was more important to obtain pure products than high yields. The bromide salts, which were greenish yellow in color, formed pink solutions with water, in which they were slightly to moderately soluble. The alkyl sulfates were brown and the iodides ranged from orange-red to brown.

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CHEMICAL LABORATORIES OF
CARSON-NEWMAN COLLEGE
JEFFERSON CITY, TENN.
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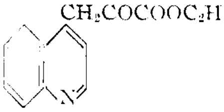
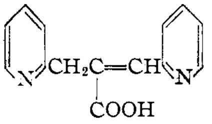
Claisen and Aldol Condensations of α-Picoline and Quinaldine with Ethyl Oxalate by Alkali Amides[1]

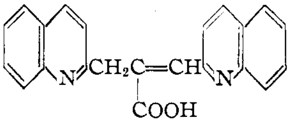
BY CHARLES R. HAUSER AND WILBERT J. HUMPHLETT[2]

It was shown recently in this Laboratory that lepidine may be acylated with ethyl oxalate by means of potassium amide to form in good yield the corresponding Claisen condensation product (I).[3] However, under similar conditions, α-picoline with this ester gave a substance which apparently was not the corresponding Claisen condensation product.

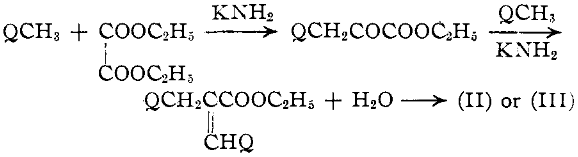
We have found that α-picoline with ethyl oxalate and either potassium amide or sodium amide forms an α,β-unsaturated pyridyl acid (II) and that quinaldine similarly gives a corresponding product (III).[4] These condensations were carried out in refluxing ether employing two molecular equivalents of the pyridyl compound and alkali amide to one of ethyl oxalate (Method B).[3] The yield of (II) was 23% and of (III), 53%.


(I)


(II)


(III)

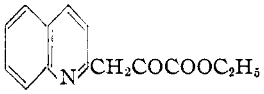
Compounds (II) and (III) evidently are formed by a Claisen condensation followed by an aldol condensation, the water thereby liberated hydrolyzing the ester group. The reactions may be represented by the following equations in which Q is α-pyridyl or α-quinolyl.



$$\mathrm{QCH_3} + \underset{\mathrm{COOC_2H_5}}{\mathrm{COOC_2H_5}} \xrightarrow{\mathrm{KNH_2}} \mathrm{QCH_2COCOOC_2H_5} \xrightarrow[\mathrm{KNH_2}]{\mathrm{QCH_3}} \mathrm{QCH_2}\underset{\mathrm{CHQ}}{\underset{\|}{\mathrm{C}}}\mathrm{COOC_2H_5} + \mathrm{H_2O} \longrightarrow \text{(II) or (III)}$$

Attempts to obtain the Claisen product in these cases were unsuccessful. When the reaction with α-picoline was stopped by acidification immediately after the addition of the ethyl oxalate, no definite product could be isolated. When the reaction with quinaldine was carried out at room temperature in pentane, instead of ether, and the mixture acidified immediately after addition of the ester, the only product isolated was (III) (20%). The reason that the Claisen product from lepidine did not undergo the aldol reaction under the conditions employed, may be attributed to its relative insolubility (see experimental).

Although sodium or potassium amide converts quinaldine and ethyl oxalate to an aldol derivative of the Claisen product, it was shown by Wislicenus[5] and confirmed by us that potassium ethoxide yields apparently only the Claisen product (IV).


(IV)

The ethoxalyl derivatives of lepidine and of quinaldine, (I) and (IV), respectively, were converted to the corresponding oximes which were hydrogenated in the presence of Raney nickel. However, the products failed to give satisfactory analytical values for the corresponding amino acid esters.

Experimental[6]

2-α-Picolal-3-α′-pyridylpropionic Acid (II).—In a one-liter three-necked flask equipped through ground glass joints with a reflux condenser (drying tube), mercury-sealed stirrer and dropping funnel, was prepared 0.40 mole of potassium amide[7] (or sodium amide) in approximately 400 ml. of anhydrous liquid ammonia. To this reagent was added 37.2 g. (0.40 mole) of α-picoline (b. p. 129–130°) in an equal volume of dry ether. The reaction flask was placed on the steam-bath and 300 ml. of ether was added gradually as the ammonia was evaporated. After the suspension was stirred and refluxed for thirty minutes,

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[1] Paper XLVI on Condensations; paper XLV, THIS JOURNAL, **72**, 1352 (1950).

