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Conversion of 6-Phenylimino-2*H*-thiopyran-4-amines to 1-Phenyl-2,3-dihydro-4(1*H*)-pyridinones

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Summary. 6-Phenylimino-3,6-dihydro-2*H*-thiopyran-4-amines (**1**) were converted to 1-phenyl-5,6-dihydropyridine-2(1*H*)-thiones (**3**). Those were akylated and hydrolyzed, thus yielding 6-methylthio-1-phenyl-2,3-dihydro-4(1*H*)-pyridinones (**5**). Finally, the methylthio group was removed with *Raney* nickel giving the title compounds **6**. The relative configurations of the formed diastereoisomeric dihydropyridinones have been investigated by NOE measurements.

Keywords. Dihydropyridine-2(1*H*)-thiones; Dihydrothiopyran-4-amines; 1-Phenyl-2,3-dihydro-4(1*H*)-pyridinones; Tetrahydropyridiniumiodides.

Umwandlung von 6-Phenylimino-2*H*-thiopyran-4-aminen zu 1-Phenyl-2,3-dihydro-4(1*H*)-pyridinonen

Zusammenfassung. 6-Phenylimino-3,6-dihydro-2*H*-thiopyran-4-amine (**1**) wurden in 1-Phenyl-5,6-dihydropyridin-2(1*H*)-thione (**3**) umgewandelt. Diese wurden alkyliert und zu 6-Methylthio-1-phenyl-2,3-dihydro-4(1*H*)-pyridinonen (**5**) hydrolysiert. Zuletzt gelangte man durch selektives Entfernen der Methylthiogruppe mit *Raney*-Nickel zu den Titelverbindungen **6**. Die relativen Konfigurationen der gebildeten diastereomeren Dihydropyridinone wurden durch NOE-Messungen aufgeklärt.

Introduction

1-Substituted 2,3-dihydro-4(1*H*)-pyridinones are valuable synthons for the preparation of analogues to natural substances and drugs [1–7] as well as for photochemical cycloadditions [8]. Therefore, many syntheses have been developed even for 1-phenyl derivatives which are not obtainable from 1-unsubstituted compounds. However, only a few of them gave 2-substituted or 2,2-disubstituted 1-phenyl-2,3-dihydro-4(1*H*)-pyridinones with no further substitution at ring positions 5 and 6, which is a requirement for most of the above-mentioned reactions: 2,2-dimethyl-1-phenyl-2,3-dihydro-4(1*H*)-pyridinone was obtained by condensation of a γ,δ-unsaturated β-ketoaldehyde with aniline [9] or by ring closure of N-(1,1-dimethyl-penta-2,4-diinyl)-aniline with aqueous acid [10]. The cyclization of *Schiff* bases with a siloxydiene yielded the 2-phenyl- and the 2-phenylethenyl-compounds [11, 12].

This paper reports the syntheses of new 2-substituted and 2,3-disubstituted 1-phenyl-2,3-dihydro-4(1*H*)-pyridinones (**6**) from 6-phenylimino-2*H*-thiopyran-4-amines (**1**) [13].

Results and Discussion

6-Phenylimino-3,6-dihydro-2*H*-thiopyran-4-amines(**1**) were converted to the corresponding 1-phenyl-5,6-dihydropyridine-2(1*H*)-thiones (**3**) by a *Dimroth* rearrangement [14]. The transposition starts with the removal of a proton in position 3 of the piperidine ring, whereupon ring cleavage between S-1 and C-2 occurs. The formed $\alpha,\beta,\gamma,\delta$-unsaturated anion **2** undergoes protonation and ring closure. The yield of that reaction varies significantly due to the substitution in position 3 of the thiopyran ring: the 3-unsubstituted compounds **1b, c** gave more than 80% of the respective pyridinethiones **3b, c**. The methyl group in **1d** decreased the yield to less than 40%, and the ethyl substituent in **1a** prevented the reaction, even when sodium ethylate as an auxiliary base was used.

