C_9H_{15}) was prepared from synthetic chrysanthemumoyl chloride according to the method of Beroza,[3] b.p. 140–141°/0.25 mm., $n_D^{25°}$ 1.5302; when the supersaturated liquid was seeded with crystals (m.p. 66–67°) obtained from Beroza, a crystalline mass was obtained which was purified by crystallization from petroleum ether; crude yield 92%.

2-Bromo-4,5-methylenedioxyphenol (III) was prepared by cooling to 0° a stirred solution of sesamol (II) (207 g.) and glacial acetic acid (450 ml.), and then slowly adding bromine (60 ml.) in glacial acetic acid (225 ml.) while holding the temperature below 10°. Immediately after the addition of bromine, the mixture was poured into ice and water, filtered quickly, and the crystals (III) washed with cold water until free of solvent; yield 90%. Although crude III is affected by light and air, when free of the acid solvent and kept in a dark bottle it was stable and could be used for further syntheses. The light green compound melted at 84° (dec.), and was very difficult to recrystallize. A small amount of III was purified by distillation under high vacuum and recrystallization from benzene; it melted at 88° (dec.); the yield from this distillation was low. III gave a positive phenol test with 2% ferric chloride solution.

Anal. Calcd. for $C_7H_5BrO_3$: C, 38.72; H, 2.32; Br, 36.8. Found: C, 39.50; H, 2.62; Br, 36.15.

2-Bromo-4,5-methylenedioxyphenyl acetate (V, R = CH_3) was prepared from III by treatment with acetyl chloride and pyridine and from IV by treatment with glacial acetic acid and halogen at 0°; recrystallized from ethanol; m.p. 84–86°; crude yield quantitative.

Anal. Calcd. for $C_9H_7BrO_4$: Br, 30.85. Found: Br, 30.65.

2-Bromo-4,5-methylenedioxyphenyl propionate (V, R = C_2H_5) was prepared *via* the acid chloride in the same way as was the acetate; b.p. 108°/0.2 mm., solidified; recrystallized from ethanol; m.p. 60–61°; yield 80%.

Anal. Calcd. for $C_{10}H_9BrO_4$: Br, 29.27. Found: Br, 28.92.

2-Bromo-4,5-methylenedioxyphenyl 1-naphthoate (V, R = $C_{10}H_7$) was prepared as described above; recrystallized from ethanol; m.p. 109–110°; crude yield quantitative.

Anal. Calcd. for $C_{18}H_{11}BrO_4$: Br, 21.53. Found: Br, 21.52.

2-Bromo-4,5-methylenedioxyphenyl benzoate (V, R = C_6H_5) was prepared as above described; recrystallized from ethanol; m.p. 131°; yield 80%.

Anal. Calcd. for $C_{14}H_9BrO_4$: Br, 24.89. Found: Br, 24.15.

2-Bromo-4,5-methylenedioxyphenyl ester of 3-(1,2-dibromo-2-methylpropyl)-2,2-dimethylcyclopropanecarboxylic acid (VII) was prepared by the bromination of 3,4-methylenedioxyphenyl chrysanthemumate (IV, R = C_9H_{15}). IV (28.8 g.) was placed in a 600-ml. beaker containing pyridine (8 g.) and glacial acetic acid (100 ml.) at 0° and bromine (32 g.) in glacial acetic acid (50 ml.) was added dropwise with continuous stirring. The whole was then poured into ice and water whereupon a yellow precipitate formed. The mixture was extracted with ether and the layers were separated. The ether layer was washed with dilute sodium bicarbonate, then water. After removal of the ether, crystallization occurred. Alcohol was added to the crystalline mass and triturated while being warmed to about 50°. The mixture was filtered and the crystals of VII were washed with alcohol; crude yield 96%; recrystallized once from a mixture of benzene and alcohol, m.p. 130–141°; and then twice from benzene alone; the product was rather soluble in benzene so that the purified yield was less than 30%; m.p. 140–142°.

Anal. Calcd. for $C_{17}H_{19}Br_3O_4$: C, 38.74; H, 3.66; Br, 45.49. Found: C, 39.16; H, 3.63; Br, 45.05.

