of nitrogen, 500 ml. of dry xylene and 23 g. of sodium. The flask and its contents were heated in an oil-bath maintained at 110°, until all of the sodium was well dispersed whereupon a mixture of 68 g. (0.25 mole) of methyl palmitate and 25 g. (0.25 mole) of methyl butyrate was slowly added during the course of 45 minutes. Stirring was continued for an additional 15 minutes, the oil-bath removed and 25 ml. of methanol slowly added to the viscous reaction mixture. When all of the sodium had disappeared 500 ml. of water was slowly added to the now fluid reaction mixture, the residual solid collected by centrifugation, washed several times with benzene, and the washings added to the xylene layer. This latter solution was washed with water until neutral, then with dilute hydrochloric acid, and finally with water. Fractional distillation gave 26.6 g. (34%) of a *n*-C_{20}-acyloin fraction, b.p. 170–180° (1.5 mm.). To 3.12 g. of this product, dissolved in 25 ml. of ethanol, was added 4.3 g. of phenylhydrazine and 3 ml. of acetic acid, the solution heated on a steam-bath for a few minutes, and sufficient water added to produce a slight turbidity. As the heating was continued the reaction mixture became more turbid and from time to time sufficient ethanol was added to restore the reaction mixture to its original state. When heating no longer led to an increased turbidity of the reaction mixture, it was cooled, the oil that formed induced to crystallize by scratching and the solid so obtained recrystallized from aqueous ethanol to give 2.9 g. (59%) of the phenylosazone of 4,5-*n*-eicosandione, m.p. 71–73°.

Anal. Calcd. for $C_{32}H_{50}N_4$ (490.8): C, 78.4; H, 10.3. Found: C, 78.5; H, 10.4.

4,5-*n*-Eicosandione.—To 10 g. of the *n*-C_{20}-acyloin fraction in 100 ml. of chloroform was added 50 ml. of a 1.05 *M* solution of iodine monochloride in glacial acetic acid[7] and the mixture allowed to stand at 25° for two days. To this solution was added 200 ml. of water and then solid sodium thiosulfate, in small portions, until the aqueous phase remained colorless after shaking. The chloroform layer was then washed with dilute aqueous sodium thiosulfate, evaporated to dryness, and the residue recrystallized from ethanol to give 6.34 g. (64%) of 4,5-*n*-eicosandione, m.p. 56.5–57.5°.

Anal. Calcd. for $C_{20}H_{38}O_2$ (310.5): C, 77.4; H, 12.3. Found: C, 77.5; H, 12.3.

Dioxime of 4,5-*n*-Eicosandione.—To a solution of 4.65 g. of 4,5-*n*-eicosandione in 75 ml. of ethanol was added a solution of 2.4 g. of sodium hydroxide and 6.3 g. of hydroxylamine hydrochloride in 30 ml. of water, and the mixture heated, under refluxing conditions, for one hour with the addition of sufficient ethanol to prevent the formation of a precipitate. The mixture was then cooled, the crystalline precipitate collected, washed with water and recrystallized from aqueous ethanol to give 4.25 g. (83%) of the dioxime, m.p. 135.5–137.5°. A second recrystallization from the same solvent gave a product, m.p. 136.5–137.5°.

Anal. Calcd. for $C_{20}H_{40}O_2N_2$ (340.5): C, 70.5; H, 11.8; N, 8.2. Found: C, 70.7; H, 11.7; N, 8.1.

4,5-Diamino-*n*-eicosane Dihydrochloride.—A solution of 1.02 g. of the dioxime of 4,5-*n*-eicosandione in 100 ml. of absolute ethanol and 1.5 ml. of concentrated hydrochloric acid was hydrogenated, under one atmosphere of hydrogen and over 0.40 g. of platinic oxide, for four hours at 25°. The solution was then freed of catalyst, evaporated to a small volume, the residue dissolved in water, the solution extracted with ether, the aqueous phase made alkaline with aqueous sodium hydroxide, extracted with ether and the ethereal extract dried over anhydrous sodium sulfate. Dry hydrogen chloride was passed into the dry ethereal extract to give a precipitate which was collected and recrystallized twice from water to give 0.385 g. of 4,5-diamino-*n*-eicosane dihydrochloride, colorless glistening plates.

