We report in this paper another approach to this structure which involves a thermal rearrangement of spiro compounds A and allows the introduction of substituents at positions 1 and 3 (Scheme B).

Scheme B

Schemes C and D describe the synthesis of our spiro compounds 6 and 12. The chloroformamidine 4, easily prepared from the known dichloromidine 3, reacted with lithium phenylacetylide to afford the amidine 5. O-Alkylation of the amide 10 was performed with triethylxonium fluoroborate.

The treatment of 5 and 11 with polyphosphoric acid according to the method described by Ried and Schweitzer2 led respectively to 6 and 12, easily identified by comparison with the methyl-aniline analogue described by these authors. A 6-methoxy quinoline 7 was observed only with the amide 5 as reported,2 but not with the imino-ether 11.

A New Synthesis of 7H-Pyrrolo[1,2-a]azepin-7-ones

M. Barreau, G. Ponsinet*

Rhone-Poulenc Sante, Centre de Recherches de Vitry, 13 Quai Jules Guesde, F-94400 Vitry-sur-Seine, France

Pyrrolo[1,2-a]azepin-7-ones 8 and 13 were prepared by heating the spiro compounds 6 and 12. This reaction proceeds probably through a tricyclic intermediate of a type already postulated in the azulene-naphthalene rearrangement.

In 1982 Jones and Radley1 published a synthesis of pyrrolo[1,2-a]azepin-7-one 1 and its protonation to give the azoniazulene 2 (Scheme A).

Scheme A

By heating at 200°–250°C, neat or in trichlorobenzene, the spiro compounds were transformed into coloured products. Analytical and spectroscopic data suggested the structures 8 and 13 for these new compounds. In particular the 1H-NMR signals of the four azepine protons are different from those in the symmetrical cyclohexadienones 6 and 12. The yellow pyrroloazepinones turned reversibly to a deep blue colour in acidic solution. The modification of their electronic structure can be measured by their UV/Visible (addition of sulfuric acid)
and $^1$H-NMR (addition of trifluoroacetic acid) spectra. In particular the strong shift of the vinylic protons after addition of trifluoroacetic acid to 13 was in agreement with the result of Jones indicating a cyclic protonation (structure E in Scheme E).

In the thermal treatment of 12 a minor colourless product was isolated and proved to be the 7-hydroxy quinoline 14. $^1$H-NMR spectra showed its substitution to be different from that of the 6-methoxy analogue 7.

Finally, we observed that, on strong acidic treatment, 8 was converted back to 6, while the same rearrangement did not occur with 13. A tentative mechanism for these reactions is shown in Scheme E.

The three structures A, B and D derive from the three possible cleavages of the aziridine ring in the tricyclic intermediate C. Other tricyclic intermediates 15, 16 and 17 were recently postulated in several analogous rearrangements and azulene derivatives were detected among the photo-products of several condensed azines.

In view of the current interest of the azulene-naphthalene rearrangement mechanism, our results provide a new non-photocatalytic route to the aza-azulene ring, probably via a tricyclic intermediate.

Melting points were determined using a Reichert-Koffer apparatus. $^1$H-NMR spectra were obtained using a Bruker WP (200 or 250 MHz) spectrometer. Infrared spectra were recorded on 580-B or 983-G Perkin-Elmer spectrophotometers. UV spectra were determined with a SP8-250 Unicam spectrometer. Mass spectra were obtained with a Finigan 3300 (electron impact: EI, chemical ionisation: CI). Column chromatography was performed on silicagel (Merck Kieselgel 60. 230–400 mesh).

1-(4-Methoxyphenylimino)-3-phenyl-1-pyrroldinyl-prop-2-yne (5):
A solution of pyrrolidine (41.0 g, 0.57 mol) in ether (250 ml) was added to a solution of N-(dichloromethylene)-p-anisidine (3, 57.2 g, 0.28 mol) in ether (500 ml) at –5°C. After 1 h at 0°C ether (300 ml) is added. The mixture is filtered to remove precipitated pyrrolidine hydrochloride and the filtrate is added slowly at –70°C to a solution of lithium phenylacetate [prepared by reacting n-butyllithium (156 ml of a 1.6 molar solution in hexane) and phenylacetylene (25.5 g, 0.25 mol) in tetrahydrofuran (150 ml)]. After 1 h at –70°C, the mixture is warmed up to 20°C and ice is added. After extraction, washing, chromatography on silica gel and recrystallization from hexane, 5 is obtained as yellow crystals; yield: 41.5 g (47%); m.p. 66°C.

C17H16N2O4 calc. C 78.92 H 6.62 N 9.20 (304.4) found 78.85 6.81 9.38
IR (KBr): ν = 2840, 2210, 1755, 1245, 830, 765, 690 cm$^{-1}$
MS (EI): m/e = 204, 289, 275, 234, 176, 129,
$^1$H-NMR (CDCl3): δ = 2.0 (m, 4 H, CH2CH2); 3.65 (m, 4 H, NCH2); 3.78 (s, 3 H, OCH3); 6.84, 6.96 (AA'BB', 4 H), 7.25–7.35 ppm (m, 5 H, C6H5).

