= R″ = H), 83-34-1; **3a**, 271-89-6; **3b**, 26278-23-9; **3c**, 39581-61-8; **3d**, 63703-24-2; **3e**, 7522-79-4; **4a**, 63703-25-3; **4b**, 63730-24-5; **4c**, 63703-29-7; **5**, 729-87-3; **7**, 2054-35-5; **8**, 63703-26-4; **12**, 54124-39-9; **13a**, 63703-27-5; **13b**, 63703-28-6; **14a**, 63730-25-6; **14b**, 63730-26-7; **17**, 39560-34-4; ethyl diazoacetate, 623-73-4; 1-methyl-1-phenylhydrazine, 618-40-6; ethyl levulinate, 539-88-8.

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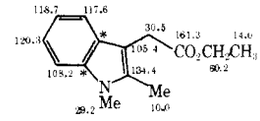

i

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Vicinal π Interactions in the Electrochemical Oxidation of a Carboxylic Acid

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Cyclic voltammetry of 5-carboxy-1,3-diphenyl-5-methyl-2-pyrazoline in acetonitrile reveals the presence a small peak at ca. 0.5 V lower overpotential than the usual peak position for diphenylpyrazolines. The peak is due to the anion form produced in the double layer and is attributed to the presence of through space interactions between the pyrazoline π system and the carboxylate group. The anodic oxidation reaction proceeds with decarboxylation to produce the aromatized pyrazole.

Although the Kolbe reaction with simple carboxylic acids appears to proceed via a concerted electron transfer–decarboxylation step to produce dimeric product,[1] in the case of phenyl-substituted propionic acids[2,3] the formation of cyclized products demonstrates that the acyloxy radical can affiliate the π system at some stage of the reaction. We should now like to present some results which show that the affiliation between the carboxyl group and a vicinal π system under anodic conditions occurs early in the reaction.

Results

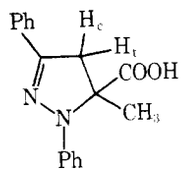
5-Carbomethoxy-1,3-diphenyl-5-methyl-2-pyrazoline (I-$COOCH_3$) is produced as the only isomer in the addition reaction of diphenylnitrilimine to methyl methacrylate.[4] Saponification of I-$COOCH_3$ in methanolic sodium hydroxide produces I-COOH in good yields. The *N*-*p*-anisyl analogues, II-COOH and II-$COOCH_3$, were prepared in the same manner. The carboxylic acids are not very stable and they decarboxylate to produce the corresponding pyrazole derivative. For example, I-COOH produces ca. 1% 1,3-diphenyl-5-methylpyrazole during the saponification reaction, while II-COOH produces ca. 12% 1-anisyl-5-methyl-3-phenylpyrazole.

Electrolytic Measurements. Cyclic voltammetry measurements for these compounds were performed in anhydrous acetonitrile containing 0.1 M tetraethylammonium tetrafluoroborate using a platinum button electrode plus a Ag/Ag^+ (0.01 M in CH_3CN) reference electrode. The cyclic voltammogram for I-COOH shows two irreversible peaks at a 200 mV/s scan rate as shown in Table I. The peak ratio varies with the basicity of the solvent. With the addition of excess sodium bicarbonate or sodium methoxide the peak at lower overpotential increases with almost the complete disappearance of the peak at +0.6 V. The reverse situation is not accomplished with the additions of methanol or benzoic acid. This result is most likely due to the fact that the inherent basicity of the double layer[5] is not completely affected by the acidity of the bulk solution. Finally, when an inherently basic electrode surface is used, e.g., Sb-doped SnO_2, the first peak is ca. 1.5 greater than the second peak.