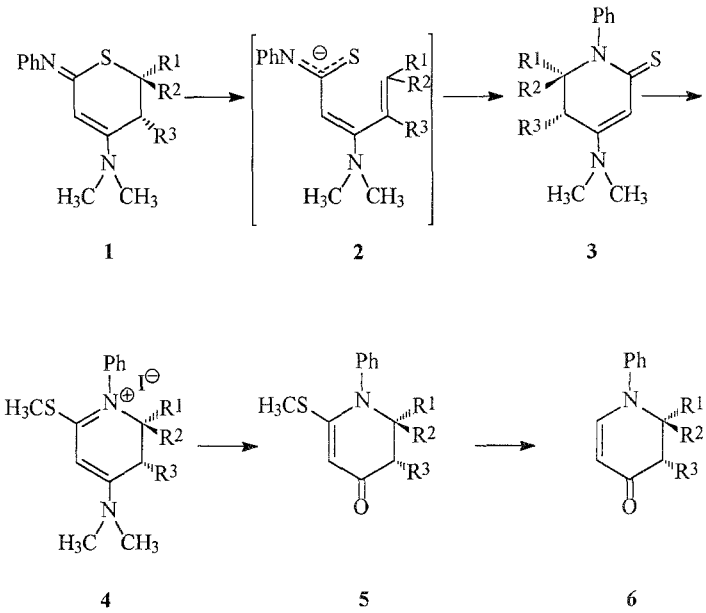
Replacement of the dimethylamino group of **3b–d** by a hydroxy group – a well-known reaction of 1-unsubstituted 5,6-dihydro-2(1*H*)-pyridinethiones[15] – failed. So we tried to introduce the desired oxo group *via* the corresponding methylthio derivatives: upon treatment of **3b–d** with iodomethane the dihydropyridiniumiodides **4b–d** were afforded quantitatively. Subsequently **4b, c** were hydrolyzed by dilute caustic soda yielding the 2,3-dihydro-4(1*H*)-pyridinones **5b, c** in good yields.

4d gave a mixture of diastereoisomers containing 70% *rac*-(2*RS*,3*SR*)-dihydropyridinone (**5e**) and 30% *rac*-(2*RS*,3*RS*)-dihydropyridinone (**5d**). The isomerization took place in position 3 of the piperidine ring *via* the enolate form as described by *Black et al.* [16]. After separation by column chromatography, both isomers were refluxed with caustic soda a second time giving the 70% **5e**: 30% **5d** – equilibrium in each case. Thus the amount of any isomer could be increased.

The final desulfurization was achieved by stirring **5b–e** with *Raney* nickel W2 [17] at atmospheric pressure giving **6b–e** in good yields. Structural evidence was furnished by compound **6c**, giving the same melting point and identical spectroscopic data as 1,2-diphenyl-2,3-dihydropyridine-4(1*H*)-one [11, 12].

In comparison to **5e** and **6e**, the methyl groups of **5d** and **6d** showed a characteristical shift to higher field in proton and carbon NMR spectra, whereas the corresponding 3-H was shifted to lower field. We assume that those effects are caused by the phenyl rings which shield the neighbouring substituents. NOE measurements proved the 3-Hs in **5e** and **6e** and the methyl groups in **5d** and **6d** to be *cis* relative to the corresponding 2-phenyl groups.

The relative configurations of **1d–4d** were also deduced from NOE data. Saturation of the methyl group always led to definite NOEs at the aromatic system. Compound **1a** was supposed to have an analogous structure due to its similar coupling constants. Most of the ^{13}C signals could be assigned by means of coupled ^{13}C NMR spectra; the distinction between C-4 and C-2 resp. C-6, however, demanded single frequency decoupling in some cases.



1–6	R^1	R^2	R^3
a	Ph	H	Et
b	iPr	H	H
c	Ph	H	H
d	Ph	H	Me
5e, 6e	H	Ph	Me

Experimental

All melting points are uncorrected (Büchi 510). IR: Perkin Elmer 2000 FT-IR; NMR: Varian Gemini (200 MHz), solvent: $CDCl_3$, internal standard: *TMS*; Microanalyses: microanalytical laboratory at the Institute of Physical Chemistry, Vienna University. All synthesized compounds were racemates.

N,N-Dimethyl-6-phenylimino-3,6-dihydro-2H-thiopyran-4-amines (**1**)

Modified general procedure [13]: The respective N,N-Dimethyl-6-methylthio-2*H*-thiopyran-4 (3*H*)-iminiumiodides [13] (0.1 mol) were dissolved in aniline (2 moles). The mixture was stirred at room temperature for 3 days, while a stream of nitrogen was passed through. The formed mercaptan was captured in a gas washing bottle with dilute caustic soda. The excess of aniline was removed *in vacuo*. The residue was triturated with ethyl acetate. The crystallizate was filtered with suction, dried, and subsequently stirred in a 2 *M* solution of caustic soda (0.2 mol) in water for one hour. The suspension was extracted with ether or toluene repeatedly. The combined extracts were washed three times with water and dried over sodium sulfate. The solvent was removed and the residue recrystallized.

