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## RESEARCH ARTICLE

### NEW ACCESS ROUTES TO 4-PHOSPHOPYRAZOLO (1,5-A)PYRIMIDINES BY ACTION OF $\alpha,\beta$ -DIKETONES AND $\alpha,\beta$ -KETOESTER ON 3,5- DIAMINO-4-PHOSPHOPYRAZOLES

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#### ABSTRACT

Constitué par la condensation de la pyrimidine et du pyrazole, la pyrazolopyrimidine serait, dans la nomenclature systématique, une pyrazolo(1,5-a)pyrimidine. Les pyrazolopyrimidines non phosphonates sont largement décrites dans la littérature (24-28). Par contre les pyrazolopyrimidinesphosphonates et fluorés ont été très peu étudiés. Il est connu que l'introduction d'un groupement phosphoré sur un hétérocycle pyrazolique par exemple modifie leurs propriétés biologiques et étend leur domaine d'application dans des importantes fonctions biologiques (25) et présentes des activités anti-inflammatoires (26). Les pyrazolopyrimidines en général sont des composés hétérocycliques qui ont donné lieu à des applications dans divers domaines : Biologique (1-4); Pharmacologique (5-7) et l'Agriculture (8-9). L'intérêt porté pour les pyrimidines a attiré l'attention de plusieurs chercheurs à développer la chimie de cette famille de composés. Dans ce travail, nous décrivons une synthèse simple et efficace par une voie nouvelle de nouveaux pyrazolopyrimidinesphosphonates possédant des groupements fluorés et aminés. En effet, l'action d'acétylacétone par chauffage à reflux sur les 4-phospho-5-aminopyrazoles conduit directement aux 4-phosphopyrazolo(1,5-a)pyrimidines attendus. Ces composés sont obtenus avec de bons rendements (68-85 %). L'étude spectroscopique par RMN (<sup>1</sup>H, <sup>13</sup>C, <sup>19</sup>F, <sup>31</sup>P) et l'analyse élémentaire centésimale des composés synthétisés, a permis de déterminer sans ambiguïté la structure et la pureté de ces hétérocycles. L'action aussi de l'acétate d'éthyle sur les 4-phospho-5-aminopyrazoles a permis d'accéder aux 4-phospho-9-hydroxy phosphopyrazolo(1,5-a)pyrimidines avec de bons rendements (68-74%). Nous n'avons pas pu isoler l'intermédiaire résultant de l'attaque du groupe carbonyle cétonique par le motif NH<sub>2</sub> du 4-phospho-5-aminopyrazole. Cet intermédiaire se cyclise au fur et à mesure de sa formation par action du doublet de l'amine N-H du noyau pyrazolique sur la fonction ester.

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#### INTRODUCTION

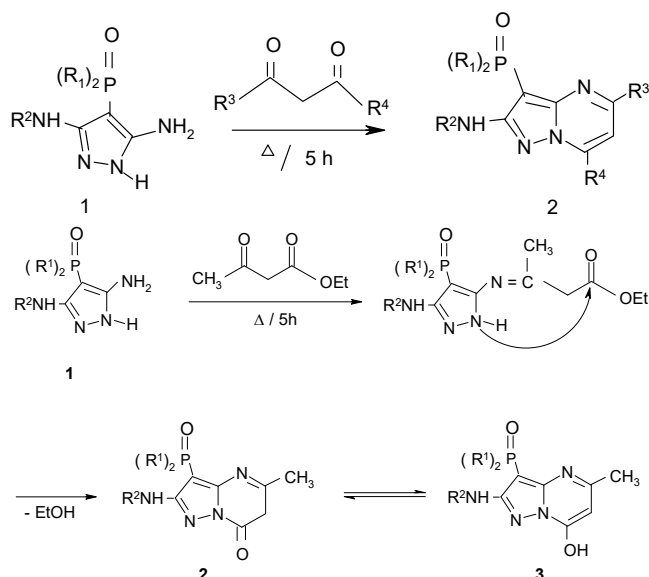
Pyrazolopyrimidines are, among heterocycles, compounds that have given rise to applications in such varied biological, pharmacological and agricultural fields. The derivatives of these products have been used as analgesics, anti-inflammatory, anti-malarial and pesticides of all kinds (10-24). The multiple applications of these pyrazolopyrimidines have attracted the attention of several laboratories to develop the chemistry of this family of compounds.

