$n^{25}{}_D$ 1.3673, d^{26} 1.435 g./cc. N.m.r. (F^{19}) showed a singlet at 18.5 p.p.m. above $CFCl_3$ characteristic for a fluoroformate group, and proton resonance at 4.3 p.p.m. consistent with a OCH_2CH_2O group. The infrared spectrum shows the following absorptions: 1830 ($\nu_{C=O}$ in fluoroformate group) and 1240 cm.$^{-1}$ (ν_{COC}), and the characteristic CH_2 and CF absorptions.

Anal. Calcd. for $C_4H_4F_2O_4$: C, 31.17; H, 2.60; F, 24.68. Found: C, 31.81; H, 2.88; F, 23.2.

Preparation of *o*-Phenylene Bisfluoroformate.—All reactions between pyrocatechol and COFCl were carried out in the same way. Pyrocatechol (0.3 mole), toluene (150 g.) as a solvent, and tertiary amine (0.5 to 20 ml.) as a catalyst were placed into a 500-ml. stainless steel lecture bottle. Carbonyl chloride fluoride (1.0 to 1.5 mole of 89% purity) was added, keeping the reaction mixture cool. The lecture bottle was shaken at different temperatures for 12 hr. The conversion of the pyrocatechol and the yield of *o*-phenyl bisfluoroformate mainly depended on the reaction temperature and time, but not on the amount of catalyst or excess of COFCl. The reaction product was analyzed and isolated as described for the ethylene bisfluoroformate.

o-Phenylene bisfluoroformate is a colorless liquid of strong fluoroformate odor. It has a b.p. 77° at 7 mm. and decomposes at higher temperature. The F^{19} n.m.r. spectrum shows a singlet at 17.6 p.p.m. above $CFCl_3$, which is characteristic for the fluoroformate group. The infrared spectrum also confirmed the structure.

Anal. Calcd. for $C_8H_4F_2O_4$: C, 47.54; H, 1.99; F, 18.80. Found: C, 47.93; H, 2.31; F, 18.7.

Decarboxylation.—All decarboxylation reactions in the liquid phase were carried out in the same way. The catalyst (15 ml. of pyridine or BF_3 etherate) wasp laced into a 50-ml., two-necked flask, equipped with a magnetic stirrer, dropping funnel, inlet for nitrogen, and a water-cooled condenser, which was connected to two cold traps (−78 and −196°) and a mercury blow off. The flask was purged with dry N_2 (50 ml./min.) for 0.5 hr. Then, the flask was heated to 120° and the bisfluoroformate was added dropwise, using stirring and a slow N_2 purge. The products, collected in the traps, and the residue in the flask were analyzed and identified by v.p.c. and infrared. The unsaturated products, such as ethylene, were brominated and identified as the bromo compound by analysis, refractive index, and their infrared spectra. The vapor phase decarboxylation was carried out by passing the bisfluoroformate vapors with dry nitrogen as carrier gas at a contact time of 10 sec. through an electrically heated quartz tube, which was connected to three cold traps (two at −78° and one at −196°) and a mercury blow off. The heated zone (300°) of the quartz tube (length, 30 cm.; o.d., 1 cm.) was filled with $Na_4P_2O_7$–$4BF_3$ as a catalyst. The gas inlet was heated by an infrared lamp to prevent condensation of the starting material.

Electrolytic Reductive Coupling. V.[1] Reactions with 2- and 4-Vinylpyridine

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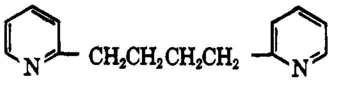
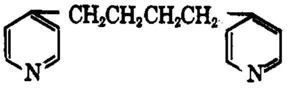
Both 2- and 4-vinylpyridine have been used extensively as acceptors in the Michael reaction.[2] Polarographic examination in this laboratory showed that these olefins in mildly alkaline solution are reduced at −1.6 and −1.5 v., respectively (beginning of wave *vs.* the saturated calomel electrode). Since these values are more positive than those reported for pyridine derivatives not bearing an unsaturated side chain,[3] it is apparent that the vinyl group reduces before the ring. Therefore, these vinylpyridines could serve as either donors or acceptors and thereby meet our criteria[1] for versatile participation in electrolytic reductive coupling.