(2RS,3SR)-(±)-3-Ethyl-N,N-dimethyl-2-phenyl-6-phenylimino-3,6-dihydro-2H-thiopyran-4-amine (**1a**)

Yield: 16.1 g (95.7%); m.p.: 162 °C (ethanol); IR (KBr): $\nu = 2937$ (w), 1598 (m), 1560 (s), 1518 (s), 1478 (m) cm^{-1}; ^1H NMR: $\delta = 0.74$ (t, $J = 7.6$ Hz, 3H, 3-CH_2CH_3), 1.71–1.93 (m, 2H, 3-CH_2CH_3), 2.88 (dt,

$J = 6.2, 2.9$ Hz, 1H, 3-H), 3.00 (s, 6H, $N(CH_3)_2$), 4.76 (d, $J = 2.9$ Hz, 1H, 2-H), 5.52 (s, 1H, 5-H), 6.97–7.08 (m, 3H, aromatic H), 7.24–7.35 (m, 7H, aromatic H) ppm; ^{13}C NMR: $\delta = 12.07$ (3-$CH_2\mathbf{C}H_3$), 20.49 (3-$\mathbf{C}H_2CH_3$), 40.14 ($N(CH_3)_2$), 42.83 (C-3), 50.52 (C-2), 96.22 (C-5), 121.24, 123.08, 127.73, 128.28, 128.41, 128.64, 138.58, 151.57 (aromatic C), 161.30 (C-4), 161.71 (C-6) ppm; $C_{21}H_{24}N_2S$ (336.49); calcd.: C 74.96, H 7.19, N 8.33, S 9.53; found: C 74.78, H 7.36, N 8.44, S 9.63.

(RS)-(±)-N,N-Dimethyl-2-(1-methylethyl)-6-phenylimino-3,6-dihydro-2H-thiopyran-4-amine (**1b**)

Yield: 13.7 g (99.8%); pale yellow oil; IR (KBr): $\nu = 2963$ (m), 1603 (m), 1580 (s), 1550 (s), 1485 (m) cm^{-1}; ^1H NMR: $\delta = 0.98$ (dd, $J = 6.8$, 1.7 Hz, 6H, $CH(\mathbf{CH}_3)_2$), 1.78–2.00 (m, 1H, $\mathbf{CH}(CH_3)_2$), 2.44 (dd, $J = 15.9$, 11.4 Hz, 1H, 3-H), 2.72 (dd, $J = 15.9$, 3.3 Hz, 1H, 3-H), 2.92 (s, 6H, $N(CH_3)_2$), 3.14 (ddd, $J = 11.4$, 5.6, 3.3 Hz, 1H, 2-H), 5.51 (s, 1H, 5-H), 6.86–7.06 (m, 3H, aromatic H), 7.23–7.32 (m, 2H, aromatic H) ppm; ^{13}C NMR: $\delta = 19.51$, 19.80 ($CH(\mathbf{CH}_3)_2$), 30.79 (C-3), 31.84 ($\mathbf{C}H(CH_3)_2$), 39.63 ($N(CH_3)_2$), 47.41 (C-2), 98.10 (C-5), 121.22, 122.85, 128.47, 151.42 (aromatic C), 156.73 (C-4), 161.27 (C-6) ppm; $C_{16}H_{22}N_2S$ (274.42); calcd.: C 70.03, H 8.08, N 10.21, S 11.68; found: C 69.80, H 8.25, N 10.34, S 11.48.

(RS)-(±)-N,N-Dimethyl-2-phenyl-6-phenylimino-3,6-dihydro-2H-thiopyran-4-amine (**1c**)

Yield: 14.6 g (94.7%); m.p.: 195 °C (chloroform/ethyl acetate); IR (KBr): $\nu = 2940$ (w), 1593 (m), 1575 (s), 1554 (s), 1483 (m) cm^{-1}; ^1H NMR: $\delta = 2.76$–3.00 (m, 2H, 3-H), 2.93 (s, 6H, $N(CH_3)_2$), 4.39 (dd, $J = 10.4$, 5.2 Hz, 1H, 2-H), 5.61 (s, 1H, 5-H), 6.89–7.03 (m, 3H, aromatic H), 7.21–7.36 (m, 7H, aromatic H) ppm; ^{13}C NMR: $\delta = 35.45$ (C-3), 39.83 ($N(CH_3)_2$), 45.31 (C-2), 97.72 (C-5), 121.29, 123.24, 127.78, 128.16, 128.65, 128.80, 139.72, 151.31 (aromatic C), 156.47 (C-4), 161.35 (C-6) ppm; $C_{19}H_{20}N_2S$ (308.44); calcd.: C 73.99, H 6.54, N 9.08, S 10.39; found: C 73.77, H 6.52, N 9.06, S 10.18.

