hydrogen), and 7.2–7.9 (m, 10.0 H, aromatic). The IR spectrum does not show peaks appropriate for the carbonyl group.[12]

The product from the electrolysis of I-$COOCH_3$ at +0.76 V was a dark oil and displayed an NMR spectra consistent with product mixture containing 5% IV and 95% 4-carbomethoxy-1,3-diphenyl-5-methylpyrazole. The NMR ($CDCl_3$) signals for IV appear as singlets at δ (Me_4Si) 2.34 and 6.42 in a 1:3 ratio, respectively, and account for 5% of the aromatic hydrogens. The signals for the ester product V appear as singlets at δ 2.53 and 3.70, where the ratio between these signals and the remaining aromatic signal is 3:3:10. Column chromatography of the dark oil on silica gel with CH_2Cl_2 solvent produced a yellow solid which had mp 240–241 °C. The NMR spectrum of this material shows signals appropriate for V, and the IR spectrum shows the carbonyl peak at 1710 cm^{-1}. Hydrolysis of this material in 0.3 N NaOH in 60% aqueous methanol produced a carboxylic acid derivative with mp 183–184 (lit. mp[4] 194 °C) which had NMR spectrum ($CDCl_3$) δ (Me_4Si) 2.54 (s, methyl) and 7.1–7.7 (m, aromatics). This material decarboxylates during GLC analysis on column 1 (T_1 = 180 °C, T_2 = 220 °C, R = 4 °C/min, 21 mL/min, injection T = 250 °C) producing two compounds appearing at 4.5 (1.5%) and 8.9 min (98.5%). On column 2 (220 °C, 21 mL/min, injection T = 250 °C) the peaks appear at 5.4 and 39.7 min and in the same ratio.

Acknowledgments. The author acknowledges R. Hernandez and M. Ochoa for technical assistance, and K. K. Kanazawa and R. Galway for providing the electrochemical instrumentation.

Registry No.—IV, 7188-89-8; V, 25113-27-3; *N*-(2-chlorobenzylidene)-*N'*-(*p*-methoxyphenyl)hydrazine, 60981-60-4; 1-*p*-anisyl-5-methyl-3-phenylpyrazole, 63534-54-3.

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Pyrrole Acylation and Spectral Studies[1]

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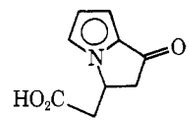
The direct acetylation of pyrrole has been found to give 3-acetylpyrrole as the minor product. Trifluoroacetic anhydride catalyzed acetylation of 2-acetylpyrrole gives the hitherto unreported 2,4-diacetylpyrrole as the major product. Methyl hydrogen β-(1-pyrrolyl)glutarate was isolated from the partial hydrolysis of the corresponding dimethyl ester. 2,3-Dihydro-1*H*-pyrrolizine-3-acetic acid (2) was prepared from 2,3-dihydro-1-oxo-1*H*-pyrrolizine-3-acetic acid (1). Attempts to cyclize 1 and 2 were unsuccessful. Certain features of the UV, IR, NMR, and mass spectra of selected compounds prepared are reported.

In contrast to the statement in most texts and reference books that the acetylation of pyrrole with acetic anhydride gives only 2-acetylpyrrole, Albert[3] asserts that "direct acetylation gives . . . mainly the 2- and 3-isomers" and Reddy[4] states that the "reaction with acetic anhydride affords the 2- and 3-isomers in about equal amounts". Neither author listed a reference and a search of the literature failed to yield supporting experimental results, although the original acetylation reaction of Ciamician and Dennstedt[5] has been repeated several times.[6] The fact that electrophilic nitration has been reported to give some (e.g. 7%[7] and 20%[8]) 3 substitution led us to reexamine acylation reactions in connection with other studies.

Acylations. From the reaction of acetic anhydride with pyrrole as described by Ciamician and Silber[6b] were isolated 2-acetylpyrrole (39.2%) and 3-acetylpyrrole (8.5%). The latter product probably was not detected in earlier work because it is not volatile in the steam-distillation step of the workup[9] and must be extracted from the residue. Acylation with acetic acid–trifluoroacetic anhydride (TFAA), in contrast, gave only 2-trifluoroacetylpyrrole in low yield. The infrared spectrum of this product is reported[10] to have bands at 3436 (NH), 3300 (CH), and 1667 cm^{-1} (CO). We have assigned the absorption at 3436 cm^{-1} to free NH stretching, that at 3289 cm^{-1} to associated NH stretching, detected both free (1684 cm^{-1}) and associated (1665 cm^{-1}) CO stretching, and attributed absorptions at 2336, 1546, 1431 and 1412 cm^{-1} to the pyrrole ring.[11,12]

