5-Methyl-2,3-phthaloylfuran (11).—A mixture of 3 g. of 10, 25 ml. of quinoline, and 0.5 g. of copper chromite was refluxed for 2 hr., cooled, diluted with chloroform, and filtered, and the filtrate was extracted with dilute hydrochloric acid. The organic phase was evaporated to dryness and the residue was recrystallized from ethanol to yield 1.8 g. of 11, m.p. 246–247°. This agrees with the reported melting point.[7]

Preparation of 15.—A solution of sodium diethyl malonate, prepared from 8 g. of malonic ester and 1.2 g. of sodium in 50 ml. of ethanol, was added to 11.3 g. of 1 dissolved in 100 ml. of dimethylformamide. The resulting solution was stirred for 3 hr. and then sodium ethyl acetoacetate, prepared from 6.5 g. of 2, 1.2 g. of sodium, and 50 ml. of ethanol, was added. After the solution had been stirred for 2 hr., 1.2 g. of sodium and 50 ml. of ethanol were added and the mixture was heated for 0.5 hr. on the steam bath and poured into a mixture of sulfuric acid and ice. The red solid was collected and recrystallized from ethanol to give 9 g. (51%) of **15**, m.p. 152°.

Anal. Calcd. for $C_{20}H_{18}O_6$: C, 68.2; H, 5.1. Found: C, 68.2; H, 5.0.

The infrared and ultraviolet absorption curves of this material were identical with those of a sample of **15** which was prepared from 1 and 2 by the published procedure.[3]

Preparation of 13.—A solution of sodium ethyl acetoacetate from 1.3 g. of 2, 0.23 g. of sodium, and 25 ml. of ethanol was added to a suspension of 3.5 g. of 12 in 20 ml. of ethanol, and the mixture was stirred for 2 hr. and allowed to stand overnight. The mixture was poured into cold dilute sulfuric acid; the sticky red solid was collected, washed with alcohol, and recrystallized from alcohol to give 0.6 g. of **15**. The combined alcoholic filtrates were evaporated to 10 ml. and chilled to give a yellow solid which was recrystallized from ligroin (b.p. 60–90°) to yield 1.2 g. of **13** as large yellow plates, m.p. 105°. Ultraviolet absorption in acetonitrile was as follows: 247 mμ (ε 25.3 × 10³), 253 (27 × 10³), ~260 (20.5 × 10³), and 335 (3.1 × 10³).

Anal. Calcd. for $C_{23}H_{24}O_9$: C, 62.3; H, 5.4. Found: C, 62.1; H, 5.5.

3-Bromo-3,5-dicarbethoxy-4-methyl-1,2-phthaloylcyclopentadiene (20).—A mixture of 3.5 g. (0.01 mole) of **15** and 2 g. (0.011 mole) of N-bromosuccinimide in 100 ml. of carbon tetrachloride was refluxed for 3 hr. The red color rapidly changed to pale yellow. The reaction mixture was filtered hot and the filtrate was evaporated to about 10 ml. and chilled. The yellow solid was collected and recrystallized from ligroin (b.p. 66–75°) to yield 2 g. of product, m.p. 135–136°. The product became orange on exposure to light.

Anal. Calcd. for $C_{20}H_{17}BrO_6$: C, 55.4; H, 3.9; Br, 18.4. Found: C, 55.8; H, 4.0; Br, 17.9.

3-Chloro-2-(1-carbethoxy-2-acetoxypropenyl)-1,4-naphthoquinone (24).—A mixture of 5 g. of **3**, 10 ml. of isopropenyl acetate, and 2 drops of sulfuric acid was refluxed for 1 hr. and cooled, and the solid was collected and recrystallized from alcohol to give 3.2 g. of light yellow crystals, m.p. 110°.

Anal. Calcd. for $C_{18}H_{15}ClO_6$: C, 59.5; H, 4.1; Cl, 9.8. Found: C, 59.3; H, 4.2; Cl, 9.7.

Acknowledgments.—We are grateful to G. P. Happ and D. P. Maier, for the mass spectral data; to O. E. Schupp, III, for the molecular weight determinations; to D. G. Bush, for the polarographic analysis and nonaqueous titration; and to J. K. O'Loane, for the n.m.r. spectra and their interpretation.

Synthesis of 2,2'-Bipyrroles from 2-Pyrrolinones[1a]

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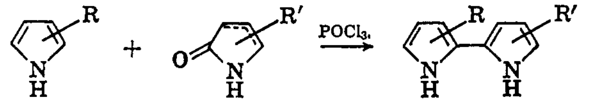
Received May 28, 1965

A series of Δ^3- and Δ^4-pyrrolin-2-ones has been prepared in which the position of the double bond has been established with certainty by reduction with diimide-d_2 and n.m.r. spectroscopy. The generalization may be drawn that Δ^3-pyrrolin-2-ones have their H-5 absorptions at lower field than the H-3 absorptions of Δ^4-pyrrolin-2-ones. Condensation of Δ^3-pyrrolin-2-ones with pyrroles leads directly in good yields to 2,2'-bipyrroles. This provides a convenient, one-step synthesis of a number of bipyrroles. However, the same reaction with Δ^4-pyrrolin-2-ones gives dipyrrylpyrrolines which may be dehydrogenated to terpyrroles. In certain instances, the presence of alkoxycarbonyl groups prevents any reaction from occurring.

