ethyl ether to the solution. The white crystalline material (28 g., 55% yield) was recrystallized from an ethanol-ethyl acetate solvent system. The compound melted at 217.0–217.8°.

Anal. Calc'd for $C_{23}H_{32}BrN$: C, 68.64; H, 8.02; Br, 19.86; N, 3.48. Found: C, 68.45; H, 7.91; Br, 19.5; N, 3.42.

1-(Diphenylmethyl)-4-methylpiperidine hydrobromide (II). 1-(Diphenylmethyl)-4-methylpyridinium bromide[2] (25 g., 0.0735 mole) was dissolved in 500 ml. of aqueous 49% ethanol and hydrogenated, in two portions, as described in the preparation of I. The reaction mixtures were combined, the platinum oxide was filtered off, and the solvents were removed under reduced pressure (max. pot temp. 50°). The crystalline residue was recrystallized from ethanol, yielding a total of 8.6 g. (33.8% yield) of product. The product was further purified by recrystallization from the ethanol-ethyl acetate solvent system. The crystalline material sintered at 160° and melted at 218.6–219.5°. The compound was dried at 130°/0.1 mm. for 1–2 hours immediately preceding analysis.[3]

Anal. Calc'd for $C_{19}H_{24}BrN$: C, 65.90; H, 6.99; Br, 23.08; N, 4.05. Found: C, 65.87; H, 7.00; Br, 22.8; N, 3.99.

The pharmacological evaluation of these compounds is in progress.

DEPARTMENT OF PHARMACOLOGY
DIVISION OF BASIC HEALTH SCIENCES
EMORY UNIVERSITY, GEORGIA

(3) The analytical laboratory reported sublimation during this operation.

Reaction Between Acrolein and Ethyl β-Aminocrotonate

K. TSUDA, Y. SATCH, N. IKEKAWA, AND H. MISHIMA

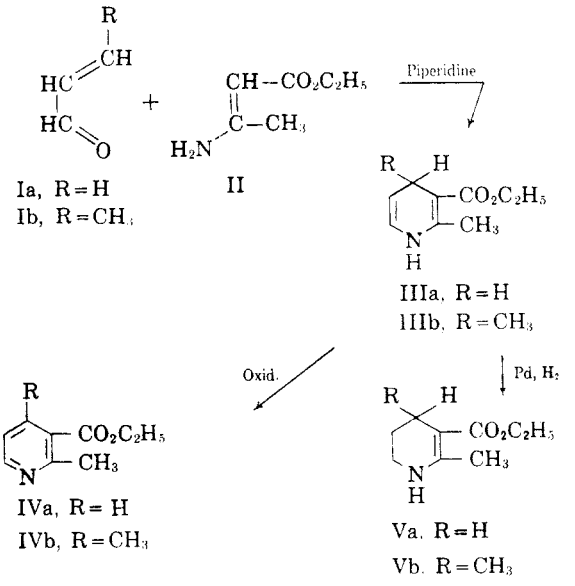
Received March 7, 1956

Reaction of acrolein (I) with ethyl β-aminocrotonate (II) in ethanol with piperidine as catalyst leads to the formation of 57% of ethyl 2-methyl-1,4-dihydronicotinate (IIIa), 15% of ethyl 2-methylnicotinate (IVa),[1] and 28% of a material assumed from ultraviolet absorption data to be a mixture of IIIa and an ethyl 2-methyltetrahydronicotinate.

The product IIIa, obtained crystalline by distillation of the crude reaction mixture, showed an infrared absorption maximum at 3500 cm.$^{-1}$, indicating the presence of the >NH function. Ultraviolet absorption maxima were observed at 220 and at 375 mμ, similar to those observed by Bohlmann and Bohlmann[2] for the 1,4-dihydro compounds obtained by lithium aluminum hydride reduction of ethyl dinicotinate and ethyl 2-methyldinicotinate. Reduction of IIIa over palladium affords ethyl 2-methyl-1,4,5,6-tetrahydronicotinate (Va).[3] Compound IIIa gives a positive reaction with silver nitrate, and is easily attacked by oxidizing agents. It is converted to IVa by such reagents as nitrous and nitric acids, picric acid, and air. Repeated recrystallization of the picrate of IIIa from ether gives the picrate of IVa. Distillation of IIIa in a vacuum leads to partial conversion of this substance to IVa, suggesting that IVa was formed from IIIa during vacuum distillation of the crude reaction product of Ia with II.

Reaction of crotonaldehyde (Ib) with II gave IIIb as the only isolated reaction product in 75% yield. Compound IIIb showed an ultraviolet absorption spectrum similar to that of IIIa. Although IIIb is less reactive toward oxidation than is IIIa, oxidation with nitric acid gives ethyl 2,4-dimethylnicotinate (IVb).

On shaking IIIa or IIIb with a palladium catalyst in methanol at room temperature, a disproportionation occurs leading to the formation of mixtures of IVa and Va or IVb and Vb respectively.