(2RS,3SR)-(±)-3,N,N-Trimethyl-2-phenyl-6-phenylimino-3,6-dihydro-2H-thiopyran-4-amine (**1d**)

Yield: 16.0 g (99.2%); m.p.: 156 °C (ethanol); IR (KBr): $\nu = 2977$ (w), 2938 (w), 1595 (m), 1572 (s), 1554 (s), 1481 (m) cm^{-1}; ^1H NMR: $\delta = 1.16$ (d, $J = 6.7$ Hz, 3H, 3-CH_3), 2.88 (dq, $J = 6.7$, 2.9 Hz, 1H, 3-H), 2.94 (s, 6H, $N(CH_3)_2$), 4.71 (d, $J = 2.9$ Hz, 1H, 2-H), 5.47 (s, 1H, 5-H), 6.95–7.06 (m, 3H, aromatic H), 7.24–7.35 (m, 7H, aromatic H) ppm; ^{13}C NMR: $\delta = 11.27$ (3-CH_3), 36.82 (C-3), 39.54 ($N(CH_3)_2$), 50.33 (C-2), 95.68 (C-5), 121.17, 122.98, 127.70, 128.23, 128.28, 128.53, 138.26, 151.45 (aromatic C), 161.40 (C-6), 161.60 (C-4) ppm; $C_{20}H_{22}N_2S$ (322.47); calcd.: C 74.49, H 6.88, N 8.69, S 9.94; found: C 74.40, H 7.09, N 8.73, S 9.97.

4-Dimethylamino-1-phenyl-5,6-dihydropyridine-2(1H)-thiones (**3**)

Modified general procedure [14]: Compounds **1** (0.05 mol) were added to 200 ml freshly distilled *DMF*. A stream of nitrogen was passed through the suspension for 30 minutes. After that, the reflux condenser was closed with a balloon and the reaction mixture was refluxed for at least 16 hours. The solvent was removed *in vacuo*. The residue was triturated with ethyl acetate or ethanol, filtered with suction, and recrystallized.

The catalytic addition of sodium ethylate (up to 0.05 mol) increased the yield of the reaction less than 3 per cent but led to products of lower purity.

(RS)-(±)-4-Dimethylamino-6-(1-methylethyl)-1-phenyl-5,6-dihydropyridine-2(1H)-thione (**3b**)

Reaction period: 16 h; yield: 12.07 g (88%); m.p.: 176 °C (ethanol); IR (KBr): $\nu = 3031$ (w), 2962 (w), 2922 (w), 1564 (s), 1492 (m), 1409 (s) cm^{-1}; ^1H NMR: $\delta = 0.88$, 0.92 (2d, $J = 7$ Hz, 6H, $CH(\mathbf{CH}_3)_2$), 2.12–2.27 (m, 1H, $\mathbf{CH}(CH_3)_2$), 2.65 (dd, $J = 16.6$, 4.1 Hz, 1H, 5-H), 2.81 (dd, $J = 16.6$, 7.1 Hz, 1H, 5-H), 2.99 (s,

6H, $N(CH_3)_2$), 3.81 (ddd, $J = 7.1$, 4.4, 4.1 Hz, 1H, 6-H), 5.82 (s, 1H, 3-H), 7.23–7.45 (m, 5H, aromatic H) ppm; ^{13}C NMR: $\delta = 17.58$, 19.99 ($CH(\mathbf{C}H_3)_2$), 25.26 (C-5), 30.08 ($\mathbf{C}H(CH_3)_2$), 39.17 ($N(CH_3)_2$), 64.72 (C-6), 101.24 (C-3), 126.87, 128.50, 128.72, 145.76 (aromatic C), 150.98 (C-4), 190.64 (C-2) ppm; $C_{16}H_{22}N_2S$ (274.42); calcd.: C 70.03, H 8.08, N 10.21, S 11.68; found: C 69.80, H 8.25, N 10.34, S 11.48.

(RS)-(±)-4-Dimethylamino-1,6-diphenyl-5,6-dihydropyridine-2(1H)-thione (**3c**)

Reaction period: 16 h; yield: 12.95 g (84%); m.p.: 214 °C (ethanol); IR (KBr): $\nu = 3018$ (w), 2880 (w), 1565 (s), 1492 (m), 1406 (s) cm^{-1}; ^1H NMR: $\delta = 2.86$ (dd, $J = 16.3$, 3 Hz, 1H, 5-H), 2.88 (s, 6H, $N(CH_3)_2$), 3.25 (dd, $J = 16.3$, 7 Hz, 1H, 5-H), 5.07 (dd, $J = 7$, 3 Hz, 1H, 6-H), 5.96 (s, 1H, 3-H), 7.15–7.37 (m, 10H, aromatic H) ppm; ^{13}C NMR: $\delta = 33.96$ (C-5), 39.18 ($N(CH_3)_2$), 63.53 (C-6), 102.04 (C-3), 126.79, 126.83, 127.44, 127.65, 128.46, 128.57, 139.71, 146.12 (aromatic C), 149.51 (C-4), 191.04 (C-2); $C_{19}H_{20}N_2S$ (308.44); calcd.: C 73.99, H 6.54, N 9.08, S 10.39; found: C 73.70, H 6.37, N 9.18, S 10.12.