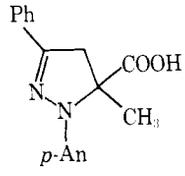
Table I. Summary of Electroanalytical Data [a]

Registry no.		$E_{pa/2}$ [b]	$i/CV^{1/2}$ [c]	α [d]	$10^3 nD^{1/2}$ [e] (E,V)	n [f]	$10^5 D$ [f]
63534-50-9	I-COOH	0.0	0.015	0.17			
		0.57	0.259	0.49	6.05 (0.7)	2	0.92
63534-51-0	II-COOH	−0.04	0.013				
		0.39	0.260	0.38	5.60 (0.5)	2	0.78
		1.09					
63534-52-1	*exo,exo*-III-COOH	0.48	0.336	0.68[g]	7.23 (0.55)	2	1.3
17660-83-2	I-$COOCH_3$	0.59	0.351	0.72[g]	5.8 (0.73)	2	0.84
63534-53-2	II-$COOCH_3$	0.366	0.196	0.48[g]	3.01 (0.45)	1	0.90
		1.02	0.145	0.11	7.04 (1.1)	1	1.2[h]

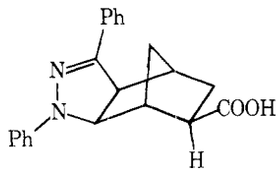
[a] 0.1 M Et_4NBF_4/CH_3CN; Pt vs. $Ag/Ag^+(CH_3CN)$. [b] V, at 200 mV/s. [c] A/M $(V/s)^{1/2}$. [d] Obtained from a plot of log i vs. E using a 5 mV/s sweep rate. [e] Obtained from a plot of integrated charge vs. $t^{1/2}$; $nD^{1/2}$ in $cm/s^{1/2}$. [f] Estimated values; D in $cm/s^{1/2}$. [g] 10 mV/s scan rate. [h] Calculated using $n = 2$.



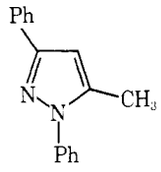
I-COOH



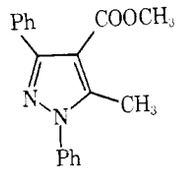
II-COOH



exo,exo-III-COOH



IV



V

The Tafel plot in the absence of added acid or base using a scan rate of 5 mV/s shows current consumption between −0.1 and +0.1 V and again between +0.5 and +0.7 V, providing α values equal to 0.17 and 0.49, respectively. Chronocoulometry provides a value for $nD^{1/2}$ from the Cottrell equation equal to 6.05×10^{-3} $cm/s^{1/2}$. This value is consistent with a two-electron process for the molecular acid where the diffusion coefficient is ca. 0.9×10^{-5} cm^2/s. Chronocoulometry measurements at lower overpotentials were not informative. Constant potential electrolysis at +0.3 V shows the consumption of 1.5 faradays/mol.

The cyclic voltammogram of II-COOH shows similar results. Not listed in Table I is an additional small peak with $E_{pa/2}$ at +0.23 V which is ca. $1/60$ the size of the main peak. Since II-COOH is partly decarboxylated, chronocoulometry measurements are not useful. Constant potential electrolysis at +0.55 V consumes approximately 2 faradays/mol.

In contrast to the free acid, the methyl ester derivative, I-$COOCH_3$, shows a single irreversible peak with $i_c/i_a < 0.4$. The oxidation peak corresponds to a two-electron process. The cyclic voltammogram for II-$COOCH_3$ shows two peaks involving one electron transfer each. The first is reversible with $i_c/i_a = 1.0$ between 50 and 800 mV/s scan rate. The second peak is irreversible.

For comparison purposes the electrochemical behavior of *exo,exo*-III-COOH is presented. This molecule is selected because it contains the pyrazoline π system and a carboxyl group held rigidly apart. This compound shows only one irreversible oxidation peak with $i_c/i_a = 0.4$. Both chronocoulometry measurements and constant potential electrolysis suggest a two-electron transfer process where in the latter the consumption is 2.1 faradays/mol.

Electrolysis Products. Constant potential electrolysis of I-COOH for product analysis was carried out in a divided cell using a platinum gauze as the working electrode. Electrolysis of +0.45 V until current flow stopped consumed 1.92 faradays/mol after 40 min. Cyclic voltammetry of the resulting solution showed no peaks up to +1.0 V. The product was recovered in 86% yield and had a simple NMR spectrum appropriate for IV with signals for the aromatic hydrogens (10 H) plus singlets at δ 6.42 (1 H) and 2.34 (3 H). No other product is detected.