Monosubstituted, deactivated pyrroles have been acetylated,[7,13] and only the 2,5-diacetyl compound (33%) was reported from 2-acetylpyrrole.[6a] In contrast, the nitration of 2-acetylpyrrole gave both the 2,5- and the 2,4-disubstitution products,[14] as did 2-carbomethoxypyrrole.[14a] The TFAA-catalyzed reaction of 2-acetylpyrrole with acetic anhydride has now been found to give the 2,5- (ca. 19%) and 2,4- (ca. 46%) diacetyl derivatives. The ultraviolet spectrum of the latter, a new compound, had the same relative intensities as those of ethyl 4-acetyl-3-ethyl-5-methylpyrrole-2-carboxylate[15] and ethyl 4-acetyl-3,5-dimethylpyrrole-2-carboxylate[16] which were the best models found. The relative intensities of the two principal bands were the inverse of those for 2,3-diacetylpyrrole. The NMR spectrum was consistent with the assigned structure. The infrared spectrum showed only associated CO stretching.[16]

Further acylations considered were the sterically strained ring closures of 2,3-dihydro-1-oxo-1*H*-pyrrolizine-3-acetic acid (1), which had been synthesized by Josey and Jenner,[17] and of 2 in an attempt to form the corresponding tricyclic



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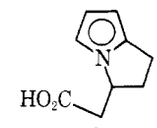

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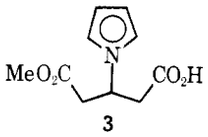
structures. Repetition of the steps leading to 1 yielded liquid dimethyl β-aminoglutaconate as described, but also an allo-

tropic form of the ester having a different melting point than reported. Saponification of the intermediate dimethyl β-(1-pyrrolyl)glutarate as described gave incomplete hydrolysis, and the new methyl hydrogen β-(1-pyrrolyl)glutarate (3) was



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isolated. High yields of β-(1-pyrrolyl)glutaric acid were obtained by stirring a methanolic solution of the diester overnight with 6 N sodium hydroxide subsequent to the reflux period.

For the cyclization of the diacid to 1 with poly(phosphoric acid) (PPA), temperature control (≤100 °C) of the exothermic reaction and the subsequent extraction of 1 ($K_a = 2 \times 10^{-4}$ as determined by potentiometric titration) at pH ≤1 were critical. The fusion of a five-membered ring to thiophene causes a hypsochromic shift in the ultraviolet absorption,[18] but this was not observed for the long-wavelength maxima for 1 or 2,3-dihydro-1-oxo-1*H*-pyrrolizine[19] as compared with the absorption for 1-methyl-2-acetylpyrrole[19] and 2-acetylpyrrole. The relative intensities of the absorptions for the last two compounds and 1 corresponded to the relative degree of planarity of the carbonyl with the ring. Treatment of the diacid with liquid HF gave no 1 (which was shown to be stable to the reaction conditions). The spectral characteristics (UV, IR, MS) of the products formed from the diacid and TFAA agreed with those expected for the 2-trifluoroacetyl substitution derivative and the corresponding anhydride. Treatment of 1 with liquid HF for periods up to 2 weeks, with PAA at 90–100 or 100–115 °C, with BF_3, or with TFAA afforded no trace of tricyclic ketone. These reagents were selected as ones which would not be expected to complex strongly with the keto carbonyl of 1.

Huang–Minlon reduction[20] of 1 gave 2,3-dihydro-1*H*-pyrrolizine-3-acetic acid (2) which, like the corresponding 2,3-dihydro-1*H*-pyrrolizine,[21] was rather unstable, and attempted cyclization with PAA was not successful. The catalytic reduction over Pd or Rh on C or Rh on Al_2O_3 of a model for the oxime of 2, 2-acetylpyrrole oxime, also failed. The ultraviolet absorption of 2 and the other 1-alkylpyrroles were very similar and, contrary to earlier reports,[21,22] showed no absorption at 204 or 263 nm. This observation and that by Cookson[16] that 1-*n*-pentyl-2-(acetamidomethyl)pyrrole exhibits no absorption above 260 nm cast doubt on the identification of a compound showing maxima at 220 and 295 nm as 1-acetamido-1*H*-pyrrolizine.[21]

