241. The Synthesis and Protonation of 1,1-Di(1-pyrrolyl)alkenes

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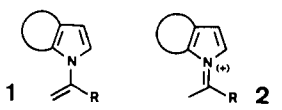
Dedicated to Prof. *Rolf Huisgen* on the occasion of his 65th birthday

(20.IX.85)

It is shown that lithiation of di(1-pyrrolyl)methane (**3**) can be directed either towards the C(α) ring positions or to the central CH_2 group, depending upon the solvent and the complexing agents chosen. Di(1-pyrrolyl)-methyllithium (**6**), resulting from CH_2 deprotonation, is intercepted by aldehydes and converted to the title alkenes in a few straightforward steps. Protonation of 1,1-di(1-pyrrolyl)ethylene (**10**) is found to occur under kinetic control at the terminal olefinic position. In $HBF_4 \cdot Me_2O$ the resulting 5-azionafulvene-type ion **14** can be observed by low-temperature NMR spectroscopy. In FSO_3H, however, protonation is directed under thermodynamic control to both pyrrole rings. The resulting symmetrical dication **13** persists even at room temperature.

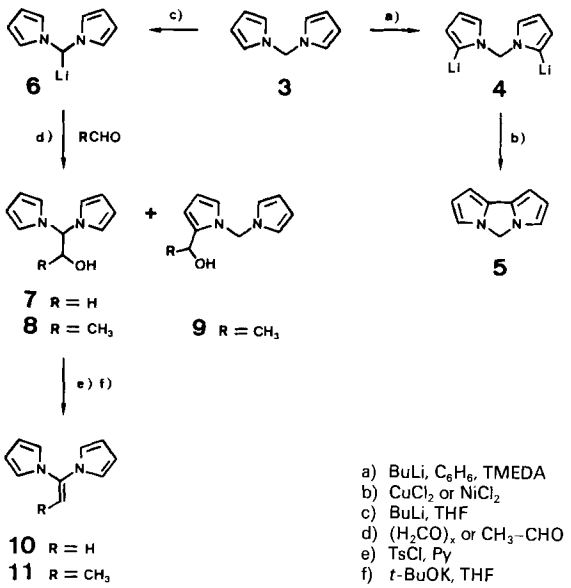
In [1], we have demonstrated that the parent 5-azionafulvene ion and related species can be prepared *in situ* by acylation or upon quaternization of appropriate N-*Mannich* bases of pyrroles and indoles. More elaborate 5-azoniafulvene ions (**2**) should be accessible by protonation of suitable *N*-vinylpyrroles or indoles **1** in the same way as iminium ions are obtained from enamines, their corresponding conjugate bases.



A few reactions are known in indole-alkaloid chemistry that are based on this relation [2]. Protonation of the unprotected *N*-vinylpyrrole, however, inevitably triggers polymerization [3], a reaction which is of some technological importance. Being interested in the spectroscopic observation of 5-azionafulvene ions, we decided to synthesize 1,1-di(1-pyrrolyl)alkenes (*e.g.* **10** and **11**), and to examine them under strongly acidic conditions. By introducing the second pyrrole unit, we hoped to delocalize the charge sufficiently, thus stabilizing the resulting iminium ions.

Results. – For the synthesis of the required di(1-pyrrolyl)alkenes, we took advantage of the solvent-dependent regioselectivity, di(1-pyrrolyl)methane (**3**) shows towards metalating agents. We had demonstrated earlier that compound **3** undergoes selective lithiation in the C(α) ring position upon treatment with BuLi in a benzene *N,N,N′,N′*-tetramethylethylenediamine (TMEDA) mixture. This feature was exploited in the synthesis of 5*H*-dipyrrolo[1,2-*c*:2′1′-*e*]imidazole (**5**) [4] and homologues thereof [5]. However, when compound **3** is allowed to react with BuLi in THF, metalation occurs preferentially (> 85%) at the central CH_2 position, as is seen from quenching experiments with both

