give 32.35 g. (80%) of benzoylacetoneimine (X), m.p. 138.5–140.5°, reported[18] m.p. 143°.

Cyclization of X with Ethyl Cyanoacetate to Form XI and its Conversion to 2-Pyridone I.—This reaction was effected by a modification of the method of Basu[6] who reported no yield.

To a solution of sodium ethoxide (prepared from 2.72 g., 0.117 mole, of sodium) in 100 ml. of absolute ethanol, was added a solution of 13.4 g. (0.117 mole) of ethyl cyanoacetate in 50 ml. of absolute ethanol, followed immediately by 19.0 g. (0.117 mole) of benzoylacetoneimine (X) in 25 ml. of absolute ethanol. The mixture was refluxed for 6 hours, and allowed to stand overnight at room temperature. Water (200 ml.) and 10 ml. (0.12 mole) of concentrated hydrochloric acid were added, and the resulting precipitate collected and recrystallized from methanol to give 4.95 g. (20%) of 3-cyano-4-phenyl-6-methyl-2-pyridone (XI), m.p. 276–277°, reported[6] m.p. 277°.

A mixture of 0.53 g. (0.0025 mole) of XI and 25 ml. of 50% sulfuric acid was heated 2 hours on the steam-bath with no apparent change, and then refluxed 30 minutes over a bunsen burner. The resulting solution was chilled in ice-water to precipitate a white solid which was triturated with saturated sodium bicarbonate solution to give 0.20 g. (44%) of 2-pyridone I, m.p. 195–198.5°. One recrystallization from methanol raised the melting point to 201–203°, 208° (Kofler micro hot-stage); reported[6] m.p. 207°. A mixed melting point with 2-pyridone I prepared in the general procedure was undepressed.

Conversion of 2-Pyridone IV to Chloro Derivative XII.—A mixture of 11.4 g. (0.042 mole) of 3,5-diphenyl-4,6-dimethyl-2-pyridone (IV), 20 g. of phosphorus pentachloride and 25 ml. of phosphorus oxychloride was refluxed on the Woods metal-bath at 140° for 24 hours. The reaction mixture was decomposed with ice and the product taken up in ether. The ether solution was washed with sodium bicarbonate solution and dried over magnesium sulfate. The solvent was removed to give 6.35 g. of a dark solid, m.p. 193–208°. One recrystallization from benzene gave 3.2 g. (26%) of 2,4-dimethyl-3,5-diphenyl-6-chloropyridine (XII), m.p. 213–220°. Two additional recrystallizations from benzene gave white crystals, m.p. 223–225°.

Anal. Calcd. for $C_{19}H_{16}NCl$: C, 77.67; H, 5.49; N, 4.77; Cl, 12.07. Found: C, 77.58; H, 5.46; N, 4.83; Cl, 12.14.

Dechlorination of XII to Form XIII.—A stirred solution of 0.4 g. (0.013 mole) of 2,4-dimethyl-3,5-diphenyl-6-chloropyridine (XII) in a mixture of 50 ml. each of absolute ethanol and ethyl acetate was hydrogenated over palladium (0.2 g.)-on-charcoal at atmospheric pressure. The theoretical amount of hydrogen was taken up overnight. The catalyst was removed (suction filtration) and the solvents were evaporated (water-pump) leaving 0.4 g. of a white solid which was triturated with sodium bicarbonate solution and taken up in ether. After drying over magnesium sulfate, the solvent was removed and the residue (0.2 g.) recrystallized from 30–60° petroleum ether to give 0.15 g. (43%) of 2,4-dimethyl-3,5-diphenylpyridine (XIII), m.p. 99–100.5°.

Anal. Calcd. for $C_{19}H_{17}N$: C, 87.99; H, 6.61; N, 5.40. Found: C, 88.18; H, 6.73; N, 5.37.

Dehydrogenation of 2-Pyridone VIII to Form XIV.—In a sublimation apparatus was placed a thoroughly mixed sample of 0.22 g. (0.001 mole) of 2-hydroxy-4-phenyl-5,6,7,8-tetrahydroquinoline (VIII) with 0.11 g. of 5% palladium-on-charcoal. The apparatus was evacuated to 30 mm. pressure and placed in a Woods metal-bath at 200°. There was collected 0.15 g. (68%) of 2-hydroxy-4-phenylquinoline (XIV), m.p. 253–256°, reported[8] m.p. 259°. One additional sublimation raised the melting point to 260–261.5° (sealed tube) which was not depressed upon admixture with a sample of XIV obtained below.

