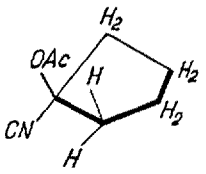
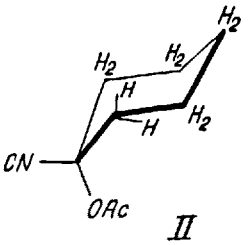
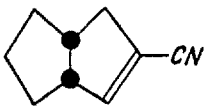


I



II



III

Δ^1-cyclopentenenitrile (b.p. 94°/60 mm; $n^{31°}$ 1·4690) in yields of 95–98% on the basis of the acetate passed; 2 g of the ester were passed per minute. BURNS, JONES, and RITCHIE[1] report a yield (calculated from their data) of 37·2% for Δ^1-cyclohexenenitrile, when (II) was pyrolysed at 440–450°. Similarly FRANK, BERRY, and SHOTWELL[2] found 575–600° as the optimum temperature for the pyrolysis of 4-isopropyl-cyclohexanone cyanohydrin acetate; the corresponding α,β-unsaturated nitrile was obtained in a yield of 74%. It has also been found that (III) can be obtained from the corresponding acetate in a yield of 96–97%, when decomposed at 480° ± 5°.

Full details will be published elsewhere.

SUKH DEV

Department of Organic Chemistry, Indian Institute of Science, Bangalore 3, September 11, 1953.

Zusammenfassung

Auf Grund stereochemischer Überlegungen wird angenommen, dass eine ionische 1,2-cis-Abspaltung in der Cyclopentan-Reihe leichter erfolgt als im Cyclohexan-System. In Übereinstimmung damit wird eine gute Methode für die Herstellung von Δ^1-Cyclopentennitril beschrieben.

[1] R. BURNS, D. T. JONES, and P. D. RITCHIE, J. Chem. Soc. *1935*, 400.

[2] R. L. FRANK, R. E. BERRY, and O. L. SHOTWELL, J. Amer. Chem. Soc. *71*, 3891 (1949).

(+)-S-Acetyl-pantetheine and (+)-S-Benzoyl-pantetheine

Recently, KING, STEWART, and CHELDELIN, and BADDILEY and THAIN[1] reported on the synthesis of S-acetyl-pantetheine (I). The few physical and chemical data given for their preparation are well in accordance with those previously published in a paper to which the aforementioned authors had not been able to refer[2].

The ultraviolet absorption spectrum of S-acetyl-pantetheine (I) shows a band (λ_{max} = 230 mμ) corresponding to the CO-S grouping[3], and is practically identical with the spectrum of N,S-diacetyl-cysteamine (IV)[4], whereas pantetheine (III)[5] shows no characteristic absorption between 210 mμ and the visible range (Fig. 1).

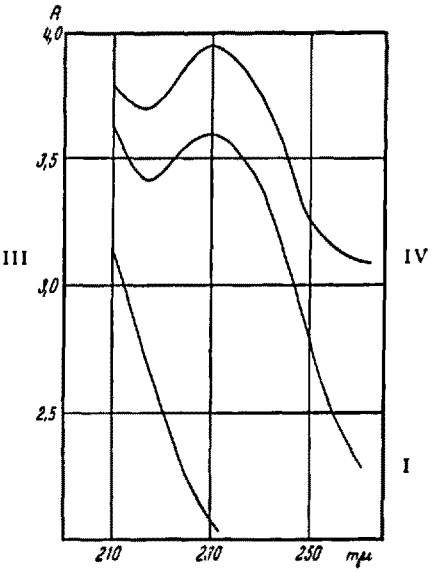


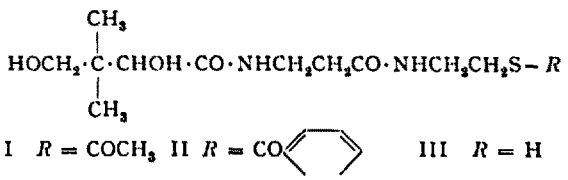
Fig. 1.