A concentrated solution of 2-vinylpyridine in 67% aqueous tetraethylammonium *p*-toluenesulfonate was electrolyzed at a mercury cathode. The expected hydro dimer I, b.p. 110° (0.15 mm.), m.p. 43–45° (m.p. of diperchlorate, 191–191.5°; of dipicrate, 226–227°; of dimethiodide, 260–261°), was obtained in 69% yield.[4] The structure was established by elemental, molecular weight, infrared, and n.m.r. analyses.



I



II

Bianchetti[5] has reported the preparation of a homologous series of α,ω-bis(2-pyridyl)alkanes by reaction of α-picolyllithium with $Br(CH_2)_nBr$. When $n = 2$ his putative product I boiled at 104–105° (0.8 mm.) and yielded a diperchlorate, m.p. 260–265°; a dipicrate, m.p. 234–240°; and a dimethiodide, m.p. 169–171°. In our hands Bianchetti's procedure was found to yield not I but the known 1,2-bis(2-pyridyl)ethane, m.p. 49–50°; dipicrate, m.p. 241–243°; and dimethiodide, m.p. 170–171°. The base was further identified by elemental analyses, mass spectral molecular weight, and comparison with an authentic sample. The abnormalities[6] in the reaction of ethylene bromide with organolithium compounds may well be due to the interchange reaction described by Wittig,[7] which, in this case,[8] would lead to the following sequence.

$$\alpha\text{-}C_5H_4NCH_2Li + BrCH_2CH_2Br \longrightarrow \alpha\text{-}C_5H_4NCH_2Br + LiBr + C_2H_4$$

$$\alpha\text{-}C_5H_4NCH_2Br + \alpha\text{-}C_5H_4NCH_2Li \longrightarrow 1,2\text{-bis(2-pyridyl)ethane} + LiBr$$

An electrolysis of a concentrated solution of 4-vinylpyridine in 85% methyltriethylammonium *p*-toluenesulfonate containing dimethylformamide[9] was conducted. The reaction was interrupted when precipitation of the product began to cause coating of the cathode. II was isolated in 82% yield[4]; previous multistep routes to II[10] have given poor yields.

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[1] Paper IV: M. M. Baizer, *J. Org. Chem.*, **29**, 1670 (1964).

[2] E. D. Bergmann, D. Ginsburg, and R. Rappo, *Org. Reactions*, **10**, 179 (1959).

[3] I. M. Kolthoff and J. J. Lingane, "Polarography," Vol. 2, 2nd Ed., Interscience Publishers, Inc., New York, N. Y., 1952, p. 812.

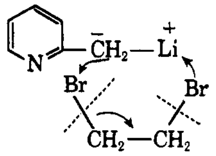
(4) Based on current input.

(5) G. Bianchetti, *Farmaco* (*Pavia*), *Ed. Sci.*, **11**, 346 (1956); *Chem. Abstr.*, **53**, 9209*g* (1959).

(6) *E.g.*, V. Ramanathan and R. Levine, *J. Org. Chem.*, **27**, 1667 (1962).

(7) G. Wittig and G. Harborth, *Ber.*, **77B**, 306 (1944).

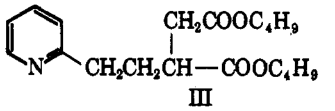
(8) One can also postulate that the α-bromomethylpyridine arises *via* a six-membered cyclic intermediate transition state.



(9) The vinylpyridine was sufficiently soluble in the quaternary salt solution that use of an auxiliary solvent would not have been necessary.