2-N-Acetylaminobenzophenone (XV).—This compound was prepared by a modification of the method of Bischler and Barad,[20] who did not report the yield.

A mixture of 8.0 g. (0.04 mole) of *o*-aminobenzophenone and 10.8 g. (0.106 mole) of acetic anhydride was stirred and heated on the steam-bath for 1 hour. The resulting dark clear solution was stirred and heated with 25 ml. of water for 1 hour to decompose the excess acetic anhydride. After neutralizing the acidic solution with an excess of sodium bicarbonate, the aqueous layer was decanted and the residual dark heavy oil was dissolved in a minimum of methanol. The solution was clarified by filtration and cooled in a Dry Ice–acetone mixture to give an oil which solidified on scratching. The white solid was collected by suction filtration to give 7.8 g. (82%) of 2-N-acetylaminobenzophenone (XV), m.p. 78–82°, reported[20] m.p. 88.5–89°.

Cyclization of XV to Form XIV.—This reaction was effected by a modification of the procedure of Camps.[8]

To a warm mixture of 6.0 g. (0.025 mole) of 2-N-acetylaminobenzophenone (XV), 50 ml. of 95% ethanol and 150 ml. of water was added 1.5 g. (0.0375 mole) of sodium hydroxide in a minimum of water. The mixture was refluxed for 2 hours, cooled in ice and the solid collected by vacuum filtration. After refluxing with 100 ml. of 3 *N* hydrochloric acid for 6 hours (to hydrolyze any uncyclized amide), the solid was collected by vacuum filtration of the cooled mixture, and recrystallized from 95% ethanol to give 4.1 g. (74%) of 2-hydroxy-4-phenylquinoline (XIV), m.p. 254–257°; reported m.p. 259°.[8] Sublimation at 180–190° (2 mm.) raised the melting point to 260–261.5°. This melting point was undepressed upon admixture with a sample of XIV prepared above.

(20) A. Bischler and D. Barad, *Ber.*, **25**, 3080 (1892).

DURHAM, N. C.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, DUKE UNIVERSITY]

Synthesis of β-Diketone Esters from Sodio Ketones and Mono Acid Chloride Esters of Succinic and Adipic Acids. Avoidance of Stobbe and Dieckmann Reactions

BY CHARLES R. HAUSER AND BRUCE O. LINN[1]

RECEIVED AUGUST 6, 1956

Sodio ketones, prepared by means of sodium amide, were acylated with the mono acid chloride-ethyl esters of succinic and adipic acids to form the corresponding β-diketone-esters. This was accomplished satisfactorily by an adaptation of an earlier method involving the use of three equivalents of the sodio ketone to one of the acid chloride. The possible Stobbe and Dieckmann reactions, which occur in attempts to acylate sodio ketones with diethyl succinate and adipate, were avoided under the present conditions. An extension of the method is indicated. The β-diketone-ester from sodio cyclohexanone and the mono acid chloride ester of adipic acid was cleaved by alkali with ring opening to form a ketone dicarboxylic acid.

It was shown recently[2] that certain β-diketones that are not obtained satisfactorily by the common base-catalyzed acylation of ketones with esters[3]

(1) American Cyanamid Co. Fellow, 1954–1955.

(2) B. O. Linn and C. R. Hauser, THIS JOURNAL, **78**, 6066 (1956).

(3) See C. R. Hauser, F. W. Swamer and J. T. Adams, "Organic Reactions," Vol. VIII, John Wiley and Sons, Inc., New York, N. Y., 1954, Chapter 3.

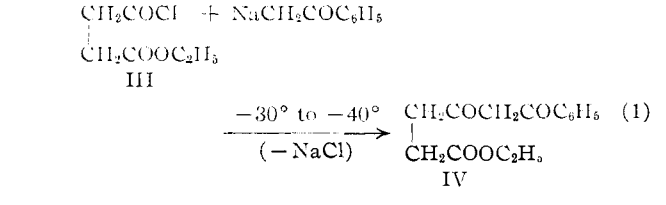
may be synthesized in good yields by the acylation of sodio ketones with acid chlorides under controlled conditions. The sodio ketones were prepared by means of sodium amide.