(5RS,6RS)-(±)-4-Dimethylamino-5-methyl-1,6-diphenyl-5,6-dihydropyridine-2(1H)-thione (**3d**)

Reaction period: 68 h; yield: 5.32 g (38.8%); m.p.: 235 °C (ethanol); IR (KBr): $\nu = 2998$ cm^{-1} (w), 2970 (w), 2937 (w), 1555 (s), 1494 (m), 1385 (s) cm^{-1}; ^1H NMR: $\delta = 1.22$ (d, $J = 6.9$ Hz, 3H, 5-CH_3), 2.64–2.78 (m, 1H, 5-H), 3.01 (s, 6H, $N(CH_3)_2$), 5.29 (d, $J = 3.6$ Hz, 1H, 6-H), 6.02 (s, 1H, 3-H), 7.01–7.17 (m, 10H, aromatic H) ppm; ^{13}C NMR: $\delta = 11.51$ (5-CH_3), 37.42 (C-5), 39.22 ($N(CH_3)_2$), 68.82 (C-6), 101.17 (C-3), 126.29, 127.50, 127.70, 127.80, 127.99, 129.82, 136.88, 144.46 (aromatic C), 158.26 (C-4), 194.55 (C-2) ppm; $C_{20}H_{22}N_2S$ (322.47); calcd.: C 74.49, H 6.88, N 8.69, S 9.94; found: C 74.30, H 6.90, N 8.64, S 9.60.

4-Dimethylamino-6-methylthio-1-phenyl-2,3dihydropyridiniumiodides (**4**)

General procedure: To an ice-cooled and stirred solution of **3** (0.05 mol) in chloroform, iodomethane (0.05 mol) was added through a dropping funnel within one hour. The reaction mixture was stirred for 18 hours at room temperature. The solvent was removed *in vacuo*. The residue was triturated with ethanol/ethyl acetate, filtered with suction, and recrystallized.

(RS)-(±)-4-Dimethylamino-2-(1-methylethyl)-6-methylthio-1-phenyl-2,3-dihydropyridiniumiodide (**4b**)

Yield: 19.7 g (94.6%); m.p.: 189 °C (chloroform/ethyl acetate); IR (KBr): $\nu = 3026$ (w), 2963 (m), 1591 (s), 1496 (s), 1426 (m), 1327 (m), 1284 (m) cm^{-1}; ^1H NMR: $\delta = 0.93$, 0.96 (2d, $J = 7.3$ Hz, 6H, $CH(\mathbf{CH}_3)_2$), 2.06–2.20 (m, 1H, $\mathbf{CH}(CH_3)_2$), 2.53 (s, 3H, SCH_3), 3.02 (dd, $J = 17.5$, 5.4 Hz, 1H, 3-H), 3.44, 3.54 (2s, 6H, $N(CH_3)_2$), 3.55 (dd, $J = 17.5$, 7.7 Hz, 1H, 3-H), 4.11 (ddd, $J = 7.7$, 5.4, 4.6 Hz, 1H, 2-H), 5.28 (s, 1H, 5-H), 7.34–7.53 (m, 5H, aromatic H) ppm; ^{13}C NMR: $\delta = 16.71$ (SCH_3), 17.39, 19.63 ($CH(\mathbf{CH}_3)_2$), 26.67 (C-3), 29.40 ($\mathbf{CH}(CH_3)_2$), 42.11, 42.45 ($N(CH_3)_2$), 65.08 (C-2), 87.22 (C-5), 128.24, 129.56, 140.09 (aromatic C), 162.31 (C-4), 173.34 (C-6) ppm; $C_{17}H_{25}IN_2S$ (416.36); calcd.: C 49.04, H 6.05, I 30.48, N 6.73, S 7.70; found: C 48.96, H 5.99, I 30.19, N 6.65, S 7.63.

(RS)-(±)-4-Dimethylamino-6-methylthio-1,2-diphenyl-2,3-dihydropyridiniumiodide (**4c**)

Yield: 21.4 g (95%); m.p.: 215 °C (chloroform/ethyl acetate); IR (KBr): $\nu = 2963$ (w), 1587 (s), 1485 (s), 1330 (m), 1318 (m) cm^{-1}; ^1H NMR: $\delta = 2.59$ (s, 3H, SCH_3), 3.30 (dd, $J = 17.2$, 6.2 Hz, 1H, 3-H), 3.37, 3.38 (2s, 6H, $N(CH_3)_2$), 3.96 (dd, $J = 17.2$, 6.8 Hz, 1H, 3-H), 5.37 (dd, $J = 6.8$, 6.2 Hz, 1H, 2-H), 5.40 (s, 1H, 5-H), 7.18–7.38 (m, 10H, aromatic H) ppm; ^{13}C NMR: $\delta = 16.89$ (SCH_3), 35.41 (C-3), 42.27, 42.56 ($N(CH_3)_2$), 64.05 (C-2), 88.07 (C-5), 127.33, 128.07, 128.82, 129.05, 129.55, 136.44, 140,32 (aromatic C), 161.58 (C-4), 173.75 (C-6) ppm; $C_{20}H_{23}IN_2S$ (450.39); calcd.: C 53.33, H 5.15, I 28.18, N 6.22, S 7.12; found: C 52.97, H 5.14, I 28.17, N 6.01, S 6.55.

