UDC 547.811'818.1'823

INTERCONVERSIONS OF HETEROCYCLES CONTAINING S, N, AND O

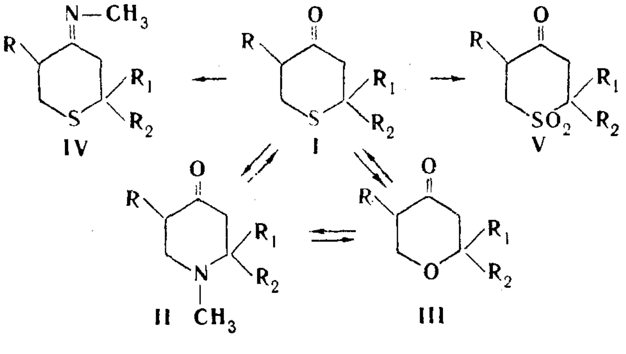
S. A. Vartanyan, A. S. Noravyan, and V. N. Zhamagortsyan

Khimiya Geterotsiklicheskikh Soedinenii, Vol. 2, No. 5, pp. 670-673, 1966

On heating with hydrogen sulfide in the presence of sulfuric acid, tetrahydropyran-4-ones (III) and 4-piperidones (II) are converted to the corresponding thiopyranones (I). The anticipated III are obtained by heating I or II in dilute sulfuric acid solution in the presence of mercuric sulfate. Analogously, I and II in aqueous methylamine solution are converted to II; 2,3,6-trimethyl-4-pyrone (VII) and 1,2,3,6-tetramethyl-4-pyridone (VIII) are also interconvertible.

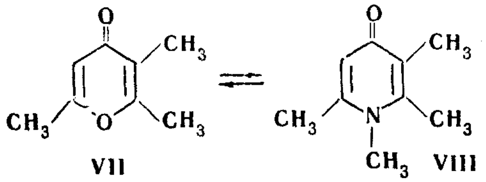
We have shown [1] that 2-methyl-2-ethyltetrahydrothiopyran-4-one, 1,2-dimethyl-2-ethyl-4-piperidone, and 2-methyl-2-ethyltetrahydropyran-4-one are interconvertible. It was of interest to study the possibility of extending this reaction to other instances. We have found that, on heating with hydrogen sulfide in the presence of sulfuric acid, tetrahydropyran-4-ones (III) and 4-piperidones (II) are converted to thiopyranones (I), which yield sulfones (V) on oxidation with potassium permanganate. Analogously, the thiopyranones I and piperidones II are converted to tetrahydropyran-4-ones (III) in dilute sulfuric acid solution in the presence of mercuric sulfate. Under the action of aqueous methylamine solution, the III are likewise smoothly converted into the anticipated II. However, under the given conditions the tetrahydrothiopyran-4-one (I, R = H, $R_1 = R_2 = CH_3$) enters into reaction with the amine at the carbonyl group, forming the corresponding imine, and the reaction stops there. The same thing happens with the thiopyranone (I, R = CH_3, R_1 = H, $R_2 = C_3H_7$).

Thus it has proved possible, depending on the conditions selected, to transform each of the three heterocycles into either of the other two:

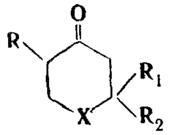


It must be noted, however, that we did not succeed in finding suitable conditions for converting the piperidone (II, R = R_1 = H, $R_2 = C_3H_7$) into the thiopyranone I and the tetrahydropyranone III, respectively. Under mild conditions the piperidone remains unchanged, and under severe conditions it resinifies.

We have found that under analogous conditions 2,3,6-trimethyl-4-pyrone (VII) in aqueous methylamine solution is converted in good yield into 1,2,3,6-tetramethyl-4-pyridone (VIII). Under the action of a dilute sulfuric acid solution in the presence of mercuric sulfate, the latter is converted to the pyrone VII.



The structure of the heterocyclic compounds thus synthesized was shown by identification of some of their crystalline derivatives with known samples.



R	R_1	R_2	X	Starting substances	Reaction time, hr	Reaction temp, °C	Molecular formula	Bp, °C (pressure, mm)	n_D^{20}	Yield, %	Notes
H	CH_3	CH_3	S	Pyranone Piperidone	42 35	80—90	$C_7H_{12}OS$	84—86°(13)*	1.4940	66.66 52.28	Semicarbazone mp 187° [5]
H	CH_3	CH_3	NCH_3	Pyranone	2.5	80—85	$C_8H_{15}NO$	56—58°(10)	1.500**	46.29	Picrate mp 139° [6]
CH_3	H	C_3H_7	NCH_3	Pyranone	24	80—82	$C_{10}H_{19}NO$	89—90°(10)	1.4650	41.07	2, 4-Dinitrophenylhydrazone mp 78°-79° [7]
H	CH_3	CH_3	O	Thiopyranone Piperidone	30 16	80—90	$C_7H_{12}O_2$	60—61°(10)	1.4990	41.09 72.22	Semicarbazone mp 165°-166°
CH_3	H	C_3H_7	O	Thiopyranone Piperidone	18 23	80—90	$C_9H_{16}O_2$	85—86°(10)	1.4630	75.22 21.73	2, 4-Dinitrophenylhydrazone mp 149°-150° [7]

---

* Mp 28°-29°.

