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SYNTHESIS AND ALKYLATION OF 4-ARYL-5-OXO-1H-2,3,4,5-TETRAHYDROINDENO[1,2-*b*]PYRIDINES*

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Reduction of 5-oxo-4-phenyl-1H-4,5-dihydroindeno[1,2-b]pyridines with triethylsilane in trifluoroacetic acid gave the corresponding 1,2,3,4-tetrahydroindeno[1,2-b]pyridines predominatly with the trans-configured substituents at atoms C(2), C(3), and C(4). Alkylation of the anionic form of the tetrahydroindenopyridines gives the N- and C(4a)-alkyl derivatives.

Keywords: 5-oxo-4,5-dihydro-1H- and 2,3,4,5-tetrahydro-1H-indeno[1,2-*b*]pyridines, N- and C(4a)-alkylation of 5-oxo-2,3,4,5-tetrahydro-1H-indeno[1,2-*b*]pyridine, triethylsilane reduction.

Depending on the reaction conditions, the reduction of Hantzsch type 1,4-dihydropyridine esters using triethylsilane in trifluoroacetic acid medium gives the *trans* isomers of the corresponding 1,2,3,4-tetrahydropyridines or piperidines [1]. Only certain representatives of the 1,2,3,4-tetrahydroindeno[1,2-*b*]pyridine series are known and they are prepared by a complex route including photosynthesis, even though they are beginning to attract interest as potential antiparasitic agents [2]. We have found that reduction of the 4-aryl-5-oxo-4,5-dihydro-1H-indeno[1,2-*b*]pyridines **1a-h** to the corresponding tetrahydroindenopyridines can also be carried out using Et_3SiH in CF_3COOH. Under these conditions selective reduction of the C(2)=C(3) bond occurs and the main products are the *trans* isomers of the 1,2,3,4-tetrahydroindenopyridines **2a-h**. Only in the single case of the reduction of compound **1b** was it possible to separate the reduction product of the C(4a)=C(9b) bond (compound **5**) in low yield (5%).

As expected, the *trans* isomer was formed as a result of the reduction since protonation of the enamine fragment as also the addition of hydride ion generated by Et_3SiH can occur at both sides of the pyridine ring plane and a *trans* orientation of all of the bulky substituents at atoms C(2), C(3), and C(4) is energetically more favored. The *cis* isomers **3a-h** are formed as minor reduction products. The remaining two possible diastereomers with reduced bond C(2)=C(3) were not observed.

Protonation of the enamine fragment at atom C(3) leads to formation of a cyclic immonium ion. Thanks to the presence of the C=C and C=N double bonds the conformation of the pyridine ring is comparatively planar, the ring atoms forming two planar fragments C(3)–C(2)=N–C(9b) and C(4)–C(4a)=C(9b)–N, the terminal atoms of which (C(3) and C(4)) are shifted to opposite sides of the mean ring plane by twisting along the C(9b)–N single bond. Such a ring conformation markedly decreases the CH_3–C(2)–C(3)–R(H) dihedral angle and makes the conformation with an axial arrangement of the substituent at C(3) more favored due to a

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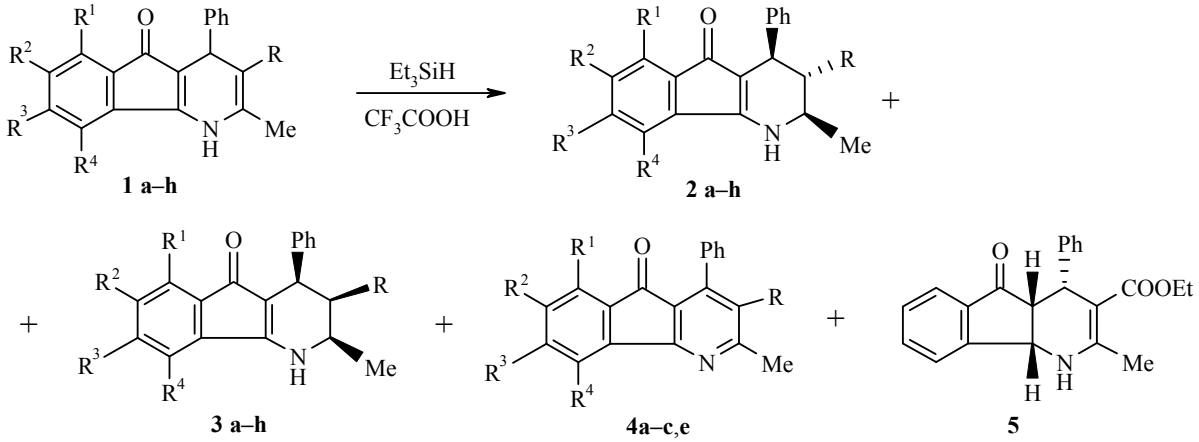
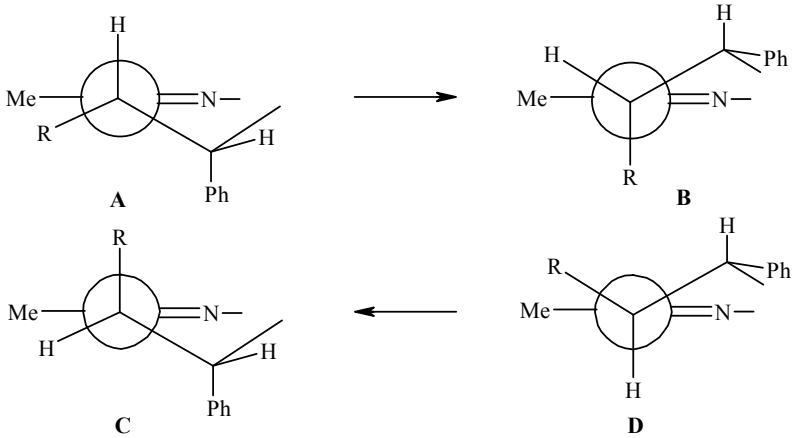
decreased Me/3-R gauche interaction. More preferred are conformation **B** with protonation on the side of the 4-phenyl substituent and conformation **C** with protonation on the side of the opposite substituent at position 4. Conformation **B** ensures free approach of the hydride-bearing agent to atom C(2) while in conformation **C** the approach is hindered by the axially placed 4-Ph group. These steric factors limit the ratio of diastereomers *trans* >> *cis* and the insignificant fraction of conformations **A** and **D** results in the absence of other stereoisomers.