The synthesis of 2,2'-bipyrroles has become of considerable interest, in part owing to the presence of such a system in the important natural products vitamin B_{12}[2] and prodigiosin.[3] Symmetrical, highly substituted 2,2'-bipyrroles are well known and are readily prepared by an Ullmann-type condensation.[4] However, unsymmetrical, simply substituted 2,2'-bipyrroles have only been prepared recently, either through the dehydrogenation of 2,2'-pyrrolidinylpyrroles (prepared from pyrroles and 1-pyrroline)[3a,5,6] or 2,2'-pyrrolinylpyrroles (synthesized from pyrroles and 2-pyrrolidinones using a Vilsmeier-type condensation).[6] Both procedures have shortcomings as general syntheses. The 1-pyrroline method suffers from both the difficulty of the initial condensation and the subsequent dehydrogenation. The Vilsmeier condensation with 2-pyrrolidinones vastly improves the condensation step, but in the case of alkylpyrroles the method is still limited by the necessary dehydrogenation step which is much improved in yield and convenience if an alkoxycarbonyl group is present somewhere in the molecule.[6b] Elimination of this troublesome dehydrogenation by employing a one-step synthesis using a 2-pyrrolinone is the next logical development in bipyrrole synthesis, and is the subject of this report.



The synthesis of 2-pyrrolinone itself has been reported[7,8] twice, the compounds obtained displaying

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[1] (a) Sponsored in part by Grant AI-04888 from the National Institutes of Health, U. S. Public Health Service; (b) Public Health Service Predoctoral Research Fellow of the National Institute of General Medical Sciences.

[2] R. Bonnett, J. R. Cannon, V. M. Clark, A. W. Johnson, L. F. J. Parker, E. L. Smith, and A. Todd, *J. Chem. Soc.*, 1158 (1957).

[3] (a) H. Rapoport and K. G. Holden, *J. Am. Chem. Soc.*, **84**, 635 (1962); H. H. Wasserman, J. E. McKeon, L. Smith, and P. Forgione, *ibid.*, **82**, 506 (1960).

[4] (a) H. Fischer and H. Stackel, *Z. physiol. Chem.*, **258**, 121 (1939); (b) J. A. Webb and R. R. Threlkeld, *J. Org. Chem.*, **18**, 1406 (1953); (c) R. Grigg, A. W. Johnson, and J. W. F. Wasley, *J. Chem. Soc.*, 359 (1963).

[5] D. W. Fuhlhage and C. A. VanderWerf, *J. Am. Chem. Soc.*, **80**, 6249 (1958).

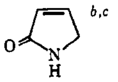
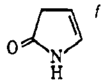
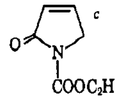
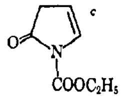
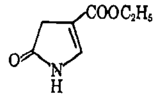
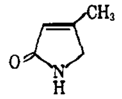
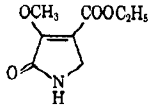
[6] (a) H. Rapoport and N. Castagnoli, Jr., *ibid.*, **84**, 2178 (1962); (b) H. Rapoport and J. Bordner, *J. Org. Chem.*, **29**, 2727 (1964).

[7] W. Langenbeck and H. Boser, *Ber.*, **84**, 526 (1951).

[8] C. A. Grob and P. Ankli, *Helv. Chim. Acta*, **32**, 2010 (1949).

TABLE I

N.M.R. ABSORPTION[a] OF SOME 2-PYRROLINONES

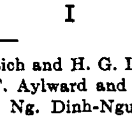
2-Pyrrolinone	Vinyl protons	Methylene protons	Others
 [b,c] (III)	7.6 (m)[d] [1][e] 6.2 (m) [1]	4.2 (m) [2]	
 [f] (IV)	7.4 (m) [1] 6.1 (m) [1]	3.2 (m) [2]	
 [c] (II)	7.2 (m) [1] 6.1 (m) [1]	4.3–4.2 (m) [4][g]	1.3 (t) [3]
 [c] (I)	6.9 (m) [1] 5.3 (m) [1]	3.1 (m) [2]	4.2 (q) [2], 1.3 (t) [3]
 (V)	7.5 (s) [1]	3.4 (s) [2]	4.3 (q) [2], 1.4 (t) [3]
 (IX)	5.4 (s) [1]	4.0 (m) [2]	2.2 (s) [3]
 (X)	. . .	4.3–4.0 (m) [4][g]	4.2 (s) [3], 1.3 (t) [3]

[a] Taken in chloroform-d and reported as δ values referred to internal tetramethylsilane. [b] In D_2O. [c] Position of the double bond was confirmed by diimide-d_2 reduction. [d] Letters in parentheses refer to singlet (s), triplet (t), quartet (q), and multiplet (m). [e] Numbers in brackets refer to number of protons obtained by integration. [f] In CD_3OD. [g] Overlap of pyrroline methylene and methylene of ethoxyl.

