sample was obtained after two crystallizations from benzene and melted at 151–152°.

Anal. Calcd. for $C_{16}H_{20}N_2O_3$: C, 66.6; H, 7.0. Found: C, 66.3; H, 6.8.

DL-*α-Amino-β-(3-methyl-2-indole) propionic acid* (DL-*3-methyl-2-isotryptophane*) (VI). Crude V (1.6 g., 0.006 mole) was mixed with a solution of sodium hydroxide (2.3 g., 0.057 mole) in water (23 ml.) and the mixture refluxed in a copper flask for 18 hr. Toward the end of this period, the reaction mixture was refluxed with Norit and filtered hot. The filtrate when acidified with glacial acetic acid gave an initial crop (125 mg.) of some infusible material. The filtrate from this initial crop was concentrated by evaporation to give successive crops totaling 0.7 g. (58%) of amino acid; m.p. 205–214°. A sample for analysis was prepared by evaporating a solution of the amino acid in hot water until enough material was obtained. This material was rinsed with a small amount of ethanol and the crystals dried *in vacuo* at 100° for 12 hr.; m.p. 219–223°.

Anal. Calcd. for $C_{12}H_{14}N_2O_2$: C, 66.0; H, 6.5. Found: C, 66.3; H, 6.8.

The aminoacid gave a positive Ninhydrin test. The R_f value found in butanol–acetic acid–water (4:1:5) was 0.69.

2-Chloracetamido-1-ethylbenzene. To a solution of *o*-aminoethylbenzene (39.1 g., 0.32 mole) in chloroform (80 ml.) was added pyridine (30 g., 0.43 mole) and chloracetyl chloride (38.4 g., 0.34 mole) with stirring and cooling. After addition was over, the reaction was completed by heating on a water bath for 0.5 hr. and the mixture poured into water (500 ml.). The chloroform layer was separated and the aqueous layer again extracted with chloroform. The combined extracts were washed with water, dried over calcium chloride, and chloroform removed. The residue was crystallized from methanol; m.p. 88–90°; yield 58 g. (91%).

Anal. Calcd. for $C_{10}H_{12}ClNO$: C, 60.7; H, 6.1. Found: C, 60.7; H, 6.3.

2-Dimethylaminoacetamido-1-ethylbenzene. A solution of 2-chloracetamido-1-ethylbenzene (33 g., 0.167 mole) in dry benzene (330 ml.) was mixed with a 4% solution (400 ml., 0.356 mole) of dimethylamine in benzene and the mixture was allowed to stand overnight. Dimethylamine hydrochloride which had separated was removed by washing with water and the base extracted from the benzene layer with 2*N* hydrochloric acid. The acid extract was made basic with ammonia and the oil which separated extracted with ether. The ether extract was stripped of solvent and the residue distilled; b.p. 174–176°/5 mm. (also 148–149°/1 mm.); yield 24.5 g. (71%). The product solidified on cooling and was crystallized from petroleum ether; m.p. 39°.

Anal. Calcd. for $C_{12}H_{18}N_2O$: C, 69.8; H, 8.8. Found: C, 69.4; H, 8.7.

The base furnished a methiodide which was crystallized from a mixture of methanol and ether; m.p. 120–125°.

Anal. Calcd. for $C_{13}H_{21}IN_2O$: C, 44.8; H, 6.1. Found: C, 45.2; H, 6.1.

Attempts to prepare a crystalline picrate of the base failed.

Reaction of 2-dimethylaminoacetamido-1-ethylbenzene with sodamide. An ether solution (25 ml.) of 2-dimethyl aminoacetamido-1-ethylbenzene (15.2 g., 0.074 mole) was mixed with sodamide (8 g., 0.205 mole) in a 250-ml. 3-necked flask in an atmosphere of nitrogen and the ether was removed. The dry residue was heated on a metal bath to 310° over a period of 0.5 hr. and maintained at that temperature for an additional 0.25 hr. The reaction mixture was then cooled, decomposed cautiously with ethanol (25 ml.) followed by water (100 ml.) and extracted with benzene. The benzene solution was extracted with two 60-ml. portions of 7% hydrochloric acid. The acid extract was made alkaline with sodium carbonate and base taken up in benzene. The benzene layer after drying over solid potassium hydroxide furnished crude liquid (11.7 g.) which was fractionated *in vacuo* through a 6″ Vigreux column. After a forerun (1.5 g.) at 113–115°/1.5 mm., the main fraction (9 g.) was collected at 170–175°/1.5 mm. Refractionation of the latter afforded fractions I (1.4 g.) and II (7 g.) with b.p. 154–158°/1.5 mm. and 165–168°/1.5 mm., respectively. Each fraction afforded a picrate which after crystallization from ethanol or methanol had m.p. and mixed m.p. 206–208° with an authentic specimen of the picrate of 2-dimethylaminomethyl-3-methylindole. With methyliodide, both fractions gave a methiodide m.p. 110–115° which after crystallization from a mixture of methanol and ether had m.p. 120–125° undepressed by the methiodide of the uncyclized base. In other runs, whereas the different fractions gave consistently the same picrate, the methiodides obtained had varying melting points and were apparently mixtures of the methiodides of both the starting material and product.