Electrolysis of I-$COOCH_3$ at +0.76 V in a similar manner consumed 2.07 faradays/mol during 80 min. Cyclic voltammetry of the resulting solution showed no peaks up to +1.0 V, but revealed that +0.76 V sits at the foot of background current. The product was recovered in 91% yield and analyzed by NMR. The spectrum showed the presence of two components in a 5:95 ratio. The minor product is IV which most likely formed from I-COOH generated during the electrolysis reaction. The major product shows two singlets at δ 3.70 (3 H) and 2.53 (3 H) plus the aromatic hydrogens suggesting structure V. The NMR spectra of the hydrolyzed material is different only by the absence of the singlet at δ 3.70. This carboxylic acid derivative decarboxylates under the GLC analysis conditions used providing only one peak consistent with compound IV.

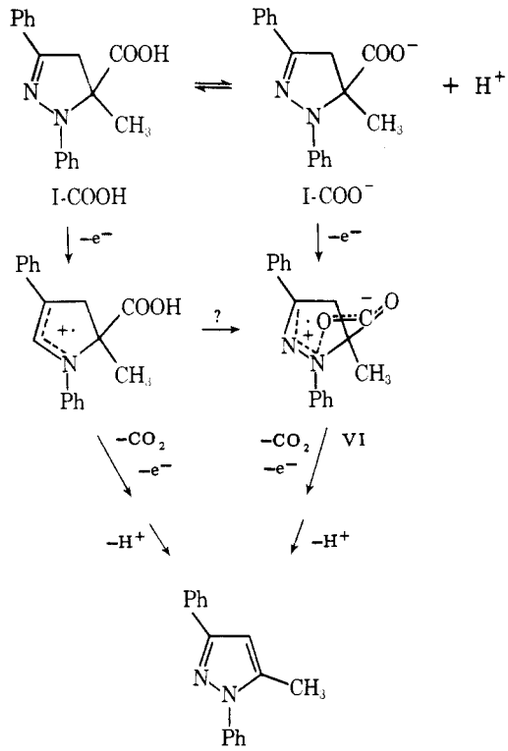
Discussion

The electrochemical results observed for I-$COOCH_3$, II-$COOCH_3$, and *exo,exo*-III-COOH are analogous to those previously reported for pyrazoline derivatives.[6] Those derivatives with a phenyl group in the 1 position show one irreversible oxidation peak at ca. +0.5 V corresponding to a two-electron transfer process. Those derivatives with a *p*-anisyl group in the 1 position show two oxidation peaks involving one electron each at ca. +0.5 and +1.0 V. In these cases, the first one is reversible.

Of particular interest are the changes in the electrochemical behavior that result when a carboxyl group is placed near the pyrazoline π system. First, a new peak is observed at ca. 0.0 V (vs. Ag/Ag^+) for both carboxylic acid derivatives and, secondly, in the case of II-COOH the peak at +0.39 V is now rendered an irreversible two-electron transfer process. Clearly, the near proximity of the carboxyl group and its anion are influencing the oxidation process of the pyrazoline π system.

The results are consistent with the enhancement of the carboxylic acid ionization at the electrode surface as shown in Scheme I. Under the present conditions, the degree of acid ionization is low where the relative peak heights in the cyclic voltammogram suggest the presence of ca. 6% carboxylate

Scheme I



anion. The total carboxylate anion concentration can be increased, of course, by the addition of base to the bulk solution. Since the amount of carboxylate anion at the electrode surface is not fully eliminated by the addition of acid to the bulk solution, the degree of carboxylic acid ionization must be enhanced and maintained at the surface.

