0.3 g (8.8%) more of compound (XIII) as a brown liquid with the R_f 0.68 (Silufol, the 5:1 mixture of heptane–ethyl acetate) and the IR spectrum characterized at 3430 cm^{-1} (NH) as well as 1.0 g of the initial compound (IV).

1,2,3,4-Tetrahydro-4-methyl-1-allylspiro[benzo(h)quinoline-2-cyclohexane] (XIV) ($C_{22}H_{27}N$). Using the method described in "C," 2.0 g (7.5 mmoles) of compound (V), 1.4 g (11.3 mmoles) of allyl bromide, and 2.0 g (14.5 mmoles) of potassium carbonate in 20 ml of DMF lead to the isolation of 0.80 g (53.3%) of compound (XIV) as a colorless liquid with the R_f 0.65 (Alufol, the 15:1 mixture of heptane–ethyl acetate). The reaction mixture affords 0.70 g more of the initial compound (V).

1,2,3,4-Tetrahydro-4-methyl-1-chloracetylspiro[quinoline-2-cyclohexane] (XVI) ($C_{17}H_{22}ClNO$). To the solution of 5.4 g (25 mmoles) of the spiro compound (I) and 2.0 g (27 mmoles) of triethylamine in 50 ml of abs. benzene at 20°C is added the solution of 2.84 g (25 mmoles) of chloroacetyl chloride in 5 ml of abs. benzene. The mixture is heated for 4 h at 50°C with the monitoring by TLC. The mixture is cooled, poured into 20 ml of water, rendered alkaline with sodium carbonate, extracted with ether (3 × 50 ml), and dried. The residue remaining after the distillation of ether crystallizes from heptane. The spiro compound (XVI) is obtained with the yield of 2.4 g (49%) as colorless crystals with the mp 70-71°C, the R_f 0.60 (Alufol, the 7:1 mixture of heptane–ethyl acetate), and the IR spectrum characterized at 1680 cm^{-1} (C=O).

1,2,3,4-Tetrahydro-4-methyl-1-(α-bromopropionyl)spiro[quinoline-2-cyclohexane] (XVII) ($C_{18}H_{24}BrNO$). Using the analogous method, 3.0 g (14 mmoles) of compound (I) and 3.1 g (14 mmoles) of α-bromopropionyl bromide in the presence of 1.5 g (15 mmoles) of triethylamine in 60 ml of abs. benzene afford 2.6 g (53.3%) of compound (XVII) as colorless crystals with the mp 130-131°C (from heptane), the R_f 0.41 (Silufol, the 5:1 mixture of heptane–ethyl acetate), and the IR spectrum characterized at 1688 cm^{-1} (C=O).

1,2,3,4-Tetrahydro-4,6-dimethyl-1-acetylspiro[quinoline-2-cyclohexane] (XVIII) ($C_{18}H_{25}NO$). Compound (II) (4.2 g, 18 mmoles) is boiled for 2 h in 13 ml of acetic anhydride. The mixture is poured onto ice, rendered alkaline with sodium carbonate to the pH ~7-8, and extracted with ether. After the distillation of the ether, compound (XVIII) is obtained with the yield of 4.6 g (90.5%) as colorless crystals with the mp 71-73°C (from heptane), the R_f 0.50 (Alufol, the 5:1 mixture of heptane–ethyl acetate), and the IR spectrum (KBr) characterized at 1655 cm^{-1} (C=O).

1,2,3,4-Tetrahydro-4,8-dimethyl-1-acetylspiro[quinoline-2-cyclohexane] (XIX) ($C_{18}H_{25}NO$). By analogy, 3.0 g (13 mmoles) of compound (III) afford 3.7 g (91.8%) of compound (XIX) as colorless crystals with the mp 89-91°C (from heptane), the R_f 0.53 (Alufol, the 5:1 mixture of heptane–ethyl acetate), and the IR spectrum (KBr) characterized at 1650 cm^{-1} (C=O).

1,2,3,4-Tetrahydro-4-methyl-1-acetylspiro[benzo(h)quinoline-2-cyclohexane] (XX) ($C_{21}H_{25}NO$). By analogy, 2.6 g (9.4 mmoles) of compound (V) afford 2.3 g (79.6%) of compound (XX) as a light brown liquid with the R_f 0.59 (Alufol, the 2:1 mixture of heptane–ethyl acetate) and the IR spectrum (in a film) characterized at 1675 cm^{-1} (C=O).