(2RS,3RS)-(±)-4-Dimethylamino-3-methyl-6-methylthio-1,2-diphenyl-2,3-dihydropyridiniumiodide (**4d**)

Yield: 21.9 g (94.3%); m.p.: 230 °C (chloroform/ethyl acetate); IR (KBr): $\nu = 2945$ (w), 1593 (s), 1490 (s), 1305 (m) cm^{-1}; ^1H NMR: $\delta = 1.28$ (d, $J = 7.2$ Hz, 3H, 3-CH_3), 2.54 (s, 3H, SCH_3), 3.26 (dq, $J = 7.2$, 3.7 Hz, 1H, 3-H), 3.49, 3.52 (2s, 6H, $N(CH_3)_2$), 5.37 (s, 1H, 5-H), 6.10 (d, $J = 3.7$ Hz, 1H, 2-H), 6.88–7.35 (m, 10H, aromatic H) ppm; ^{13}C NMR: $\delta = 10.78$ (3-CH_3), 16.82 (SCH_3), 36.97 (C-3), 41.90, 42.53 ($N(CH_3)_2$), 68.19 (C-2), 87.63 (C-5), 127.11, 127.82, 128.05, 128.70, 129.62, 129.80, 129.95, 133.37, 137.29 (aromatic C), 168.67 (C-4), 174.86 (C-6) ppm; $C_{17}H_{25}IN_2S$ (464.41); calcd.: C 54.31, H 5.43, I 27.33, N 6.03, S 6.90; found: C 54.31, H 5.44, I 27.34, N 5.92, S 6.70.

6-Methylthio-1-phenyl-2,3-dihydropyridin-4(1H)-ones (**5b, c**)

General procedure: Compounds **4** (5 mmol) were refluxed in a 2 *M* aqueous solution of caustic soda (50 mmol) for 2 hours. The aqueous phase was extracted with toluene repeatedly. The extract was washed three times with water and dried over sodium sulfate. The solvent was removed *in vacuo*. The residue was triturated with ethanol/water, filtered with suction, dried, and recrystallized.

(RS)-(±)-2-(1-Methylethyl)-6-methylthio-1-phenyl-2,3-dihydropyridin-4(1H)-one (**5b**)

Yield: 1.12 g (85.7%); m.p.: 108 °C (heptane); IR (KBr): $\nu = 2961$ (m), 1621 (s), 1505 (s), 1393 (m), 1360 (m), 1280 (s) cm^{-1}; ^1H NMR: $\delta = 0.94$ (dd, $J = 6.8$, 2 Hz, 6H, $CH(CH_3)_2$), 2.05–2.17 (m, 1H, $CH(CH_3)_2$), 2.22 (s, 3H, SCH_3), 2.55 (dd, $J = 16.6$, 6.2 Hz, 1H, 3-H), 2.79 (dd, $J = 16.6$, 6.2 Hz, 1H, 3-H), 3.69 (ddd, $J = 6.2$, 6.2, 6 Hz, 1H, 2-H), 5.24 (s, 1H, 5-H), 7.25–7.47 (m, 5H, aromatic H) ppm; ^{13}C NMR: $\delta = 15.46$ (SCH_3), 17.29, 20.01 ($CH(CH_3)_2$), 28.73 ($CH(CH_3)_2$), 35.86 (C-3), 67.99 (C-2), 98.28 (C-5), 127.88, 128.39, 129.10, 143.06 (aromatic C), 167.58 (C-6), 189.18 (C-4) ppm; $C_{15}H_{19}NOS$ (261.38); calcd.: C 68.93, H 7.33, N 5.36, O 6.12, S 12.27; found: C 68.85, H 7.43, N 5.46, S 11.93.