Scheme 1

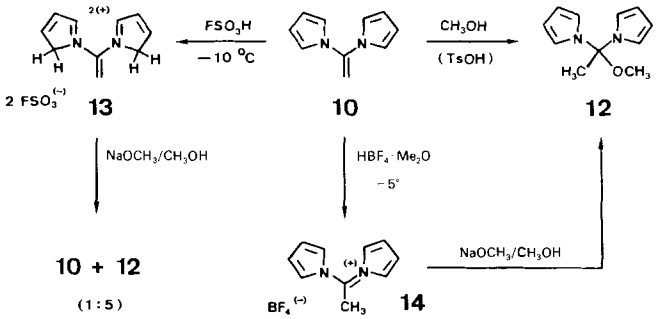


D_2O and MeI. Reaction of **6** with either paraformaldehyde or acetaldehyde provides alcohols **7** and **8** in 86% and 77% yields, respectively. In the latter case 1-(1-pyrrolylmethyl-2-(1-hydroxyethyl)pyrrole (**9**) is obtained as a by-product in 11% yield. Tosylation of alcohols **7** and **8** followed by treatment with *t*-BuOK in THF gives the desired crystalline dipyrrolylalkenes **10** and **11** in 81% and 54% yields, respectively *(Scheme 1)*.

The acid-catalyzed addition of MeOH to compound **10** reveals that protonation occurs at the terminal olefinic position: adduct **12** is obtained at room temperature in quantitative yield. Treating olefin **10** at −78°, under rigorous exclusion of air, with a large excess of $HBF_4 \cdot Me_2O$ gave, after warming to −5°, a homogeneous orange-rose colored solution. Its ^{1}H-NMR spectrum shows besides the solvent peaks an *AA'MM'* spin pattern of double intensity centered at 7.18 and 6.52 ppm, together with a 3-proton singlet at 3.00 ppm. Quenching of this solution with MeONa/MeOH also gave compound **12**. On the basis of these features, we assign the structure of the 1,1-di(pyrrolyl)-methyl-carbinyl ion **14** to the orange-rose colored ion. The ^{1}H-NMR spectrum is consistent with either a planar or a propeller-like species, rotation around the exocyclic C–N bonds being rapid on the NMR time scale at −5°. The freezing point of $HBF_4 \cdot Me_2O$ (*ca.* −10°) prevents us from obtaining more precise information about the molecular dynamics of the ion; above + 10° the solution decomposes. To our knowledge, the ion **14** is the first 5-azoniafulvene-type ion to be observed directly.

When we dissolved **10** at −70° in FSO_3H, a deep green colored solution was obtained. Its ^{1}H-NMR spectrum was found to be temperature-independent apart from the progressive sharpening of signals upon warming from −45° to +20°. The five distinct signals between 8.7 and 4.9 ppm resembled those of α-protonated *N*-alkylpyrroles [6]. Their intensity ratio of 1:1:1:1:2 immediately suggested that double protonation of **10** had occurred, to give the dication **13**. This found corroboration in the ^{13}C-NMR spectrum and the associate ^{13}C-{^{1}H} off resonance decoupling experiment recorded at −10°.

Scheme 2



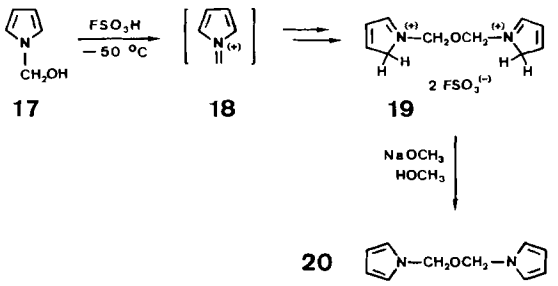
Quenching of the deep-green colored solution with excess MeONa/MeOH resulted in the isolation of starting olefin **10** with adduct **12** in a ratio of 1:5 *(Scheme 2)*.

The behavior of dipyrrolylpropene **11** in FSO_3H is analogous to that of the ethylene derivative **10**. Again, the resulting deep green colored solution was found to be stable up to room temperature. Both the ^{1}H-NMR and the ^{13}C-NMR spectra attest to the formation of dication **15** distinguished from **13** by the presence of two non-equivalent heterocyclic groupings. In contrast to the behavior of **10**, dipyrrolylpropene **11** in $HBF_4 \cdot Me_2O$ is not simply monoprotonated. Instead of a 5-azoniafulvene-type ion **16**, dication **15** is again observed. Clearly, introduction of the additional CH_3 group makes **16** slightly more basic than **14**, thereby tipping the balance between mono and double protonation. Thus, it becomes clear that the pH range in which azoniafulvene ions of type **14** can be observed is rather narrow.

15 **16**

It should finally be mentioned that on dissolution of 1-hydroxymethylpyrrole **17** [7] in FSO_3H, the parent 5-azoniafulvene ion **18** was not observed but only the doubly protonated ether **19**. Quenching with MeONa/MeOH gave di(1-pyrrolylmethyl) ether **20** *(Scheme 3)*.