I (+)-S-acetyl-pantetheine (alcohol) . . $\log E^{1\,m}_{1\,cm}$ = A

IV N,S-diacetyl-cysteamine (alcohol) . . $\log E^{1\,m}_{1\,cm}$ = A − 0·4

III Pantetheine (alcohol) . . . . . $\log E^{1\,m}_{1\,cm}$ = A + 0·4

From a practical point of vue (+)-S-benzoyl-pantetheine (II)[1] is more interesting. It is obtained in yields of 70 to 80% even in experiments delivering as much as 20 g of material, and is, up to the present, the only simple, crystalline derivative showing full activity for *Lactobacillus helveticus* 80 (21000 to 22000 units per milligram, calculated for pantetheine)[2], and which is easily accessible and easily converted *in vitro* to pantetheine-pantethine. Its ultraviolet spectrum is shown in Figure 2. The CO-S band is shifted by 8 mμ towards longer wave lengths, and a band corresponding to the phenyl group shows up at approximately 266 mμ. This same sort of spectrum is characteristic also for other mercapto-esters of benzoic acid, viz. S-benzoyl-N-acetyl-cysteamine (V), S-benzoyl-α-mercapto-acetic acid (VI), and S-benzoyl-β-mercapto-propionic acid (VII) (Fig. 2).



[1] R. SCHWYZER, Helv. chim. Acta *35*, 1903 (1952).

[2] Private communication from Prof. E. E. SNELL.

[1] T. E. KING, C. J. STEWART, and V. H. CHELDELIN; J. BADDILEY and E. M. THAIN, Science *117*, 139 (1953).

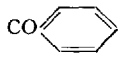
[2] R. SCHWYZER, Helv. chim. Acta *35*, 1903 (1952).

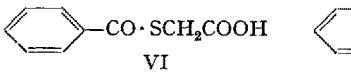
[3] B. SJÖBERG, Z. physik. Chem. *52*, 209 (1942). – H. P. KOCH, J. chem. Soc. *1949*, 387.

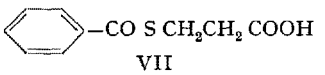
[4] R. KUHN and G. QUADBECK, Ber. dtsch. chem. Ges. *84*, 844 (1951).

[5] E. E. SNELL, G. M. BROWN, V. J. PETERS, J. A. CRAIG, E. L. WITTLE, J. A. MOORE, V. M. MCGLOHON, and O. D. BIRD, Amer. Soc. *72*, 5349 (1950).

$CH_3CO{\cdot}NHCH_2CH_2S-R$

IV $R = COCH_3$ V $R = CO$ 


VI


VII

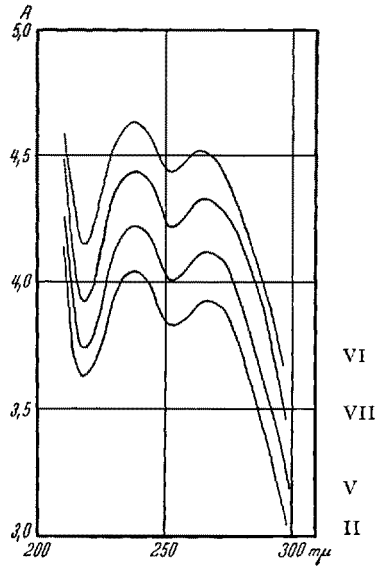


Fig. 2.

II (+)-S-benzoyl-pantetheine (alcohol) . . $\log E \frac{1\text{ m}}{1\text{ cm}} = A$

V S-benzoyl-N-acetyl-cysteamine (alcohol) $\log E \frac{1\text{ m}}{1\text{ cm}} = A - 0{\cdot}2$

VII S-benzoyl-β-mercapto-propionic acid (alcohol) . . . . . $\log E \frac{1\text{ m}}{1\text{ cm}} = A - 0{\cdot}4$

VI S-benzoyl-α-mercapto-acetic acid (alcohol) . . . . . $\log E \frac{1\text{ m}}{1\text{ cm}} = A - 0{\cdot}6$

Figreu 3*a* shows the spectrum of the copper-II-complex obtained from 2 molecules of pantetheine and one "formula weight" of copper-II-acetate in alkaline solution. The violet complex can best be obtained in solution by dissolving (+)-S-benzoyl-pantetheine in a 1:1 mixture of alcohol-water (10^{-3} molar) containing copper-II-acetate (10^{-3} normal), and adding slowly

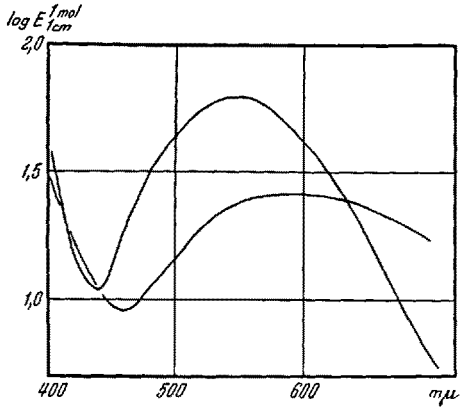


Fig. 3.–Curve *a*: violet complex of Cu^{++} with pantetheine, Curve *b*: blue product of deterioration of *a* (The values of $\log E \frac{1\text{ m}}{1\text{ cm}}$ are calculated on the basis of pantetheine present in solution).