It has now been found that this acid chloride method may be adapted successfully to the synthesis of certain β-diketone-esters from sodio ketones and the mono acid chloride–ethyl esters of succinic and adipic acids. The corresponding diethyl esters of these dicarboxylic acids are not suitable for the acylation of ketones. Diethyl succinate is unsuitable because it undergoes instead the base-catalyzed Stobbe condensation[4] in which the α-hydrogen of the ester and carbonyl group of the ketone are involved. We have observed this reaction even when the α-hydrogen of the ketone was first ionized by sodium amide and the resulting sodio ketone then treated with diethyl succinate. Evidently a sodium–hydrogen exchange first occurs to form the sodio ester which condenses with the regenerated ketone to give the Stobbe product (I).

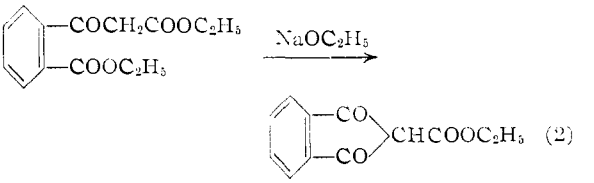
Diethyl adipate is unsuitable for the acylation of ketones because it readily undergoes the Dieckmann intramolecular cyclization involving the α-hydrogen of the ester. We have observed this cyclization even when the α-hydrogen of acetophenone was first ionized and the resulting sodio ketone then treated with diethyl adipate. Apparently a sodium–hydrogen exchange first occurs to form the sodio ester which cyclizes to give the Dieckmann product (II).

Both the Stobbe and Dieckmann reactions were avoided and the acylations of sodio ketones realized by the use of more reactive acylating agents such as the mono acid chloride-esters of the appropriate dicarboxylic acids. As usual[2] the sodio ketone was prepared by means of sodium amide in ether and three molecular equivalents of it treated with one equivalent of the acid chloride. The large excess of sodio ketone was employed to avoid its diacylation.[2] The reaction was carried out at relatively low temperatures (−30 to −40°) in order to minimize the possible cyclization of the product or the further acylation of the excess sodio ketone by the free ester group of the product.

The acylation of sodio acetophenone with the mono acid chloride-ester of succinic acid, β-carbethoxypropionyl chloride (III), produced β-diketone-ester IV in 64% yield (equation 1). In such acylations[2,3] the reactive hydrogen of the β-diketone is ionized by the sodio ketone to form the sodio β-diketone from which the free β-diketone is subsequently liberated by acidification of the reaction mixture.

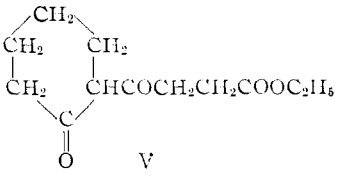


Since a somewhat related β-ketoester-ester has been reported to undergo cyclization on treatment with sodium ethoxide (equation 2),[5] the possibility of IV being cyclized was considered. However, in line with well known failure of ordinary sodio β-



diketones or sodio β-ketoesters to undergo appreciable acylation with esters,[6] β-diketone-ester IV was largely recovered (69%) after refluxing it with an equivalent of sodium ethoxide for 67 hr. in ether.

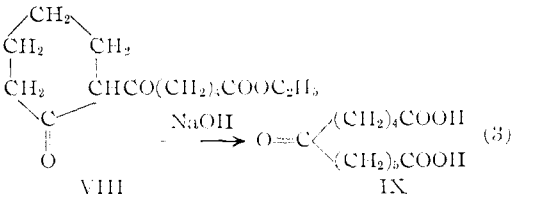
Similarly the acylation of sodio cyclohexanone with acid chloride-ester III gave β-diketone-ester V in 44% yield.



The acylation of sodio acetophenone with the mono acid chloride-ester of adipic acid, δ-carbethoxyvaleroyl chloride (VI), formed β-diketone-ester VII in 64% yield.

Although the sodio derivative of VII was stable, treatment of VII with two equivalents of sodium ethoxide in refluxing ether for 27 hr. gave an unidentified product. Cyclization might have occurred.

Similarly the acylation of sodio cyclohexanone with acid chloride-ester VI formed β-diketone-ester VIII in 32% yield. It is possible that this low yield was due to a Dieckmann cyclization of product VIII.[7] This β-diketone-ester is of particular interest since it was cleaved and hydrolyzed by dilute alkali to form ketone dicarboxylic acid IX in 63% yield (equation 3). Similar ring openings of acyl cyclohexanones have been described previously.[8]



The general formulas for the β-diketone-esters from the acylations of sodio acetophenone and sodio cyclohexanone with acid chloride-esters III and VI and also those from the possible acylations of these sodio ketones with other straight chain acid chloride-esters may be represented by X and XI, respectively.