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Syntheses of Pyrrolizidine, Indolizidine, and Related Compounds

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We[1] found that the treatment of diethyl 5-oxoazelate (Ia) with ammonia afforded a compound of Δ^5-piperidone type (IIa) and subsequent high-pressure hydrogenation of it with copper chromite catalyst proceeded successfully to quinolizidine (IIIa). An application of these reactions for preparing a diazatricyclo compound, 9-methyl-9-azahexahydrojulolidine (VIa), from 1-methyl-3,5-bis(β-ethoxycarbonylethyl)-4-piperidone (IVa) was also reported by us.[1] It is, therefore, of interest to study this reaction on other keto diesters.

When diethyl 4-oxopimelate (Ib),[2] diethyl 4-oxosuberate (Ic),[2] 1-methyl-3,5-bis(ethoxycarbonylmethyl)-4-piperidone (IVb), and 1-methyl-3-(β - ethoxycarbonylethyl) - 5 - (ethoxycarbonylmethyl)-4-piperidone (IVc) were treated with ammonia in alcohol or water, all were converted to monocyclic (IIb and IIc, in 40–50% yield), or bicyclic (Vb and Vc, in 20–30% yield) lactams respectively.

These lactams did not show any absorption bands in the ultraviolet region above 200 mμ (*cf.* the lactams,[1] IIa and Va showed their maxima at 203 mμ in water). In the infrared, the stretching vibrational bands for the ring carbonyl (-CONH-)[1] were observed at 1724, 1712, 1725, and 1704 $cm.^{-1}$ respectively for IIb, IIc, Vb, and Vc, while the bands of IIa and Va were located at 1675 and 1684

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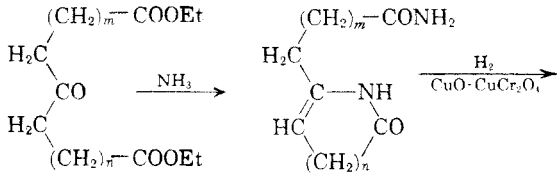
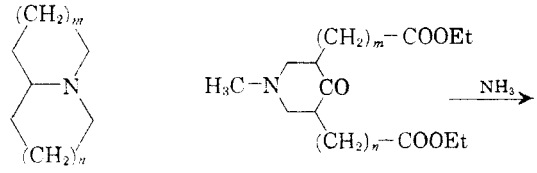
(2) N. J. Leonard and W. E. Goode, *J. Am. Chem. Soc.*, 72, 5404 (1950).

cm.$^{-1}$ IIb and Vb must possess the 5-membered Δ^4-pyrrolidone structure. A comparison of the spectra of these compounds with the previously reported IIa and Va, which must possess a 6-membered ring structure, shows the hypsochromic displacements of IIc and Vc analogous to that shown by IIb and Vb, thus favoring the Δ^4-pyrrolidone structure for IIc and Vc.

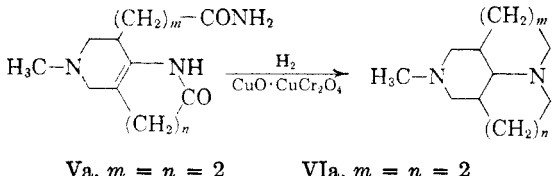
Hydrogenations of IIb and IIc with copper chromite catalyst at high pressure and high temperature afforded pyrrolizidine (IIIb)[2,3] and indolizidine (IIIc)[2,4] in about 60% yield. Hexahydropyrido[3,4,5-*g*,*h*]pyrrolizidine (VIb) and hexahydropyrido[3,4,5-*h*,*i*]indolizidine (VIc) were produced in 40–50% yield respectively from Vb and Vc in the same manner.