1–4 a–c $R^2 = R^3 = R^4 = H$, **a** R = COMe, R^1 = H; **b** R = CO_2Et, R^1 = H; **c** R = CO_2Pr-*i*; R^1 = H; **1–3 d** R = CO_2Me, R^1 = Me, $R^2 = R^3 = R^4 = H$; **1–4 e** R = CO_2Et, $R^1 = NH_2$, $R^2 = R^3 = R^4 = H$; **1–3 f** R = CO_2Et, $R^1 = R^2 = R_3 = H$, $R^4 = NO_2$; **g** R = CO_2Me, $R^1 = R^2 = H$, R^3 = OMe, R^4 = OEt; **h** R = CO_2Et, $R^1 = R^4 = H$, $R^2 = R^3$ = Cl

It was interesting to note that the substituent in the indene part of the molecule affects the t*rans*/*cis* isomers ratio. On comparing the yields of the *trans* and *cis* isomers of the compounds **2b**,**f** the *trans*/*cis* ratio are 72:12 and 86:4. Reduction of the dihydroindenopyridines with Et_3SiH/CF_3COOH is accompanied by partial oxidation of the dihydropyridine derivative to a pyridine, even though the reduction is carried out under an argon atmosphere. The tetrahydroindenopyridines are not oxidized by atmospheric oxygen to indenopyridines but undergo a rearrangement which will be reported separately. Hence the source of the oxidized form is the starting dihydropyridine and the oxidant may be the atmospheric oxygen in the reaction medium. We were unable to avoid this side reaction by either simple passage of argon through the reaction vessel or by repeated freeze/evacuation/argon fill. It can be proposed that, along with the Et_3SiH, the hydride ion donor may be the dihydropyridine when converted to the indenopyridine. This hypothesis is indirectly confirmed by the absence of the oxidized form in the case of reduction of indenopyridines having acceptor substituents in the indane ring (**1f**,**h**) since such a substitution must lower the reductive ability of the dihydropyridine.



The 3-acetyl derivative of dihydroindenopyridine **1a** undergoes reduction in the same way as the dihydroindenopyridine-3-carboxylates but we were unable to reduce the corresponding 3-cyano derivative with Et_3SiH in trifluoroacetic acid.

The structures of the diastereomers **2a-h** and **3a-h** and the reduction product **5** were proved using NMR spectroscopy and X-ray structural analysis (compounds **2b**, **3b** and **5**, see Figs. 1-3 respectively). Hence the ^1H NMR spectra of the *trans* isomers **2a-h** show a large proton spin-spin coupling constants for the protons of the pyridine ring with $J_{2,3} \approx J_{3,4}$ = 9.4-10.0 Hz and this agrees well with an antiperiplanar arrangement of H(2),

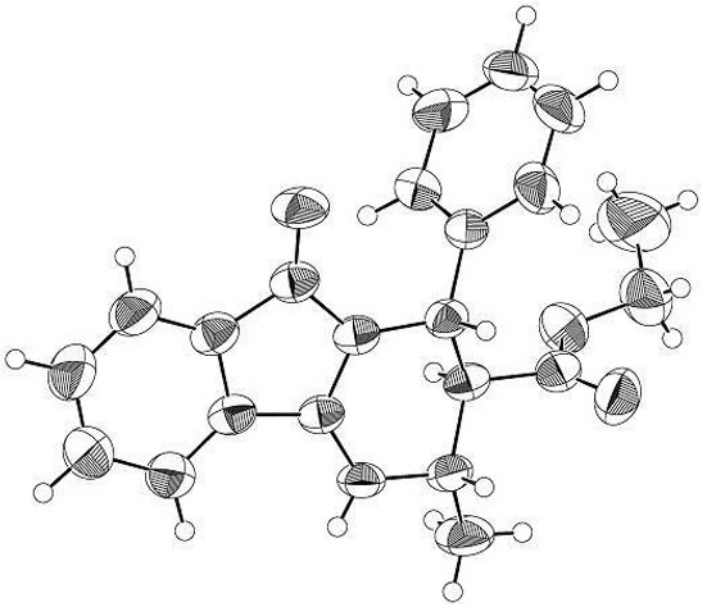


Fig. 1. Structure of ethyl (2*R**,3*S**,4*R**)-2-methyl-5-oxo-4-phenyl-2,3,4,5-tetra-hydro-1H-indeno[1,2-*b*]pyridine-3-carboxylate (**2b**).

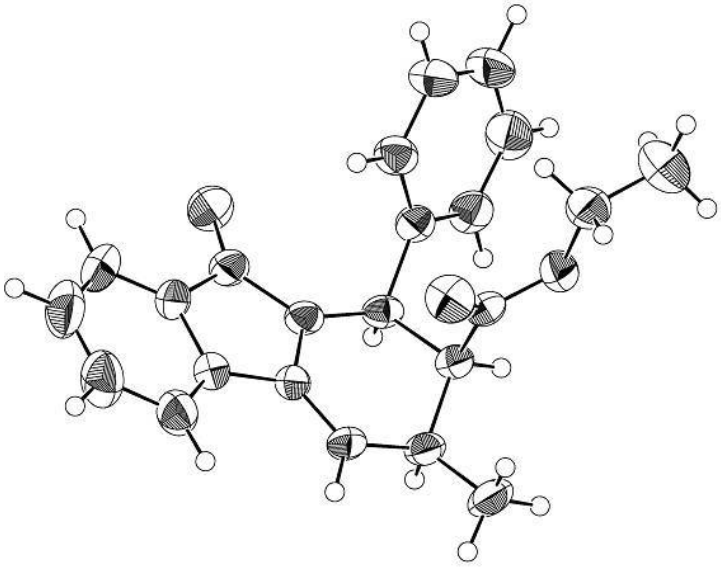


Fig. 2. Structure of ethyl (2*R**,3*R**,4*R**)-2-methyl-5-oxo-4-phenyl-2,3,4,5-tetra-hydro-1H-indeno[1,2-*b*]pyridine-3-carboxylate (**3b**).