Scheme 3



We wish to thank Miss *P. Millasson* (syntheses), Mr. *J. P. Saulnier* (NMR) and Mrs. *D. Clément* (MS) for valuable technical assistance. Financial support by the *Swiss National Science Foundation* is gratefully acknowledged (grant No. 2.033–0.83).

Experimental Part

General. IR spectra [cm^{-1}]: *Perkin-Elmer IR-257* spectrometer. UV spectra (λ[nm](logε)): *Kontron Uvikon 820* spectrometer. ^{1}H-NMR spectra (δ[ppm] relative to internal TMS; J[Hz]: apparent scalar coupling constant): *Varian XL-100-FT* spectrometer operating at 100.1 MHz and *Bruker WM-360* spectrometer operating at 360 MHz. ^{13}C-NMR spectra (δ[ppm] relative to internal or external TMS, (multiplicity for off-resonance decoupling)): *Bruker WM-360* spectrometer operating at 90.56 MHz. Mass spectra (MS) (m/z(% relative to base peak)): *Finnigan-4023* spectrometer with *INCOS* data system; electron impact, 70 eV.

2,2-Di(1-pyrrolyl)ethanol (**7**). To a soln. of 2.92 g (20 mmol) of **3** [5] in 60 ml anh. THF under Ar at −40°, was added 20 ml of a 1.1M soln. of BuLi in THF (22 mmol). The resulting violet soln. was allowed to warm to 20°, at which time 2.0 g (66 mmol CH_2O) of paraformaldehyde was added. The mixture was stirred for 2 h at 20°. The reaction was quenched by the addition of 2M HCl then extracted with Et_2O (3 × 100 ml). The combined org. extracts were washed with sat. brine, dried ($MgSO_4$), and concentrated to give a yellow oil. Bulb-to-bulb distillation at 5×10^{-3} Torr afforded 3.03 g (86%) of a crystalline solid. Recrystallization (pentane/Et_2O 1:1) gave an anal. sample of m.p. 96.5–97.5°. IR (nujol): 3490*m*, 1270*m*, 1050*m*. ^{1}H-NMR ($CDCl_3$,100 MHz): 2.21(*t*, J = 7.0, 1 H, exchangeable with D_2O); 4.15 (*t*, J = 7.0, CH_2); 5.89 (*t*, J = 7.0, 1 H); 6.11 (*AA* of *AA'MM'*, of double intensity, 4 H); 6.72 (*MM'* of *AA'MM'*, of double intensity, 4 H). ^{13}C-NMR ($CDCl_3$, 90.56 MHz): 63.9 (*t*); 7.25 (*d*); 109.5 (*d*); 119.0 (*d*). MS ($C_{10}H_{12}N_2O$; 176): 176 (35, M^+), 146 (40), 80 (100).

1,1-Di(1-pyrrolyl)-2-propanol (**8**) *and 1-[1-(1-Pyrrolyl)methyl-2-pyrrolyl]ethanol* (**9**). Same procedure as described for **7**, with paraformaldehyde being replaced by 0.90 g (20 mmol) of acetaldehyde. The crude product is a mixture of two components which are separated by medium-pressure chromatography [8] (silica gel 40–63 μm, hexane/Et_2O 1:4): 2.9 g (77%, R_f 0.2) of **8**, and 0.42 g (11%, R_f 0.1) of **9**.

8: Colorless needles of m.p. 62–63°. IR (CCl_4): 3590*m*, 3430*w*(br.), 1480*m*, 1270*s*, 1082*s*. ^{1}H-NMR ($CDCl_3$,100 MHz): 1.18 (*d*, J = 7.0, 3 H); 1.85 (*d*, J = 6.2, 1 H, exchangeable with D_2O); 4.58 (*m*, 1 H); 5.55 (*d*, J = 7.6, 1 H); 6.2 (*m*, overlapping of *AA* of 2 × *AA'MM'*, 4 H); 6.78 (apparent *t*, *MM* of *AA'MM'*, 2 H); 6.88 (apparent *t*, *MM* of *AA'MM'*, 2 H). MS ($C_{11}H_{14}N_2O$; 190): 190 (50, M^+), 172 (5), 145 (42), 124 (100).