Ia, $m = n = 2$ IIa, $m = n = 2$
Ib, $m = n = 1$ IIb, $m = n = 1$
Ic, $m = 2; n = 1$ IIc, $m = 2; n = 1$



IIIa, $m = n = 2$ IVa, $m = n = 2$
IIIb, $m = n = 1$ IVb, $m = n = 1$
IIIc, $m = 2; n = 1$ IVc, $m = 2; n = 1$



Va, $m = n = 2$ VIa, $m = n = 2$
Vb, $m = n = 1$ VIb, $m = n = 1$
Vc, $m = 2; n = 1$ VIc, $m = 2; n = 1$

EXPERIMENTAL[5]

1-Methyl-3,5-bis(ethoxycarbonylmethyl)-4-piperidone (VIb). A mixture of 88 g. (1 mole equivalent) of diethyl 3,5-diethoxycarbonyl-4-oxopimelate,[2] 16.2 g. (1 mole equivalent) of methylamine hydrochloride, and 24.3 g. (1 mole equivalent) of potassium bicarbonate was dissolved in aqueous alcohol containing 44.8 ml. (2 mole equivalent) of 33% formaldehyde. The mixture was allowed to stand at 25–28° for 4 days. After condensing the mixture under reduced pressure, the residue was treated with 10% hydrochloric acid and the insoluble material was removed by ether. The aqueous layer was made basic with potassium carbonate and the oily base was extracted with ether. The extract was washed and dried and the ether was evaporated. The residue was distilled under reduced pressure to give *1-methyl-3,5-diethoxycarbonyl-3,5-bis(ethoxycarbonylmethyl)-4-piperidone* (VII), b.p. 165–167°/0.2 mm., yield 42 g. (45%).

The *picrate* was obtained as yellow needles from ethanol, m.p. 112–113°.

Anal. Calcd. for $C_{20}H_{31}NO_9.C_6H_3N_3O_7$: C, 47.41; H, 5.16; N, 8.52. Found: C, 47.53; H, 5.32; N, 8.90.

A solution of 42 g. of VII dissolved in a mixture of 300 ml. of concentrated hydrochloric acid and 120 ml. of water was refluxed for 25 hr. After distilling the water under reduced pressure, a crystalline salt remained. Recrystallization from ethanol gave colorless plates, m.p. 198° (decomp.).

Anal. Calcd. for $C_{10}H_{15}NO_5.HCl$: C, 45.50; H, 6.07; N, 5.32. Found: C, 45.66; H, 6.26; N, 5.71.

A solution of 280 ml. of absolute ethanol and 1.5 ml. of concentrated sulfuric acid was added to the salt, and the mixture was refluxed for 30 hr. The solvent was removed under reduced pressure. The residue was dissolved in 10% hydrochloric acid, the solution was made basic with potassium carbonate, and the base was extracted with ether. The extract was washed and dried and the ether was evaporated. The residue was distilled to give IVb, b.p. 135–139°/0.2 mm., in a yield of 20 g. (75%). Crystallization from petroleum ether gave colorless plates, m.p. 45.5–46.5°.

Anal. Calcd. for $C_{14}H_{23}NO_5$: C, 58.98; H, 8.08; N, 4.92. Found: C, 59.13; H, 8.12; N, 5.06.

The *picrate* was obtained as yellow needles from ethanol, m.p. 148–149°, and the *picrolonate* as yellow plates from ethanol, m.p. 174–175°.

1-Methyl-3-(β-ethoxycarbonylethyl)-5-(ethoxycarbonylmethyl)-4-piperidone (IVc). A mixture of 116 g. of diethyl 3,5-diethoxycarbonyl-4-oxosuberate,[2] 23 g. of methylamine hydrochloride, 30 g. of potassium hydrogen carbonate, and 46 g. of 30% formaldehyde was treated as described above to yield 64 g. (48%) of 1-methyl-3,5-diethoxycarbonyl-3-(ethoxycarbonylmethyl) - 5 - (β - ethoxycarbonylethyl) - 4-piperidone, b.p. 179–182°/0.1 mm. To 60 g. of this product, 520 ml. of concentrated hydrochloric acid and 200 ml. of water were added and the mixture was refluxed for 24 hr. After evaporating the solvent under reduced pressure, the residue was again refluxed for 30 hr. in a solution of 450 ml. of absolute ethanol and 3 ml. of concentrated sulfuric acid. IVc was obtained after the treatment described above, b.p. 155–159°/0.2 mm., in a yield of 33 g. (80%).