NMR Spectra. The spectrum of 2,5-diacetylpyrrole in Me_2SO was as expected except for an apparent doublet at δ 6.99 for which the coupling constant was 0.5–0.7 Hz smaller than those reported for 1,3 or 1,4 coupling in monoacetylpyrroles.[23,24] The virtual elimination of coupling of the NH with ring hydrogens in Me_2SO has been reported.[23,25] Yet, the absence of mutual splitting by H-3 and H-4 appears to rule out nonequivalence for these hydrogens,[25] as does the single absorption for the acetyl methyl groups. The sharp singlet for methyl hydrogens excludes ring hydrogen coupling with these. Thus, coupling of H-1 with H-3 and H-4 is the best explanation provided by simple splitting rules. In the spectrum of 2,4-diacetylpyrrole the singlets for the nonequivalent methyl groups were clearly separated. The lower field ring hydrogen signal was assigned to H-5.

In the spectrum for 2-trifluoroacetylpyrrole H-4 and H-5 were mutually coupled with H-1 and H-3 and the multiplet for H-3 was not well resolved.[23,15] The fluorine signal was split by coupling with H-3.[26]

The spectrum of 1 had two pairs of doublets (H-5 at lower field) for each pyrrole ring hydrogen (ABC pattern) with the spin–spin coupling very similar to that of H-1 decoupled 2-acetylpyrrole.[23] The assignment of the aromatic hydrogen signals for 2 (ABC pattern; H-5 at lowest field, then H-6 and H-7) paralleled those for methylpyrroles[27] with apparent H-7 α-methylene coupling.[23,28–30]

Mass Spectra. The electron-impact fragmentation pattern for 1 corresponded to that observed for 2,3-dihydro-1-oxo-1*H*-pyrrolizine,[31] and the ions of *m/e* 93 and 66 have also been reported from 2-acyl- and 2-carboxylpyrroles.

The molecular ion of 2 was indicated by the metastable peaks at *m/e* 87.5 and 68.2 to decompose by two routes to ions of *m/e* 120 (loss of CO_2H) and 106 (loss of CH_2CO_2H), respectively. The base peak, *m/e* 106, then lost C_2H_3 (indicated by the metastable peak at *m/e* 60) to form a methylenepyrrole ion (*m/e* 80). The analogous *N*-methylene ion has been reported to arise from *N*-butyl- and *N*-pentylpyrroles.[33] No peak at *m/e* 81, which is present in the spectra of *N*-alkylpyrroles having more than three carbons in the side chain,[33,34] was detected.

For the ions of *m/e* 120 and 162 in the spectrum of β-(2-trifluoroacetyl-1-pyrrolyl)glutaric anhydride, ring closures to 2,3-dihydro-1-oxo-1*H*-pyrrolizine and the corresponding 3-acylium ions, respectively, are proposed, although interactions of 1-alkyl groups with the pyrrole ring have been reported[33] and a 1-vinyl-1-acylium structure can be written for *m/e* 120. Also of interest were the peaks at *m/e* 202, which possibly represents the (2-trifluoroacetyl-1-pyrrolyl)cyclopropyl ion, and at 93 for the pyrroleacylium ion commonly observed from 2-acylpyrroles.[32]

None of the metastable peaks found for the anhydride were present in the spectrum of β-(2-trifluoroacetyl-1-pyrrolyl)-glutaric acid, but several of the fragment ions appeared to be the same. The latter did not arise from anhydride formed in the mass spectrometer, since a number of the other ions from the anhydride were absent. Of the three transformations *m/e* 247 → 216 (calcd 189.0), *m/e* 224 → 206 (calcd 189.5), and *m/e* 216 → 202 (calcd 189.2) which fit the metastable peak at *m/e* 189.5, the first required a nonsimple loss of OCH_3 from the assigned structure, the second (which is favored) involved simple loss of H_2O to form the anhydride, and no reasonable transformation was deduced for the third.

Experimental Section

Melting points were taken on a calibrated Kofler hot stage and are corrected, or, when noted, on a Hoover apparatus and are uncorrected. Boiling points are uncorrected. Automatic collection of column chromatograph fractions was performed by a Warner-Chilcott Laboratories Instruments Division Model A1205 with volumetric siphoning. UV spectra were recorded in balanced 1-cm quartz cells on a calibrated Cary Model 11 or 14 spectrophotometer. IR spectra were recorded on a calibrated Perkin-Elmer Model 21 instrument. NMR spectra were taken on a Varian A-60 with Me_4Si as an internal standard or, for F^{19}, on a Varian HR-60 spectrometer, the latter at 40 MHz. Chemical shifts are given in δ (ppm). Mass spectra were obtained on an Associated Electrical Industries MS-9 at 70 eV employing a direct insertion probe. Analyses were performed by A. Bernhardt, Mülheim (Ruhr), Germany.