H(3), and H(4) protons. Hence all of the bulky groups in the tetrahydropyridine ring occupy equatorial positions. The spin-spin couplings constants of the isomers **3a-h** occur in the range $J_{2,3}$ = 3.3-3.6 and $J_{3,4}$ = 6.3-6.7 Hz, corresponding to a *cis* arragement of the H(2), H(3), and H(4) protons. An increased value for the $J_{3,4}$ constant points to a decrease in the H–C(3)–C(4)–H dihedral angle due to flattening of the ring conformation.

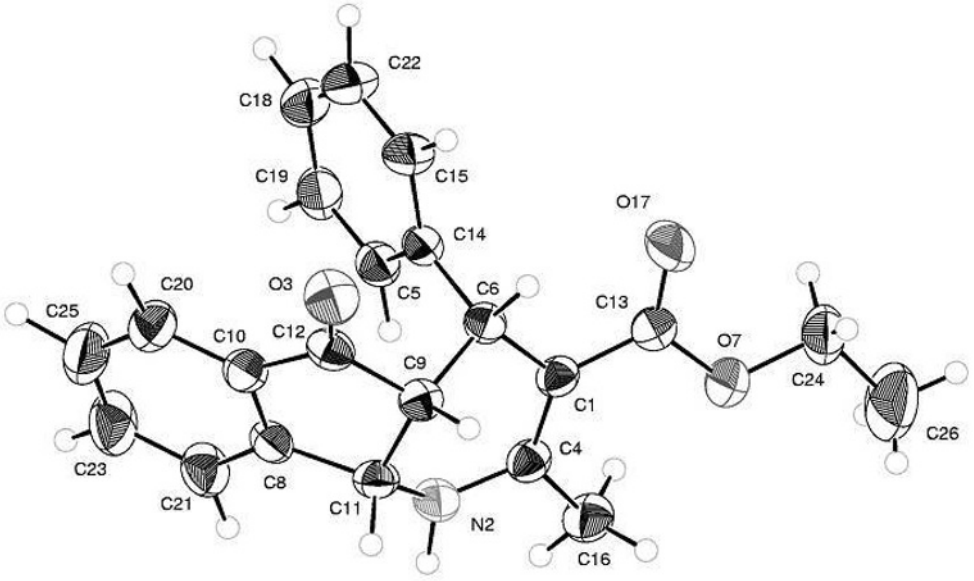
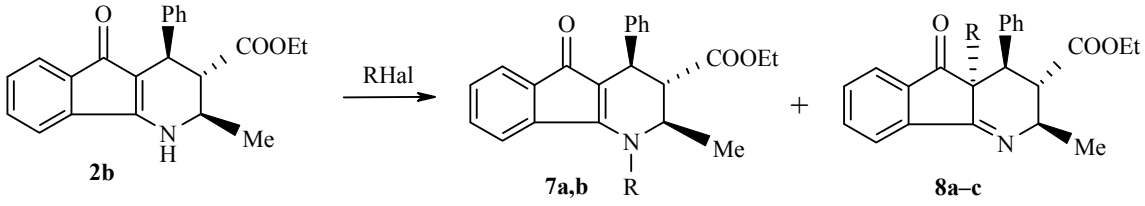


Fig. 3. Structure of ethyl (4*R**,4a*R**,9b*S**)-2-methyl-5-oxo-4-phenyl-4,4a,5,9b-tetrahydro-1H-indeno[1,2-*b*]pyridine-3-carboxylate (**5**).

Alkylation of the tetrahydroindenopyridine **2b** using iodomethane, allyl bromide, or ethyl bromoacetate was carried out in DMF in the presence of sodium hydride. The action of NaH on the tetrahydroindenopyridine **2b** forms an anion, the ambidentate properties of whose enamino ketone fragment are similar to those of dihydroindenopyridine anions [3]. Reaction of the tetrahydropyridine anion with an alkylating agent gives a mixture of the N- and C-alkylated products **7a**,**b** and **8a-c**. Similar methylation of the diastereomer **3b** gave the N-isomer **10** as the main product.



7 a R = Me, **b** R = CH_2CO_2Et; **8 a** R = Me, **b** R = CH_2CO_2Et, **c** R = $CH_2CH{=}CH_2$

The spatial positioning of the substituent in the alkylation product **8c** was determined from the results of a 2D NOESY correlation spectroscopic experiment. This spectrum clearly showed an interaction between the 4a-allyl substituent and the H(4) proton and the complete absence of corresponding cross peak with the phenyl group. Hence the substituent R on atom C(4a) had added to the ring plane opposite to the 4-Ph substituent. In the spectra of compounds **7a**,**b** the spin-spin couplings $J_{2,3} \approx J_{3,4}$ = 2.3-3.0 Hz are nontypical for *trans*-orientated substituents at atoms C(2), C(3), and C(4).

Selective reduction of the C(2)=C(3) bond occurs upon reduction of 1-methyl-5-oxo-4,5-dihydroindeno[1,2-*b*]pyridine **9** and the main product is the *trans* isomer of 1,2,3,4-tetrahydroindenopyridine **7a**, the fraction of the *cis* isomer **10** being markedly greater when compared with the N-unsubstituted analogs.