(10) M. W. Goldberg and L. M. Jampolsky, U. S. Patent 2,624,735 (1953); *Chem. Abstr.*, **47**, P12426*i* (1953); L. M. Jampolsky, *et al.*, *J. Am. Chem. Soc.*, **74**, 5222 (1952); G. Magnus and R. Levine, *ibid.*, **78**, 4127 (1956); *J. Org. Chem.*, **22**, 270 (1957).

An attempt to use dibutyl maleate (−1.38 to 1.48 v.)[11] as a donor toward 2-vinylpyridine (−1.6 v.) was successful. A solution containing the ester and the pyridine in a 1:5 molar ratio was electrolyzed at the cathode voltage required for the first monomer. The individual hydro dimers were obtained as well as the product of mixed coupling, III. The structure



III

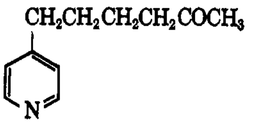
of III was established by elemental analysis, molecular weight, infrared and n.m.r. spectroscopy, and mass spectrometric fragmentation studies.

Reduction and ring closure of III would offer a route to new 4-ketoquinolizidines.[12]

Since the "reduction potentials" for methyl vinyl ketone (−1.4 v.)[11] and 4-vinylpyridine (−1.5 v.) are fairly close, three products (IV, V, and II) were expected[13] and were indeed obtained in a mixed reductive coupling of these two components.

$(CH_3COCH_2CH_2-)_2$

IV



V

Experimental[14]

Apparatus and General Procedure.—These have been described before.[15]

Hydrodimerization of 2-Vinylpyridine.—The catholyte contained 100 g. of 2-vinylpyridine,[16] 100 g. of tetraethylammonium *p*-toluenesulfonate, and 50 g. of water. The anolyte was a 50% solution of the above salt. Electrolysis was conducted at 25–30° at 1.5–2.0 amp.; total amp.-hr., 8.67. The pH was moderated by the addition of 4.4 ml. of acetic acid in the course of the run. The catholyte was then diluted with 200 ml. of water and extracted with five 50-ml. portions of methylene chloride. The extracts were washed with water, dried over Drierite, and filtered. The solvent and unchanged 2-vinylpyridine were removed at 10 mm. The residue was distilled and 23.6 g. (68.8%[4]) of crude I was collected from 125 (0.2 mm.) to 140° (0.3 mm.). For analysis a sample was redistilled through a spinning-band column and the (major) portion boiling at 110° (0.15 mm.), n^{25}D 1.5519, was collected. On storage the sample solidified, m.p. 43–45°. V.p.c. examination showed only one component.

Anal. Calcd. for I, $C_{14}H_{16}N_2$: C, 79.20; H, 7.60; N, 13.20; mol. wt., 212. Found: C, 78.55; H, 7.60; N, 13.29; mol. wt. (benzene), 211.

The **dipicrate** prepared in alcohol melted at 226–227°.

Anal. Calcd. for $C_{26}H_{22}N_8O_{14}$: C, 46.57; H, 3.31; N, 16.72. Found: C, 46.53; H, 3.66; N, 16.72.

The **diperchlorate** was prepared in acetic acid, m.p. 191–191.5°.

Anal. Calcd. for $C_{14}H_{18}Cl_2N_2O_8$: C, 40.69; H, 4.39; Cl, 17.16; N, 6.78. Found: C, 40.94; H, 4.59; Cl, 17.38; N, 6.55.

The **dimethiodide** was prepared according to Bianchetti,[5] m.p. 260–261°.

Anal. Calcd. for $C_{16}H_{22}I_2N_2$: C, 38.73; H, 4.47; N, 5.65. Found: C, 39.47; H, 4.96; N, 5.44.

The proton magnetic resonance spectrum of I was determined at room temperature on a Varian A-60 spectrometer operating at 60 Mc./sec. Spectrograde carbon tetrachloride was used as solvent and tetramethylsilane as internal standard. The δ-values for the ring protons were found at −8.31, −7.33, and −6.88 (total 7.98H); the side-chain α-protons had a δ-value of −2.74 (for 4.01H) and the β-protons −1.84 (for 3.97H). It is obvious that no CH_3 protons arising from α- to β- or α- to α-coupling of the monomer units were found.