Acetylation of Pyrrole with Acetic Anhydride. From 13.0 g (0.194 mol) of dried redistilled pyrrole and 108 g (106 mol) of acetic anhydride, which were allowed to react in a high-pressure bomb heated to 300–320 °C as described by Ciamician and Silber,[6b] was obtained 1.1 g of 2-acetylpyrrole, mp 89.5–90.5 °C (uncorrected) (lit.[7] 89–89.5 °C), from the distillate from the neutralized aqueous workup solution. Addition of bomb rinsings to the residue and then steam distillation gave an additional 2.7 g of product, mp 89–90 °C. Repeated steam distillation of the dark residue, continuous ether extraction of the distillate, and sublimation (1 atm) of the crude material gave 4.41 g of colorless solid: mp 89–90 °C; total yield 8.21 g (39.2%); UV (EtOH) ($\epsilon \times 10^{-3}$) 250 (sh, 3.8), 288 (14.5), and (Et_2O) (intensity ratio) 245 (sh, 1), 277 (4.3), and 285 nm (sh, 3.8); IR (CCl_4) 3425 (free NH s), 3268 (assoc NH s), 1653 (free CO), 1645 (assoc CO), 1543, 1439, and 1425

cm^{-1}; NMR (CH_2Cl_2), 7.05 (8 line m, $J_{1,5}$ = 3 Hz, $J_{3,5}$ = 1.4 Hz, $J_{4,5}$ = 2.4 Hz, H-5), 6.92 (7 line m, $J_{1,3}$ = 2.4 Hz, $J_{3,4}$ = 3.9 Hz, $J_{3,5}$ = 1.4 Hz, H-3), 6.23 (two overlapping t, $J_{1,4}$ = 2.4 Hz, $J_{3,4}$ = 3.9 Hz, H-4), and 2.37 (s, CH_3CO) of the corresponding areas.

The remaining dark residue was triturated with hot H_2O and then continuously extracted with ether for 2 days. Concentration of the ethereal solution gave 1.8 g (8.5%) of 3-acetylpyrrole as a colorless powder: mp 114–114.5 °C (uncorrected). Recrystallization from benzene raised the melting point to 114–115 °C (lit.[35] 112.5–113.5 °C): UV (Et_2O) $\epsilon \times 10^{-3}$) 234 (7.62), 258 (5.07) and (EtOH) (intensity ratio) 234 (6.9), 272 (sh, 3.2), 300 (sh, 1.6), and 320 nm (sh, 1.0); IR ($CHCl_3$), 3448 (free NH s), 3279 (assoc NH s), 2985 (CH s), 1661 (C=O), 1548, 1502, and 1420 cm^{-1}; NMR (CH_3NO_2), 10.1 (br s, $J_{1,4}$ = 2.8 Hz, $J_{1,5}$ = 3 Hz, NH), 7.57 (two overlapping t, $J_{1,2}$ = 3.2 Hz, $J_{2,4}$ = 1.6 Hz, $J_{2,5}$ = 1.9 Hz, H-2), 6.89 (8 line m, $J_{1,5}$ = 3 Hz, $J_{2,5}$ = 1.9 Hz, $J_{4,5}$ = 2.8 Hz, H-5), 6.63 (6 line m, $J_{1,4}$ = 2.8 Hz, $J_{2,4}$ = 1.6 Hz, $J_{4,5}$ = 2.8 Hz, H-4), and 2.40 (s, CH_3O)[29] having the corresponding areas.

2-Acetylpyrrole Oxime Acetate. A mixture of 0.112 g (0.9 mmol) of 2-acetylpyrrole oxime, mp 147–148.5 °C (lit.[36] 145–146 °C), 3 mL of dry ether, 0.101 g (1 mmol) of dry triethylamine, and 0.078 g (1 mmol) of acetyl chloride was stirred for 2 h and filtered, and the precipitate was washed with ether. The 0.1535 g of oil obtained from the filtrate was chromatographed over silica gel (1 × 60 cm). Elution with 20% ethyl acetate–hexane separated 0.1345 g (90%) of 2-acetylpyrrole oxime acetate; mp 46–55 and 79.5–81.5 °C after recrystallization, with charcoal decolorization, from ethyl acetate–hexane: UV (Et_2O) ($\epsilon \times 10^{-3}$) 242 (sh, 3.9), 286 (17.6), and (EtOH) 245 (sh, 3.8), 290 nm (17.3); IR ($CHCl_3$) 3413 (free NH s), 3226 (assoc NH s), 1757 (C=O), 1597 (C=NO), 1449, 1414, 1361, 1325, 1211, 1198, 1143, 1111, 1071, 1037, 992, 948, 913, 892, 880, and 673 cm^{-1}.