NaOH solution to a concentration of about $5 \cdot 10^{-2}$ normal. On standing, the violet colour appears, accompanied by dissolution of the first precipitated copper hydroxide. As saponification of the mercapto-ester proceeds, the odour of benzoic acid ethyl ester develops (in the case of benzoyl-pantetheine). After some days the violet colour yields to a cornflower blue of the same hue as of the copper complex of pantothenic acid (Fig. 3*b*); the conversion is accelerated by aeration. Neither N-acetyl-cysteamine, nor N, S-diacetyl-cysteamine, nor S-benzoyl-pantetheine-2′, 4′-phosphate develop any colour under the same conditions. These findings suggest that the hydroxyl as well as the thiol groups are involved in complex formation. Besides offering a possibility for identification of pantetheine and its acyl-derivatives, the reaction has some bearing on the explanation of the activation of the CO-S bond observed for certain metal ions, and communicated some time ago[1]. Experiments on this subject will be published in detail elsewhere.

I am indebted to Drs. H. GYSEL and R. ROMETSCH for help in the determination of the spectra reported here, and to Prof. E. E. SNELL for the determination of the biological activity.

R. SCHWYZER

Research Laboratories of Ciba Pharmaceutical Products, Inc., Basle, October 6, 1953.

Zusammenfassung

Die UV.-Spektren von (+)-S-Acetyl-pantethein, (+)-S-Benzoyl-pantethein und von Pantethein wurden bestimmt und werden mit denjenigen anderer Thiosäureester verglichen. Pantethein und seine beiden S-Acylderivate geben in alkalischer Lösung mit Kupfer-II-Salzen eine violette Färbung. Die biologische Aktivität des stabilen, kristallisierten (+)-S-Benzoyl-pantetheins entspricht seinem Gehalt an Pantethein.

[1] R. SCHWYZER, abstract of paper read at the "Chemiker-Treffen 1953, Innsbruck" in Angew. Chem. *65*, 267 (1953) and Österr. Chem. Ztg. *54*, 155 (1953); Helv. chim. Acta *37*, 155 (1954).

Über Mercapto-triazinone mit tuberkulostatischer Wirkung

Thiosemicarbazone von aromatischen Aldehyden bzw. Ketonen zeichnen sich durch ihre Wirkung gegenüber Tuberkelbazillen aus[1]. In einer früheren Mitteilung[2] haben wir über einige Thiosemicarbazone von heterocyclischen Aldehyden berichtet. In Fortsetzung obiger Arbeiten haben wir α-Ketoaldehyde mit Thiosemicarbazid umgesetzt und dabei zum Beispiel aus Phenylglyoxal-monothiosemicarbazon das 5-Phenyl-3-mercapto-1, 2, 4-triazin erhalten[3], das sich *in vivo* als tuberkulostatisch unwirksam erwies. Lässt man an Stelle von α-Ketoaldehyden aromatische α-Ketosäuren auf Thiosemicarbazid einwirken, so lassen sich die gebildeten Thiosemicarbazone zu 6-substituierten 3-Mercapto-1, 2, 4-triazin-5-onen gemäss folgender Gleichung cyclisieren:[4]

[1] G. DOMAGK, R. BEHNISCH, F. MIETZSCH und H. SCHMIDT, Naturwissenschaften *33*, 315 (1946).

[2] R. E. HAGENBACH und H. GYSIN, Exper. *8*, 184 (1952).

[3] L. WOLFF und H. LINDENHAYN, Ber. dtsch. chem. Ges. *36*, 4126 (1903). – R. FUSCO, S. ROSSI, G. MANTEGAZZA und R. TOMMASINI, Ann. Chimica *42*, 94 (1952).

[4] J. BOUGAULT und L. DANIEL, C. r. Acad. Sci. *186*, 151 (1928).