[2] Eli Lilly Fellow, 1949–1950.

[3] Weiss and Hauser, THIS JOURNAL, **71**, 2023 (1949).

[4] α-Picoline failed to react appreciably with ethyl oxalate in the presence of diethylaminomagnesium bromide in refluxing ether for three hours, 75% of the α-picoline being recovered. Quinaldine and ethyl oxalate with sodium hydride in refluxing ethyl ether liberated only about 25% of the calculated amount of hydrogen and no definite product was isolated. Perhaps the condensation might be realized in a higher boiling solvent; see Swamer and Hauser, THIS JOURNAL, **72**, 1352 (1950).

[5] Wislicenus and Kleisinger, *Ber.*, **42**, 1140 (1909).

[6] Analyses are by Clark Microanalytical Laboratory, Urbana, Illinois.

[7] Yost and Hauser, THIS JOURNAL, **69**, 2325 (1947).

the steam-bath was removed and 29.2 g. (0.20 mole) of ethyl oxalate (b. p. 184°) in ether was added at a rate to maintain gentle refluxing. The reaction mixture was refluxed and stirred rapidly for two hours with the formation of a yellow precipitate and then decomposed with cooling by addition of 120 ml. of 6 *N* acetic acid. Dilute (5 *N*) ammonium hydroxide (60 ml.) was added until the solution was neutral or faintly acid. The yellow solid was filtered from the cold solution and washed with ether yielding 11 g. (23%) of (II) melting at 161–163°. The aqueous filtrate was extracted with benzene, but very little more of the substance was obtained. After recrystallization from benzene, the yellow needles melted at 163–164°.

Anal. Calcd. for $C_{14}H_{12}N_2O_2$: C, 69.98; H, 5.04. Found: C, 70.00, 70.02; H, 4.80, 4.93.

This yellow water-soluble amino acid (II) decolorized dilute potassium permanganate solution and reacted with bromine in carbon tetrachloride to form an orange hygroscopic addition product. The amino acid (II) formed a dipicrate which, after recrystallization from ethanol, melted at 146–148°.

Anal. Calcd. for $C_{26}H_{18}O_2N_8$: C, 44.73; H, 2.60; N, 16.04. Found: C, 45.04; H, 2.68; N, 15.88.

2-α-Quinaldal-3-α′-quinolylpropionic Acid (III).—In a similar manner 43.5 g. (0.3 mole) of quinaldine (b. p. 245–246°) treated with 0.3 mole of potassium amide (or sodium amide) and then with 21.9 g. (0.15 mole) of ethyl oxalate in ether. After refluxing for one hour the reaction mixture was decomposed by pouring into 75 ml. of glacial acetic acid and 75 g. of ice. The resulting solution was neutralized by the addition of solid anhydrous sodium carbonate, the final neutralization being adjusted with a solution of sodium bicarbonate. The thick orange precipitate was filtered and washed twice with ether yielding 27 g. (53%) of (III), m. p. 219–223°. After recrystallization from large volumes of benzene, the orange-red crystals melted at 221–223°.

Anal. Calcd. for $C_{22}H_{16}O_2N_2$: C, 77.63; H, 4.74; N, 8.23. Found: C, 77.56; H, 4.90; N, 8.05.

This substance (III) in carbon tetrachloride solution reacted with bromine in this solvent to form an orange precipitate which was shown by sodium fusion to contain halogen. A red monopicrate of (III) was obtained by filtering a hot benzene solution of (III) into boiling ethanolic picric acid. After recrystallization of 0.4 g. of this picrate from one liter of acetone, the red crystals melted with decomposition at 220°.

Anal. Calcd. for $C_{28}H_{19}O_9N_5$: C, 59.05; H, 3.36. Found: C, 59.25; H, 3.42.