1,2,3,4-Tetrahydro-N-(α-bromopropionyl)-4-methylspiro[benzo(h)quinoline-2-cyclohexane] (XXI) ($C_{22}H_{26}BrNO$). Using the method described for the isolation of compound (XVI), 1.0 g (3.8 mmoles) of compound (V) and 0.85 g (3.9 mmoles) of α-bromopropionyl bromide in the presence of 0.4 g (3.9 mmoles) of triethylamine are utilized to synthesize 0.90 g (59.6%) of compound (XXI) as colorless crystals with the mp 148.5-150°C (from heptane), the R_f 0.57 (Alufol, the 2:1 mixture of heptane–ethyl acetate), and the IR spectrum characterized at 1690 cm^{-1} (C=O).

Recyclization of N-Acyl-substituted Spiro[tetrahydroquinoline-2-cyclohexanes] (XV)-(XX). A. The N-acyl-substituted compounds (XV) and (XVII)-(XX) (5 mmoles) are heated for 1.5 h at 100°C in phosphoric acid; 8-10 ml of the acid are taken for 1 g of the spiro compound. The mixture is cooled, poured onto ice, and made alkaline with aqueous sodium carbonate solution. The mixture is extracted with ether and dried. The residue remaining after the distillation of the ether is chromatographed on a column using the eluent of heptane or the 25:1, 15:1, and 5:1 mixtures of heptane–ethyl acetate. Compounds isolated sequentially are the spiro compounds (I)-(III), (V), the 4-aminospiro[indan-1-cyclohexanes] (XXVIII)-(XXXI), the 4-acylaminospiro[indan-1-cyclohexanes] (XXII)-(XXIV), (XXVI), and (XXVII). The characteristics of the compounds (XXII)-(XXXI) are presented in Table 3.

B. The compounds (XVI) or (XVII) (1.4 mmoles) are boiled for 1 h in 1 ml of boron trifluoride etherate with the monitoring by TLC. The mixture is cooled, poured into water, made alkaline with an aqueous solution of sodium carbonate, extracted with ether (50 × 2 ml), and dried. The residue remaining after the distillation of the ether is chromatographed on a column. The compounds (XXV) and (XXVI) are isolated.

3-Methyl-4-(α-bromopropionyl)aminospiro[indan-1-cyclohexane] (XXVI). To the solution of 0.2 g (1 mmole) of compound (XXVIII) and 0.14 g (1.4 mmoles) of triethylamine in 5 ml of abs. benzene is added 0.3 g (1.4 mmoles) of α-bromopropionyl bromide in 5 ml of abs. benzene. The mixture is stirred for 4 h at 20°C and poured into 20 ml of water. It is extracted with ether and dried. The residue remaining after the distillation of the ether is chromatographed on a column using the 10:1 mixture of heptane–ethyl acetate as the eluent. Compound (XXVI) is isolated with the yield of 0.14 g (43%) as colorless crystals with the mp 174-176°C (from heptane).

REFERENCES

1. R. A. Johnson, J. Org. Chem., **33**, 3627 (1968).
2. N. S. Prostakov, V. V. Kuznetsov, and E. E. Stashenko, Khim. Geterotsikl. Soedin., No. 1, 1514 (1989).
3. V. V. Kuznetsov, R. A. Pal'ma, M. Fernandes, A. É. Aliev, V. K. Shevtsov, A. V. Varlamov, and N. S. Prostakov, Khim. Geterotsikl. Soedin., No. 10, 1350 (1991).
4. V. V. Kuznetsov, A. É. Aliev, R. A. Pal'ma, A. V. Varlamov, and N. S. Prostakov, Zh. Org. Khim., **27**, 1579 (1991).
5. V. V. Kuznetsov, A. É. Aliev, A. V. Varlamov, and N. S. Prostakov, Khim. Geterotsikl. Soedin., No. 7, 947 (1991).
6. W. H. Cliffe, D. Dodman, and O. Meth-Cohn, J. Chem. Soc. (C), No. 5, 514 (1966).
7. B. I. Ionin, B. A. Ershov, and A. I. Kol'tsov, NMR Spectroscopy in Organic Chemistry [in Russian], Khimiya, Leningrad (1983), p. 250.