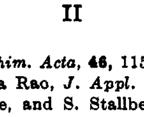
distinctly different properties. One was a solid (prepared by ring closure of methyl γ-aminocrotonate) melting above 140°,[7] and the other a colorless liquid (synthesized by hydrolysis and decarboxylation of 4-ethoxycarbonyl-Δ^4-pyrrolin-2-one[8]); both substances were characterized further only by an elemental analysis. The difference between the two compounds of course may be explained by assigning one the Δ^3 structure and the other the isomeric Δ^4 structure. In an effort to make these assignments, we attempted this synthesis of the high-melting 2-pyrrolinone, but in our hands it proved unsatisfactory, the product being obtained in poor yield and in very impure form. Since the liquid 2-pyrrolinone also was prepared only in a very poor yield,[8] we investigated the recent convenient synthesis of N-ethoxycarbonyl $\Delta^{3(\text{or }4)}$-pyrrolin-2-one (from furan by heating with ethyl azidoformate)[9] as a possible alternate route to the 2-pyrrolinones. The expected product was obtained, but, when more efficient cooling was employed to decrease polymerization, a new compound resulted.

This compound was a clear liquid which resembled the reported solid pyrrolinone in its n.m.r. spectrum except that the vinyl and methylene protons of the liquid were shifted upfield (see Table I). The infrared spectrum of the liquid was very similar to that of the solid in the carbonyl region, and it could be converted to the solid by heating at 120°. Both liquid solid were reduced to N-ethoxycarbonyl-2-pyrrolidinone. Therefore, both compounds are 2-pyrrolinones and must be double-bond isomers, but the position of the double bond could not be definitely assigned by the ultraviolet or infrared absorption. Both compounds displayed $\lambda_{\max}^{H_2O}$ 210 mμ, while only the solid showed a shift to 225 mμ in n-hexane. However, no assignment of structure based on this small difference could be made, particularly since diacylamines absorb in this region.[10] Also, there was insufficient analogy for an assignment to be made on the basis of the rather complex infrared spectra.

Because of the above difficulties, the structural assignments were made by employing a reduction[11] with diimide, generated from hydrazine-d_4 and atmospheric oxygen, in conjunction with n.m.r. examination of the products. This method of reduction prevented scrambling of the deuterium which occurs on catalytic deuteration, while integration of the resulting N-ethoxycarbonyl-2-pyrrolidinone-d_2 (I-d and II-d) spectra located the position of the deuterium, and thus the position of the original double bond. Using this technique



I



II

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[9] K. Hafner and W. Kaiser, *Tetrahedron Letters*, 2185 (1964). We would like to thank Professor Hafner for kindly providing additional experimental details and a sample of his 2-pyrrolinone.

[10] K. Stich and H. G. Leeman, *Helv. Chim. Acta*, **46**, 1151 (1963).

[11] (a) F. Aylward and C. V. Narayana Rao, *J. Appl. Chem.*, **6**, 559 (1956); (b) Ng. Dinh-Nguyen, R. Ryhage, and S. Stallberg-Stenhagen, *Arkiv Kemi*, **15**, 433 (1960); (c) A. Furst, R. C. Berlo, and S. Hooton, *Chem. Rev.*, **65**, 51 (1965); (d) E. L. Bulgozdy and E. L. Wagner, *J. Am. Chem. Soc.*, **73**, 5866 (1951).