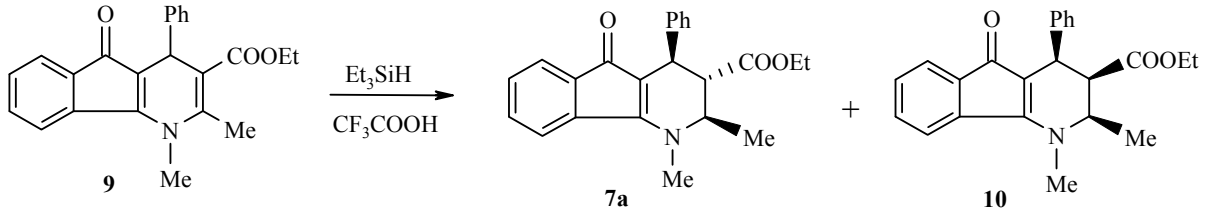


TABLE 1. Physicochemical Characteristics of the Compounds Prepared

Compound	Empirical formula	Found, % / Calculated, %			mp, °C	Yield, %
		C	H	N		
2b	$C_{22}H_{21}NO_3$	75.96 76.06	6.08 6.09	4.04 4.03	227-227.5	23
2c	$C_{23}H_{23}NO_3$	76.18 76.43	6.23 6.41	3.81 3.88	230	67
2d	$C_{22}H_{21}NO_3$	75.62 76.06	5.98 6.09	3.93 4.03	345-347	80
2e	$C_{22}H_{22}N_2O_3$	72.51 72.91	5.59 6.12	7.39 7.73	193-195	50
2f	$C_{22}H_{20}N_2O_5$	67.32 67.34	5.07 5.14	7.09 7.14	148	86
2g	$C_{24}H_{25}NO_5$	70.44 70.75	6.12 6.18	3.32 3.44	116-118	83
3a	$C_{21}H_{19}NO_2$	79.70 79.47	6.15 6.03	4.20 4.41	158-159	24
3b	$C_{22}H_{21}NO_3$	75.80 76.06	6.03 6.09	3.98 4.03	251-252	12
3c	$C_{23}H_{23}NO_3$	76.21 76.43	6.26 6.41	3.67 3.88	212	6
3f	$C_{22}H_{20}N_2O_5$	67.09 67.34	5.32 5.14	6.92 7.14	148	4
4c	$C_{23}H_{19}NO_3$	76.99 77.29	5.30 5.36	3.75 3.92	124	17
4e	$C_{22}H_{22}N_2O_3$	73.58 73.73	4.84 5.06	7.61 7.82	262-265	11
5	$C_{22}H_{21}NO_3$	75.82 76.06	6.02 6.09	3.98 4.03	201	5
7a	$C_{23}H_{23}NO_3$	76.42 76.43	6.45 6.41	3.77 3.88	168-170	35*, 65*[2]
7b	$C_{26}H_{27}NO_5$	71.84 72.04	6.27 6.28	3.09 3.23	148-150	14
8a	$C_{23}H_{23}NO_3$	76.29 76.43	6.42 6.41	3.81 3.88	140-141	27
8b	$C_{26}H_{27}NO_5$	71.86 72.04	6.24 6.28	3.10 3.23	140-141	61
8c	$C_{25}H_{25}NO_3$	77.41 77.49	6.49 6.50	3.58 3.60	77-79	54
10	$C_{23}H_{23}NO_3$	76.01 76.43	6.41 6.41	3.79 3.88	149-150	48*, 32*[2]

* Yield in the alkylation reaction.

*[2] Yield in the reduction reaction.