** From the neutral products, there was obtained 3.5 g pyranone (III, R=H, $R_1=R_2=CH_3$), bp 60° (10 mm); n_D^{20} 1.4460.

Experimental

2-Propyltetrahydrothiopyran-4-one (I, $R = R_1 = H$, $R_2 = C_3H_7$). 8 g propylpyranone (III, $R = R_1 = H$, $R_2 = C_3H_7$) was added to a solution of 70 ml 90% methanol and 4.9 g sulfuric acid, saturated with hydrogen sulfide at – 10–0°. The mixture was heated 40 hr at 80°–90° in a sealed tube. After the methanol was distilled off, the reaction product was extracted with ether, neutralized with soda solution, and dried with magnesium sulfate. Yield 5.3 g (59.10%) (I, $R = R_1 = H$, $R_2 = C_3H_7$). Bp 84°–86° (4 mm); n_D^{20} 1.5002; d_4^{20} 1.0270, MR_D 45.26. calc. 44.95. Found: C 61.05; H 9.10; S 19.98%. Calculated for $C_8H_{14}OS$: C 60.76; H 8.86; S 20.25%. Semicarbazone, mp 81°–82° (from alcohol). Found: N 19.87; S 14.62%. Calculated for $C_9H_{17}N_3OS$: N 19.54; S 14.89%. The remaining experiments were carried out similarly. The constants are presented in the table.

Oxidation of the thiopyranone (I, $R = R_1 = H$, $R_2 = C_3H_7$). 65 ml 4% aqueous potassium permanganate was added with vigorous stirring to a solution of 2 g thiopyranone in 20 ml acetone and 80 ml 10% sulfuric acid. Crystals of the sulfone (V, $R = R_1 = H$, $R_2 = C_3H_7$) were obtained. Mp 43°–44° (from 1:1 ether-petroleum ether). Found: C 50.73; H 7.56; S 17.38%. Calculated for $C_8H_{14}O_3S$: C 50.53; H 7.37; S 16.84%.

5-Methyl-2-propyltetrahydrothiopyran-4-one (I, $R = CH_3$, $R_1 = H$, $R_2 = C_3H_7$: a) from 10 g pyranone (III, $R = CH_3$, $R_1 = H$, $R_2 = C_3H_7$), there was obtained, under the conditions described above, 4.6 g (41.81%) of the substituted tetrahydrothiopyran-4-one [2]. Bp 89°–90° (10 mm); n_D^{20} 1.4825. Semicarbazone, mp 174°–176°.

b) Under analogous conditions, 2 g (39.37%) was obtained from 5 g piperidone (II, $R = CH_3$, $R_1 = H$, $R_2 = C_3H_7$) on heating 72 hr. There was also obtained 0.9 g (17.71%) of a crystalline isomer of the thiopyranone (I, $R = CH_3$, $R_1 = H$, $R_2 = C_3H_7$). Mp 111°–112° (from alcohol). Found: C 62.53; H 9.41; S 18.72%. Calculated for $C_9H_{16}OS$: C 62.79; H 9.30; S 18.60%. This isomer gives no crystalline derivative with semicarbazide.

Interaction of methylamine with 2,2-dimethyltetrahydrothiopyran-4-one (I, $R = H$, $R_1 = R_2 = CH_3$). A mixture of 5 g thiopyranone (I, $R = H$, $R_1 = R_2 = CH_3$), 20 ml 25% aqueous methylamine, and 10 ml ethyl alcohol was heated 21 hr at 80°–90° in a sealed tube. After the usual work up, 1.5 g imine (IV, $R = H$, $R_1 = R_2 = CH_3$) was obtained. Bp 83°–84° (10 mm); n_D^{20} 1.5060. From the neutral products, 1 g thiopyranone (I, $R = H$, $R_1 = R_2 = CH_3$) was isolated. Bp 83°–86° (12 mm); n_D^{20} 1.4930.

Hydrolysis of the imine (IV, $R = H$, $R_1 = R_2 = CH_3$). A mixture of 1.5 g imine (IV, $R = H$, $R_1 = R_2 = CH_3$) and 8 ml 18% hydrochloric acid was heated 2 hr 30 min on a water bath at 50°–60°. The work up was as usual. There was obtained 0.9 g thiopyranone (I, $R = H$, $R_1 = R_2 = CH_3$). Bp 81°–83° (10 mm); n_D^{20} 1.4950. The semicarbazone, mp 187° (from alcohol), gave no melting point depression when mixed with the foregoing sample.