(RS)-(±)-6-Methylthio-1,2-diphenyl-2,3-dihydropyridin-4(1H)-one (**5c**)

Yield: 1.28 g (86.7%); m.p.: 145 °C (ethanol); IR (KBr): $\nu = 3018$ (w), 3000 (w), 1620 (s), 1495 (s), 1387 (s), 1268 (s) cm^{-1}; ^1H NMR: $\delta = 2.29$ (s, 3H, SCH_3), 2.81 (dd, $J = 16.4$, 6.1 Hz, 1H, 3-H), 3.15 (dd, $J = 16.4$, 6.3 Hz, 1H, 3-H), 5.00 (dd, $J = 6.2$, 6.2 Hz, 1H, 2-H), 5.29 (s, 1H, 5-H), 7.11–7.32 (m, 10H, aromatic H) ppm; ^{13}C NMR: $\delta = 15.49$ (SCH_3), 43.14 (C-3), 66.56 (C-2), 97.94 (C-5), 127.04, 127.84, 127.96, 128.09, 128.58, 128.95, 138.87, 142.64 (aromatic C), 167.53 (C-6), 187.43 (C-4) ppm; $C_{18}H_{17}NOS$ (295.40); calcd.: C 73.19, H 5.80, N 4.74, O 5.42, S 10.85; found: C 73.10, H 5.55, N 4.59, S 10.98.

3-Methyl-6-methylthio-1,2-diphenyl-2,3-dihydropyridin-4(1H)-ones (**5d** and **5e**)

4d (5 mmol) was refluxed in a 2 *M* aqueous solution of caustic soda (50 mmol) for 16 hours. The aqueous phase was extracted with benzene, washed with water, and dried over sodium sulfate. The solvent was removed *in vacuo*. The oily residue was separated by flash chromatography [18]: column diameter 30 mm, layer thickness 300 mm, Merck silicagel 60, 0.040–0.063 mm (230–400 mesh), rate of flow 35 ml/min, eluent toluene:ethyl acetate = 1:2.

(2RS,3RS)-(±)-3-Methyl-6-methylthio-1,2-diphenyl-2,3-dihydropyridin-4(1H)-one (**5d**)

Yield: 0.34 g (22%); m.p.: 142 °C (ethanol); $R_f = 0.26$ (toluene:ethyl acetate = 1:2); IR (KBr): $\nu = 3053$ (w), 2927 (w), 1632 (s), 1514 (s), 1414 (m), 1223 (m) cm^{-1}; ^1H NMR: $\delta = 1.00$ (d, $J = 7$ Hz, 3H, 3-CH_3), 2.30 (s, 3H, SCH_3), 3.39 (dq, $J = 7.1$, 7.1 Hz, 1H, 3-H), 4.72 (d, $J = 7.2$ Hz, 1H, 2-H), 5.25 (s, 1H, 5-H), 7.02–7.32 (m, 10H, aromatic H) ppm; ^{13}C NMR: $\delta = 11.14$ (3-CH_3), 15.63 (SCH_3), 43.23 (C-3), 72.18

(C-2), 95.64 (C-5), 128.21, 128.33, 128.47, 128.53, 128.67, 129.05, 136.84, 142.71 (aromatic C), 166.46 (C-6), 190.34 (C-4) ppm; $C_{19}H_{19}NOS$ (309.43); calcd.: C 73.75, H 6.19, N 4.53, O 5.17, S 10.36; found: C 73.78, H 6.30, N 4.51, S 10.68.

(2RS,3SR)-(±)-3-Methyl-6-methylthio-1,2-diphenyl-2,3-dihydropyridin-4(1H)-one (**5e**)

Yield: 0.81 g (52.4%); m.p.: 140 °C (ethanol); $R_f = 0.17$ (toluene:ethyl acetate = 1:2); IR (KBr): $\nu = 3088$ (w), 2924 (w), 1636 (s), 1514 (s), 1490 (m), 1396 (m), 1224 (m) cm^{-1}; ^1H NMR: $\delta = 1.39$ (d, $J = 7.2$ Hz, 3H, 3-CH_3), 2.32 (s, 3H, SCH_3), 2.73 (dq, $J = 7.2$, 4.5 Hz, 1H, 3-H), 4.62 (d, $J = 4.5$ Hz, 1H, 2-H), 5.22 (s, 1H, 5-H), 7.11–7.33 (m, 10H, aromatic H) ppm; ^{13}C NMR; $\delta = 15.50$ (SCH_3), 17.28 (3-CH_3), 47.02 (C-3), 73.19 (C-2), 95.81 (C-5), 127.11, 127.80, 128.05, 128.11, 128.63, 129.08, 138.84, 143.10 (aromatic C), 166.11 (C-6), 191.43 (C-4) ppm; $C_{19}H_{19}NOS$ (309.43); calcd.: C 73.75, H 6.19, N 4.53, O 5.17, S 10.36; found: C 73.84, H 6.33, N 4.69, S 10.27.

1-Phenyl-2,3-dihydropyridin-4(1H)-ones (**6**)

General procedure: *Raney* nickel W2 (17) was added in portions to a solution of compounds **5** (10 mmol) in 50 ml ethanol which was stirred at room temperature under an atmosphere of nitrogen. The addition of the catalyst was stopped upon completion of the reaction which was monitored by TLC. The reaction mixture was filtered and the solvent was removed *in vacuo*. The residue was dissolved in chloroform, washed with water, and dried over sodium sulfate. The solvent was evaporated. The oily residue was triturated with ethanol/water or heptane, filtered with suction, dried, and recrystallized.