The *picrate*, yellow needles from ethanol, melted at 114–115°.

Anal. Calcd. for $C_{15}H_{25}NO_5.C_6H_3N_3O_7$: N, 10.64. Found: N, 10.21.

The *picrolonate*, yellow needles from ethanol, melted at 169–170° (decomp.).

Anal. Calcd. for $C_{15}H_{25}NO_5.C_{10}H_8N_4O_5$: C, 53.30; H, 5.86; N, 12.40. Found: C, 53.29; H, 5.94; N, 12.30.

Cyclization reaction of oxocarboxylic diesters (Ib, Ic, IVb, IVc) *with ammonia. General procedure.* Ammonia was passed into a solution of one part of Ib (or Ic) in 10 parts (v.) of absolute ethanol and the precipitated crystalline product (IIb or IIc) was collected. In the case of IVb (or IVc), a mixture of one part of IVb (or IVc) and 10 parts (v.) of 28% ammonia water was agitated until it was completely dissolved. After evaporating the aqueous ammonia under diminished pressure, the residue was dried with heating for 1 hr. to give crystalline Vb (or Vc). IIb: colorless prisms from ethanol, m.p. 274° (decomp.); yield 46%.

Anal. Calcd. for $C_7H_{10}N_2O_2$: C, 54.53; H, 6.54; N, 18.17. Found: C, 54.70; H, 6.31; N, 18.48.

IIc: Colorless prisms from methanol, m.p. 285° (decomp.); yield 43%.

Anal. Calcd. for $C_8H_{12}N_2O_2$: C, 57.13; H, 7.19; N, 16.66. Found: C, 57.05; H, 7.38; N, 16.40.

Vb: Colorless prisms from ethanol, m.p. 268° (decomp.); yield 25%.

Anal. Calcd. for $C_{10}H_{15}N_3O_2$: C, 57.41; H, 7.23; N, 20.08. Found: C, 57.32; H, 7.08; N, 20.15.

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(5) All melting and boiling points were uncorrected.

Vc: Colorless prisms from methanol, m.p. 276° (decomp.); yield 27%.

Anal. Calcd. for $C_{11}H_{17}N_3O_2$: C, 59.20; H, 7.63; N, 18.80. Found: C, 59.53; H, 7.62; N, 18.87.

High pressure hydrogenations of IIb, IIc, Vb, and Vc. General procedure. A mixture of one part of IIb (or IIc, Vb, Vc) and 1–2 parts of copper chromite in 20–30 parts of dioxane (v.) was submitted to hydrogenation at 250° and 130 atmospheres (initial pressure) for 1 hr. In the case of IIb or IIc, the reaction mixture was filtered, dry hydrogen chloride was passed into the filtrate, and dioxane was removed under reduced pressure. After adding water to the residue, it was made basic with potassium carbonate, the base was extracted with ether, the extract was washed and dried, the ether was evaporated, and the remaining material was distilled. In the case of Vb or Vc, the filtrate was directly stripped under reduced pressure and the residual oil was distilled. *Pyrrolizidine* (IIIb), b.p. 135°, yield 55%, formed a picrate, longish yellow needles from ethanol, m.p. 253° (decomp.). A mixed melting point with the sample prepared by the method of Leonard, *et al.*[2] showed no depression. *Indolizidine* (IIIc): b.p. 70–80° (bath temp.)/30 mm., yield 66%. *Picrate:* yellow needles from ethanol, m.p. 233°. A mixed melting point with the sample prepared by the method of Leonard, *et al.* showed no depression. *2-Methyl-hexahydropyrido[3,4,5-g,h]-pyrrolizidine* (VIb): b.p. 70–90°/4 mm., yield 40%. This was dissolved in ethanol containing sulfamic acid and the separated sulfamate solidified on standing for several days. It melted at 127° and was difficult to recrystallize because of its hygroscopic nature. The salt was dissolved in water, the solution was made basic with potassium hydroxide, and the base was extracted with ether. The purified oil distilled at 70–72°/4 mm.

Anal. Calcd. for $C_{10}H_{18}N_2$: C, 72.24; H, 10.91; N, 16.85. Found: C, 72.35; H, 10.91; N, 16.70.