Ia, R = H
Ib, R = CH_3

II

IIIa, R = H
IIIb, R = CH_3

IVa, R = H
IVb, R = CH_3

Va, R = H
Vb, R = CH_3

EXPERIMENTAL[4]

Condensation of acrolein with ethyl β-aminocrotonate. Acrolein, 31 g. (0.55 mole), was added during a period of two hours to a stirred solution of 65 g. (0.5 mole) of ethyl β-aminocrotonate and 2 g. of piperidine in 250 ml. of anhydrous ethanol at 40–50°. After addition was complete, the solution was heated to reflux for 3 hours, during which time the color changed from yellow to brown. The ethanol was removed by distillation, and the residue was distilled under reduced pressure to give: (1) 7.5 g. of oil, b.p. 100–120° (5 mm.); (2) 27.6 g. of crystalline material, b.p. 125–127° (5 mm.); and (3) 13.6 g. of oil, b.p. 130–140° (5 mm.).

Fraction (1) showed λ_{max}^{EtOH} 220 mμ (ε = 7.55) and 268 mμ (ε = 3.47) and gave a *picrate*, needles, m.p. 146°, which did not depress the m.p. of a known sample of ethyl 2-methylnicotinate picrate.

Anal. Calc'd for $C_{15}H_{14}N_4O_9$: C, 45.69; H, 3.58; N, 14.21. Found: C, 45.74; H, 3.34; N, 14.01.

Fraction (2) showed m.p. 50–60°; recrystallization from

(1) P. Baumgarten and A. Dornow, *Ber.*, **72**, 564 (1939); A. Dornow and H. Bormann, *Ber.*, **82**, 216 (1949); E. Ochiai and Y. Ito, *Ber.*, **74**, 1111 (1941).

(2) F. Bohlmann and M. Bohlmann, *Ber.*, **85**, 1419 (1953).

(3) N. F. Albertson, *J. Am. Chem. Soc.*, **74**, 3816 (1952).

(4) Melting and boiling points are uncorrected.

petroleum ether gave plates, m.p. 71–72°, which liquified on exposure to air at room temperature. The substance showed λ_{max}^{EtOH} 210 mμ (ε = 11.52) and 349–350 mμ (ε = 6.00). Infrared absorption maxima were observed at 3500, 1690, and 1614 cm.$^{-1}$, indicating the presence of >NH, >CO and >C=C< respectively. The substance is assigned the structure of ethyl 2-methyl-1,4-dihydronicotinate (IIIa).

Anal. Calc'd for $C_9H_{13}NO_2$: C, 64.7; H, 7.78; N, 8.39. Found: C, 64.81; H, 7.57; N, 8.56.

Compound IIIa gave a *red picrate* from ether solution which changed to yellow needles on repeated crystallization, m.p. 146°. The recrystallized material failed to depress the m.p. of known ethyl 2-methylnicotinate picrate. Redistillation of fraction (2) gave about 50% conversion to ethyl 2-methylnicotinate.

Fraction (3) exhibited a broad absorption band at 270–290 mμ and another band at 350 mμ, suggesting that this fraction is a mixture of IIIa and ethyl 2-methyl-1,4,5,6-tetrahydronicotinate.

Oxidation of ethyl 2-methyl-1,4-dihydronicotinate. The crude reaction product of condensation of acrolein with ethyl β-aminocrotonate, 48 g., was added to a mixture of 28 g. of conc'd sulfuric acid, 30 g. of conc'd nitric acid, and 90 g. of water. The mixture was cautiously warmed on a water-bath with occasional shaking; effervescence occurred for about 10 minutes. The resulting mixture was extracted with ether to remove a neutral substance, made basic, and again extracted with ether. Drying of the ether extract over sodium sulfate, removal of ether, and distillation of the residue gave 28.7 g. (61%) of ethyl 2-methylnicotinate, b.p. 107° (13 mm.), m.p. of *picrate* 146°, λ_{max}^{EtOH} 220 mμ (ε = 7.55) and 268 mμ (ε = 3.47).

Condensation of crotonaldehyde with ethyl β-aminocrotonate. Crotonaldehyde, 23 g. (0.33 mole), was condensed with 39 g. (0.30 mole) of ethyl β-aminocrotonate in 20 ml. of anhydrous ethanol containing 1 g. of piperidine by the procedure described above for the acrolein condensation. There was obtained 41 g. (75%) of ethyl 2,4-dimethyl-1,4-dihydronicotinate (IIIb), b.p. 115–130° (2 mm.). Recrystallization of this material from petroleum ether gave plates, m.p. 66°, which liquified on exposure to air at room temperature for 1 week. The recrystallized material showed λ_{max}^{EtOH} 210 mμ (ε = 13.40) and 330–331 mμ (ε = 7.74). Infrared absorption maxima were observed at 3500, 1683, and 1605 cm.$^{-1}$, indicating the presence of >NH, >CO and >C=C< functions respectively.