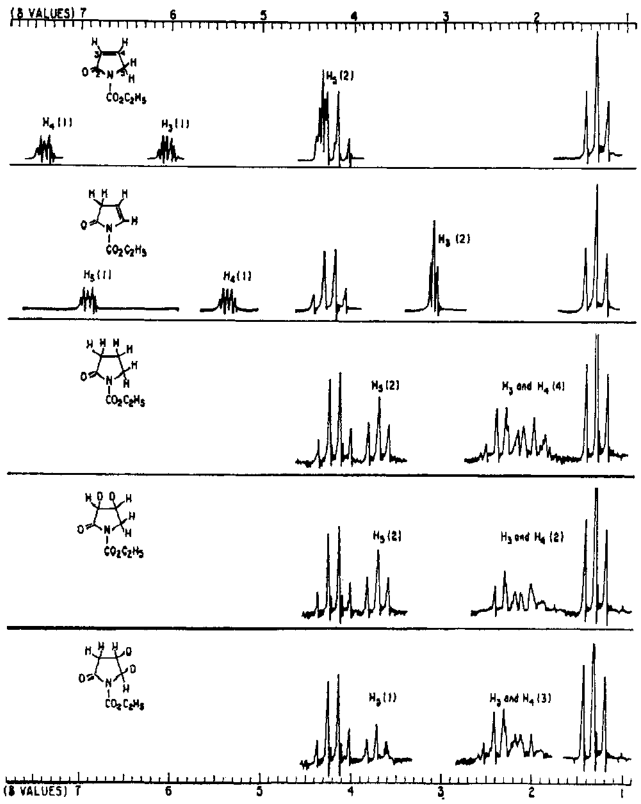


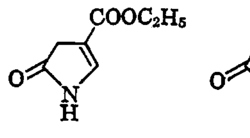
Figure 1.—N.m.r. absorption in $CDCl_3$ of N-ethoxycarbonyl-Δ^3-pyrrolin-2-one (II), N-ethoxycarbonyl-Δ^4-pyrrolin-2-one (I), N-ethoxycarbonyl-2-pyrrolidinone, N-ethoxycarbonyl-2-pyrrolidinone-3,4-d_2 (II-*d*), and N-ethoxycarbonyl-2-pyrrolidinone-4,5-d_2 (I-*d*).

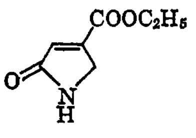
the liquid was assigned the Δ^4 structure I and the solid the Δ^3 structure II (see Figure 1).

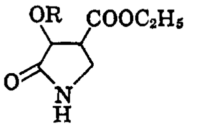
Decarbethoxylation of both 2-pyrrolinones was then investigated. Isomer II was readily hydrolyzed in dilute sodium hydroxide within 1 hr. and the product was isolated after acidification and sublimation. The resulting pyrrolinone, m.p. 165°, would have the structure Δ^3-pyrrolin-2-one (III) if no rearrangement occurred, and this was established as the case by diimide reduction as described above. The resulting deuterium containing 2-pyrrolidinone showed absorption at δ 3.40, integrating for two protons, and an additional two protons at δ 1.8–2.5. The former absorption can clearly be assigned to the H-5 methylene and the latter to the combined H-3 and H-4, thus confirming the Δ^3 assignment. The unstable, liquid isomer I decomposed into an intractable tar upon the first addition of alkali, and none of the desired decarbethoxylated compound could be detected.

Another isomeric ethoxycarbonyl-2-pyrrolinone, 4-ethoxycarbonyl-Δ^4-pyrrolin-2-one (V), has been synthesized,[8] but no proof was provided for the position of the double bond. The method of synthesis (ring closure of diethyl aminomethylenesuccinate by alkoxide in benzene) suggested the Δ^4 structure; however, isomerization of the double bond to VI was possible, although unlikely, since ring closure appeared to occur under nonequilibrating conditions. Also the ultraviolet spectrum suggested, a 3-acetamidoacrylate chromophore, $\lambda_{\max}^{C_2H_5OH}$ 271 mμ (ε 18,600),[12] rather than a fumarate chromophore, $\lambda_{\max}^{C_2H_5OH}$ 211 mμ (ε 16,600).[13]

Various attempts to prepare the other isomer by treatment under acidic or alkaline equilibrating conditions failed, and in all cases the position of the double bond remained unchanged. Another approach to preparation of the Δ^3 isomer was attempted *via* the alcohol VII. However, although elimination took place readily from the alcohol VII on treatment with acetic anhydride and from the tosylate VIII either on treatment with ethoxide or chromatography on alumina, in all cases the product was the same ethoxycarbonyl-2-pyrrolinone to which structure V had been assigned. Obviously, this is the much more stable isomer. An examination of its n.m.r. spectrum showed a methylene absorption at δ 3.4, and in comparison with the other compounds of Table I this can be assigned to C-3, thus confirming structure V. The methylene of isomer VI at C-5 would be expected at δ ~4.0–4.3.


V


VI


VII, R = H
VIII, R = Ts

The hydrolysis and decarboxylation of 4-ethoxycarbonyl-Δ^4-pyrrolin-2-one (V) to Δ^4-pyrrolin-2-one (IV) in very poor yield has already been described,[8] and we were unable to improve it. The resulting Δ^4-pyrrolin-2-one (IV) was a viscous liquid differing markedly from the crystalline Δ^3 isomer III. Since the structure III had been clearly established by examination of its reduction product from diimide-d_2, the new pyrrolinone must be the Δ^4 isomer IV. This is confirmed by examination of the n.m.r. spectra (Table I) which shows methylene absorption at δ 4.2 for III (C-5 methylene) and 3.2 for IV (C-3 methylene).