2-Bromo-4,5-methylenedioxyphenyl chrysanthemumate (V, R = C_9H_{15}) was prepared from synthetic chrysanthemumoyl chloride in the same manner as were the halopiperonyl chrysanthemumates[1]; b.p. 163–171°/0.11 mm., $n_D^{25°}$ 1.5483; yield 67%.

Anal. Calcd. for $C_{17}H_{19}BrO_4$: C, 55.60; H, 5.21; Br, 21.76. Found: C, 55.27; H, 5.18; Br, 21.70.

The chloro derivative (V, R = C_9H_{15}), prepared in the same manner, boiled at 142–157°/0.2 mm. and had $n_D^{25°}$ 1.5355.

BELTSVILLE, MD.

[CONTRIBUTION FROM THE RESEARCH LABORATORY, DAINIPPON PHARMACEUTICAL CO.]

Palladium Dehydrogenation of Methyl Reserpate and Yohimbine in Cymene[1]

HIDEHIKO KANEKO

Received July 1, 1958

On dehydrogenation with palladium-carbon in boiling cymene, methyl reserpate yielded 7-methoxyyobyrine and *Py*-tetradehydroreserpic acid lactone and yohimbine gave *Py*-tetradehydroyohimbic acid or *Py*-tetradehydroyohimbine.

The selenium dehydrogenation procedure has been widely employed for elucidation of the structure of indole alkaloids, for example yohimbine,[2] corynantheine,[3] reserpine,[4] and ajmaline.[5] Since this reaction has usually been carried out at temperatures about 300°, dehydrogenation has sometimes been accompanied by rearrangement and cleavage of the ring system of the alkaloids. I, therefore, thought it of some interest to investigate the dehydrogenation under milder conditions. The present paper describes the products of the dehydrogenation of methyl reserpate and yohimbine by palladium-carbon in boiling *p*-cymene.

Methyl reserpate (Ia) is a minor constituent of *Rauwolfia serpentina*,[6] but can most conveniently be obtained by methanolysis of reserpine[7] (Ib).

(1) Presented at the annual meeting of the Pharmaceutical Society of Japan held in Fukuoka, Japan, April, 1956.

(2) G. Barger and C. Scholtz, *Helv. Chim. Acta*, **16**, 1343 (1933); **18**, 923 (1935).

(3) P. Karrer and P. Enslin, *Helv. Chim. Acta*, **32**, 1390 (1949).

(4) J. M. Muller, E. Schlittler, and H. Bein, *Experientia*, **8**, 338 (1952).

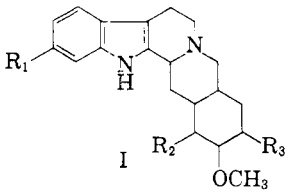
(5) F. A. L. Anet, D. Chakravarti, R. Robinson, and E. Schlittler, *J. Chem. Soc.*, 1242 (1954).

(6) A. Hofmann, *Helv. Chim. Acta*, **37**, 849 (1954).

(7) L. Dorfman, A. Furlenmeier, C. F. Huebner, R. Lucas, H. B. Macphillamy, J. M. Mueller, E. Schlittler, and A. F. Andre, *Helv. Chim. Acta*, **37**, 59 (1954).

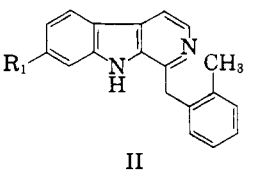
Several years ago Schlittler and his collaborators dehydrogenated the alkaloid over selenium and isolated 7-hydroxyyobyrine (IIa) together with a small amount of yobyrine (IIb).

When a solution of methyl reserpate in *p*-cymene was refluxed in an atmosphere of carbon dioxide with palladium-carbon, dehydrogenation took place readily with evolution of hydrogen. The reaction mixture was divided into chloroform- and water-soluble fractions.