Anal. Calcd. for $C_{20}H_{46}N_2Cl_2$ (385.5): C, 62.3; H, 12.0; N, 7.3. Found: C, 62.6; H, 12.2; N, 7.2.

The above dihydrochloride was converted into the dipicrate, m.p. 138–140.5° after two recrystallizations from aqueous ethanol.

Anal. Calcd. for $C_{32}H_{50}O_{14}N_8$ (770.8): C, 49.9; H, 6.5; N, 14.5. Found: C, 50.2; H, 6.5; N, 14.6.

The ethereal solution remaining after the collection of the ether-insoluble dihydrochloride was evaporated to dryness and the residue recrystallized from ethyl acetate containing a small amount of absolute ethanol to give 0.332 g. of a second 4,5-diamino-*n*-eicosane dihydrochloride.

Anal. Calcd. for $C_{20}H_{46}N_2Cl_2$ (385.5): C, 62.3; H, 12.0; N, 7.3. Found: C, 62.6; H, 12.0; N, 7.2.

In contrast to the ether-insoluble dihydrochloride, the ether-soluble dihydrochloride was appreciably soluble in cold water. All attempts to prepare a dipicrate from the latter compound failed in that only oils were obtained.

Mixed Iso-C_{20}-acyloins.—The acyloin condensation of methyl palmitate and methyl isobutyrate, conducted as described above, gave 36% of an iso-C_{20}-acyloin fraction, b.p. 175–190° (2 mm.).

2-Methyl-3,4-*n*-nonadecandione.—The oxidation of 17.7 g. of the iso-C_{20}-acyloin fraction, dissolved in 100 ml. of chloroform, with 87 ml. of 1.05 *M* iodine monochloride in glacial acetic acid gave after fractional distillation 13.4 g. (76%) of crude 2-methyl-3,4-nonadecandione, b.p. 140–145° (0.1 mm.), m.p. 18–20°, and a small amount, *i.e.*, 0.48 g., of an unidentified product, m.p. 58–61°.

Dioxime of 2-Methyl-3,4-*n*-nonadecandione.—To a solution of 4.65 g. of the crude diketone in 75 ml. of ethanol was added a solution of 6.3 g. of hydroxylamine hydrochloride and 2.4 g. of sodium hydroxide in 30 ml. of water and the reaction conducted as previously described for the corresponding derivative of *n*-eicosane. The solid which was obtained was recrystallized from ethanol to give 4.5 g. of an impure product, m.p. 60–90°. On further recrystallization from ethanol a product, m.p. 113–115°, was obtained.

Anal. Calcd. for $C_{20}H_{40}O_2N_2$ (340.5): C, 70.5; H, 11.8; N, 8.2. Found: C, 71.6; H, 11.8; N, 7.6.

2-Methyl-3,4-diamino-*n*-nonadecane Dihydrochloride.—A solution of 0.80 g. of the crude dioxime, m.p. 60–90°, in 80 ml. of absolute ethanol and 1.5 ml. of concentrated hydrochloric acid was hydrogenated as before using 0.3 g. of platinic oxide. After removal of the catalyst the filtrate was evaporated to dryness, the residue dissolved in water, the solution extracted with ether, the aqueous phase made alkaline with aqueous sodium hydroxide, extracted with ether, the ethereal solution acidified with methanolic hydrogen chloride and evaporated to dryness. The residue was extracted with dry ether to give an ether-soluble and an ether-insoluble fraction. The ether-insoluble fraction was recrystallized from ethanol to give 0.173 g. of a 2-methyl-3,4-diamino-*n*-nonadecane dihydrochloride.

Anal. Calcd. for $C_{20}H_{46}N_2Cl_2$ (385.5): C, 62.3; H, 12.0; N, 7.3. Found: C, 62.4; H, 11.9; N, 7.4.