An alkyl-substituted pyrrolinone, 4-methyl-Δ^3-pyrrolin-2-one (IX) was synthesized as described.[14] Its structure had been assigned by comparison of its ultraviolet spectrum ($\lambda_{\max}^{C_2H_5OH}$ 210 mμ) with that of the crotonic acid system which absorbs at $\lambda_{\max}^{C_2H_5OH}$ 204,[15] whereas N-vinylpyrrolidinone absorbs at $\lambda_{\max}^{C_2H_5OH}$ 235 mμ.[16] This assignment is confirmed by the n.m.r. data of Table I which clearly distinguishes the C-5 (δ 4.0–4.3) from the C-3 (δ 3.0–3.4) methylene in 2-pyrrolinones. The correlation is firmly based on structures established by the diimide-d_2 reduction and is very useful in ascertaining the position of the double bond in 2-pyrrolinones.

It is of interest to note the difference in the position of the double bond between 4-methyl-Δ^3-pyrrolin-2-one (IX) and 4-ethoxycarbonyl-Δ^4-pyrrolin-2-one (V). Both compounds may be synthesized from the appropriate alcohol (4-hydroxy-4-methyl-2-pyrrolidinone for IX and alcohol VII for V) by dehydration using acetic anhydride followed by alkaline hydrolysis of the N-acetyl group. In the case of 4-methyl-Δ^3-pyrrolin-2-one, the double bond remained Δ^3 as it was generated, while in the formation of 4-ethoxycarbonyl-Δ^4-pyrrolin-2-one the double bond has rearranged. The steric factor should favor Δ^4 in both cases, since Δ^3 results in

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[12] C. A. Grob, *Helv. Chim. Acta*, **33**, 1787 (1950).

[13] R. F. Rekker, P. H. Brombacher, H. Hamann, and W. T. Nauta, *Rec. trav. chim.*, **73**, 410 (1954).

[14] H. Pleininger and M. Decker, *Ann.*, **598**, 198 (1956).

[15] H. Mohler and H. Lohr, *Helv. Chim. Acta*, **21**, 485 (1938).

[16] G. Oster and E. H. Immegul, *J. Am. Chem. Soc.*, **76**, 1396 (1954).

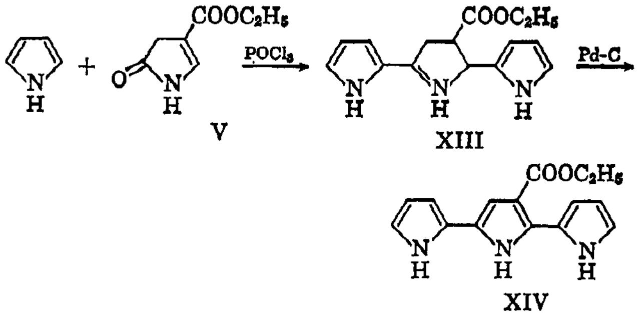
the unfavorable steric environment of three contiguous trigonal carbons and the consequent three coplanar substituents in a five-membered ring. This is not enough to overcome the conjugation in IX that would be lost, but the added conjugation of the N—C=C—C(=O)OR system permits the rearrangement VI → V.

A pyrrolinone containing both electron-withdrawing and -releasing groups, 3-methoxy-4-ethoxycarbonyl-Δ^3-pyrrolin-2-one (X), was synthesized as described[17] and the structural assignment was confirmed since no vinyl absorption was evident in its n.m.r. spectrum.

With a variety of 2-pyrrolinones in hand, their condensation reactions with pyrrole under conditions of the Vilsmeier reaction were investigated. First tried was 4-methyl-Δ^3-pyrrolin-2-one (IX) since the expected product already had been prepared in this laboratory.[6b] The ultraviolet absorption of the reaction mixture indicated that the desired 2,2′-bipyrrole had been formed, but neither crystallization nor sublimation, the only two purification techniques reported[4,6] for 2,2′-bipyrroles, led to a pure product. However, chromatography on activity III alkaline alumina and gas chromatography were found to be generally applicable to 2,2′-bipyrroles and led to isolation of a product identical with the previously prepared[6b] 4-methyl-2,2′-bipyrrole (XI). Similar satisfactory results were obtained with Δ^3-pyrrolin-2-one (III), the resulting product being 2,2′-bipyrrole,[6a] and with 3-methoxy-4-ethoxycarbonyl-Δ^3-pyrrolin-2-one (X) which gave 3-methoxy-4-ethoxycarbonyl-2,2′-bipyrrole (XII).

The use of pyrroles bearing electron-withdrawing groups in the condensation reaction with 2-pyrrolinones was next investigated. Both ethyl 3,4-dimethylpyrrole-2-carboxylate and ethyl 4-methylpyrrole-3-carboxylate failed to react with 4-methyl-Δ^3-pyrrolin-2-one (IX). This failure to react was independent of the stoichiometry and of the order of addition of reactants.