Hydrodimerization of 4-Vinylpyridine.—The cathode contained 43 g. each of 4-vinylpyridine,[16] 85% aqueous methyltriethylammonium *p*-toluenesulfonate, and dimethylformamide. The anolyte had 20 g. of 64% quaternary salt solution. Electrolysis was at 30° and 2.0 amp. for a total of 3.8 amp.-hr. At this time sufficient solid had deposited on the cathode to make further operation inconvenient. The product II was removed by filtration, washed, and dried: 6.0 g., m.p. 116–118°. The original mother liquor was diluted with 300 ml. of water and extracted with five 50-ml. portions of methylene chloride. The extracts were washed, dried, filtered, and freed of solvent and excess starting material. The dark residue was dissolved in methylene chloride and purified by passage through a column of activated alumina. From the effluent there was isolated 6.4 g. of II which, after trituration with methanol, melted at 119–121° (lit.[17] m.p. 117.5–118.5°). The **dipicrate** melted at 220–221° (lit.[17] m.p. 219.5–220.5°).

Mixed Reductive Coupling of Dibutyl Maleate and 2-Vinylpyridine.—The catholyte contained 79.8 g. of 2-vinylpyridine, 39.4 g. of dibutyl maleate, 86.5 g. of tetraethylammonium *p*-toluenesulfonate, 10.4 g. of water, and 68.0 g. of dimethylformamide. The electrolysis was conducted at 25–33° and an average of 2 amp. for a total of 10.1 amp.-hr. The catholyte was worked up by the procedure described above. The methylene chloride residue was fractionated through a spinning-band column. The fractions boiling below 120° (0.25 mm.) contained dibutyl maleate and I. The residue was distilled from a semimicro apparatus without a column and 12.9 g. of pale yellow liquid A was collected at 174–186° (0.2 mm.). V.p.c. examination showed two components in A (ratio 1:3); they were separated in the F and M Model 770 automatic preparative gas chromatograph using a 12-ft. column of 12% silicone grease on 48-mesh Chromosorb W at 300°. The smaller fraction was III, n^{25}D 1.4779.

Anal. Calcd. for $C_{19}H_{29}NO_4$: C, 68.03; H, 8.71; N, 4.18; mol. wt., 335. Found: C, 67.80; H, 8.61; N, 4.15; mol. wt. (mass spectrometer), 335.

The n.m.r. spectrum was consistent with structure III. Furthermore, the base peak obtained by mass spectrometric fragmentation was at *m/e* 93 (calcd., 93 for formation of $C_5H_4NCH_2$ fragment plus H migration). If the coupled product had been formed by attachment of the α-position of 2-vinylpyridine to dibutyl maleate, the corresponding fragment would have had *m/e* 106.[18]

The second fraction obtained by v.p.c., n^{25}D 1.4472, was tetrabutyl butane-1,2,3,4-tetracarboxylate identified by elemental analysis, molecular weight, and identity of retention time in v.p.c. with that of an authentic sample.[19]

Mixed Reductive Coupling of 4-Vinylpyridine and Methyl Vinyl Ketone.—The catholyte contained 24.4 g. of 4-vinylpyridine,[16] 50.0 g. of methyl vinyl ketone, 70.0 g. of tetraethylammonium *p*-toluenesulfonate, 10 ml. of water, and 150 ml. of dimethylformamide. Current input at 25° and *ca.* 2 amp. was 10.7 amp.-hr. From the methylene chloride residue excess monomers and dimethylformamide were removed at 13 mm. The residue was fractionated through a spinning-band column: (i) 4.0 g., b.p. mainly 74–76° (0.2 mm.); (ii) 2.6 g. of an intermediate fraction boiling up to 110° (0.06 mm.); (iii) 8.3 g. of a fraction boiling from 102 (0.09 mm.) to 110° (0.06 mm.), n^{25}D 1.5040; and (iv) a higher boiling residue. Fraction i solidified and was found to be IV: m.p. (from benzene–hexane) 39° (lit.[20] m.p. 43°), m.p. of the bis-2,4-dinitrophenylhydrazone 214–215° (lit.[20] m.p. 216–218°), m.p. of the bissemicarbazone 226–227° (lit.[21] m.p. 226°), and m.p. of the dioxime 154–155°

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(11) Figures in parentheses represent the cathode voltage, *vs.* the saturated calomel electrode, observed in the hydrodimerization of the individual monomers.