The ether-soluble fraction was evaporated to dryness to give a partially crystalline sirup which was triturated and washed with ethyl acetate and then recrystallized from ethyl acetate to give 0.065 g. of a second 2-methyl-3,4-diamino-*n*-nonadecane dihydrochloride.

Anal. Calcd. for $C_{20}H_{46}N_2Cl_2$ (385.5): C, 62.3; H, 12.0; N, 7.3. Found: C, 62.2; H, 12.1; N, 7.2.

All attempts to prepare the dipicrates from the above two diamine dihydrochlorides gave only oils.

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Correlation of Entropies of Transition and Fusion

BY GEORGE C. HOOD

RECEIVED AUGUST 28, 1953

Certain molecules which approach spherical symmetry possess the ability to rotate in the solid phase. In general, the very existence and entropy change of a transition believed to indicate the onset of molecular rotation in a crystal must be determined experimentally. Similarly, the entropy change of a fusion is difficult to estimate. However, with the aid of the external symmetry number (σ), certain correlations and predictions can be made for members of a substitution series, such as CX_4, CX_3Y . . ., CY_4.

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(7) V. L. Hansley, THIS JOURNAL, **57**, 2305 (1935).

The entropy of fusion[1] for the molecules CF_4, CCl_4, CH_4, CBr_4, $C(CH_3)_4$, $C(CH_3)_3Cl$, $C(CH_3)_2Cl$ and $C(CH_3)Cl_3$, all of which rotate in the solid phase, is essentially constant with a value of 2.6 ± 0.4 e.u.[2] The entropy of transition for the molecules CF_4, CCl_4, CBr_4 and $C(CH_3)_4$, all of which have a symmetry number of 12, is essentially constant with a value of 4.6 ± 0.1 e.u. Thus it appears that the rotational contribution to the entropy change $\Delta S_t + \Delta S_f$ is constant for substituted methanes with equal symmetry numbers.

One obtains the following expressions by assuming the effect of the symmetry number can be calculated in a manner analogous to the symmetry number contribution to the rotational entropy of a gas:

$$\Delta S_{\sigma_3-\sigma_{12}} = -2.303R\,(\log 3-\log 12) = 2.76 \text{ e.u.}$$
$$\Delta S_{\sigma_2-\sigma_3} = -2.303R\,(\log 2-\log 3) = 0.81 \text{ e.u.}$$

Consequently, a substituted methane with a symmetry number of 3 should have a transitional entropy change of 7.4 e.u. if it is freely rotating, or a fusional entropy change of 10.0 e.u. if it does not rotate in the solid phase. The molecule $C(CH_3)Cl_3$, known to rotate in the solid phase, has a ΔS_t of 7.97 e.u. The molecules $CFCl_3$, CH_3Cl, $CHCl_3$, $CHBr_3$ and CHI_3 have an average ΔS_f of 9.7 ± 0.5 e.u. Thus it would not be expected that these molecules rotate in the solid phase. This is substantiated by the lack of any observed rotational transition points for these molecules, and the low dielectric constant values for solid CH_3Cl and $CHCl_3$, which indicate no molecular rotation, at least around any axis perpendicular to a carbon–halogen axis.[3] The molecule CH_3Br has a ΔS_t of 0.650 e.u. and a ΔS_f of 7.96 e.u. The observed transition point probably is not a rotational effect.