The effect of an electron-withdrawing group on reactivity of the pyrrolinone was also investigated. It has already been noted that the combination found in 3-methoxy-4-ethoxycarbonyl-Δ^3-pyrrolin-2-one (X) permits condensation with pyrrole. However, when only an ester group is present, the reaction becomes more complicated. In the case of 4-ethoxycarbonyl-Δ^4-pyrrolin-2-one (V), no bipyrrole was detected. However, a compound was isolated in good yield that had a spectrum in ethanol reminiscent of a pyrrolinylpyrrole ($\lambda_{\max}^{H^+}$ 322 mμ, $\lambda_{\max}^{OH^+}$ 283 mμ) and for which structure XIII is proposed. Such a trimer-type structure may arise from an addition of pyrrole to the conjugate double bond in the pyrrolinone followed by a Vilsmeier-type condensation. The addition reaction must occur rapidly and precede the Vilsmeier condensation since 2,2′-bipyrrole systems do not undergo such additions. Based on this proposed mechanism, the $\Delta^{1'}$ structure has been assigned, although we have no data to rule out the $\Delta^{5'}$ structure. The n.m.r. spectrum of XIII was revealing. Six pyrrole-type protons (δ 6.6–6.2) were observed in addition to the ester protons (δ 4.3 and 1.3) and four higher field protons (δ 3.4–4.0). Further evidence for the pyrrolinylpyrrole structure was obtained by dehydrogenating XIII with 30% palladium on carbon. The ultraviolet absorption of the resulting compound XIV [$\lambda_{\max}^{CH_3OH}$ 355 mμ (ϵ 28,000)] resembled very closely that of 5-methoxycarbonyl-2,2′:5′,2″-terpyrrole [$\lambda_{\max}^{CH_3OH}$ 358 mμ (ϵ 28,800)].[18]



The coupling reaction of pyrrole and Δ^4-pyrrolin-2-one (IV) also yielded a compound with a pyrrolinylpyrrole-type ultraviolet spectrum ($\lambda_{\max}^{OH^-}$ 283 mμ, $\lambda_{\max}^{+H}$ 322 mμ). It appears, therefore, that a Δ^4 double bond is especially susceptible to addition, and that Δ^4-pyrrolin-2-ones may afford a possible new route to terpyrroles.

Further studies with substituted pyrrolinones indicated that if an ester group were attached to the nitrogen as in compounds I and II, the condensation reaction fails and no bipyrroles are produced.

The results represented in this report have shown that the 2-pyrrolinone condensation reaction has some restrictions, namely, it leads to pyrrolinylpyrroles of the trimer type when the double bond is Δ^4 and fails to occur in some instances of ester-substituted pyrroles or pyrrolinones. For the latter type of substitution pattern, the previous condensation with 2-pyrrolidinones[6b] provides an adequate procedure for bipyrrole synthesis. In many other instances, the pyrrolinone condensation reaction proceeds smoothly and in good yield to give the bipyrrole directly, and thus conveniently supplements the existing synthetic methods.

Experimental Section[19]

N-Ethoxycarbonyl-Δ^4-pyrrolin-2-one (I) and N-Ethoxycarbonyl-Δ^3-pyrrolin-2-one (II).—A solution of 10.5 g. (91.2 mmoles) of ethyl azidoformate[20] in 60 ml. of freshly distilled furan was placed in a Magne Drive 300-cc. autoclave equipped with a Honeywell Pyr-o-vane temperature control and an internal cooling coil. The temperature was gradually increased to 120° over a 1-hr. period. After the pressure had risen to 200 p.s.i., the heater was turned off and ice–water was circulated through the cooling coil. The resulting yellow liquid was evaporated and the residual viscous yellow oil was distilled at 90° and 10^{-3} μ to give N-ethoxycarbonyl-Δ^4-pyrrolin-2-one as a colorless liquid, 4.2 g. (30%), $\lambda_{\max}^{H_2O \text{ or hexane}}$ 210 mμ.

Anal. Calcd. for $C_7H_9NO_3$: C, 54.2; H, 5.9; N, 9.0. Found: C, 54.0; H, 5.7; N, 8.7.

If the pressure was allowed to increase to its maximum value (470 p.s.i.) before cooling, the residue, after evaporation of the excess furan, slowly crystallized. This solid was sublimed at 80° at 0.1 mm., giving N-ethoxycarbonyl-Δ^3-pyrrolin-2-one (II), 4.0 g. (28%), m.p. 60.5° (lit.[9] m.p. 60.5–61.5°), $\lambda_{\max}^{\text{hexane}}$ 225 mμ (lit.[9] $\lambda_{\max}$ 225 mμ), $\lambda_{\max}^{H_2O}$ 210 mμ. Isomer I could be converted to II by heating at 120° under nitrogen for 10 min.

Decarbethoxylation of I and II.—To 300 mg. (1.9 mmoles) of N-ethoxycarbonyl-Δ^3-pyrrolin-2-one (II) was added 1.91 ml.

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[17] P. L. Southwick and R. T. Crouch, *J. Am. Chem. Soc.*, **75**, 3413 (1953).

[18] H. Rapoport, N. Castagnoli, Jr., and K. G. Holden, *J. Org. Chem.* **29**, 833 (1964).