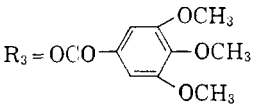
I

Ia, R_1 = OCH_3; R_2 = $COOCH_3$ R_3 = OH
Ib, R_1 = OCH_3; R_2 = $COOCH_3$

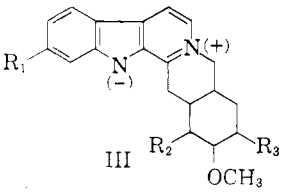


II

IIa, R_1 = OH
IIb, R_1 = H
IIc, R_1 = OCH_3



Ic, R_1 = OCH_3; R_2–R_3 = COO



III

IIIa, R_1 = OCH_3; R_2–R_3 = COO
IIIb, R_1 = OCH_3; R_2 = $COOH$; R_3 = OH

Chromatographic separation of the chloroform-soluble fraction yielded along with unchanged methyl reserpate (Ia), reserpic acid lactone (Ic), and a compound which had m.p. 230–232° and the formula $C_{20}H_{18}N_2O$ containing one methoxyl group. These properties and the fact that the ultraviolet spectrum of the compound was almost superimposable upon that of 7-hydroxyyobyrine (IIa) suggested that it must be identical with 7-methoxyyobyrine (IIc) and this inference was proved beyond doubt by direct comparison with an authentic sample.[8]

Acidification and concentration of the water-soluble fraction mentioned above gave a product which analyzed for $C_{22}H_{22}N_2O_4$.HCl, and showed a strong band in the infrared spectrum at 5.62 μ, characteristic of a γ-lactone. Hydrolysis gave as expected a hydroxy acid with a band at 6.39–6.41 μ (—COO—), while its hydrochloride absorbed strongly at 5.79 μ (—COOH). The same hydroxy acid was also isolable from the mother liquor of the above lactone when it was concentrated further after neutralization. The lactone was reformed upon treatment of the acid with acetic anhydride in pyridine. The ultraviolet absorption spectra of the lactone and its corresponding acid were very similar to that of harmine methiodide[9] as shown in Table I, a fact which indicates clearly that they

TABLE I

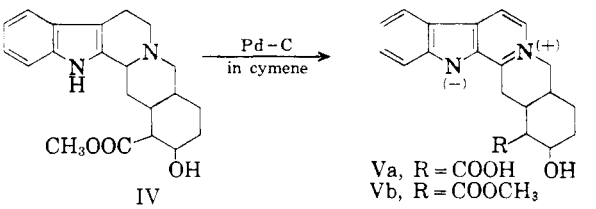
	Max (log ϵ) mμ		Min (log ϵ) mμ	Shoulder (log ϵ) mμ
Harmine-CH_3I	255 (4.38)	327 (4.28)	287 (3.04)	360 (3.98)
IIIa	252 (4.46)	332 (4.33)	285 (2.99)	365–367 (3.86)
IIIb	254 (4.47)	330 (4.30)	287 (3.14)	365 (3.83)

both contain a β-carboline chromophore, which leads to the structures, (IIIa) and (IIIb) for the lactone and the hydroxy acid, respectively.[10]

When the lactone (IIIa) was reduced with sodium borohydride, methyl isoreserpate[11] was obtained as expected. In a similar manner, the hydroxy acid (IIIb) gave isoreserpic acid.[12]

When yohimbine (IV) was subjected to dehydrogenation with palladium-carbon in *p*-cymene, the only product which could be isolated from the many experiments was *Py*-tetradehydroyohimbic acid (Va), m.p. 330–332°. It was identified by analysis and optical rotation as well as mixed melting point and comparison of ultraviolet and infrared spectra with an authentic sample prepared by oxidation of yohimbine with lead tetraacetate.[13]

In one case, though which could not be reproduced, *Py*-tetradehydroyohimbine (Vb) was isolated, as shown by direct comparison with a sample obtained by esterification of *Py*-tetradehydroyohimbic acid with methanolic hydrochloric acid.



IV

Va, R = COOH
Vb, R = $COOCH_3$

From the above results it may be concluded that, in contrast with selenium dehydrogenation, which

(8) I am indebted to Dr. W. I. Taylor of the Ciba Pharmaceutical Industries, Inc., Summit, N. J., for a mixed melting point determination and comparison of the infrared spectra.