TABLE 2. ^{1}H NMR Spectra of the Compounds Prepared

Compound	Chemical shifts, δ, ppm (*J*, Hz)*
1	2
2a	1.30 (3H, d, *J* = 6.5, 2-CH_3); 1.72 (3H, s, $COCH_3$); 2.78 (1H, dd, *J* = 9.5, *J* = 9.4, H-3); 3.12 (1H, dq, *J* = 9.4, *J* = 6.5, H-2); 3.91 (1H, d, *J* = 9.5, H-4); 5.27 (1H, br. s, NH); 6.87-7.82 (9H, m, Ar)
2b	1.01 (3H, t, *J* = 7.0, $OCH_2C\underline{H}_3$); 1.33 (3H, d, *J* = 6.4, 2-CH_3); 2.53 (1H, t, *J* = 9.7, H-3); 3.80 (1H, m, H-2); 3.97 (2H, q, *J* = 7.0, $OC\underline{H}_2CH_3$), 4.01(1H, d, *J* = 9.7, H-4); 5.31 (1H, br. s, NH); 7.00-7.38 (9H, m, Ar)
2c	0.86 (3H, d, *J* = 6.3, $CH(C\underline{H}_3)_2$); 1.15 (3H, d, *J* = 6.3, $CH(C\underline{H}_3)_2$); 1.35 (3H, d, *J* = 6.4, 2-CH_3); 2.48 (1H, dd, *J* = 9.8, *J* = 9.7, H-3); 3.90 (1H, m, H-2); 4.01 (1H, d, *J* = 9.8, H-4); 4.89 (1H, sept, *J* = 6.3, $C\underline{H}(CH_3)_2$); 5.47 (1H, br. s, NH); 7.02-7.35 (9H, m, Ar)
2d	1.18 (3H, d, *J* = 6.4, 2-CH_3); 2.33 (3H, s, 6-CH_3); 2.43-2.51 (1H, m, H-3); 3.43 (3H, s, OCH_3); 3.69-3.78 (1H, m, H-2); 3.83 (1H, d, *J* = 9.4, H-4); 6.98-7.07 (3H, m, Ar); 7.10-7.24 (4H, m, Ar); 7.34 (1H, d, *J* = 7.0, Ar); 8.60 (1H, br. s, NH)
2e	1.00 (3H, t, *J* = 7.1, $OCH_2C\underline{H}_3$); 1.32 (3H, d, *J* = 6.5, 2-CH_3); 2.50 (1H, dd, *J* = 9.9, *J* = 9.8, H-3); 3.76-4.05 (3H, m, $OC\underline{H}_2CH_3$, H-2); 4.25 (1H, m, H-4); 4.98 (2H, br. s, NH_2); 5.05 (1H, br. s, NH); 6.50 (2H, m, H-7,8); 6.90-7.53 (6H, m, Ar)
2f	1.02 (3H, t, *J* = 7.1, $OCH_2C\underline{H}_3$); 1.40 (3H, d, *J* = 6.5, 2-CH_3); 2.55 (1H, t, *J*= 10.0, *J* = 9.8, H-3); 3.85-4.08 (3H, m, $OC\underline{H}_2CH_3$, H-2); 4.10 (1H, d, *J* = 10.0, H-4); 7.13-7.66 (8H, m, Ar)
2g	1.30 (3H, d, *J* = 6.4, 2-CH_3); 1.41 (3H, t, *J* = 7.0, $CH_2C\underline{H}_3$); 2.52 (1H, t, *J* = 9.6, H-3); 3.52 (3H, s, $COOCH_3$); 3.81-3.95 (4H, m, H-2, OCH_3); 4.02 (1H, d, *J* = 9.6, H-4); 4.14-4.41 (2H, m, $C\underline{H}_2CH_3$); 6.20 (1H, br. s, NH); 6.65 (1H, d, *J* = 7.7, H-7); 7.04 (1H, d, *J* = 7.7, H-6); 7.09-7.37 (5H, m, Ar)
2h,3h	0.83 (0.5H, t, *J* = 7.1, *cis*-$OCH_2C\underline{H}_3$); 1.01 (2.5H, t, *J* = 7.1, *trans*-$OCH_2C\underline{H}_3$); 1.31 (2.5H, d, *J* = 6.5, *trans*-2-CH_3); 1.40 (0.5H, d, *J* = 6.9, *cis*-2-CH_3); 2.51 (0.83H, t, *J* = 9.6, *trans*-H-3); 3.06 (0.17H, m, *cis*-H-3); 3.67-4.08 (3.83H, m, *trans*-H-2, *cis*-H-2, *trans*-H-4, *cis*-$OC\underline{H}_2CH_3$, *trans*-$OC\underline{H}_2CH_3$); 4.22 (0.17H, d, *J* = 6.6, *cis*-H-4); 5.47 (0.17H, br. s, NH); 5.52 (0.83H, br. s, NH); 7.08-7.38 (7H, m, H-6,9, Ar)
3a	1.37 (3H, d, *J* = 6.5, 2-CH_3); 1.91 (3H, s, $COCH_3$); 3.30 (1H, m, H-3); 3.94 (1H, m, H-2); 4.28 (1H, d, *J* = 6.5, H-4); 5.23 (1H, br. s, NH); 7.04–7.67 (9H, m, Ar)
3b	0.85 (3H, t, *J* = 7.0, $OCH_2C\underline{H}_3$); 1.41 (3H, d, *J* = 6.8, 2-CH_3); 3.08 (1H, dd, *J* = 6.6, *J* = 3.5, H-3); 3.74 (2H, m, $OC\underline{H}_2CH_3$); 3.98 (1H, m, H-2); 4.26 (1H, d, *J* = 6.6, H-4); 5.22 (1H, br. s, NH); 7.02-7.42 (9H, m, Ar)
3c	0.65 (3H, d, *J* = 6.3, $CH(C\underline{H}_3)_2$); 1.05 (3H, d, *J* = 6.3, $CH(C\underline{H}_3)_2$); 1.40 (3H, d, *J* = 6.9, 2-$C\underline{H}_3$); 3.04 (1H, dd, *J* = 6.6, *J* = 3.6, H-3); 3.96 (1H, qd, *J* = 6.9, *J* = 3.6, H-2); 4.23 (1H, d, *J* = 6.6, H-4); 4.62 (1H, sept, *J* = 6.3, $C\underline{H}(CH_3)_2$); 5.27 (1H, br. s, NH); 7.02-7.42 (9H, m, Ar)
3d	1.21 (3H, d, *J* = 6.8, 2-CH_3); 2.37 (3H, s, 6-CH_3); 3.03 (1H, dd, *J* = 6.4, *J* = 3.5, H-3); 3.15 (3H, s, OCH_3); 3.86-3.94 (1H, m, H-2); 4.12 (1H, d, *J* = 6.4, H-4); 6.99-7.07 (3H, m, Ar); 7.08-7.23 (4H, m, Ar); 7.31 (1H, d, *J* = 7.0, Ar); 8.27 (1H, br. s, NH)
3e	0.73 (3H, t, *J* = 7.0, $OCH_2C\underline{H}_3$); 1.20 (3H, d, *J* = 6.8, 2-$C\underline{H}_3$); 2.97 (1H, dd, *J* = 6.3, *J* = 3.3, H-3); 3.52-3.69 (2H, m, $OC\underline{H}_2CH_3$); 3.79-3.90 (1H, m, H-2); 4.09 (1H, d, *J* = 6.3, H-4); 5.75 (2H, br. s, NH_2); 6.55 (1H, d, *J* = 8.2, Ar); 6.75 (1H, d, *J* = 6.8, Ar); 6.93-7.24 (6H, m, Ar); 8.03 (1H, br. s, NH)
3f	0.86 (3H, t, *J* = 7.1, $OCH_2C\underline{H}_3$); 1.45 (3H, d, *J* = 6.9, 2-CH_3); 3.10 (1H, dd, *J* = 6.7, *J* = 3.6, H-3); 3.76 (2H, m, $OC\underline{H}_2CH_3$); 4.00 (1H, m, H-2); 4.28 (1H, d, *J* = 6.7, H-4); 7.08-8.03 (9H, m, NH, Ar)
3g	1.33 (3H, d, *J* = 6.8, 2-CH_3); 1.39 (3H, t, *J* = 7.0, $CH_2C\underline{H}_3$); 3.03-3.08 (1H, m, H-3); 3.26 (3H, s, $COOCH_3$); 3.84 (3H, s, OCH_3); 3.90-3.96 (1H, m, H-2); 4.16-4.33 (3H, m, $C\underline{H}_2CH_3$, H-4); 6.23 (1H, br. s, NH); 6.64 (1H, d, *J* = 7.6, H-7); 7.05 (1H, d, *J* = 7.6, H-6); 7.10-7.26 (5H, m, Ar)
4c	0.97 (3H, d, *J* = 6.3, $CH(C\underline{H}_3)_2$); 2.68 (3H, s, 2-CH_3); 4.93 (1H, sept, *J* = 6.3, $C\underline{H}(CH_3)_2$); 7.32-7.94 (9H, m, Ar)
4e	0.93 (3H, t, *J* = 7.1, $CH_2C\underline{H}_3$); 2.68 (3H, s, 2-CH_3); 4.02 (2H, q, *J* = 7.1, $C\underline{H}_2CH_3$); 5.50 (2H, br. s, NH_2); 6.62 (1H, dd, *J* = 6.0, *J* = 2.4, H-7); 7.19-7.48 (7H, m, Ar)