(RS)-(±)-2-(1-Methylethyl)-1-phenyl-2,3-dihydropyridin-4(1H)-one (**6b**)

Reaction period: 18 h; yield: 1.89 g (87.8%); colourless oil; IR (KBr): $\nu = 2963$ (m), 1648 (s), 1579 (s), 1495 (s), 1266 (m), 1226 (s), 1207 (m) cm^{-1}; ^1H NMR: $\delta = 0.90$, 0.95 (2d, $J = 6.7$ Hz, 6H, $CH(CH_3)_2$), 2.15–2.37 (m, 1H, $CH(CH_3)_2$), 2.61 (dd, $J = 16.8$, 3.3 Hz, 1H, 3-H), 2.90 (dd, $J = 16.8$, 7 Hz, 1H, 3-H), 4.08 (ddd, $J = 7$, 6.7, 3.3 Hz, 1H, 2-H), 5.15 (d, $J = 7.8$ Hz, 1H, 5-H), 7.13–7.44 (m, 6H, 6-H and aromatic H) ppm; ^{13}C NMR: $\delta = 18.06$, 19.83 ($CH(CH_3)_2$), 29.33 ($CH(CH_3)_2$), 36.95 (C-3), 63.13 (C-2), 100.97 (C-5), 120.72, 124.72, 129.60, 144.96 (aromatic C), 148.83 (C-6), 191.85 (C-4) ppm; $C_{14}H_{17}NO$ (215.30); calcd.: C 78.10, H 7.96, N 6.51, O 7.43; found: C 77.79, H 8.14, N 6.49.

(RS)-(±)-1,2-Diphenyl-2,3-dihydropyridin-4(1H)-one (**6c**)

Reaction period: 18 h; yield: 1.52 g (75.5%); m.p.: 97 °C (ethanol/water Ref. [12]: 96–97 °C); IR, ^1H NMR, and ^{13}C NMR: identical with Ref. [11].

(2RS,3RS)-(±)-3-Methyl-1,2-diphenyl-2,3-dihydropyridin-4(1H)-one (**6d**)

Reaction period: 12 h; yield: 2.16 g (82%); m.p.: 105 °C (ethanol/water); IR (KBr): $\nu = 2927$ (w), 1647 (s), 1575 (s), 1494 (s), 1202 (s) cm^{-1}; ^1H NMR: $\delta = 1.03$ (d, $J = 7.1$ Hz, 3H, 3-CH_3), 3.40 (dq, $J = 7$, 7 Hz, 1H, 3-H), 5.05 (d, $J = 7$ Hz, 1H, 2-H), 5.30 (d, $J = 7.8$ Hz, 1H, 5-H), 7.01–7.39 (m, 10H, aromatic H), 7.63 (d, $J = 7.8$ Hz, 1H, 6-H) ppm; ^{13}C NMR: $\delta = 11.08$ (3-CH_3), 43.69 (C-3), 67.90 (C-2), 101.29 (C-5), 119.16, 124.42, 127.88, 128.20, 128.69, 129.42, 136.31, 145.09 (aromatic C), 148.38 (C-6), 193.37 (C-4) ppm; $C_{18}H_{17}NO$ (263.34); calcd.: C 82.10, H 6.51, N 5.32, O 6.08; found: C 82.18, H 6.51, N 5.24.

(2RS,3SR)-(±)-3-Methyl-1,2-diphenyl-2,3-dihydropyridin-4(1H)-one (**6e**)

Reaction period: 12 h; yield: 2.24 g (85.1%); m.p.: 130 °C (heptane); IR (KBr): $\nu = 2924$ (w), 1645 (s), 1559 (s), 1495 (s), 1209 (s) cm^{-1}; ^1H NMR: $\delta = 1.41$ (d, $J = 7.3$ Hz, 3H, 3-CH_3), 2.74 (dq, $J = 7.3$, 2.2 Hz, 1H,

3-H), 4.92 (d, $J = 2.2$ Hz, 1H, 2-H), 5.21 (d, $J = 8$ Hz, 1H, 5-H), 7.02–7.37 (m, 10H, aromatic H), 7.65 (d, $J = 8$ Hz, 1H, 6-H) ppm; ^{13}C NMR: $\delta = 18.32$ (3-CH_3), 47.88 (C-3), 68.14 (C-2), 100.93 (C-5), 118.55, 124.45, 126.09, 127.76, 128.89, 129.55, 137.62, 145.34 (aromatic C), 146.93 (C-6), 194.77 (C-4) ppm; $C_{18}H_{17}NO$ (263.34); calcd.: C 82.10, H 6.51, N 5.32, O 6.08; found: C 82.00, H 6.52, N 5.34.

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