Anal. Calcd for $C_8H_{10}N_2O_2$: C, 57.81; H, 6.07; N, 16.86. Found: C, 57.79, H, 6.21; N, 16.03.

Acylation of Pyrrole with Acetic Acid–Trifluoroacetic Anhydride. To a stirred, ice-cooled solution of 24.2 g (0.25 mol) of trifluoroacetic anhydride and 2 g (0.15 mol) of glacial acetic acid was added 6.71 g (0.1 mol) of freshly distilled pyrrole over a 30-min period. The dark solution was stirred for 45 min and then poured into a solution of 50 g of $NaHCO_3$ in 300 mL of H_2O. This mixture plus 400 mL of H_2O was steam distilled. Water (500 mL) was added to the residue and steam distillation continued until the yellow distillate amounted to 1 L. Refrigeration of the distillate yielded 1 g of colorless crystals, mp 40–45 °C, which after sublimation at 15 mm and 60 °C gave 0.9 g (5.8%) of 2-trifluoroacetylpyrrole: mp 47–47.5 °C (lit.[10] 46–47 °C); UV (EtOH) ($\epsilon \times 10^{-3}$) 260 (sh, 5) and 303 nm (16.2); IR (CCl_4), 3436 (free NH s), 3289 (assoc NH s), 2336 (ring), 1684 (free CF_3CO), 1664 (assoc CF_3CO), 1546, 1431, and 1412 cm^{-1}; NMR (CCl_4), 11.0 (br s, $J_{1,5}$ = 3.2 Hz, 60 Hz, H-1), 7.31 (3-line, broadened m partially resolved at 100 sweep width into 7.34, (8-line m), and 7.20 (poorly resolved m, $J_{3,4}$ = 4 Hz, $J_{3,5}$ = 1.6 Hz, $J_{1,5}$ = 3.2 Hz, $J_{4,5}$ = 2.5 Hz, H-3 and H-5), 6.38 (two overlapping t, $J_{1,4}$ = 2.4 Hz, $J_{3,4}$ = 4 Hz, $J_{4,5}$ = 2.5 Hz, H-4) of the corresponding areas. The signal for fluorine was a doublet, $J_{F,H-3}$ = 0.86 Hz.

Acetylation of 2-Acetylpyrrole with Acetic Acid and Trifluoroacetic Anhydride. To a stirred mixture of 0.91 g (15 mmol) of glacial acetic acid and 2.42 g (25 mmol) of trifluoroacetic anhydride under N_2 was added dropwise a solution of 1.09 g (10 mmol) of 2-acetylpyrrole in 15 mL of dry benzene. The whole was stirred for 2 weeks during which the color turned from cranberry to black. The mixture was poured into 10 mL of H_2O containing 5.04 g (0.6 mol) of $NaHCO_3$, and the resulting solution (pH 7) was extracted with ether. The aqueous layer was set aside. Evaporation of the solvent from the dried ($MgSO_4$) extract left 1.5 g of red-black solid which was triturated with hot H_2O for 2 h. The cooled filtrate was extracted with ether. Removal of the solvent from the dried extract gave 0.948 g of solid which was chromatographed on basic Al_2O_3. Elution with CCl_4 followed by gradually increasing amounts (up to 30%) of $HCCl_3$ in CCl_4 separated 0.2813 g (18.7%) of 2,5-diacetylpyrrole as colorless needles, mp 158–158.5 °C (uncorrected) after sublimation and recrystallization from H_2O–ethanol and, after recrystallization from dry nitromethane, 159.5–160 °C (lit.[37] 161–162 °C): UV (Et_2O) (intensity ratio) 222 (sh, 1), 227 (1,3), 234 (sh, 1.1), 293 (2.2), 303 (2.2), and (EtOH) 230 (1.1), 234 (sh, 1) 302 nm (2.4); IR ($CHCl_3$), 3390 (NH s), 2985 (CH s), 1672 (free CH_3CO), 1664 (assoc CH_3CO), 1536, and 1425 cm^{-1}; NMR (Me_2SO), 12.15 (br s, $J_{1,3}$ = $J_{1,4}$ = 1.9 Hz, H-1), 6.99 (d, $J_{1,3}$ = 1.9 Hz, H-3), and 2.47 (s, CH_3CO). Juxtaposition of the signal at 2.47 to Me_2SO absorption precluded peak area integration.