Monohydrate crystallized from this oil on standing in air. Recrystallization from petroleum ether gave colorless prisms, m.p. 160°.

Anal. Calcd. for $C_{10}H_{18}N_2.H_2O$: C, 65.17; H, 10.94; N, 15.21. Found: C, 65.41; H, 10.70; N, 15.38.

2-Methyl-hexahydropyrido[3,4,5-h,i]-indolizidine (VIc): b.p. 140–180° (bath temp.)/12 mm., yield 54%. Purified base prepared through its flavianate distilled at 145–150° (bath temp.)/12 mm.

Anal. Calcd. for $C_{11}H_{20}N_2$: C, 73.28; H, 11.18; N, 15.55. Found: C, 73.01; H, 11.01; N, 15.32. *flavianate:* yellow needles from water, m.p. 267° (decomp.).

Anal. Calcd. for $C_{11}H_{20}N_2.2C_{10}H_6N_2O_8S$: C, 46.05; H, 3.96; N, 10.04. Found: C, 46.33; H, 3.90; N, 9.92.

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Infrared Spectra of Some Naturally Occurring Flavonoids

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Numerous infrared spectra of some naturally occurring flavonoids have been recorded for rapid structural elucidation of these structures in the course of studying the occurrence of flavonoids in allergenic pollens. Flavonoid pigments have been found to be widely distributed in pollen. In 1919 Heyl isolated a quercetin glucoside and isorhamnetin from ragweed pollen.[2] Stevens, Moore, and Baer[3] have recently shown a quercetin glucoside from giant ragweed pollen to be isoquercitrin. Some of the other flavonoids isolated from pollen are rutin,[4] isorhamnetin-3,4′-diglucoside,[5,6] and a isorhamnetin-3-trisaccharide.[7]

EXPERIMENTAL

Materials: Samples of apiin (5,7,4′-trihydroxyflavone-7-apioside), chrysosplenin (5,4′-dihydroxy-6,7,3′-trimethoxyflavone-3-glucoside), luteolin-7-glucoside (5,3′,4′-trihydroxyflavone-7-glucoside), pectolinarin (5-hydroxy-6,3′-dimethoxyflavone-7-rhamnoglucoside), reynoutrin (5,7,3′,4′-tetrahydroxyflavone-3-xyloside), robinin (5,4′-dihydroxyflavone-3-robinobio-7-rhamnoside), chrysosplenetin (3,5,4′-trihydroxy-6,7,3′-trimethoxyflavone), and luteolin (5,3′,4′-trihydroxyflavone) were kindly supplied by Dr. Tashichiro Nakaoki. Dr. Richard Kuhn kindly supplied samples of isorhamnetin (3,5,7,4′-tetrahydroxy-3′-methoxyflavone) and 3,4′-dihydroxy-5,7,3′-trimethoxyflavone, and Dr. Simon H. Wender kindly supplied the samples of apigenin-7-rhamnoglucoside (5,7,4′-trihydroxyflavone-7-rhamnoglucoside) and naringin (5,7,4′-trihydroxyflavanone-7-rhamnoglucoside). The sample of flavone was kindly sent to us by Dr. T. S. Wheeler. Dactylin (isorhamnetin-3,4′-diglucoside) was isolated from timothy pollen.[6]

Infrared spectra. The spectral data recorded in Table I were obtained by a recording Perkin-Elmer infrared spectrometer, Model 21. The flavonoids were dissolved in dimethylformamide and placed on a micro silver chloride plate. The solvent was removed by means of an infrared heat lamp. A smooth film of flavonoid was deposited on the plate. A drop of Nujol on the film gave sharp spectra.

DISCUSSION

Hergert and Kurth[8] in 1953 reported some infrared spectral studies on some flavanones, flavones, chalcones, and acetophenones. The small number of naturally occurring flavones and flavonols employed in their study did not make it possible to assign any specific absorption region for the carbonyl band. In the present study, the naturally occurring flavonoids recorded in Table I reveal a specific carbonyl region for naturally occurring flavones and flavonols. The flavones, apigenin-7-rhamnoglucoside, apiin, pectolinarin, luteolin, and luteolin-7-glucoside, recorded in Table I have carbonyl absorption bands between 1660 cm.$^{-1}$ and 1655 cm.$^{-1}$

The flavonols, chrysosplenetin, chrysosplenin, dactylin, isorhamnetin, quercetin, quercitrin, rey-

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