(4) See W. S. Johnson and G. H. Daub, "Organic Reactions," Vol. VI, John Wiley and Sons, Inc., New York, N. Y., 1951, Chapter 1.

(5) W. Wislicenus, *Ann.*, **246**, 349 (1888).

(6) See ref. 2, note 7.

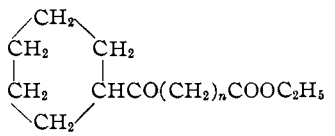
(7) The yield was increased from 22 to 32% by decreasing the normal reaction time of 1 hr. (found to be optimum for the preparation of VII) to 0.5 hr. It is possible that even a higher yield could be obtained by minimizing the cyclization tendency of VIII through the use of the *t*-butyl or a more complex ester instead of the ethyl ester.

(8) C. R. Hauser, F. W. Swamer and B. I. Ringler, THIS JOURNAL, **70**, 4023 (1948); R. M. Manyik, F. C. Frostick, J. J. Sanderson and C. R. Hauser, *ibid.*, **75**, 5031 (1953).

The present acid chloride method or an extension of it should be useful for the synthesis of various β-diketone-esters of types X and XI except when n is

$C_6H_5COCH_2CO(CH_2)_nCOOC_2H_5$

X



XI

zero. In the latter case the product can be prepared more conveniently with diethyl oxalate.[3] However, oxalic esters are apparently the only dicarboxylic acid ethyl esters that have produced good yields in the acylations of ketones. Diethyl malonate would presumably be unsuitable because of its reactive α-hydrogen. Diethyl succinate and adipate are unsatisfactory for the reasons discussed above, and diethyl pimelate might be expected to undergo the Dieckmann cyclization like the adipic ester. Even diethyl or dimethyl glutarate, which shows little tendency to cyclize, has given only 25–26% yields of β-diketone-esters X and XI (n = 3) with acetophenone[9] and cyclohexanone,[10] respectively. The former acylation was effected by sodium amide and the latter, by sodium. Apparently no study has been made of acylations of ketones with higher dicarboxylic acid ethyl esters.

Experimental[11]

Sodium–Hydrogen Exchange and Stobbe Reaction with Sodio Acetophenone and Ethyl Succinate.—To a stirred suspension of 0.30 mole of sodium amide in 300 ml. of dry ether[3] was added 36.0 g. (0.30 mole) of acetophenone in 75 ml. of dry ether, followed after 10 minutes by 52.4 g. (0.30 mole) of ethyl succinate in 100 ml. of dry ether. After stirring and refluxing for 2 hr., the reaction mixture was cooled and acidified with cold hydrochloric acid. The ether layer was extracted with sodium bicarbonate solution until a sample of the extract failed to produce cloudiness on acidification. No β-diketone ester was found upon fractionation of the ether solution. The combined bicarbonate extracts was acidified with hydrochloric acid and the liberated carboxylic acid taken up in ether. The ether solution was dried, concentrated and evacuated over a steam-bath giving 47.6 g. (64%) of crude, yellow, semi-solid acid I. A chloroform solution of a sample of this crude acid was chromatographed through an alumina column to give the "*cis*" isomer of acid I, m.p. 110–111°, reported m.p. 111–112°.[12]

Sodium–Hydrogen Exchange and Dieckmann Cyclization with Sodio Acetophenone and Ethyl Adipate.—To a stirred suspension of 0.20 mole of sodium amide in 200 ml. of dry ether[3] was added 24.0 g. (0.20 mole) of acetophenone in 50 ml. of dry ether, followed after 10 minutes by 40.4 g. (0.20 mole) of ethyl adipate in 75 ml. of dry ether. After 10 minutes at room temperature, the solidified reaction mixture was acidified with cold hydrochloric acid. The ether layer was washed with saturated sodium bicarbonate solution and dried over Drierite. The solvent was removed and the liquid residue was fractionated to give 16.3 g. (68%) of recovered acetophenone, b.p. 94–96° at 20 mm., and 11.3 g. (36%) of 2-carbethoxycyclopentanone (II), b.p. 109–111° at 14 mm., $n^{25}D$ 1.4495, reported b.p. 114° at 20 mm., $n^{20}D$ 1.4519.[13] This product gave a semicarbazone, m.p. 142–143°, reported m.p. 143°.[14] No β-diketone ester was found.