Elution with 50–70% $HCCl_3$ in CCl_4 separated 0.7043 g (46.6%) of 2,4-diacetylpyrrole, mp 139.5–140 °C, after two recrystallizations from ligroin–THF: UV (MeOH) ($\epsilon \times 10^{-3}$) 228 (21), 260 (sh, 8), and 286 nm (16.2); IR ($HCCl_3$), 3401 (free NH s), 3236 (assoc NH s), 2347, 1656 (CH_3CO), 1553, 1488, 1420, 1385, 1351, 1271, 1222, 1168, 1136, 1126, 943, 928, and 849 cm^{-1}; NMR (CH_3NO_2), 10.68 (br s, $J_{1,3}$ = 2.5 Hz, $J_{1,5}$ = 3.2 Hz, H-1), 7.77 (two overlapping d, $J_{1,5}$ = 3.2 Hz, $J_{3,5}$ = 1.6 Hz, H-5), 7.40 (two overlapping d, $J_{1,3}$ = 2.5 Hz, $J_{3,5}$ = 1.6 Hz, H-3), 2.47 (s, CH_3CO), and 2.43 (s, CH_3CO) of the appropriate areas; the mass spectrum was recorded.

Anal. Calcd for $C_8H_9NO_2$: C, 63.58; H, 6.00; N, 9.27. Found: C, 63.45; H, 6.07; N, 9.36.

Dimethyl β-Aminoglutaconate. The procedure of Josey and Jenner[17] gave 72.2% of colorless liquid: bp 130–132 °C (2.8 mm); $n^{22}D$ 1.5055 (lit.[17] bp 120–130 °C/ca. 1 mm; $n^{25}D$ 1.5067). Concomitantly distilled was a colorless, cubic crystalline solid, mp 75–80 °C (lit.[17] 50–52 °C), which readily sublimed but did not induce crystallization of the liquid ester. The IR spectra (thin film) of the solid and liquid were identical: 3390 (NH s), 3279 (NH s), 2959 (CH s), 2924 (CH s), 1739 (C=O), 1667 (C=N?), 1626 (C=CC=O), and 1563 cm^{-1}.

Methyl Hydrogen β-(1-Pyrrolyl)glutarate (3). A solution of 32.5 g (0.144 mol) of dimethyl β-(1-pyrrolyl)glutarate,[17] 67.5 mL of 6 N NaOH (0.405 mol), and 87 mL of absolute methanol was refluxed for 2 h and the methanol then distilled slowly at 1 atm. The residual solution was acidified with 48 mL of 12 N hydrochloric acid and refrigerated. The yellow oil which separated was extracted into ether. Evaporation of the solvent from the dried ($MgSO_4$) extracts left 25.3 g of brown oil. The oil (15.04 g) was chromatographed over silica gel with an automatic fraction (50 mL) collector over a 2-week period. Elution with 10% ethyl acetate–hexane removed small amounts of oils which were discarded. Then, 20% ethyl acetate–hexane removed, successively, unchanged starting material (1.77 g, 5.5%), methyl hydrogen β-(1-pyrrolyl)glutarate (some overlapping) (6.29 g, 20.6%), and β-(1-pyrrolyl)glutaric acid (7.21 g, 25.4%). Rechromatography of the middle fraction with 30% ethyl acetate–hexane yielded colorless crystals of methyl hydrogen β-(1-pyrrolyl)glutarate: mp 102.8–103.3 °C; NMR (CH_2Cl_2), 10.1 (s, OH), 6.69 and 6.66 (two d, J = 2.0–2.5 Hz, H-2 and H-5), 6.08 (t, J = 2.0 Hz, H-3 and H-4), 4.88 (q, J = 7.0 Hz, CH_2CHCH_2), 3.56 (s, OMe), 2.87 (d, J = 7.0 Hz, CH_2CO_2H), and 2.83 (d, J = 7.0 Hz, CH_2CO_2Me) of the corresponding areas. The IR spectrum was recorded.

Anal. Calcd for $C_{10}H_{13}NO_4$: C, 56.86; H, 6.20; N, 6.63. Found: C, 56.97; H, 6.16; N, 6.75.

