

Tetrahedron Letters, Vol. 36, No. 43, pp. 7859-7862, 1995 Elsevier Science Ltd Printed in Great Britain 0040-4039/95 \$9.50+0.00

0040-4039(95)01636-8

## Tandem Wolff Rearrangement -"tert-Amino Effect" Sequence : Synthesis of 2-Oxoindolinium Enolate and 1H-2-Benzopyrane Derivatives.

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Abstract : The thermal decomposition of dimethyl 1-diazo-2-oxo-(2-N,N-disubstituted aminophenyl)ethylphosphonates 1 gave rise to 2-oxoindolinium enolates 3 resulting from a Wolff rearrangement followed by an attack of the nitrogen atom on the intermediate ketene moiety. Annuonium ylides 5 resulting from the decomposition of 1 were also formed through a carbene path. The thermal decomposition of dimethyl 1-diazo-2-oxo-(2-(N,N-disubstituted aminomethyl)phenyl) ethylphosphonates 6 followed a different course and afforded 1*H*-2-benzopyranes 9 as the sole isolated products through a Wolff rearrangement - [1,5] H shift - ring closure sequence. The structures of 3a and 5a were confirmed by X-ray crystallography.

Cyclizations of certain *ortho*-substituted N,N-dialkylanilines, known as the "*tert*-amino effect",<sup>1</sup> can proceed through N-alkylation (I) or [1,5] or [1,6] hydrogen shift followed by heterocyclization (II and III) depending on the nature of the *ortho* substituent  $X=Y^2$ .



Although various "*ortho*  $2\pi$  substituents" have been reported, such as C=C, C=O, C=N, NO<sub>2</sub>, N=N, N=SO<sub>2</sub>, we found no example of a ketene moiety as the X=Y substituent.

We have recently reported that the thermal decomposition of some  $\alpha$ -diazo- $\beta$ -keto- $\gamma$ , $\delta$ -alkenylphosphonates substituted in the  $\delta$  position by an alkyl, aryl or alkenyl group led to the formation of cyclobutenones or of various phenolic compounds, these products being formed by the electrocyclization of a vinyl or dienyl ketene resulting from a thermal Wolff rearrangement.<sup>3</sup> We have applied this ketene aromatic annulation to the field of isoxazole chemistry.<sup>4</sup> These results have demonstrated that dimethylphosphono vinyl or dienyl ketenes are easily generated by a thermal Wolff rearrangement. Consequently, it became interesting to investigate the thermal decomposition of 1-diazo-2-oxo-(2-N,N-disubstituted aminophenyl)ethylphosphonates 1 which could possibly lead to intermediate 2-ketenyl-N,N-disubstituted anilines 2 and thus allow to study their behaviour.

The  $\alpha$ -diazo- $\beta$ -ketophosphonates 1<sup>5</sup> were prepared in three steps (overall yields : 1a [58%], 1b [42%]) from ethyl 2-fluorobenzoate by fluorine substitution with piperidine or pyrrolidine in the presence of potassium carbonate,<sup>6</sup> condensation with dimethyl lithiomethylphosphonate and diazo-transfer with tosyl azide. Thermal decomposition of 1 by heating in boiling toluene<sup>7</sup> gave mixtures of 3 and 5 (Yields : 3a [43%] and 5a [44%], 3b [88%] and 5b [2%]).<sup>8</sup>

The <sup>13</sup>C-nmr spectra of  $3a^9$  and  $5a^{10}$  showed the presence of three methylenes, respectively at 55.79, 20.99, 20.26 and 64.40, 22.72, 19.50 ppm, indicating that ring opening or hydrogen shift related to the piperidino moiety did not occur; the presence of two deshielded protons in the <sup>1</sup>H-nmr spectra of  $3a^9$  and  $5a,^{10}$  respectively at 3.55 and 4.87 ppm, suggested the presence of a positively charged nitrogen. Formulation of the structures as 3-dimethylphosphono-2-oxo-1-spiropiperidinoindolinium enolate for 3a and 2-dimethylphosphono-3-oxo-1-spiropiperidinoindolinium enolate for 5a was derived on the basis of the expected decomposition paths of the  $\alpha$ -diazo- $\beta$ -ketophosphonates 1 : mesoionic compounds 3 would result from a Wolff transposition followed by an attack of the nitrogen atom lone pair on the intermediate ketenes 2, whereas ammonium ylides 5 would be obtained through the transient carbenes 4.



We found no example in the literature of mesoionic compounds like 3 or stable cyclic ammonium ylides like 5. Ammonium ylides are intermediate species which can evolve, according to their structures, by Stevens [1,2] shift or [2,3] signatropic rearrangement<sup>11-14</sup>; stable cyclic sulfonium ylides<sup>15-16</sup> are known, but comparison of their spectral data with those of 5a was not conclusive. Consequently the structures of 3a and 5a were ascertained by X-ray crystallography (Figure).<sup>17</sup> The structures of 3b and 5b were established by their spectral similarities with 3a and 5a.