9: Colorless needles of m.p. 53–54°. IR (CCl_4): 3580*s*; 3420*w*(br.), 1500*s*, 1480*s*, 1280*s*. ^{1}H-NMR ($CDCl_3$, 100 MHz): 1.53 (*d*, J = 6.5, 1 H, exchangeable with D_2O); 1.60 (*d*, J = 7, 3 H); 4.88 (~ *quint.*, J = 7, 1 H); 5.88, 6.12 (*AB* of CH_2, J = 14); 6.20 (*m*, 4 H); 6.80 (*m*, 3 H). MS ($C_{11}H_{14}N_2O$; 190): 190 (4, M^+), 123 (50), 108 (10), 94 (55), 80 (100).

Tosylate of **7**. TsCl (1.08 g, 5.7 mmol) is added at +5° to a soln. of 1.0 g (5.7 mmol) of **7** in 8 ml of pyridine. After 3 h, the mixture is hydrolyzed by addition of cold 2N HCl and rapidly extracted with $CHCl_3$. Drying ($MgSO_4$) and removal of the solvent leaves 1.9 g of a solid. Recrystallization from EtOH gives 1.6 g (85%) of colorless needles of m.p. 114–115°. ^{1}H-NMR ($CDCl_3$, 100 MHz): 2.46 (*s*, 3 H); 4.61 (*d*, J = 6.8, 2 H); 6.14 (*t*, J = 6.8, 1 H) overlapping with 6.16 (apparent *t*, *AA* of 2× pyrrolic *AA'MM'*, 4 H); 6.65 (apparent *t*, *MM* of 2× pyrrolic *AA'MM'*, 4 H); 7.32 (*m*, 2 H); 7.69 (*m*, 2 H). MS ($C_{17}H_{18}N_2O_3S$; 330): 330 (62 M^+), 264 (75), 155 (100), 108 (92).

Tosylate of **8**. Same procedure as for tosylate of **7**. Yield 59%. Colorless needles of m.p. 78–79° (from EtOH). ^{1}H-NMR ($CDCl_3$, 100 MHz): 1.35 (*d*, J = 7.0, 3 H); 2.43 (*s*, 3 H); 5.41 (*dq*, J = 8.0, 7.0, 1 H); 5.75 (*d*, J = 8.0, 1 H); 6.14 (*m*, *AA* of 2× pyrrolic overlapping *AA'MM'*, 4 H); 6.73 (*m*, *MM* of 2× pyrrolic overlapping *AA'MM'*, 4 H); 7.24 (*m*, 2 H); 7.51 (*m*, 2 H). MS ($C_{18}H_{20}N_2O_3S$; 344): 344 (24, M^+), 278 (43), 155 (60), 145 (40), 139 (31), 122 (39), 91 (100).

1,1-Di(1-pyrrolyl)ethylene (**10**). A soln. of 2.0 g (6.0 mmol) of the tosylate of **7** in 20 ml of THF is added slowly at 0° to 1.02 g (9.0 mmol) of *t*-BuOK in 10 ml of THF. The mixture is stirred for 2 h at r.t., hydrolyzed, and extracted with Et_2O. The solid, remaining after drying ($MgSO_4$) and solvent removal, is purified by chromatography over a short column (Al_2O_3, basic; pentane/Et_2O 1:1). Yield: 0.92 g (95%) of colorless prisms of m.p. 50–51°. UV (hexane): 202 (4.33); 236 (4.16); 249 (4.14). IR (nujol): 3100*m*, 1640*s*, 1365*m*. ^{1}H-NMR ($CDCl_3$, 100 MHz): 4.80 (*s*, 2 H); 6.31 (apparent *t*, *AA* of *AA'MM'*, 4 H); 6.87 (apparent *t*, *MM* of *AA'MM'*, 4 H). ^{13}C-NMR ($CDCl_3$, 90.56 MHz): 91.6 (*t*); 110.3 (*d*); 120.8 (*d*); 141.3 (*s*). MS ($C_{10}H_{10}N_2$; 158): 158 (71, M^+), 92 (55), 67 (100).

1,1-Di(1-pyrrolyl)propene (**11**). Same procedure as described for compound **10** but using tosylate of **8**. Yield: 92%, of colorless crystals of m.p. 49–50°. ^{1}H-NMR ($CDCl_3$, 100 MHz): 1.75 (*d*, J = 7.1, 3 H); 5.51 (*q*, J = 7.1, 1 H); 6.20, 6.65 and 6.29, 6.74 (two closely spaced *AA'MM'* patterns, 8 H). ^{13}C-NMR ($CDCl_3$, 90.56 MHz): 12.1 (*q*); 106.1 (*d*); 109.5 (*d*); 109.8 (*d*); 119.6 (*d*); 121.8 (*d*); 135.5 (*s*). MS ($C_{11}H_{12}N_2$; 172): 172 (80, M^+), 106 (100), 78 (56).