TABLE 2 (continued)

1	2
5	1.12 (3H, t, *J* = 7.1, $CH_2C\underline{H}_3$); 2.55 (3H, s, 2-CH_3); 3.32 (1H, t, *J* = 7.4, *J* = 7.1, H-4a); 3.98 (2H, m, $C\underline{H}_2CH_3$); 4.65 (1H, d, *J* = 7.4, H-4); 4.94-5.06 (2H, m, NH, H-9b); 6.73-6.78 (5H, m, Ar); 7.10-7.17 (2H, m, H-6,8); 7.46-7.51 (2H, m, H-7,9)
7a	0.90 (3H, d, *J* = 7.1, 2-CH_3); 1.22 (3H, t, *J* = 7.1, $OCH_2C\underline{H}_3$); 1.14 (1H, t, *J* = 2.3, H-3); 3.60 (3H, s, N-CH_3); 3.91 (1H, m, H-2); 4.12 (1H, q, *J* = 7.1, $OC\underline{H}_2CH_3$); 4.14 (1H, q, *J* = 7.1, $OC\underline{H}_2CH_3$); 4.57 (1H, m, H-4); 7.10-7.50 (9H, m, Ar)
7b	0.98 (3H, d, *J* = 7.1, 2-CH_3); 1.21 (3H, t, *J* = 7.1, $OCH_2C\underline{H}_3$); 1.29 (3H, t, *J* = 7.1, $OCH_2C\underline{H}_3$); 3.11 (1H, t, *J* = 3.0, H-3); 3.98 (1H, qd, *J* = 7.1, *J* = 3.0, H-2); 4.13 (2H, q, *J* = 7.1, $OC\underline{H}_2CH_3$); 4.27 (1H, q, *J* = 7.1, $OC\underline{H}_2CH_3$); 4.28 (1H, q, *J* = 7.1, $OC\underline{H}_2CH_3$); 4.33 (1H, d, *J* = 18.5, CH_2CO); 4.54 (1H, d, *J* = 3.0, H-4); 4.76 (1H, d, *J* = 18.5, CH_2CO); 7.05 (1H, m, Ar); 7.14-7.35 (7H, m, Ar); 7.45 (1H, m, Ar)
8a	1.26 (3H, t, *J* = 7.0, $OCH_2C\underline{H}_3$) ; 1.49 (3H, s, 4a-CH_3); 1.64 (3H, d, *J* = 6.6, 2-CH_3); 2.64 (1H, dd, *J* = 9.9, *J* = 5.1, H-3); 3.64 (1H, d, *J* = 5.1, H-4); 4.05-4.29 (1H, m, H-2) and (2H, q, *J* = 7.0, $OC\underline{H}_2CH_3$); 6.86 (2H, m, Ar); 7.05 (3H, m, Ar); 7.49-7.78 (3H, m, H-7,8,9); 8.11 (1H, m, H-6)
8b	0.87 (3H, t, *J* = 7.1, $OCH_2C\underline{H}_3$); 1.28 (3H, t, *J* = 7.1, $OCH_2C\underline{H}_3$); 1.68 (3H, d, *J* = 7.1, 2-CH_3); 2.77 (1H, dd, *J* = 10.0, *J* = 4.0, H-3); 3.21 (1H, d, *J* = 16.0, CH_2CO); 3.42 (1H, d, *J* = 16.0, CH_2CO); 3.64 (1H, d, *J* = 4.0, H-4); 3.79 (2H, q, *J* = 7.1, $OC\underline{H}_2CH_3$); 4.18 (1H, qd, *J* = 10.0, *J* = 6.5, H-2); 4.23 (2H, q, *J* = 7.1, $OC\underline{H}_2CH_3$); 6.85 (2H, m, Ar); 6.99 (3H, m, Ar); 7.48 (2H, m, Ar); 7.67 (1H, ddd, *J* = 7.6, *J* = 6.0, *J* = 2.4, H-8); 8.07 (1H, ddd, *J* = 7.6, *J* = 6.0, *J* = 2.4, H-7)
8c	1.25 (3H, t, *J* = 7.1, $OCH_2C\underline{H}_3$) ; 1.63 (3H, d, *J* = 6.6, 2-CH_3); 2.66 (1H, dd, *J* = 9.9, *J* = 5.2, H-3); 2.74 (1H, dd, *J* = 14.0, *J* = 7.0, $C\underline{H}_2CH$=); 2.90 (1H, dd, *J* = 14.0, *J* = 7.0, $C\underline{H}_2CH$=); 3.63 (1H, d, *J* = 5.2, H-4); 4.17 (1H, qd, *J* = 9.9, *J* = 6.6, H-2); 4.20 (2H, q, *J* = 7.1, $OC\underline{H}_2CH_3$); 4.84 (1H, dd, *J* = 9.9, *J* = 1.8, CH_2=); 5.01 (1H, dd, *J* = 16.9, *J* = 1.8, CH_2=); 5.31 (1H, ddt, *J* = 16.9, *J* = 9. 9, *J* = 7.0, CH=); 6.85 (2H, m, Ar); 7.03 (3H, m, Ar); 7.53 (2H, m, Ar); 7.70 (1H, ddd, *J* = 7.6, *J* = 6.0, *J* = 2.2, H-7); 8.08 (1H, d, *J* = 7.6, H-6)
10	1.18 (3H, d, *J* = 6.8, 2-CH_3); 1.29 (3H, t, *J* = 7.1, $OCH_2C\underline{H}_3$); 3.29 (1H, dd, *J* = 6.2, *J* = 3.9, H-3); 3.57 (3H, s, N-CH_3); 3.80 (1H, m, H-2); 4.19 (2H, m, $OC\underline{H}_2CH_3$); 4.65 (1H, d, *J* = 6.2, H-4); 7.11-7.49 (9H, m, Ar)