Anal. Calc'd for $C_{10}H_{15}NO_2$: C, 66.3; H, 8.35; N, 7.73. Found: C, 66.36; H, 8.16; N, 7.74.

Ethyl 2,4-dimethyl-1,4-dihydronicotinate gave a *picrate* from ether solution as brown plates, m.p. 160° (decomp.).

Oxidation of IIIb by the procedure described above gave ethyl 2,4-dimethylnicotinate in 65% yield, λ_{max}^{EtOH} 263 mμ (ε = 2.55), m.p. of *picrate*, 175°.

Anal. Calc'd for $C_{16}H_{16}N_4O_9$: C, 47.1; H, 3.94; N, 13.73. Found: C, 47.87; H, 4.18; N, 14.03.

Treatment of IIIb with boiling ethanolic potassium hydroxide gave the potassium salt which on dry distillation with soda lime gave 2,4-lutidine, b.p. 165°. The *picrate*, m.p. 182–183°, failed to depress the m.p. of an authentic specimen.

Catalytic hydrogenation of ethyl 2-methyl-1,4-dihydronicotinate. Hydrogenation of 0.18 g. (0.0011 mole) of ethyl 2-methyl-1,4-dihydronicotinate in 20 ml. of methanol over 0.08 g. of 15% palladium on calcium carbonate catalyst led to absorption of 23 ml. of hydrogen (0.001 mole) in 20 minutes. Removal of catalyst and solvent and distillation of the residue gave ethyl 2-methyl-1,4,5,6-tetrahydronicotinate (Va), b.p. 115–120° (0.08 mm.), λ_{max}^{EtOH} 290 mμ (ε = 14.50).[3]

Catalytic hydrogenation of ethyl 2,4-dimethyl-1,4-dihydronicotinate. Hydrogenation of ethyl 2,4-dimethyl-1,4-dihydronicotinate as described above gave ethyl 2,4-dimethyl-1,4,5,6-tetrahydronicotinate, λ_{max}^{EtOH} 285 mμ (ε = 17.80), m.p. of *3,5-dinitrobenzoate*, 102–103°.

Anal. Calc'd for $C_{17}H_{19}N_3O_7$: C, 54.11; H, 5.08; N, 11.14. Found: C, 54.05 H, 4.50; N, 11.45.

Disproportionation of ethyl 2-methyldihydronicotinate. A mixture of 0.15 g. of ethyl 2-methyldihydronicotinate, 0.08 g. of a 15% palladium on calcium carbonate catalyst, and 15 ml. of methanol was shaken for 1 hour in a nitrogen atmosphere. Removal of the catalyst and solvent gave a base from which there was obtained a *picrate*, m.p. 146°, identical with that of ethyl 2-methylnicotinate. The ultraviolet absorption spectrum of this base showed maxima at 220 and 290 mμ and was identical with that of an equimolar mixture of IVa and Va.

Similar treatment of IIIb gave an equimolar mixture of IVb and Vb.

Acknowledgment. The author is indebted to Dr. E. Earl Royals who kindly read the manuscript and assisted in its arrangement with respect to English idiom and current Journal usage.

INSTITUTE OF APPLIED MICROBIOLOGY
UNIVERSITY OF TOKYO, AND
TAKAMINE RESEARCH LABORATORY
SANKYO CO., LTD.
TOKYO, JAPAN

Basic Alcoholysis of the Trifluoromethyl Group in 1,1,1-Trifluoro-2,2-diarylethanes

R. MECHOULAM, S. COHEN, AND A. KALUSZYNER

Received March 8, 1956

Buxton, Stacey, and Tatlow[1] have recently summarized the state of our knowledge on the alkaline hydrolysis of trifluoromethyl groups in aliphatic compounds. Of special interest for the experiments reported here is the observation of these authors that α-trifluoromethylpropionic acid is hydrolyzed to methylmalonic acid while α-hydroxy-α-trifluoromethylpropionic acid remains unchanged, and the report[2] that 3,3,3-trifluoropropene is alcoholyzed to 3-ethoxy-3,3-difluoropropene. Also the diaryltrifluoromethylcarbinols[3] show this resistance to alkaline hydrolysis which appears to be connected with the presence of the hydroxyl in the immediate vicinity of the trifluoromethyl group. It seemed, therefore, of interest to study the basic alcoholysis of 1,1,1-trifluoro-2,2-diarylethanes, CF_3CHAr_2, with Ar = C_6H_4, *p*-ClC_6H_4, and *p*-BrC_6H_4.

Basic alcoholysis under anhydrous conditions converts these compounds into the corresponding esters Ar_2CHCO_2R. When alcoholic sodium hydroxide is used, the esters remain the predominant

(1) Buxton, Stacey, and Tatlow, *J. Chem. Soc.*, 366 (1954).

(2) Henne, Smook, and Pelley, *J. Am. Chem. Soc.*, **72**, 4756 (1950).

(3) Kaluszyner, Reuter, and Bergmann, *J. Am. Chem. Soc.*, **77**, 4164 (1955).