(9) F. Pruckner and B. Witkop, *Ann.*, **554**, 127 (1943).

(10) After this work was completed, a U. S. Patent (**2,786,843**) by Huebner (to Ciba Pharmaceutical Products, Inc.) was abstracted in *Chem. Abstr.* [**51**, 12989 (1957)] in which a preparation of tetradehydroreserpic acid by the dehydrogenation of reserpic acid with lead tetraacetate was described.

(11) H. B. MacPhillamy, C. F. Huebner, and E. Schlittler, *J. Am. Chem. Soc.*, **77**, 4335 (1955).

(12) R. B. Woodward, F. E. Bader, H. Bickel, A. J. Frey, and R. W. Kierstead, *J. Am. Chem. Soc.*, **78**, 2023 (1956).

(13) G. Hahn, E. Kappes, and H. Ludewig, *Ber.*, **67**, 686 (1934).

affords yobyrine, tetrabyrine, and ketoyobyrine, but no *Py*-tetradehydroyohimbine from yohimbine, palladium-charcoal dehydrogenation in boiling *p*-cymene is, as expected, milder in behavior and resembles lead tetraacetate,[13] only ring C being dehydrogenated, while rings D and E remain unattacked.[14] The same conclusion is applicable for the case of methyl reserpate.

EXPERIMENTAL[15]

Dehydrogenation of methyl reserpate (Ia). An intimate mixture of 1 g. of methyl reserpate and 2 g. of 30% palladium-carbon prepared by the Linstead method,[16] was added to 12 ml. of *p*-cymene and the mixture refluxed gently in an atmosphere of carbon dioxide for 30 min.

After cooling, the precipitate was separated from the solution by filtration and extracted with benzene in a continuous extractor. The benzene extract and the *p*-cymene solution were combined and extracted with dilute hydrochloric acid. The aqueous layer was basified with ammonium hydroxide and extracted with chloroform (Fraction A).

The residue which was insoluble in benzene was further extracted continuously with hot methanol for 1 day, the extract concentrated to dryness, and the residue shaken with chloroform and water to give a chloroform-soluble fraction B and a water-soluble fraction C. Fractions A and B were combined, dried over sodium sulfate, and concentrated to dryness to yield a dark brown residue (200 mg.) which was chromatographed in chloroform over alumina (Brockmann, Merck).

Elution with 50 ml. of chloroform gave 70 mg. of a crystalline product, m.p. 226–229° (dec.). Recrystallization from methanol yielded pure 7-methoxyyobyrine (IIc), needles, m.p. 230–232° (dec.), (lit.[7] 230–232°) λ_{max}^{alc} 244, 303, 326, 339 mμ (log ε 4.53, 4.33, 3.86, 3.79).

Anal. Calcd. for $C_{20}H_{18}N_2O$: C, 79.44; H, 6.00; N, 9.27; 1 CH_3O, 10.26. Found: C, 79.69; H, 6.39; N, 9.05; CH_3O; 10.33.

The melting point was not depressed on admixture with an authentic sample of 7-methoxyyobyrine and the infrared spectra were identical. Further elution of the above column with 50 ml. of chloroform-methanol (200:1) gave 10 mg. of reserpic acid lactone (Ic), needles from acetone, m.p. and mixed m.p. 309–310° (dec.); λ_{max}^{alc} 229, 267, 297 mμ (log ε 4.57, 4.07, 4.14).

Anal. Calcd. for $C_{22}H_{26}N_2O_4$: C, 69.09; H, 6.85; N, 7.33. Found: C, 69.21; H, 6.89; N, 7.11.

Finally, the column was eluted with 100 ml. of chloroform-methanol (50:1) and the eluate rechromatographed on alumina and eluted with chloroform to afford 5 mg. of recovered starting material. The water-soluble fraction C was brought to *p*H 4.5 with dilute hydrochloric acid and evaporated to dryness on a steam bath, yielding 500 mg. of a dark brown residue which was dissolved in ethanol, decolorized with charcoal, and concentrated to dryness to furnish 70 mg. of pale yellow needles. Recrystallization from ethanol gave *Py*-tetradehydroreserpic acid lactone hydrochloride (IIIa), needles, m.p. 275–277.5° (dec.), $[\alpha]_D^{15}$ −63 ± 4° (C, 0.44, CH_3OH).