(12) V. Boekelheide and S. Rothschild, *J. Am. Chem. Soc.*, **71**, 879 (1949).

(13) M. M. Baizer, *Tetrahedron Letters*, 973 (1963).

(14) Boiling points are uncorrected. Mercury was used as a cathode throughout. Elemental analyses of all previously reported compounds were checked and found to be satisfactory.

(15) M. M. Baizer, *J. Electrochem. Soc.*, **111**, 215 (1964).

(16) A trace of hydroquinone was included.

(17) G. Magnus and R. Levine, *J. Am. Chem. Soc.*, **78**, 4127 (1956).

(18) J. H. Beynon, "Mass Spectrometry and Its Application to Organic Chemistry," Elsevier Publishing Co., New York, N. Y., 1960, pp. 340–345.

(19) M. M. Baizer and J. D. Anderson, *J. Electrochem. Soc.*, **111**, 223 (1964).

(20) E. Buchta and H. Weidinger, *Ann.*, **580**, 109 (1953).

(21) S. Shimizu, *J. Agr. Chem. Soc. Japan*, **23**, 288 (1950); *Chem. Abstr.*, **44**, 8868*i* (1950).

(lit.[21] m.p. 155°). Fraction iii was found to be pure by v.p.c. and was analyzed as V [lit.[22] b.p. 129–130° (1 mm.)].

Anal. Calcd. for $C_{19}H_{29}NO_4$: C, 74.58; H, 8.47; N, 7.91. Found: C, 73.91; H, 8.56; N, 7.63.

The semicarbazone of V melted at 160° (lit.[22] m.p. 158°).

Acknowledgment.—The authors are particularly grateful to the following members of Donald Beasecker's group for performing the instrumental analyses: J. C. Edwards, O. P. Tanner, D. J. Bauer, and R. A. Anderson.

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[22] M. Miocque, *Bull. soc. chim. France*, 322 (1960).

The Acyloin Condensation. II. The Conjugate Addition of Some α,β-Unsaturated Esters Followed by a Dieckmann Cyclization[1]

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The acyloin-type condensation with ethyl *p*-methylcinnamate, ethyl *o*-chlorocinnamate, and ethyl *p*-chlorocinnamate gave the respective phenyl-substituted cyclopentane carboxylic acid, ethyl 5-oxo-2,3-diphenylcyclopentane carboxylate, when refluxed with sodium in ether. These were hydrolyzed, respectively, with 48% hydrobromic acid and 10% sodium hydroxide to give the respective diphenyl-substituted cyclopentanones and the diphenyl-substituted adipic acids. The treatment of the following esters of cinnamic acids, *n*-propyl, *n*-butyl, *n*-amyl, isopropyl, isobutyl, isoamyl, *sec*-butyl, *t*-butyl, cyclohexyl, benzyl, and β-phenylethyl, with sodium in ether gave the corresponding 5-oxo-2,3-diphenylcyclopentane carboxylic acid esters. The course of these reactions and products, respectively corresponded to the course of the reactions and products obtained with ethyl cinnamate.[3]

The need for certain starting compounds for the syntheses of potential physiologically active compounds inspired this work. The acyloin condensation with α,β-unsaturated esters of the cinnamic acid variety have been shown to proceed by way of conjugate addition followed by a Dieckmann ring closure.[3-5] The results obtained in this work extend the generality of this reaction.