[19] All melting points are corrected and were taken in evacuated capillaries; microanalyses were performed by the Microchemical Laboratory, University of California, Berkeley, Calif.; all evaporations were *in vacuo* at 50° using a rotary evaporator; λ^{H^+} denotes 0.1 *M* ethanolic hydrochloric acid and λ^{OH^-} denotes 0.1 *M* ethanolic sodium hydroxide as solvent.

[20] M. O. Foster and H. E. Fierz, *J. Chem. Soc.*, **93**, 81 (1908).

of 1 *N* sodium hydroxide. The reaction mixture was stirred under nitrogen at room temperature for 3 hr., acidified to pH 2, and evaporated. The resulting solid was sublimed at 120° and 0.1 mm., yielding 30 mg. (19%) of **Δ^3-pyrrolin-2-one** (II), m.p. 165° (lit.[7] m.p. >140°), $\lambda_{\max}^{H_2O}$ 210 mμ.

Anal. Calcd. for C_4H_5NO: C, 57.8; H, 6.1; N, 16.9. Found: C, 57.7; H, 6.0; N, 16.7.

An identical experiment with N-ethoxycarbonyl-Δ^4-pyrrolin-2-one (I) yielded only a dark brown polymeric material.

Reduction of I and II. A. Catalytic Hydrogenation.—To 200 mg. (1.3 mmoles) of N-ethoxycarbonyl-Δ^4-pyrrolin-2-one (I) in 20 ml. of absolute ethanol was added 250 mg. of 10% palladium on carbon. The mixture was hydrogenated at 30 p.s.i. and room temperature for 12 hr., after which the catalyst was removed and the solvent was evaporated. The resulting liquid was distilled at 100° and 0.1 mm., and a quantitative yield of N-ethoxycarbonyl-2-pyrrolidinone was obtained.

Anal. Calcd. for $C_7H_{11}NO_3$: C, 53.5; H, 7.1; N, 8.9. Found: C, 53.0; H, 6.9; N, 8.9.

Hydrogenation of isomer II gave the same compound.

B. Reduction with Diimide.[11]—N-Ethoxycarbonyl-Δ^3-pyrrolin-2-one (II, 75 mg., 0.48 mmole) in 0.1 ml. of deuterium oxide, 0.25 ml. of dioxane, and 0.1 ml. of hydrazine hydrate-d_6 was heated at 60° for 6 hr. with vigorous stirring and then evaporated. Distillation of the resulting residue at 120° and 0.1 mm. gave N-ethoxycarbonyl-2-pyrrolidinone-3,4-d_2 (II-*d*) as a liquid. N-Ethoxycarbonyl-2-pyrrolidinone-4,5-d_2 (I-*d*) was prepared similarly from I. The n.m.r. spectra of I-*d* and II-*d* are given in Figure 1.

4-Ethoxycarbonyl-3-hydroxy-2-pyrrolidinone (VII).—To 5.0 g. (29 mmoles) of 2,3-dioxo-4-ethoxycarbonylpyrrolidine[17] dissolved in 250 ml. of absolute ethanol was added 1.0 g. of 30% palladium on carbon. This mixture was hydrogenated overnight at 60° and 30 p.s.i., the catalyst was removed, and the solvent was evaporated. The residue was crystallized from benzene–chloroform to give a quantitative yield of the desired alcohol VII, m.p. 113–114°.

Anal. Calcd. for $C_7H_{11}NO_4$: C, 48.5; H, 6.4; N, 8.1. Found: C, 48.4; H, 6.4; N, 8.1.

The tosylate was prepared by adding 1.14 g. (6 mmoles) of *p*-toluenesulfonyl chloride to a solution of 1.0 g. (5.8 mmoles) of 4-ethoxycarbonyl-3-hydroxy-2-pyrrolidinone (VII) in 1.0 ml. of pyridine at 0°. The reaction mixture was stirred at 0° under nitrogen for 1.5 hr., poured into 75 ml. of ice–water, and extracted with chloroform. The chloroform extracts were washed with 10% sulfuric acid, water, and saturated aqueous sodium bicarbonate, and then dried over magnesium sulfate. Evaporation of the solvent and crystallization of the residue from benzene–hexane gave 0.8 g. (42%) of the **tosylate VIII**, m.p. 101–102°.

Anal. Calcd. for $C_{14}H_{17}NO_6S$: C, 51.4; H, 5.2; N, 4.3. Found: C, 51.3; H, 5.4; N, 4.3.