A substituted methane molecule with a symmetry number of 2 should have a transitional entropy change of 8.3 e.u. if it is freely rotating in the solid phase, or a fusional entropy change of 10.8 e.u. if it does not rotate in the solid phase. The molecule CH_2I_2 has a ΔS_t of 0.5 e.u. and a ΔS_f of 10.3 e.u. Again, the small entropy of transition probably is not a rotational effect. No transitions have been observed for the molecules CH_2Cl_2, CH_2Br_2 or CF_2Cl_2. In addition, the low dielectric constant value for solid CH_2Cl_2 again indicates no molecular rotation around any axis perpendicular to a carbon–halogen axis. However, the entropies of fusion are CH_2Cl_2 6 e.u., CH_2Br_2 4 e.u. and CF_2Cl_2 8.4 e.u. These values are too high to indicate complete rotation in the solid phase and too low to indicate no rotation in the solid phase. Admittedly, the data for CH_2Cl_2 and CH_2Br_2 are the most uncertain herein, but they would have to be considerably in error to fit the correlation either way. Then too, the value of 8.4 e.u. for the fusion of CF_2Cl_2 is more firmly experimentally established. Hence it would appear that these molecules possess a certain amount of rotation in the solid and have transition points with fairly large transitional entropy changes or the entropy of fusion data for these compounds are seriously in error.

This correlation for the type of series considered seems to fit the available data reasonably well and allows prediction of transitional entropy changes or fusional entropy changes, provided one or the other is known. The accuracy is generally better than one entropy unit. The correlation also provides information concerning the rotation of molecules in the solid phase.

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(1) All the data used herein were taken from *Selected Values of Chemical Thermodynamic Properties*, Circular of the National Bureau of Standards 500, Washington, D. C., 1950, except the data for $C(CH_3)_4$, $C(CH_3)_3Cl$, and $C(CH_3)_2Cl_2$, which were taken from A. Turkevich, and C. P. Smyth, THIS JOURNAL, **62**, 2468 (1940).

(2) All uncertainties used herein are average deviations.

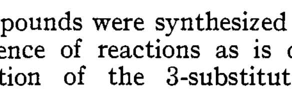
(3) C. P. Smyth, *Chem. Revs.*, **19**, 329 (1936).

The Preparation and Properties of a Few ω-(N,N-Dialkylamino)-alkyl-2-thienyl Sulfide Hydrochlorides and 2-Thiophenethiol

BY WM. H. HOUFF AND ROBERT D. SCHUETZ

RECEIVED JULY 6, 1953

A recent report[1] indicated the possibility that there are differences between the physiological properties of 2- and 3-substituted thiophene isomers. The already known pronounced local anesthetic activity of a series of ω-(N,N-dialkylamino)-alkyl-3-thienyl sulfide hydrochlorides[2] prompted an investigation of their corresponding 2-thienyl analogs. The latter substances can be represented by the general formula



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These compounds were synthesized by the same general sequence of reactions as is described for the preparation of the 3-substituted isomers.[2] The reaction can be summarized as

$$R_2NH + Cl(CH_2)_nOH \xrightarrow[\text{EtOH}]{\text{NaI}} R_2N(CH_2)_nOH \qquad \text{II}$$
$$\xrightarrow[\text{CHCl}_3]{\text{SOCl}_2} R_2N(CH_2)_nCl\cdot HCl \qquad \text{III}$$
$$\xrightarrow[\text{2. HCl}]{\text{1. } C_4H_3SSH + NaOH} \text{(I)}$$

A secondary amine was allowed to react with the appropriate polymethylene chlorohydrin in ethanolic sodium iodide solution and the resulting ω-hydroxy alkyl amine (II) was converted to the corresponding chloro compound III by interaction with thionyl chloride in dry chloroform. The latter material was added to a refluxing solution of 2-thiophenethiol in aqueous sodium hydroxide and the oily ω-(N,N-dialkylamino)-alkyl-2-thienyl sulfide was converted to its hydrochloride salt I and characterized as such. A few properties of two tertiary amine derivatives of mixed thienyl alkyl sulfides not previously reported are listed in Table I.

Two new synthetic routes were investigated for the preparation of 2-thiophenethiol. One of these involved the interaction of sulfur and 2-thienylmagnesium bromide, and was similar to that used by

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(1) E. Campaigne, Abstracts of Papers, Division of Medicinal Chemistry, American Chemical Society, Los Angeles, California, March 15, 1953, p. 7 L.

(2) W. H. Houff and R. D. Schuetz, THIS JOURNAL, **75**, 2072 (1953).