The new observed peak corresponds to the reaction of the anion, and its position at a lower overpotential compared to that of the molecular acid suggests the presence of an intramolecular stabilizing interaction between the carboxylate anion and the pyrazoline π system which influences the oxidation transition state. Since *exo,exo*-III-COOH does not show a similar behavior, the effect can not be due to an intermolecular interaction nor can it be a matter of selective adsorption at the electrode surface. This interaction shown in structure VI could be a form of tight ion pair[7] or could be due to homoconjugation.[8] While it is not clear whether VI is a transition state or an intermediate, its lifetime is very limited and it undergoes a decarboxylation reaction to produce the aromatized pyrazole. The mechanism of product formation was not investigated, but it is interesting to note that the reaction is a very clean, two-electron process.

From the results with II-COOH it can be deduced that the un-ionized carboxyl group also intervenes in the oxidation reaction. In this case, however, the carboxyl group must intervene after the first electron step, influencing the radical cation character and making the reaction step irreversible. The overall reaction characteristics is the same as with the anion. It is a two-electron oxidation that proceeds with decarboxylation.

In contrast, the carbomethoxy group in I-$COOCH_3$ does not influence the oxidation of the pyrazoline π system. This pyrazoline undergoes a two-electron oxidation with rearrangement to produce the 4,5-disubstituted pyrazole V as the only product.

In conclusion, the oxidation of the carboxylate anion (I-COO^-) proceeds via a reaction pathway that differs from that for the free acid or the ester derivative even before the first electron-transfer steps and produces a radical structure with a stabilizing O–π interaction. This same separation of reaction pathways may be influencing the formation of cyclization product found in some Kolbe reactions.[2,3]

Experimental Section

5-Carbomethoxy-1,3-diphenyl-5-methylpyrazoline (I-$COOCH_3$). This ester was obtained as the only isomer in the addition reaction of diphenylnitrilimine to methyl methacrylate as previously described.[4] The yellow waxy solid had: NMR ($CDCl_3$) δ (Me_4Si) 1.60 (s, 3 H, methyl), 3.20 (d, 1 H, H_{4c}), 3.64 (d, 1 H, H_{4t}), 3.66 (s, 3 H, methoxy) and 7.0–7.7 (10 H, aromatics), $J_{4c,4t}$ = 16 Hz.

1,3-Diphenyl-5-methylpyrazoline-5-carboxylic acid (I-COOH). The above ester was heated in 75% aqueous methanol containing 0.25 M NaOH for 2 h at 50 °C. The acid was recovered by extraction of the neutralized reaction mixture with ether. The recovered white solid (95% yield) decarboxylates at 86 °C and had: NMR ($CDCl_3$) δ (Me_4Si) 1.32 (s, 3 H, methyl), 2.9 plus 3.32 (d, 1 H each, H_{4c} and H_{4z}), and 6.8–7.8 (m, 10 H, aromatics), $J_{4c,4t}$ = 14 Hz. Since even our best sample contained ca. 2% of 1,3-diphenyl-5-methylpyrazole, an analysis was not obtained.

***N*-(α-Chlorobenzylidene)-*N'*-(*p*-methoxyphenyl)hydrazine** was prepared by the reaction of PCl_5 with β-benzoyl(*p*-methoxyphenyl)hydrazide following previously reported procedures.[4] The recrystallized product (48% yield) had: mp 91–92 °C; NMR (CCl_4) a singlet for the methyl hydrogens at δ (Me_4Si) 3.63 aside from the aromatic hydrogens; the analytical value for C was 0.3% low.

1-*p*-Anisyl-5-carbomethoxy-5-methyl-3-phenylpyrazoline (II-$COOCH_3$) was prepared as above as a yellow oil: NMR ($CDCl_3$) δ (Me_4Si) 1.46 (s, 3 H, methyl), 3.15 plus 3.60 (d, 1 H each, methylenes), 3.66 (s, 6 H, methyls), 6.70 plus 6.96 (dd, 4 H, *N*-aryl), and 7.23 plus 7.6 (m, 5 H, C-phenyl), $J_{4c,4t}$ = 16 Hz; IR (neat) 3100–3000, 2980, 2920, 2890, 2820, 1730 cm^{-1}.