β-Carbethoxypropionyl Chloride (III).—Ethyl hydrogen succinate was prepared in 73% yield from succinic anhydride and absolute ethanol and then treated with thionyl chloride to give a 91% yield of β-carbethoxypropionyl chloride (III), b.p. 87–88° at 10 mm., as described by Cason.[15]

Acylation of Sodio Acetophenone with Acid Chloride III to Form β-Diketone-ester IV.—A suspension of 0.30 mole of sodium amide in 200 ml. of ether (prepared in the usual manner)[3] was stirred and refluxed for 15 minutes and dry ether added until the volume was about 700 ml. Dry nitrogen was passed through for 15 minutes with stirring and refluxing and the suspension cooled to room temperature. A solution of 36.0 g. (0.30 mole) of acetophenone in 75 ml. of dry ether was added over 15 minutes, and dry nitrogen bubbled through the stirred mixture for 20 minutes longer to remove the liberated ammonia. During the last few minutes, more dry ether was added to bring the volume to about 600 ml. The resulting suspension of the sodio ketone was cooled to −40° by means of a Dry Ice–acetone-bath and a solution of 16.46 g. (0.10 mole) of β-carbethoxypropionyl chloride (III) in 50 ml. of dry ether added rapidly (one minute) with vigorous stirring. The reaction mixture was stirred for 30 minutes[16] keeping the temperature at −30 to −40° and then acidified by the cautious addition of a solution of 27 ml. of concentrated hydrochloric acid in 100 ml. of ice-water. The ether layer (with which was combined an ether extract of the aqueous layer) was washed with saturated sodium bicarbonate solution. After extracting the bicarbonate solution with ether, the combined ethereal solution was dried over Drierite and concentrated. The liquid residue was fractionated to give 21.7 g. of recovered acetophenone, b.p. 106–107° at 39 mm., and 15.89 g. (64%) of 1-phenyl-5-carbethoxy-1,3-pentanedione (IV), b.p. 168–169° at 1.4 mm., $n^{25}D$ 1.5533.

Anal. Calcd. for $C_{14}H_{16}O_4$: C, 67.73; H, 6.50. Found: C, 67.92; H, 6.50.

This product (IV) was further identified by a positive red enol test with ferric chloride, by the formations of a gray copper chelate, m.p. 169–170°, and a pyrimidol, m.p. 167–168° dec.[17]

A sample (0.065 mole) of IV was stirred and refluxed for 67 hr. with 0.065 mole of sodium ethoxide in 150 ml. of dry ether. On acidification there was recovered 69% of slightly impure starting material (IV), b.p. 161–168° at 0.9 mm., $n^{25}D$ 1.5573, and 1.87 g. of red tar. A sample of the recovered starting material was converted to the copper chelate which was identified by the mixed melting point method.

Acylation of Sodio Cyclohexanone with Acid Chloride III to Form β-Diketone-ester V.—To a suspension of 0.60 mole of sodium amide in 1.2 liters of dry ether was added 58.9 g. (0.60 mole) of cyclohexanone in 125 ml. of dry ether followed by 32.9 g. (0.20 mole) of β-carbethoxypropionyl chloride (III) in 100 ml. of dry ether essentially as described above for the acylation of sodio acetophenone. The reaction mixture was stirred for 40 minutes (at −30 to −40°) and then acidified. After saturating with sodium chloride, the aqueous layer was extracted with ether and the combined ethereal layers washed with a bicarbonate solution as previously described. After drying and concentrating the ethereal solution, the liquid residue was fractionated giving 39.3 g. of recovered cyclohexanone, b.p. 154–155°, and 19.64 g. (44%) of 2-(β-carbethoxypropionyl)-cyclohexanone (V), b.p. 137–138° at 1.2 mm., $n^{25}D$ 1.4940.

Anal. Calcd. for $C_{12}H_{18}O_4$: C, 63.70; H, 8.02. Found: C, 63.58; H, 8.09.

This product was further identified by a positive purple enol test with ferric chloride and by the formation of a gray copper chelate, m.p. 138.5–139°.