β-(1-Pyrrolyl)glutaric Acid. A mixture of 22.5 g (0.1 mol) of dimethyl β-(1-pyrrolyl)glutarate,[17] 45 mL of 6 N NaOH (0.3 mol) and 56 mL of absolute methanol was refluxed for 3 h. Water (10 mL) was added to dissolve the remaining suspended solids and the solution was stirred overnight. The volume was reduced to 100 mL by the slow distillation of solvent. The residual solution was acidified to pH 2–3 with 12 N hydrochloric acid and then refrigerated. The collected precipitate was pressed dry under reduced pressure, washed three times with ice water, and air dried. The tan crystals (12.6 g) had mp 127.5–130.5 °C.[17] Extraction of the filtrate with ether afforded an additional 6.2 g of product: mp 124–130 °C; total yield 18.8 g (95%). Colorless crystals, mp 129.5–130.5 °C, UV (H_2O) 210 nm (ϵ = 5100), were obtained by chromatography on silica gel with 4% methanol–benzene or 30–50% ethyl acetate–hexane as the eluant.

2,3-Dihydro-1-oxo-1*H*-pyrrolizine-3-acetic Acid (1). The procedure of Josey and Jenner[17] was followed on a reduced scale [7 g of β-(1-pyrrolyl)glutaric acid] except that the initial hydrolyzed reaction mixture was extracted with six 85-mL protions of ether and then subjected to continuous ether extraction for 2 weeks. The yield was 4.5 g (64.3%), mp 126–132 °C, and 1.3 g of less pure material.

Chromatography on silica gel with elution with 20% ethyl acetate–hexane and then 30% ethyl acetate–hexane removed minor impurities, then β-(1-pyrrolyl)glutaric acid along with traces of pyrrolizinecarboxylic acid, and finally 1 as colorless crystals, mp 130–133 °C (capillary); UV (Et_2O) ($\epsilon \times 10^{-3}$) 250 (sh, 4.35), 276 (sh, 18), 283 (20.1), (EtOH) 250 (sh, 3.4), 288.5 (20.3), (H_2O) 260 (sh, 3.8), and 293 nm (18.4); IR ($CHCl_3$), 3077 (br, H-bonded CO_2H), 2358 (ring), 1724 (acid C=O), 1698 (C=O), 1658 sh (C=O), and 1520 cm^{-1} (ring); NMR [$(CD_3)_2CO$], 7.29 (two d, $J_{5,7}$ = 1.3 Hz, $J_{5,6}$ = 2.3 Hz, H-5), 6.62 (q, $J_{6,7}$ = 4 Hz, $J_{5,7}$ = 1.3 Hz, H-7), 6.48 (q, $J_{6,7}$ = 4 Hz, $J_{5,6}$ = 2.3 Hz, H-6), 6.43 (br, OH), 5.00 (octet, $J_{2,3}$ = 3.8, 6.5 Hz, J_{3,CH_2CO_2H} = 6.5 Hz, H-3), 3.04 (m, $J_{2,3}$ = 3.8, 6.5 Hz, J_{3,CH_2CO_2H} = 6.5 Hz, H-2, CH_2CO_2H) of the appropriate areas; K_a = 2 × 10^{-4} (potentiometric titration with aqueous NaOH by the method of Meites and Thomas[38]); neutral equiv 180 (calcd 179; lit.[14] 180).

Reaction of 1 with Trifluoroacetic Anhydride. A mixture of TFAA (1.49 g, 7.1 mmol), β-(1-pyrrolyl)glutaric acid (0.5 g, 2.45 mmol), and 45 mL of dry CH_2Cl_2 was stirred until the absorption at 298 nm showed no change (45 h). The liquids were removed by distillation. Chromatography of the residual solid over silica gel (20% ethyl acetate–hexane) removed a mixture of β-(2-trifluoroacetyl-1-

pyrrolyl)glutaric acid and anhydride which gave 0.1 g (14%) of the acid, mp 141–147 °C. The second fraction yielded 0.2433 g (34.8%) of the acid anhydride (needles from 25% ethyl acetate–hexane): mp 120–120.5 °C; UV (ether) 299 and 268 nm (sh) (intensity ratio 2.4:1); IR ($CHCl_3$), 1821 (anhydride), 1776 (anhydride), 1675 (CF_3CO), 1524 (ring), 1414, 1376, 1330, 1266 (CF_3CO), 1198 (CH_3CO), 1156 (CF_3CO), 1099 (CF_3CO), 1070 (CF_3CO), 1053 (CF_3CO), 939, and 729 cm^{-1}; the mass spectrum was recorded.