1-Methyl-2-propyl-4-piperidone (II, $R = R_1 = H$, $R_2 = C_3H_7$). a) 7 g pyranone (III, $R = R_1 = H$, $R_2 = C_3H_7$) and 32 ml 25% aqueous methylamine were heated 32 hr at 80°–82° in a sealed tube. There was obtained 2 g (36.63%) of the piperidone. Bp 86°–87° (7 mm); n_D^{20} 1.4680; d_4^{20} 0.9286. Found: C 69.81; H 11.15; N 9.06%. Calculated for $C_9H_{17}NO$: C 69.68; H 10.96; N 9.03%. Picrate, mp 148°–149° (from alcohol). Found: N 14.32%. Calculated for $C_{15}H_{20}N_4O_8$: N 14.58%.

b) On heating 18 hr at 80°–90°, 1.1 g (56.12%) was obtained from 2 g thiopyranone (I, $R = R_1 = H$, $R_2 = C_3H_7$).

Interaction of methylamine with 5-methyl-2-propyltetrahydrothiopyran-4-one (I, $R = CH_3$, $R_1 = H$, $R_2 = C_3H_7$). Under analogous conditions, 2 g imine (IV, $R = CH_3$, $R_1 = H$, $R_2 = C_3H_7$) was obtained from 4 g thiopyranone (I, $R = CH_3$, $R_1 = H$, $R_2 = C_3H_7$). Bp 80°–81° (5 mm); n_D^{20} 1.4920; d_4^{20} 0.9311; MR_D 57.64, calc. 56.78. Found: C 65.10; H 10.42; N 7.78%. Calculated for $C_{10}H_{19}NS$: C 64.87; H 10.27; N 7.56%. By hydrolysis of 1 g of the imine (IV, $R = CH_3$, $R_1 = H$, $R_2 = C_3H_7$), there was obtained 0.6 g tetrahydrothiopyran-4-one (I, $R = CH_3$, $R_1 = H$, $R_2 = C_3H_7$). Bp 88° (10 mm); n_D^{20} 1.4830. 2,4-Dinitrophenylhydrazone, mp 124°–125°; semicarbazone, mp 174°; these gave no melting point depression when mixed with the samples described above.

2-Propyltetrahydropyran-4-one (III, $R = R_1 = H$, $R_2 = C_3H_7$). A mixture of 2 g thiopyranone (I, $R = R_1 = H$, $R_2 = C_3H_7$), 25 ml 7% sulfuric acid, and 1 g mercuric sulfate was heated 24 hr at 80°–85°. During this time a further 1.5 g mercuric sulfate was added in portions. There was obtained 0.8 g (44.44%), bp 84°–86° (10 mm); n_D^{20} 1.4545. Semicarbazone, mp 148°. The constants agreed with the constants of a known sample [3].

1,2,3,6-Tetramethyl-4-pyridone ($VIII$). A mixture of 10 g pyrone VII and 105 ml 25% aqueous methylamine was shaken 6 hr at room temperature, then heated 4 hr at 80°–90°. There was obtained 6.4 g (58.71%), bp 100°–103° (10 mm); n_D^{20} 1.5200; d_4^{20} 0.9553; MR_D 48.06; calc. 44.58. Found: C 71.65; H 8.50; N 9.48%. Calculated for $C_9H_{13}NO$: C 71.52; H 8.60; N 9.27%. Hydrochloride, mp 252°–254°. Found: N 7.32%. Calculated for $C_9H_{13}NO \cdot HCl$: N 7.46%. 2,4-Dinitrophenylhydrazone, mp 112°–113°. Found: N 21.21%. Calculated for $C_{15}H_{17}N_5O_4$: N 21.15%.

2,3,6-Trimethyl-4-pyrone (VII). A mixture of 2.7 g pyridone VIII, 20 ml 20% sulfuric acid, and 1 g mercuric sulfate was heated 30 hr at 80°–90°. There was obtained 0.7 g (31.25%), mp 78° (from petroleum ether) [4].

REFERENCES

1. S. A. Vartanyan, A. S. Noravyan, and V. N. Zhamagortsyan, Izv. AN SSSR, OKhN, 17, 436, 1964.
2. S. A. Vartanyan, A. S. Noravyan, and V. N. Zhamagortsyan, Izv. AN Arm. SSR, KhN, 18, 124, 1965.
3. I. N. Nazarov, I. V. Torgov, and L. N. Terekhova, Izv. AN SSSR, OKhN, 50, 1943; I. N. Nazarov and A. N. Elizarova, Izv. AN SSSR, OKhN, 647, 1947.
4. Beilst, 17, 296.
5. I. N. Nazarov and A. N. Kuznetsova, Izv. AN SSSR, OKhN, 118, 1948.
6. I. N. Nazarov, S. G. Matsoyan, and S. A. Vartanyan, ZhOKh, 23, 1990, 1953.
7. S. A. Vartanyan, V. N. Zhamagortsyan, and A. S. Noravyan, Izv. AN Arm. SSR, KhN, 16, 391, 1963.

12 November 1964 Institute of Organic Chemistry, AS Armenian SSR