Anal. Calcd. for $CuC_{24}H_{34}O_8$: Cu, 12.36; C, 56.07; H, 6.67. Found: Cu, 12.82; C, 55.88; H, 6.75.

(9) H. Wieland and I. Drishaus, *Ann.*, **473**, 111 (1929).

(10) R. Robinson and E. Seijo, *J. Chem. Soc.*, 582 (1941).

(11) Melting and boiling points are uncorrected. Analyses are by Galbraith Microanalytical Laboratories, Knoxville, Tenn.

(12) Reference 4, p. 47. Our purified sample amounted to approximately one-third by weight of the crude product in agreement with the results obtained by Johnson and Daub (ref. 4) for the Stobbe reaction under the usual conditions.

(13) M. Von Rysselberge, *Bull. classe sci., Acad. roy. Belg.*, [5] **12**, 173 (1926).

(14) M. L. Bouveault, *Bull. soc. chim. France*, [3] **21**, 1021 (1899).

(15) J. Cason, "Organic Syntheses," Coll. Vol. III, John Wiley and Sons, Inc., New York, N. Y., 1955, p. 169.

(16) When 1 hr. was allowed only a 45% yield of the β-diketone-ester was obtained.

(17) The details for the preparation of the pyrimidol will be published soon.

δ-Carbethoxyvaleroyl Chloride (VI).—Monethyl adipate obtained from Eastman Distillation Products was treated with excess thionyl chloride as described previously[18] to give on distillation a 91% yield of δ-carbethoxyvaleroyl chloride, b.p. 128–130° at 17 mm.

Acylation of Sodio Acetophenone with Acid Chloride VI to Form β-Diketone-ester VII.—A suspension of 0.30 mole of sodio acetophenone in 600 ml. of ether (essentially free from ammonia) was prepared as described above and cooled to −40°. To the stirred suspension was added 19.27 g. (0.10 mole) of δ-carbethoxyvaleroyl chloride (VI) in 50 ml. of dry ether and the reaction allowed to proceed for 1 hr.[19] at −30 to −40°. The reaction mixture was acidified and worked up as described above (see IV) to give on fractionation, 21.9 g. of recovered acetophenone, b.p. 106–107° at 39 mm., and 17.67 g. (64%) of 1-phenyl-7-carbethoxy-1,3-heptanedione (VII), b.p. 197–198° at 2.3 mm., $n^{25}D$ 1.5471. The product crystallized slowly to give a white solid, m.p. 34.5°.

Anal. Calcd. for $C_{16}H_{20}O_4$: C, 69.54; H, 7.30. Found: C, 69.68; H, 7.21.

This product was further identified by a positive red enol test with ferric chloride, by the formations of a gray copper chelate, m.p. 76.5–77°, and a yellow pyrimidol, m.p. 148.5–149°.[17]

A sample (0.04 mole) of VII was stirred and refluxed for 27 hr. with 0.08 mole of sodium ethoxide in 150 ml. of dry ether. The reaction mixture was acidified, washed with bicarbonate solution and dried. After removal of the ether, the viscous liquid residue gave a positive red enol test and a green copper chelate (stable up to 340°). The product was not identified.

(18) D. Papa, E. Schwenk and H. Hankin, THIS JOURNAL, **69**, 3021 (1947).

(19) Reaction times of 5 and 15 minutes gave yields of only 39 and 41% of VII, respectively.

Acylation of Sodio Cyclohexanone with Acid Chloride VI to Form β-Diketone-ester VIII.—A suspension of 0.60 mole of sodio cyclohexanone in 1.2 liters of ether was prepared essentially as described above (see IV) and cooled to −40°. To the stirred suspension was added 38.54 g. (0.20 mole) of δ-carbethoxyvaleroyl chloride (VI) in 100 ml. of dry ether and the reaction allowed to proceed for 30 minutes[7] at −30 to −40°. The reaction mixture was then acidified and worked up as described above (see IV). There was obtained 33.5 g. of recovered cyclohexanone, b.p. 74° at 53 mm., and 16.10 g. (32%) of 2-(δ-carbethoxyvaleroyl)-cyclohexanone (VIII), b.p. 152–154° at 0.7 mm., $n^{25}D$ 1.4906.

Anal. Calcd. for $C_{12}H_{18}O_4$: C, 66.11; H, 8.72. Found: C, 65.78; H, 8.78.