Elution with 50% ethyl acetate–hexane afforded 0.36 g (48%) of the substituted glutaric acid as colorless crystals from the same solvent, mp 152–153.5 °C after two recrystallizations and drying over P_2O_5: UV (MeOH) ($\epsilon \times 10^{-3}$) 270 (sh, 5.95) and 303 nm (13.1); IR ($CHCl_3$), 2941 (H-bonding), 1718 (CO_2H), 1667 (CF_3CO), 1527 (ring), 1412, 1374, 1307, (CF_3CO), 1282 (CF_3CO), 1263 (CF_3CO), 1241, 1225, 1211, 1190 (CF_3CO), 1149 (CF_3CO), 1101 (CF_3CO), 1042 (CF_3CO), 952, 909, and 873 cm^{-1}; the mass spectrum was recorded.

2,3-Dihydro-1*H*-pyrrolizine-3-acetic Acid (2). A mixture of 2.1 g (32 mmol) of crushed 85% KOH pellets, 1.75 mL (1.8 g, 36 mmol) of 95% hydrazine hydrate, 1.97 g (10 mmol) of 1, and 12 mL of diethylene glycol under dry N_2 was heated over a 20-min period (external oil bath) to 150 °C (gas evolution). The distillative removal of H_2O and continued heating raised the temperature to 185 °C where it was maintained until N_2 evolution ceased (1.5 h). The cooled mixture was combined with ice–water and extracted with ether. The acidified solution was extracted with ether. Evaporation of the solvent from the dried ($MgSO_4$) extracts left 1.56 g (96.5%) of crude **2** as a greenish oil which solidified on chilling. The portion soluble in hot hexane was crystallized (seeding) and recrystallized from this solvent. Recrystallization of the solid material from the concentration of the mother liquors gave a total of 1.137 g (69%) of **2** as needles, mp 73–78 °C (not sharpened by further recrystallizations), unstable to exposure to light plus air and to polar solvents: UV (Et_2O) 215 (ϵ = 6500) and (MeOH) 213 nm (ϵ = 6100); IR (CCl_4), 3058 sh, 2915, 2632 sh (H-bonded CO_2H), 2347 (ring), 1724 sh, 1701 (C=O), 1538 (ring), 1464, 1414, 1366, 1299, 1222, 1185, 1144, 1119, 1053, 1010, 930, 909, 847, and 693 cm^{-1}; NMR (CCl_4), 11.4 (s, OH), 6.6 (two d, $J_{5,6} \simeq 3.0$, $J_{5,7} \simeq 1.0$ Hz, H-5), 6.2 (t, $J_{5,6} \simeq J_{6,7} \simeq 3.0$ Hz, H-6), 5.77 (br d, $J_{6,7} \simeq 3.5$ Hz, $J_{5,7} \simeq 1.0$ Hz, H-7), 4.61 (q, $J \simeq 6.5$, methyne), and ca. 2.8 (m, CH_2); the mass spectrum was recorded.

Anal. Calcd for $C_9H_{11}NO_2$: C, 65.42; H, 6.71; N, 8.48. Found: C, 65.50; H, 6.72; N, 8.39.

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Supplementary Material Available. Mass spectral data with assigned structures of ions (Tables I–V) (8 pages) for 2,4-diacetylpyrrole and compounds indicated in the text. Ordering information is given on any current masthead page.

Registry No.—1, 63547-56-8; **2,** 63547-57-9; **3,** 63547-58-0; pyrrole, 109-97-7; 2-acetylpyrrole, 1072-83-9; 3-acetytpyrrole, 1072-82-8; 2-acetylpyrrole oxime, 63547-59-1; acetyl chloride, 75-36-5; 2-acetylpyrrole oxime acetate, 63547-60-4; 2-trifluoroacetylpyrrole, 2557-70-2; 2,5-diacetylpyrrole, 31685-34-4; 2,4-diacetylpyrrole, 63547-61-5; dimethyl β-aminoglutaconate, 63547-62-6; dimethyl β-(1-pyrrolyl)-glutarate, 63547-63-7; β-(1-pyrrolyl)glutaric acid, 23757-03-1; β-(2-trifluoroacetyl-1-pyrrolyl)glutaric acid, 63547-64-8; β-(2-trifluoroacetyl-1-pyrrolyl)glutaric acid anhydride, 63547-65-9.

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