Anal. Calcd. for $C_{22}H_{23}ClN_2O_4$: C, 63.68; H, 5.35; N, 6.75; 2 CH_3O, 14.95. Found: C, 63.58; H, 5.56; N, 6.65; CH_3O, 14.51. Ultraviolet: λ_{max}^{alc} 252, 332 mμ (log ε 4.46, 4.33); λ_{min}^{alc} 285 mμ (log ε 2.99); shoulder, 265–276 mμ. Infrared: 5.64 μ (γ-lactone).

Further concentration of the mother liquor gave 140 mg. of a product which was dissolved in water and neutralized with ammonium hydroxide solution to yield *Py*-tetradehydroreserpic acid (IIIb), needles, m.p. 248–249° (dec.), after recrystallization from a mixture of methanol and ethanol. Ultraviolet: λ_{max}^{alc} 254, 330 mμ (log ε 4.47, 4.30); λ_{min}^{alc} 287 mμ (log ε 3.14). Infrared: 6.39–6.41 μ (COO—).

Anal. Calcd. for $C_{22}H_{24}N_2O_5 \cdot 3H_2O$: C, 58.65; H, 6.71; N, 6.21; 1 CH_3O, 13.88. Found: C, 59.19; H, 6.54; N, 6.34; CH_3O, 13.61. The hydrochloride formed needles, m.p. 246–248° (dec.) lit.[10] 260–261°, from methanol. Infrared: 5.79 μ (—COOH).

Both hydrochlorides (IIIa) and (IIIb) were soluble in water with intensive fluorescence.

Py-tetradehydroreserpic acid lactone (IIIa). A mixture of 177 mg. of *Py*-tetradehydroreserpic acid (IIIb), 1.5 ml. of acetic anhydride, and 14 ml. of pyridine were allowed to stand at room temperature for 2 days. After removal of reagents under reduced pressure, the residue was dissolved in ethanol, acidified with a few drops of concentrated hydrochloric acid to yield 103 mg. of needles, m.p. 276–278° (dec.), after recrystallization from ethanol which were identical with *Py*-tetradehydroreserpic acid lactone hydrochloride obtained above as shown by mixed melting point determination and comparison of the infrared spectra. The lactone (IIIa) was readily hydrolyzed to the acid (IIIb) m.p. 245–248° (dec.), on heating with 5% aqueous sodium hydroxide for 30 min.

Sodium borohydride reduction of Py-tetradehydroreserpic acid lactone (IIIa). To a solution of 95 mg. of (IIIa) in 5 ml. of methanol, 0.5 g. of sodium borohydride was added portionwise. After the vigorous reaction had ceased, the mixture was refluxed for 1.5 hr. After removal of the solvent a small amount of water was added and the mixture extracted with chloroform. The chloroform solution was extracted with dilute hydrochloric acid, the acid layer made alkaline with ammonium hydroxide and extracted into chloroform. Removal of the chloroform afforded 80 mg. of a gum which after chromatography in chloroform-on-alumina, followed by conversion into its picrate, formed reddish orange needles (40 mg.), m.p. 212–213° (dec.), after recrystallization from methanol, which was identical in all respects with an authentic sample of methyl 3-isoreserpate picrate. The infrared spectrum contained a band at 5.72 μ.

Anal. Calcd. for $C_{29}H_{33}N_5O_{12} \cdot H_2O$: C, 52.64; H, 5.17; N, 10.57. Found: C, 52.89; H, 5.24; N, 10.58.