This product was further identified by a positive red enol test with ferric chloride and by the formation of a gray copper chelate, m.p. 107.5–108°.

Anal. Calcd. for $CuC_{28}H_{42}O_8$: Cu, 11.14; C, 58.98; H, 7.43. Found: Cu, 11.19; C, 59.30; H, 7.33.

Alkaline Cleavage of β-Diketone-ester VIII to Form Ketone Dicarboxylic Acid IX.—A mixture of 10.18 g. (0.040 mole) of 2-(δ-carbethoxyvaleroyl)-cyclohexanone (VIII) and 73 ml. (0.088 mole, 2 equivalents plus 10%) of 5% aqueous sodium hydroxide was refluxed for 2 hr. After cooling in an ice-bath, the alkaline reaction was extracted with ether. The aqueous alkaline layer was boiled for a short time in order to remove the dissolved ether and after cooling, the solution was acidified with 6 *M* hydrochloric acid. The precipitate was collected and washed several times with water. After recrystallization from chloroform and petroleum ether, 6.13 g. (63%) of 1,10-dicarboxydecanone-5 (IX), m.p. 114–114.5°, was obtained.

Anal. Calcd. for $C_{12}H_{20}O_5$: C, 59.00; H, 8.25; neut. equiv., 122.1. Found: C, 59.05; H, 8.28; neut. equiv., 121.9.

DURHAM, NORTH CAROLINA

[CONTRIBUTION NO. 2132 FROM THE GATES AND CRELLIN LABORATORIES OF CHEMISTRY, CALIFORNIA INSTITUTE OF TECHNOLOGY]

Stereochemistry of the Opening of the Imine Ring with Ethylamine[1,2]

BY ROBERT GHIRARDELLI[3] AND HOWARD J. LUCAS[4]

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Four openings of imine rings and one opening of an oxide ring have been found to occur in a *trans* manner. Of the first, three are reactions of ethylamine with L(−)-*trans*-2,3-iminobutane, L(+)-*trans*-N-ethyl-2,3-iminobutane and *cis*-N-ethyl-2,3-iminobutane, and one is the reaction of ammonia with L(+)-*trans*-N-ethyl-2,3-iminobutane. The *trans* opening of an oxide ring occurs in the reaction of ethylamine with D(+)-*trans*-2,3-epoxybutane. The configuration of DL-*threo*-2,3-bis-(ethylamino)-butane has been established as *threo* by resolution with (−)-dibenzoyltartaric acid. The configuration of the (+)-isomer has been established as L by relating it to L(+)-*threo*-2,3-diaminobutane. The configuration of (+)-*erythro*-3-ethylamino-2-butanol has been established by relating it to L(+)-*erythro*-3-amino-2-butanol. Zinc chloride forms a 1-to-1 complex with D(−)-*threo*-2,3-bis-(ethylamino)-butane. The enhancement of rotation in its formation suggests that it may have a cyclic structure, but its low solubility in organic solvents suggests a polymeric structure.

The isomeric N-ethyl-2,3-iminobutanes have been synthesized by methods which are strictly analogous to those described for the 2,3-iminobutanes[5] except that ammonia is replaced by ethylamine. In Figs. 1 and 2 are shown the steps in the synthesis of *cis*-N-ethyl-2,3-iminobutane and L-(+)-*trans*-N-ethyl-2,3-iminobutane, respectively. The openings of oxide rings by ethylamine and the closings of the N-ethylimine rings are depicted as *trans* openings and closings, respectively, similar to the former results.[5] A *trans* opening in Fig. 2 must be regarded as proven because the identity of the resulting amino alcohol has been established as L(+)-*erythro*-3-ethylamino-2-butanol. The single Walden inversions occurring during the ring openings and ring closings in Figs. 1 and 2 are shown at carbon atoms C-3.

Proof of *trans* Openings of Imine Rings by Ethylamine.—This is given by four independent results, as outlined in Figs. 3, 4, 5 and 6, respectively. In Fig. 3 *cis*-N-ethyl-2,3-iminobutane is converted into 2,3-bis-(ethylamino)-butane which is resolvable into (+)- and (−)-isomers. It therefore is the DL-*threo*-isomer. Carbon atom C-3 is inverted on the formation of the L-isomer and C-2 on that of the D.

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(5) F. H. Dickey, W. Fickett and H. J. Lucas, THIS JOURNAL, **74**, 944 (1952).