Synthesis of 2,2′-Bipyrroles from 2-Pyrrolinones.—All the 2-pyrrolinone coupling reactions were carried out by the general procedure for which the synthesis of 4-methyl-2,2′-bipyrrole serves as an example. To 225 mg. (2.3 mmoles) of 4-methyl-Δ^3-pyrrolin-2-one (IX), m.p. 111–112°, $\lambda_{\max}^{CH_3OH}$ 210 mμ (lit.[14] m.p. 112–113°, $\lambda_{\max}^{C_2H_5OH}$ 210 mμ), dissolved in 680 mg. (10 mmoles) of pyrrole was added 0.23 ml. of phosphorus oxychloride (2.5 mmoles) at 25° under a nitrogen atmosphere. The reaction mixture was stirred for 1.5 hr. at 25° and then added to 100 ml. of 5 *M* aqueous sodium acetate. Extracting with chloroform, washing the chloroform with pH 4 phosphate buffer, drying over magnesium sulfate, and evaporating the chloroform left a residue which was dissolved in benzene and chromatographed on alumina (alkaline, activity III). The 2,2′-bipyrrole was eluted with benzene–hexane (50:50), dissolved in a minimum volume of chloroform, and gas chromatographed (15% Sf-96 on HMDS-treated Chromosorb W, 218°, flow rate 100 cc./min.). The peak at 2 min. 42 sec. was collected and identified as 4-methyl-2,2′-bipyrrole (XI), 266 mg. (79%), by comparison with an authentic sample.[6b]

In subsequent preparations, alumina chromatography followed by sublimation provided sufficient purification and the gas chromatography could be eliminated.

The above coupling reaction was applied to Δ^3-pyrrolin-2-one and the product obtained was identical with **2,2′-bipyrrole**[6a] in its infrared and ultraviolet spectra and g.c. retention time (1 min. 31 sec., 205°, 100 cc./min.)

3-Methoxy-4-ethoxycarbonyl-2,2′-bipyrrole (XII).—Following the general procedure, 150 mg. (0.81 mmole) of 3-methoxy-4-ethoxycarbonyl-Δ^3-pyrrolin-2-one (X), m.p. 102–103° (lit.[17] m.p. 105–106°), $\lambda_{\max}^{C_2H_5OH}$ 246 mμ (ϵ 9600), $\lambda_{\max}^{OH^-}$ 241 mμ (ϵ 8100), a fourfold excess of pyrrole, and 125 mg. (0.83 mmole) of phosphorus oxychloride were allowed to react. The resulting product (118 mg., 65%) was identified as **3-methoxy-4-ethoxycarbonyl-2,2′-bipyrrole**: m.p. 175–177°; $\lambda_{\max}^{CH_3OH}$ 333 mμ; n.m.r. spectrum in acetone-d_6, δ 6.60 (m) [1], 6.38 (m) [1], 6.03 (m) [1], 5.90 (m) [1], 4.14 (q) [2], 3.54 (s) [3], 1.18 (t) [3].

Anal. Calcd. for $C_{12}H_{14}N_2O_3$: C, 61.5; H, 6.0; N, 12.0. Found: C, 61.5; H, 6.1; N, 11.8.

Condensation of 4-Ethoxycarbonyl-Δ^4-pyrrolin-2-one (V).—When the general procedure was applied to 500 mg. (3.2 mmoles) of 4-ethoxycarbonyl-Δ^4-pyrrolin-2-one,[8] a fourfold excess of pyrrole, and 490 mg. (3.2 mmoles) of phosphorus oxychloride, no 2,2′-bipyrrole was isolated. The pH 4 phosphate buffer extract was adjusted to pH 10 with 10 *N* potassium hydroxide and extracted with chloroform, and the chloroform was dried and evaporated. The residue, dissolved in benzene, was applied to an alumina column (alkaline, activity III) and eluted with chloroform. Evaporation of the chloroform and crystallization of the residue from benzene–hexane gave 310 mg. (36%) of the dipyrrylpyrroline (XIII), m.p. 167–168°, $\lambda_{\max}^{H^+}$ 322 mμ (ϵ 25,300), $\lambda_{\max}^{OH^-}$ 283 mμ (ϵ 18,200).

Anal. Calcd. for $C_{15}H_{17}N_3O_2$: C, 66.4; H, 6.3; N, 15.5. Found: C, 66.2; H, 6.4; N, 15.5.

Decreasing the amount of pyrrole to less than 100 mole % still led to the dipyrrylpyrroline as the only detectable product.

The dipyrrylpyrroline could be dehydrogenated to a carbethoxyterpyrrole by heating at 200° with 30% palladium on carbon in di-*n*-hexyl ether. Removal of the catalyst, addition of a twofold volume of hexane to the solution, and cooling to −80° gave the terpyrrole XIV as a solid, m.p. 184–188° dec., $\lambda_{\max}^{CH_3OH}$ 355 mμ (ϵ 28,000).

Condensation of Δ^4-Pyrrolin-2-one (IV).—The general procedure was applied to 20 mg. (0.24 mmole) of Δ^4-pyrrolin-2-one, a fourfold excess of pyrrole, and 37 mg. (0.24 mmole) of phosphorus oxychloride. Isolation as in the case of the 4-ethoxycarbonyl-Δ^4-pyrroline-2-one (V) established the absence of any bipyrrole and the formation of a dipyrrylpyrroline, $\lambda_{\max}^{OH^-}$ 284 mμ, $\lambda_{\max}^{H^+}$ 322 mμ.