Reduction of (IIIb) *with sodium borohydride* (*formation of 3-isoreserpic acid*). To a solution of 150 mg. of (IIIb) in 10 ml. of methanol was added in portions 1 g. of sodium borohydride and the mixture heated under reflux for 1 hr. After concentration of the reaction mixture, water was added, neutralized with hydrochloric acid, and extracted with a mixture of chloroform and methanol (1:1). The extract, when evaporated to dryness, gave a residue which was recrystallized from methanol or ethanol yielding 50 mg. of needles, m.p. 261–262° (dec.), identical with an authentic sample of 3-isoreserpic acid. The hydrochloride formed needles, m.p. 275–279° (dec.), from methanol. The picrate was obtained as yellow prisms from ethanol, m.p. 234–235° (dec.), and identical with 3-isoreserpic acid picrate prepared from isoreserpine as shown by the infrared spectra.

Anal. Calcd. for $C_{28}H_{31}N_5O_{12}$: C, 53.41; H, 4.96; N, 11.13. Found: C, 53.33; H, 5.08; N, 11.11.

Dehydrogenation of yohimbine (IV). (*a*) One g. of yohimbine

(14) It may be mentioned that Le Hir, Goutarel, and Janot [*Bull. soc. chim.*, 866 (1954)] reported a few years ago that yohimbane gave *Py*-tetradehydroyohimbane on dehydrogenation over palladium-carbon at 280° while alloyohimbane afforded under the same conditions sempervirine, an octadehydro derivative.

(15) All melting points are uncorrected. Ultraviolet absorption spectra were determined by a Beckman DK spectrophotometer and infrared determinations were by means of Nujol mull, using a Perkin-Elmer Model 21 recording spectrophotometer. Microanalyses were performed by Mr. Y. Utsui of this laboratory.

(16) R. P. Linstead, A. F. Millidge, S. L. S. Thomas, and A. L. Walpole, *J. Chem. Soc.*, 1146 (1937).

and 2 g. of 30% palladium-carbon were heated under reflux in 12 ml. of *p*-cymene under carbon dioxide atmosphere for 2 hr., during which time 70 ml. of gases evolved. After cooling, the precipitate was collected by filtration, washed with benzene, and extracted with methanol in a continuous extractor. After evaporation of the methanol and addition of water, the mixture was acidified with dilute hydrochloric acid to *p*H 4.8 and extracted with chloroform to remove the unchanged starting material. The aqueous layer was treated with decolorizing charcoal, and concentrated to dryness to give a brown material (580 mg.) which was crystallized from methanol-acetone and then from methanol to give 60 mg. of *Py*-tetradehydroyohimbine hydrochloride (Vb), yellow prisms, m.p. 234–234.5° (dec.), $[\alpha]_D^{17}$ +216.3° (C, 0.36, AcOH). Ultraviolet: λ_{max}^{alc} 255, 306, 361 mμ (log ε 4.45, 4.35, 3.71); λ_{min}^{alc} 226, 280, 325 mμ (log ε 4.13, 3.78, 3.25).

Anal. Calcd. for $C_{21}H_{23}ClN_2O \cdot {}^3/_5CH_3OH$: C, 63.88; H, 6.30; N, 6.89; ${}^3/_5CH_3O$, 12.23. Found: C, 63.47; H, 6.34; N, 6.70; CH_3O, 12.22.

(*b*) In a second run, 1.0 g. of yohimbine was dehydrogenated as above and the precipitate was extracted with benzene and then with methanol. The methanol extract was evaporated to give a brown oil (780 mg.) which was washed with chloroform and then crystallized from methanol to give 80 mg. of needles. Recrystallization from methanol gave *Py*-tetradehydroyohimbic acid (Va), pale yellow needles m.p. 330–332° (dec.), $[\alpha]_D^{16}$ +241.4° (C, 0.319, AcOH). Ultraviolet: λ_{max}^{alc} 225, 306, 364 mμ (log ε 4.37, 4.26, 3.62); λ_{min}^{alc} 226, 280, 325 mμ (log ε 4.03, 3.70, 3.16).

Anal. Calcd. for $C_{20}H_{20}N_2O_3$: C, 71.39: H, 5.99; N, 8.33. Found: C, 71.91; H, 5.97; N, 8.35.