No hydrogen shift was observed during the decomposition of the  $\alpha$ -diazo- $\beta$ -ketophosphonates 1, possibly because unfavorable 7-membered transition states would have been involved. So we decided to investigate the effect of the introduction of a methylene between the *tert*-nitrogen and the aromatic ring. The requisite 1-diazo-2-oxo-(2-(N,N-disubstituted aminomethyl)phenyl)ethylphosphonates 6 were synthesized in four steps (overall yields : **6a** [45 %]; **6b** [40 %]) starting from ethyl *o*-toluate by benzylic bromination with N-bromo-succinimide, bromine substitution with piperidine or N-methylaniline, condensation with dimethyl

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lithiomethylphosphonate and diazo-transfer with tosyl azide. Thermal decomposition of 6 by heating in boiling toluene for 2.5 h gave the 1*H*-2-benzopyranes  $9a^{18}$  (yield : 38 %) and  $9b^{19}$  (yield : 78 %) as the sole isolated products. The formation of 9 from 6 results from a Wolff transposition giving rise to the intermediate ketene 7 followed by a [1,5] hydrogen shift and subsequent ring closure of the iminium 8. The transformation  $7 \rightarrow 9$  appears as a new example of an " $\alpha$ -Cyclization of a Tertiary Amine".<sup>2,20</sup>



We are currently investigating the scope and limitations of these sequences, especially the influence of the *tert*-amino moiety and its replacement by other nucleophilic groups.