4-Phenyl-2-pyrroldinyl-1-azaspiro[4,5]deca-1,3,6,9-tetraen-8-one (6) and 6-Methoxy-4-phenyl-2-pyrroldinylquinoline (7):
Amidine 5 (14.1 g, 0.46 mol) is added to polyphosphoric acid [prepared from phosphoric acid (47 ml, d = 1.7) and phosphorus pentoxide (63 g)]. After 2 h at 100°C the mixture is cooled and ice is added. The mixture is made alkaline with sodium hydroxide to pH 9 and extracted with dichloromethane (3 × 200 ml). The organic phase is washed with water (2 × 500 ml), dried with sodium sulfate and evaporated. The residue is chromatographed on silica gel using ethyl acetate as eluent to give 2 fractions:

7: Fraction one is crystallized from isopropyl ether, affording 7 as yellow crystals; yield: 3.7 g (26%); m.p. 127°C.

C17H10N2O4 calc. C 78.92 H 6.62 N 9.20 (304.4) found 78.80 6.82 9.12
IR (KBr): ν = 1610, 1600, 1575, 1550, 1495, 1480, 1450, 1420, 1265, 1045, 700 cm$^{-1}$
MS (EI): m/e = 304, 275, 249, 235.
$^1$H-NMR (CDCl3): δ = 2.03 (m, 4 H, CH2CH2); 3.62 (m, 4 H, NCH2); 3.72 (s, 3 H, OCH3); 6.62 (s, 1 H, H-3); 7.00 (d, J = 2.5 Hz, 1 H, H-5); 7.20 (dd, J = 8.5 Hz, J = 2.5 Hz, 1 H, H-7); 7.45–7.63 (m, 5 H, C6H5).

7.22 ppm (d, J = 8.5 Hz, 1 H, H-8).
1-Phenyl-3-pyridinyl-7H-pyrido[1,2-e]azepin-7-one (8):

Compound 6 (11.0 g, 0.038 mol) is heated for 30 min at 250°C. After cooling, chromatography on silica gel (eluent: dichloromethane) and recrystallization from ethyl acetate, 8 is obtained as orange crystals; yield: 8.3 g (75%); m. p. 135°C.

C_{21}H_{18}N_{2}O_{4} calc. C 78.59 H 6.25 N 9.65 (290.4) found 78.82 6.35 9.60
IR (KBr): v = 1660, 1615, 1550, 860, 765, 700 cm⁻¹.
MS (EI): m/e = 265, 250, 236, 208, 180, 102.

1H-NMR (CDCl₃): δ = 2.02 (m, 4H, CH₂CH₂); 3.58 (m, 4H, NCH₂); 6.37 (d, J = 10 Hz, 2H, H-6, H-10); 6.84 (d, J = 10 Hz, 2H, H-7, H-9); 6.88 (s, 1H, H-3); 7.3–7.5 ppm (m, 5H, C₆H₅).

13C-NMR (CDCl₃): δ = 76.3 (C-5); 122.0 (C-3); 126.5 (C-7, 9); 149.5 (C-6, 10); 162.2 (C-4); 167.8 (C-2); 186.3 ppm (C-8).

3-Ethoxy-1-phenyl-7H-pyrido[1,2-e]azepin-7-one (13) and 2-Ethoxy-7-hydroxy-4-phenylquinoline (14):

A solution of 12 (2.75 g, 0.01 mol) in 1,2,4-trichlorobenzene (15 ml) is heated for 4 h at 200°C. After cooling, cyclohexane (50 ml) is added and filtered. The filtrate and the precipitate are worked up separately.

13: The filtrate is evaporated and the residue is chromatographed on silica gel (eluent: dichloromethane/methanol, 99:1). The product obtained is recrystallized from ethanol/diisopropyl ether: brown crystals; yield: 0.9 g (32%); m. p. 162°C.
C_{21}H_{18}N_{2}O_{4} calc. C 76.96 H 5.70 N 5.28 (265.3) found 76.60 5.70 5.12
IR (KBr): v = 1540, 1610, 1580, 1550, 845, 760, 705 cm⁻¹.
UV (CH₃OH): λ_{max} = 276 (4.45), 320 (sh), 444 nm (3.62).
UV (CH₃OH + 1% H₂SO₄): λ_{max} = 278 (4.37), 342 (4.08), 544 nm (3.62).

Rearrangement of 8 into 6:

48% Hydrogen bromide (0.05 ml) is added to a solution of 8 (0.1 g, 0.34 nmol) in acetic acid (1 ml). On heating for 1 min at 100°C the blue-violet colour is vanished. The mixture is cooled, diluted with water (50 ml), adjusted to pH 10 with ammonium hydroxide and extracted with dichloromethane. The product recovered proved to be indelible with 6 by TLC (dichloromethane/methanol, 95:5), melting point and IR spectrum.

N-(4-Methoxy-phenyl)-phenylpropiolamide (10):

A solution of para-nitroaniline (64.0 g, 0.6 mol) in ether (600 ml) is added slowly to a solution of the acid chloride⁹ (9, 49.4 g, 0.53 mol) in ether (250 ml) cooled at 3°C. The mixture stirred for 1 h more at 3°C. The mixture is decomposed with ice and the product is extracted with ether (3 x 500 ml). Evaporation of solvent affords 10 which is recrystallized from ethanol; yield: 71.0 g (97%); m. p. 131°C.
C₁₈H₁₇NO₂ calc. C 76.48 H 5.22 N 5.57 (251.3) found 76.43 5.26 5.50
IR (KBr): v = 2920, 2840, 2210, 1630, 1540, 1250, 830, 765, 695 cm⁻¹.
MS (EI): m/e = 251, 250, 208, 180, 129.

1H-NMR (CDCl₃): δ = 3.74 (s, 3H, OCH₃); 6.81 (d, J = 8.5 Hz, 2H, arom ortho from OCH₃); 7.22–7.45 ppm (m, 7H, arom).