The above benzene extract was shaken with dilute hydrochloric acid. The aqueous layer was made alkaline with ammonium hydroxide and extracted with chloroform. The chloroform extract was chromatographed over alumina to furnish 10 mg. of unchanged yohimbine.

Esterification of (Va) [*formation of Py-tetradehydroyohimbine* (Vb)]. Eight mg. of *Py*-tetradehydroyohimbic acid (Va) was heated under reflux in 5 ml. of 5% methanolic hydrochloric acid for 2 hr. After removal of the solvent under reduced pressure, the residue was triturated with methanol to yield pale brownish crystals, m.p. 227–230° (dec.), after recrystallization from methanol, the infrared spectrum of which was identical with that of the hydrochloride of (Vb).

Acknowledgment. The author is indebted to Professor S. Uyeo of the University of Osaka for helpful discussions and suggestions. The continued interest of Dr. S. Kato, Director of this laboratory, and the invaluable help and advice of Dr. S. Ose of this laboratory are gratefully acknowledged.

OSAKA, JAPAN

[CONTRIBUTION NO. 20 FROM THE L. G. RYAN RESEARCH LABORATORIES, MONSANTO CANADA LTD.]

Amino Acids. IX.[1] 1,3-Di(ω-carbamylalkyl)-ureas and -thioureas and Their Chemistry

E. J. TARLTON, S. GELBLUM, M. A. MOSLEY, AND A. F. McKAY

Received July 7, 1958

1,3-Di(ω-carbamylalkyl)-ureas and -thioureas were prepared by the ammonolysis and aminolysis of 1,3-di(ω-carbalkoxyalkyl)-ureas and -thioureas. The nitrosation of these amides and the properties of the resulting nitrosamide derivatives are described.

In conjunction with studies on 1,3-di(ω-carboxyalkyl)-thioureas and -ureas,[2] a series of diamides of these dicarboxylic acids have been synthesized. These derivatives (Table I) were prepared by two general methods: A, aminolysis or ammonolysis of the dicarboxylic acid dimethyl esters and B, the reaction of amines with the mixed dianhydrides from 1,3-di(ω-carboxyalkyl)ureas and ethyl hydrogen carbonate.

The aminolysis and ammonolysis reactions were performed in methanolic solution in the presence of sodium methoxide[3,4] as catalyst. Under similar reaction conditions, ammonia, benzylamine, and most primary straight chain amines reacted with 1,3-di-(ε-carbomethoxypentyl)urea (Ia) to give good yields of the corresponding diamides (II). With dodecylamine, hexadecylamine, and octadecylamine, the intermediate monoamide-monoesters (Table II) separated from solution readily and hence prevented complete aminolysis. These latter products were identified by their analyses and infrared spectra which showed the presence of carbonyl bands due to the ester group (1729 cm.$^{-1}$) together with those of the amide (1634–1637 cm.$^{-1}$) and urea (1610–1618 cm.$^{-1}$) functions.

Of the branched chain primary amines, those with branching on the carbon alpha to the nitrogen atom (isopropylamine, *t*-butylamine, cyclohexylamine) failed to react under the same experimental conditions. However, with the branching farther along the chain (2-*N*,*N*-dimethylaminoethylamine, 2-*N*,*N*-diethylaminoethylamine, 3-*N*,*N*-dimethylaminopropylamine) the aminolysis proceeded normally. With secondary amines (dimethylamine, diethylamine, di-*n*-butylamine), only dimethylamine reacted to give a diamide (II), while the remaining reaction mixtures yielded starting material. These

(1) Paper VIII: A. F. McKay, D. J. Whittingham, and M.-E. Kreling, *J. Am. Chem. Soc.*, **80**, 3339(1958).

(2) A. F. McKay, E. J. Tarlton, S. I. Petri, P. R. Steyermark, and M. A. Mosley, *J. Am. Chem. Soc.*, **80**, 1510 (1958).

(3) R. L. Betts and L. P. Hammett, *J. Am. Chem. Soc.*, **59**, 1568 (1937).

(4) P. B. Russell, *J. Am. Chem. Soc.*, **72**, 1853 (1950).