1-Methoxy-1,1-di(1-pyrrolyl)ethane (**12**). A soln. of 160 mg (1.0 mmol) of **10** and 17 mg (0.1 mmol) of TsOH in 45 ml of MeOH was allowed to react for 2 h at 20°. The mixture was neutralized by the addition of solid Na_2CO_3, filtered, concentrated, and passed through a short column of *Florisil* (Et_2O) to give 186 mg (98%) of a colorless

liquid (**12**). IR (CCl_4): 2990*w*, 2950*m*, 1465*m*, 1375*m*, 1260*s*. ^{1}H-NMR ($CDCl_3$, 100 MHz): 2.15 (*s*, 3 H); 3.24 (*s*, 3 H); 6.22 (*AA* of *AA'MM'*, 4 H); 6.73 (*MM* of *AA'MM'*, 4 H). ^{13}C-NMR ($CDCl_3$, 90.56 MHz): 25.8 (*q*); 50.9 (*q*); 96.3 (*s*); 109.1 (*d*); 118.7 (*d*). MS ($C_{11}H_{14}N_2O$; 190): 190 (5, M^+), 158 (10), 124 (20), 83 (45), 57 (100).

Protonation in Superacid Media. General procedure. Ca. 0.1 mmol of the solid olefin to be protonated, is dissolved in 0.3 ml of CCl_4 and transfered to an ordinary NMR tube of 5 mm outer diameter. The NMR tube is then fitted to an inclinable *Büchi* rotavapor and brought into a nearly horizontal position. Slow evaporation of the solvent leaves the olefin as a thin solid film in the NMR tube. The tube is then fitted by means of an O-ring connector below the injection membrane of a vacuum line. After deoxygenation, the sample is cooled under Ar to *ca.* −100° and the appropriate amount of acid is injected. The NMR tube then is sealed. Mixing of its content is achieved by repeatedly inverting the tube in a spacious cooling bath, kept slightly above the freezing point of the acid. Finally the NMR tube is inserted in the precooled probe of the spectrometer for recording.

Cation **14**. ^{1}H-NMR ($HBF_4 \cdot Me_2O$ (*Aldrich* product No. 17.640–0), −5°, 360 MHz, external TMS): 3.00 (*s*, 3 H); 6.52 (*m*, *AA* of *AA'MM'*-type double intensity, 4 H); 7.18 (*m MM* of *AA'MM'*-type double intensity, 4 H).

Dication **13**. ^{1}H-NMR (FSO_3H, −20°, 100 MHz, external TMS): 4.90 (*m*, 4 H); 5.78 (*s*, 2 H, terminal CH_2); 6.90 (br. *d*, J = 6, 2 H); 8.07 (*d*, J = 6, 2 H); 8.64 (*m*, 2 H). ^{13}C-NMR (FSO_3H, −10°, 90.56 MHz, external TMS): 67.8 (*t*); 117.6 (*t*); 128.0 (*d*); 133.6 (*s*); 166.4 (*d*); 176.7 (*d*).

Dication **15**. ^{1}H-NMR ($HBF_4 \cdot Me_2O$, −5°, 360 MHz, external TMS): 1.55 (*d*, J = 7, 3 H); 5.05, 5.07 (2 narrow *m*, 4 H, CH_2N groups); 6.58 (*q*, J = 7, 1 H, couples with the CH_3 group); 6.90, 7.10, 8.04, 8.28 (4 *dm*, all J = 4.9, 4 H); 8.60, 9.02 (2 narrow *m*, 2 H).

Doubly Protonated Ether **19**. ^{1}H-NMR (FSO_3H, 0°, 100 MHz, external TMS): 4.89 (*m*, 4 H); 5.80 (*s*, 2 NCH_2O); 6.88 (*dm*, J = 6, 2 H); 8.07 (*dm*, J = 6, 2 H); 8.82 (narrow *m*, 2 H).

Di(1-pyrrolylmethyl) Ether (**20**). ^{1}H-NMR ($CDCl_3$, 100 MHz): 5.10 (*s*, 2 NCH_2O); 6.26, 6.79 (pyrrolic *AA'MM'*, 8 H). MS ($C_{10}H_{12}N_2O$; 176): 176 (12, M^+), 81 (22), 80 (100), 53 (23).

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