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- 5. All new compounds described therein gave satisfactory elemental analysis except 5b for which no microanalysis was made because only a very small quantity of this compound was isolated.
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- 7. Time of decomposition : 3.5 h for 1a, 1h for 1b.
- 8. The interpretation of the 3/5 ratios appears difficult in view of these preliminary results.
- 9. 3-Dimethylphosphono-2-oxo-1-spiropiperidinoindolinium enolate (3a) : Mp = 170-172 °C. IR (CHCl<sub>3</sub>) : 1750, 1600, 1580, 1055, 1025 cm<sup>-1</sup>. <sup>1</sup>H-RMN (300 MHz, CDCl<sub>3</sub>) :  $\delta$ (ppm) 7.57 (d, 1H, J = 8.0 Hz) ; 7.52 (d, 1H, J = 7.9 Hz) ; 7.30 (pt, 1H, J = 7.7 Hz) ; 6.94 (pt, 1H, J = 7.8 Hz) ; 3.69 (d, 6H, <sup>3</sup>J<sub>HP</sub> = 11.5 Hz) ; 3.55 (td, 2H, J = 13.2 Hz, J = 3.8 Hz) ; 2.88 (pd, 2H, J = 13.2 Hz) ; 2.33-2.18 (m, 2H) ; 2.07-1.98 (m, 3H) ; 1.76-1.71 (m, 1H). <sup>13</sup>C-RMN (75 MHz, CDCl<sub>3</sub>) :  $\delta$ (ppm) 170.15 (d, <sup>2</sup>J<sub>CP</sub> = 24.8 Hz) ; 139.32 (<sup>3</sup>J<sub>CP</sub> = 15.0 Hz) ; 137.66 (<sup>2</sup>J<sub>CP</sub> = 13.0 Hz) ; 130.14 ; 120.02 ; 119.87 ; 118.74 ; 62.32 (d, <sup>1</sup>J<sub>CP</sub> = 219.3 Hz) ; 55.79 ; 52.26 (d, <sup>2</sup>J<sub>CP</sub> = 5.3 Hz) ; 20.99 ; 20.26.
- 10. 2-Dimethylphosphono-3-oxo-1-spiropiperidinoindolinium enolate (**5a**) : Mp = 219-221 °C. IR (CHCl<sub>3</sub>) : 1620, 1585, 1035 cm<sup>-1</sup>. <sup>1</sup>H-RMN (300 MHz, CDCl<sub>3</sub>) :  $\delta$ (ppm) 7.95 (d, 1H, J = 8.2 Hz) ; 7.82 (d, 1H, J = 6.4 Hz) ; 7.65 (pt, 1H, J = 7.4 Hz) ; 7.52 (pt, 1H, J = 6.8 Hz) ; 4.87 (td, 2H, J = 13.4 Hz, J = 4.0 Hz) ; 3.74 (d, 6H, <sup>3</sup>J<sub>HP</sub> = 12.1 Hz) ; 3.22 (pd, 2H, J = 13.4 Hz) ; 2.47-2.31 (m, 2H) ; 2.12-1.97 (m, 3H) ; 1.89-1.77 (m, 1H). <sup>13</sup>C-RMN (75 MHz, CDCl<sub>3</sub>) :  $\delta$ (ppm) 172.11 (d, <sup>2</sup>J<sub>CP</sub> = 16.8 Hz) ; 150.88 (d, <sup>3</sup>J<sub>CP</sub> = 8.6 Hz) ; 135.44 (d, <sup>3</sup>J<sub>CP</sub> = 15.7 Hz) ; 130.85 ; 129.10 ; 123.79 (d, J<sub>CP</sub> = 0.7 Hz) ; 119.27 (d, J<sub>CP</sub> = 1.2 Hz) ; 105.75 (d, <sup>1</sup>J<sub>CP</sub> = 226.8 Hz) ; 64.40 ; 52.77 (d, <sup>2</sup>J<sub>CP</sub> = 5.6 Hz) ; 22.72 ; 19.50.
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- 17. Crystal data. (3a) : C<sub>15</sub>H<sub>20</sub>NO<sub>4</sub>P, M = 309.30, triclinic, space group P1, a = 6.476(1), b = 9.384(2), c = 13.054(1) Å,  $\alpha$  = 94.74(1),  $\beta$  = 100.79(1),  $\gamma$  = 98.22(1)°, V = 766.3(2) Å<sup>3</sup>, Z = 2, D<sub>c</sub> = 1.341 g.mL<sup>-1</sup>. (5a) : C<sub>15</sub>H<sub>20</sub>NO<sub>4</sub>P, M = 309.30, monoclinic, space group C2, a = 28.252(2), b = 6.478(1), c = 8.707(1) Å,  $\beta$  = 105.59(1)°, V = 1534.9(4) Å<sup>3</sup>, Z = 4, D<sub>c</sub> = 1.339 g.mL<sup>-1</sup>.
- 18. 4-Dimethylphosphono-1-piperidino-1*H*-2-benzopyrane (9a) : Mp = 94°C. IR (CHCl<sub>3</sub>) : 1600, 1565, 1250, 1055, 1025 cm<sup>-1</sup>. <sup>1</sup>H-RMN (200 MHz, CDCl<sub>3</sub>) :  $\delta$ (ppm) 7.59 (d, 1H, <sup>3</sup>J<sub>HP</sub> = 9.4 Hz) ; 7.50-7.40 (m, 1H) ; 7.40-7.20 (m, 3H) ; 6.08 (s, 1H) ; 3.75 (d, 3H, <sup>3</sup>J<sub>HP</sub> = 11.4 Hz) ; 3.72 (d, 3H, <sup>3</sup>J<sub>HP</sub> = 11.4 Hz) ; 2.90-2.55 (m, 4H) ; 1.60-1.40 (m, 6H).<sup>13</sup>C-RMN (50 MHz, CDCl<sub>3</sub>) :  $\delta$ (ppm) 159.04 (d, <sup>2</sup>J<sub>CP</sub> = 21.7 Hz) ; 128.68 ; 128.10 (d, <sup>2</sup>J<sub>CP</sub> = 7.8 Hz) ; 127.25 ; 126.87 (d, <sup>3</sup>J<sub>CP</sub> = 3.2 Hz) ; 126.79 (d, <sup>3</sup>J<sub>CP</sub> = 10.8 Hz) ; 122.84 (d, <sup>4</sup>J<sub>CP</sub> = 2.5 Hz) ; 98.47 (d, <sup>1</sup>J<sub>CP</sub> = 200.6 Hz) ; 95.48 ; 52.21 (d, <sup>2</sup>J<sub>CP</sub> = 4.8 Hz) ; 52.12 (d, <sup>2</sup>J<sub>CP</sub> = 4.8 Hz) ; 48.01 ; 26.01 ; 24.39.
- 19. 4-Dimethylphosphono-1-phenylmethylamino-1*H*-2-benzopyrane (9b) : Mp = 87°C. IR (CHCl3) : 1600, 1570, 1260, 1225, 1055, 1025 cm<sup>-1</sup>.<sup>1</sup>H-RMN (200 MHz, CDCl3) :  $\delta$ (ppm) 7.60-6.92 (m, 11 H with a doublet at 7.58, <sup>3</sup>J<sub>HP</sub> = 9.6 Hz) ; 3.77 (d, 3H, <sup>3</sup>J<sub>HP</sub> = 11.4 Hz) ; 3.75 (d, 3H, <sup>3</sup>J<sub>HP</sub> = 11.4 Hz) ; 2.75 (s, 3H). <sup>13</sup>C-RMN (50 MHz, CDCl3) :  $\delta$ (ppm) 158.17 (d, <sup>2</sup>J<sub>CP</sub> = 21.7 Hz) ; 148.57 ; 129.19 ; 129.15 (d, <sup>3</sup>J<sub>CP</sub> = 3.0 Hz) ; 127.83 (d, <sup>2</sup>J<sub>CP</sub> = 7.7 Hz) ; 127.71 ; 126.29 (d, <sup>4</sup>J<sub>CP</sub> = 1.4 Hz) ; 126.24 (d, <sup>3</sup>J<sub>CP</sub> = 10.8 Hz) ; 123.52 (d, <sup>4</sup>J<sub>CP</sub> = 2.5 Hz) ; 120.93 ; 116.75 ; 98.84 (d, <sup>1</sup>J<sub>CP</sub> = 200.7 Hz) ; 89.69 ; 52.25 (d, <sup>2</sup>J<sub>CP</sub> = 4.9 Hz) ; 52.15 (d, <sup>2</sup>J<sub>CP</sub> = 5.0 Hz) ; 32.76.
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