* The spectra of compounds **2a-c**,**e**,**f**,**h, 3a-c**,**f**,**h**, **4c**,**e**, **5**, **7a**,**b**, **8a-c** (in $CDCl_3$) were recorded on a Varian Mercury 200 (200 MHz) and compounds **2**, **3d** (in DMSO-d_6) and **2g**, **3e**,**g** (in $CDCl_3$) on a Varian Mercury 400 (400 MHz) instrument.

The structure of the *cis*-1-methyl-1,2,3,4-tetrahydroindenopyridine **10** was proved by ^{1}H NMR spectroscopy. The spin-spin couplings constants in compound **10** are close to those in the N-unsubstituted analogs **3a-h** ($J_{2,3}$ = 3.3-3.6, $J_{3,4}$ = 6.3-6.7 Hz). As noted above, this spin-spin coupling in the N-methyl-*trans* isomer **7a** contrasts strongly with the measured constants in the precursor compounds **2a-h**. This is explained by the fact that, in the conformations with equatorial substituents at the C(2)–C(4) atoms, the NCH_3 and 2-CH_3 groups occupy an almost screened orientation. The unfavorable steric interaction is decreased by rotation around the N–C(2) bond so leading to a tetrahydropyridine ring conformation with an axial orientation of the C(2) and C(3) substituents.