Ethyl *p*-methylcinnamate, ethyl *o*-chlorocinnamate, and ethyl *p*-chlorocinnamate were prepared by the Claisen condensation by the treatment of the respective aldehydes with ethyl acetate and sodium.[6] The acyloin-type condensation was carried out by refluxing the esters with powdered sodium in dry ether. Ethyl *p*-methylcinnamate gave a 25% yield of the condensation product. Ethyl *o*-chlorocinnamate and ethyl *p*-chlorocinnamate gave 9% yields of the corresponding condensation products. In consideration of the evidence for the proposed mechanism for this reaction,[3,5] ethyl cinnamate with a methyl substituent in the *ortho* or *para* position in the phenyl moiety would be expected to give a higher yield of the condensation product I than the unsubstituted ethyl cinnamate, as a positive methyl group would be expected to enhance the electron density of the carbonyl oxygen in the cinnamate ester, facilitating reduction by sodium and thus favoring the increase of the yield of I. The yield was found to be slightly higher. Ethyl cinnamate in this reaction gave a 20% yield of the corresponding product.[7] The chloro substituent being a negative group would be expected to decrease the electron density on the carbonyl oxygen of the cinnamate ester making reduction by sodium more difficult, and thus favoring lower yields of II and III. This was found to be the case.

The structures for I, II, and III were demonstrated by their analysis, acid hydrolysis and basic hydrolysis products, and their characteristic infrared spectra (see Table I).

Although for compounds VIII and IX, the carbon and hydrogen values were high and the chlorine values were low, the correct values of carbon, hydrogen, and chlorine for compounds II and III together with the infrared spectra of VIII and IX help to make these values acceptable.

The 2-carbethoxycyclopentanone group has been shown to absorb strongly in the carbonyl region giving a very characteristic doublet at about 5.7–5.8 μ.[3] Compounds I, II, and III absorbed strongly in the carbonyl region, giving a doublet at 5.72–5.83 μ. The hydrolysis products gave absorption maxima in the infrared region characteristic of ketones and dibasic acids.

The preparation of compounds X through XX was important for finding if the ester group in the α,β-unsaturated ester would affect the yield of the 5-oxo-2,3-diphenylcyclopentane carboxylic acid nucleus in the acyloin-type condensation, and also to produce model compounds of this class to learn if large ester groups in these β-keto esters would decrease ring opening by basic reagents in the syntheses of pyrimidines.

No complete uniform effect regarding yields could be observed; however, yields of 24, 31, 35, and 41% were obtained, respectively, from the butyl, isoamyl, isobutyl, and cyclohexyl cinnamic esters, while the ethyl ester gave a 20% yield.[3,7]

The evidence for the demonstration of the structures of the compounds X through XX was furnished by their carbon and hydrogen analyses and their infrared spectra (see Table II). Compounds X through XX absorbed strongly at about 5.7–5.8 μ, giving a doublet.

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(1) Grateful acknowledgment is made to the Department of Health, Education, and Welfare, Public Health Service, and National Institutes of Health, Bethesda, Md., for the support of this work by the Grant CA-05465-02-MC.

(2) Taken in part from theses submitted to North Carolina College in partial fulfillment of the requirements for M.S. degrees, June 1962, by G R. Kilpatrick and, June 1963, by N. Horton and S. A. Blakeney.

(3) E. L. Totton, R. C. Freeman, H. Powell, and T. Yarboro, *J. Org. Chem.*, **26**, 343 (1961).

(4) K. Bernhauer and R. J. Hoffmann, *Pract. Chem.* (N.F.), **149**, 317 (1937).

(5) H. A. Weidlich, *Ber.*, **71**, II, 1601 (1938).

(6) "Organic Syntheses," Coll. Vol. I, Gilman and Blatt, Ed.; John Wiley and Sons, Inc., New York, N. Y., 1941, p. 252.

(7) We wish to report a correction: the yield of 2-carbethoxy-3,4-diphenylcyclopentanone[3] was 20%, not 10%.