1-*p*-Anisyl-5-methyl-3-phenylpyrazoline-5-carboxylic acid (II-COOH) was prepared as above as a yellow oil in 80% yield: NMR ($CDCl_3$) δ (Me_4Si) 1.32 (s, 3 H, methyl), 3.06 plus 3.44 (d, 1 H each, methylene), 3.62 (s, 3 H, *O*-methyl), and 6.75 plus 7.05 (dd, 4 H, *N*-aryl) and 7.25 plus 7.60 (m, 5 H, C-phenyl), $J_{4c,4t}$ = 16 Hz. The NMR spectra for material treated with base for 1 h showed the presence of 12% 1-*p*-anisyl-5-methyl-3-phenylpyrazole with singlets at δ 2.26 (3 H) and 6.42 (1 H).

***exo,exo*-3,4-Diaza-3,5-diphenyltricyclo[5.2.1.$0^{2,6}$]dec-4-ene-9-carboxylic acid (*exo,exo*-III-COOH)** was prepared by the addition of diphenylnitrilimine to 6-carbomethoxynorbor-2-ene.[4] Hydrolysis of the ester adduct with methanolic NaOH produced *exo,exo*-III-COOH in good yield. The details of this preparation will be published elsewhere.[9]

All electrochemical experiments were performed using 0.1 M tetraethylammonium fluoroborate solutions in previously purified acetonitrile. For the electroanalytical measurements, a two-compartment cell containing ca. 10^{-3} M electroactive species, a platinum-button-working electrode, a Ag/Ag^+ (0.01 M in CH_3CN) reference electrode, and a copper-coil counter electrode was used.

In the electrolysis experiments for product analysis, 55 mg of compound in 25 mL of solution was typically used and a platinum gauze was used. The counter electrode was separated from the bulk solution by a glass frit. The products were isolated by extraction between ether and water. The ether solution was dried with anhydrous magnesium sulfate and evaporated to constant weight without heating before making the spectral determinations. The recovered yields averaged 88%.

The reaction product mixtures were purified by column chromatography using silica gel and methylene chloride–pentane solvent mixtures. Analytical gas chromatography was done using a Hewlett Packard Model 5320 instrument employing the following columns: column 1, 4 ft × 0.125 in., 10% GE SE30 on 100/120 Chromosorb Q; column 2, 6 ft × 0.125 in., 10% Carbowax 20M on 100/120 Chromosorb Q.

The product from the electrolysis of I-COOH at +0.48 V was a dark oil and displayed a clean NMR spectra consistent with 1,3-diphenyl-5-methylpyrazole (IV) as the only product. GLC analysis (column 1, T_1 = 180 °C, T_2 = 220 °C, R = 4 °C/min, 21 mL/min) revealed the presence of one major volatile component (>99%) with a retention time of 8.9 min. Liquid column chromatography of the material provided a light yellow solid with mp 43–44 °C [lit. mp[10,11] 47 (labile form) and 77 °C (stable form)]. GLC analysis as above showed the presence of only one volatile component with a retention time of 8.9 min (>99.9%). Analysis on column 2 (220 °C, 21 mL/min) gave the same results with the peak appearing at 39.5 min. The NMR spectra ($CDCl_3$) had δ (Me_4Si) 2.34 (s, 2.8 H, methyl), 6.42 (s, 1.0 H, vinylic

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.

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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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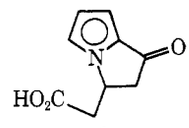
The direct acetylation of pyrrole has been found to give 3-acetylpyrrole as the minor product. Trifluoroacetic anhydride catalyzed acetylation of 2-acetylpyrrole gives the hitherto unreported 2,4-diacetylpyrrole as the major product. Methyl hydrogen β-(1-pyrrolyl)glutarate was isolated from the partial 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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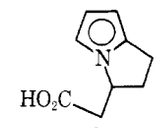

2

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