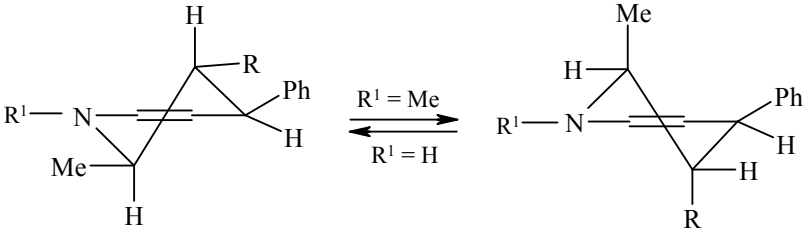


TABLE 3. ^{13}C NMR Spectra of the Compounds Prepared

Compound	Chemical shifts, δ, ppm (*J*, Hz)*
2b	14.25 ($CH_2\underline{C}H_3$); 19.46 (CH_3); 41.99 (C-4); 50.74 (C-2); 56.93 (C-3); 60.91 ($\underline{C}H_2CH_3$); 103.69 (C-4a); 117.07; 120.64; 126.99; 127.94; 128.47; 130.50; 130.54; 136.10; 136.61; 140.86; 162.09; 173.01 ($\underline{C}OOCH_2$); 189.08 (C=O)
2c	19.43 (CH_3); 21.26 ($CH(\underline{C}H_3)_2$); 22.00 ($CH(\underline{C}H_3)_2$); 42.06 (C-4); 50.80 (C-2); 57.01 (C-3); 68.37 ($\underline{C}H(CH_3)_2$); 104.12; 116.75; 120.74; 126.98; 128.04; 128.45; 130.50; 130.52; 136.12; 136.51; 140.73; 172.49; 189.05 ($\underline{C}OOPr$-2); 201.95 (C=O)
2e	14.03 ($CH_2\underline{C}H_3$); 19.50 (CH_3); 41.95 (C-4); 50.43 (C-2); 56.71 (C-3); 60.60 ($\underline{C}H_2CH_3$); 103.61 (C-4a); 106.96; 114.03; 120.30; 126.82; 127.73; 128.21; 131.42; 136.87; 140.74; 143.36; 159.57; 172.87 ($\underline{C}OOCH_2$); 192.07 (C=O)
2f	14.09 ($CH_2\underline{C}H_3$); 19.27 (CH_3); 42.05 (C-4); 50.76 (C-2); 50.81 (C-3); 61.65 ($\underline{C}H_2CH_3$); 119.60 (C-4a); 121.79; 127.99; 128.31; 129.10; 132.44; 133.28; 135.55; 144.45; 147.10; 161.20; 163.62; 167.68 ($\underline{C}OOCH_2$); 187.54 (C=O)
2g	15.9; 19.6; 41.7; 50.1; 51.7; 55.9; 56.5; 69.3; 103.4; 111.4; 116.9; 126.5; 126.6; 127.5; 128.2; 129.2; 140.6; 141.6; 155.3; 160.5; 173.3 (COOMe); 187.70 (C=O)
3a	18.08 ($COCH_3$); 31.19 (CH_3); 40.90 (C-4); 52.42 (C-2); 56.34 (C-3); 117.26 (C-4a); 120.46; 127.05; 128.10; 128.42; 128.76; 130.50; 136.17; 138.54; 143.65; 162.77; 164.10; 176.71 ($COCH_3$); 208.40 (C=O)
3b	20.84 ($CH_2\underline{C}H_3$); 21.27 (CH_3); 39.33 (C-4); 40.58 (C-2); 40.63 (C-3); 45.70 ($\underline{C}H_2CH_3$); 116.35 (C-4a); 126.10; 127.48; 127.55; 128.36; 128.47; 128.77; 132.01; 145.36; 149.48; 152.97; 155.38; 174.20($\underline{C}OOCH_2$); 192.89 (C=O)
3c	18.36 (CH_3); 21.34 ($CH(\underline{C}H_3)_2$); 22.03 ($CH(\underline{C}H_3)_2$); 42.21 (C-4); 50.04 (C-2); 51.78 (C-3); 67.59 ($\underline{C}H(CH_3)_2$); 101.93 (C-4a); 116.78; 120.52; 126.90; 128.02; 128.94; 130.40; 130.42; 136.29; 136.84; 138.80; 163.64; 169.41 ($\underline{C}OOPr$-2); 189.53 (C=O)
3e	14.1; 18.1; 49.3; 51.3; 59.3; 98.6; 108.2; 120.1; 126.3; 127.6; 129.0; 131.2; 137.5; 140.5; 143.8; 162.1; 169.8 (COOEt); 191.3 (C=O)
3f	14.56 ($CH_2\underline{C}H_3$); 19.18 (CH_3); 41.77 (C-4); 51.10 (C-2); 56.23 (C-3); 60.85 ($\underline{C}H_2CH_3$); 102.90 (C-4a); 121.69; 124.10; 127.09; 128.40; 128.63; 132.96; 138.15; 141.38; 143.85; 161.13; 164.22; 166.88 ($\underline{C}OOCH_2$); 172.75 (C=O)
3g	15.8; 18.4; 40.1; 49.1; 50.8; 51.4; 55.9; 69.4; 101.3; 111.2; 116.7; 126.6; 127.0; 127.8; 128.4; 129.6; 138.7; 141.5; 155.3; 162.0; 170.0 (COOMe); 188.0 (C=O)

* The spectra of compounds **2b**,**c** and **3a**,**c**,**f** (in $CDCl_3$) were recorded on a Varian Mercury 200 (200 MHz) and compounds **3e** (in DMSO-d_6) and **2e**,**f**,**g**, **3b**,**g** (in $CDCl_3$) on a Varian Mercury 400 (400 MHz) instrument.

The N-methyltetrahydroindenopyridine **7a** was prepared by two independent methods, i.e. by reduction of the dihydroindeno[1,2-*b*]pyridine **9** and by alkylation of the tetrahydroindenopyridine **2b** and this is an additional confirmation of its steric structure.

EXPERIMENTAL

^1H and ^{13}C NMR spectra were obtained on Varian Mercury 200 and 400 MHz instruments using TMS as internal standard and mass spectra on a Micromass Q-TOF mass spectrometer. X-ray structural investigation was carried out on a Bruker-Nonius Kappa automatic X-ray diffractometer using a CCD detector. Preparative column chromatography was performed on Acros Kieselgel (0.035-0.070 mm) grade silica gel.

Synthesis of the 5-Oxo-4-phenyl-1H-2,3,4,5-tetrahydroindeno[1,2-*b*]pyridines 2a-h, 3a-h, 7a, 10 (General Method). Triethylsilane (1.0 ml) was added to a solution of the dihydropyridines **1a-h**, **9** (4.3 mmol) in trifluoroacetic acid (5 ml). The reaction mixture was stirred under an argon atmosphere for 1 h and added to a mixture of ice (100 g) and bicarbonate (15 g). The precipitate formed was filtered off, dried, and placed on a chromatographic column. The *cis* and *trans* isomers **3a-c**,**f**, **10** and **2a-g**, **7a** were separated using the following eluents: ethyl acetate–petroleum ether (6:1), methylene chloride–acetone (20:1), and methylene chloride–

petroleum ether–acetone (9:7:1). The *cis* isomers **3d**,**e**,**g** were separated after a repeated chromatography, their yields not exceeding 5% (**3d**, mp 347-348ºC; **3g**, mp 191-193ºC; **3e**, mp 176-178ºC (sinters), 178-180ºC (melts). Mass spectra: **3d**, *m/z* 348 $[M+1]^+$; **3e**, *m/z* 363 $[M+1]^+$. The mixture of **2h**, **3h** *trans* and *cis* isomers (in the ratio 5:1) could not be separated, the overall yield being 66%. Compound **2a** was separated in 45% yield and had *m/z* 318 $[M+1]^+$.

Alkylation of (2*R,3*S**,4*R**)-5-Oxo-4-phenyl-1H-2,3,4,5-tetrahdroindeno(1,2-*b*)pyridines (General Method).** A suspension of sodium hydride (0.26 g) in mineral oil (60%) was added with stirring to a solution of the tetrahydroindenopyridines **2b** or **3b** (4.3 mmol) in DMF (15 ml) and stirred for a further 0.5 h. The reaction mixture was then treated with the alkylating agent (12.9 mmol) and monitored using TLC. The reaction mixture was poured into an aqueous solution of sodium chloride at the end of the reaction. The oily precipitate formed was separated, dried, and placed on a silica gel chromatographic column. The C- and N-isomers **8a-c** and **7a**,**b**, **10** were separated using the following eluents: ethyl acetate – petroleum ether (1:1) or petroleum ether–acetone (4:1).

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