Ethyl (γ-Quinolyl)-pyruvate (I).—This ester was prepared by a modification of the method previously described.[3] To 0.60 mole of potassium amide in liquid ammonia was added 86 g. (0.60 mole) of lepidine (b. p. 262°) in ether. After the liquid ammonia was removed and replaced with ether, refluxing was continued thirty minutes. To this metal derivative was added dropwise 43.8 g. (0.30 mole) of ethyl oxalate in ether. After refluxing for one hour, the cooled reaction mixture was decomposed with 6 *N* acetic acid and neutralized with sodium carbonate. After filtering and washing with ether and water, there was obtained 62 g. (85%) of crude ethyl-(γ-quinolyl)-pyruvate, m. p. 185–189°. This product was insoluble in ether and only slightly soluble in boiling alcohol or benzene. Recrystallization from dioxane gave the pure compound, m. p. 188–189°, as previously reported.[3]

Ethyl (γ-Quinolyl)-pyruvate Oxime.—To a hot solution of 7.5 g. (0.31 mole) of compound (I) in 150 ml. of dioxane was added 7.5 g. of hydroxylamine hydrochloride, 7.5 g. of sodium acetate and sufficient water to effect solution. The solution was evaporated to a volume of 100 ml. and poured onto ice. There was obtained 7.1 g. (90%) of the oxime, m. p. 183–184°, after recrystallization from ethanol–water.

Anal. Calcd. for $C_{14}H_{14}O_3N_2$: C, 65.10; H, 5.46; N, .84. Found: C, 65.19; H, 5.74; N, 10.60.

The oxime (12.5 g., 0.048 mole) in 250 ml. of absolute ethanol was hydrogenated in the presence of Raney nickel at 800 pounds pressure and 75° for six hours yielding an amine, b. p. 193–198° at 3 mm. This amine formed a picrate and a picrolonate, but neither of these derivatives, after recrystallization from ethanol, gave satisfactory analytical values.

Ethyl (α-Quinolyl)-pyruvate Oxime.—Ethyl (α-quinolyl)-pyruvate (m. p. 130–131°), prepared by means of potassium ethoxide as previously described,[5] was readily soluble in alcohol or ether. This ester (10 g., 0.41 mole) yielded 9.1 g. (85%) of the corresponding oxime, which after recrystallization from ethanol melted at 162–163°.

Anal. Calcd. for $C_{14}H_{14}O_3N_2$: C, 65.10; H, 5.45; N, 10.84. Found: C, 65.32; H, 5.29; N, 11.03.

Hydrogenation of the oxime yielded an amine b. p. 178–183° at 2 mm. The picrate salt failed to analyze satisfactorily.

DEPARTMENT OF CHEMISTRY
DUKE UNIVERSITY
DURHAM, NORTH CAROLINA

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The Degradation of Silver Trifluoroacetate to Trifluoroiodomethane

BY ALBERT L. HENNE[1] AND WILLIAM G. FINNEGAN

Trifluoroiodomethane, CF_3I, has been shown to break homolytically and is presently the only source of trifluoromethyl free-radicals. Its value has been proved by efficient addition across a carbon to carbon double or triple bond. Its preparation has called for carbon tetraiodide and iodine pentafluoride, neither of which is current or convenient to handle.[2,3,4]

The degradation of silver trifluoroacetate by means of an excess of iodine appealed to us as a more promising synthesis. It can be written: $CF_3COOAg + I_2 \rightarrow CF_3I + AgI + CO_2$. The first step is the formation of an iodinated complex such as $CF_3CO_2AgI_2$, in which iodine has a definitely positive character. The electropositive nature of the CF_3 group should enhance its ability to migrate as a negative fragment toward the positive, iodinated end of the molecule and form CF_3I in preference to CF_3COOCF_3; this is the opposite of the reaction with unfluorinated silver salts, which favors ester formation.

Experimentally, the careful heat-decomposition of an equimolecular mixture of dry silver salt and iodine gave an 80% yield of CF_3I and no other compound was traced. The mechanical losses, estimated at 10% were relatively high because no solvent or dispersing medium could be used, as all were affected by the silver or the positive iodine. A one-step synthesis of CF_3I from commercially available reagents is thus at hand.[5]

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(1) Visiting Professor from Ohio State University.

(2) Haszeldine and Emeleus, *Research*, **1**, 715 (1948).

(3) Banks, Emeleus, Haszeldine and Kerrigan, *J. Chem. Soc.*, 2188 (1948).

(4) Haszeldine, *ibid.*, 2856 (1949); *Nature*, **165**, 152 (1950).

(5) A letter from R. N. Hazseldine, Cambridge University, informs us that he has obtained parallel results, which he is now submitting to *Nature*.