In this work we describe the reactivity of 3,5-diamino-4-phosphopyrazoles type 1 vis-à-vis biselectrophile compounds of  $\alpha,\beta$ -diketones and  $\alpha,\beta$ -ketoesters in order to access pyrazolopyrimidines 2 and hydroxypyrazolopyrimidines 3 phosphorylated. The spectroscopic NMR study of <sup>1</sup>H, <sup>13</sup>C, <sup>19</sup>F, <sup>31</sup>P and centesimal analysis of synthesized compounds, made it possible to determine unambiguously the structure of these heterocycles.

#### MATÉRIELS AND MÉTHODES

**Matériels:** Melting points are determined in capillary with a Büchi device. NMR spectra were recorded in chloroform or DMSO deuterized with a Bruker AC spectrometer at 300 MHz for <sup>1</sup>H, 75.47 MHz for <sup>13</sup>C, 121.49 MHz for <sup>31</sup>P and 282.39 MHz for <sup>19</sup>F.

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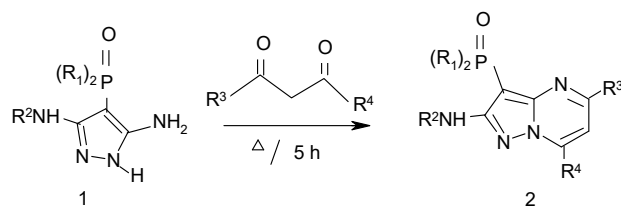


Chemical shifts are given in ppm and are counted positively towards weak fields relative to TMS as internal reference ( $^1\text{H}$ ,  $^{13}\text{C}$ ) and  $\text{C}_6\text{F}_6$  ( $^{19}\text{F}$ ),  $\text{H}_3\text{PO}_4$  to 85% ( $^{31}\text{P}$ ) as external references. The allocation of  $^{13}\text{C}$  NMR signals was done by the broadband decoupling technique based on chemical displacements. The values of the coupling constants are given in Hz. The elemental analysis was carried out at the Centre d'AnalyseElementaire of the Université P. et M. Curie (PARIS VI). Melting points are determined in capillary with a Büchi device. NMR spectra were recorded in chloroform or DMSO deuterized with a Bruker AC spectrometer at 300 MHz for  $^1\text{H}$ , 75.47 MHz for  $^{13}\text{C}$ , 121.49 MHz for  $^{31}\text{P}$  and 282.39 MHz for  $^{19}\text{F}$ . Chemical shifts are given in ppm and are counted positively towards weak fields relative to TMS as internal reference ( $^1\text{H}$ ,  $^{13}\text{C}$ ) and  $\text{C}_6\text{F}_6$  ( $^{19}\text{F}$ ),  $\text{H}_3\text{PO}_4$  to 85% ( $^{31}\text{P}$ ) as external references. The allocation of  $^{13}\text{C}$  NMR signals was done by the broadband decoupling technique based on chemical displacements. The values of the coupling constants are given in Hz. The elemental analysis was carried out at the Centre d'AnalyseElementaire of the Université P. et M. Curie (PARIS VI).

**Méthods:** Preparation of 4-phosphopyrazolo (1,5-a) pyrimidines 2. Pyrazolo (1,5-a) pyrimidines 2 a-d are obtained according to the following procedure: On reflux heats for 5 hours, 5 millimoles of 4-phosphopyrazole 1 in 10 ml of acetylacetone. After concentration of the reaction mixture, 5 ml of light petroleum was added. It precipitates a product that is recrystallized in a mixture of benzene - petroleum ether (80 - 20%). Pyrazolo (1,5-a) pyrimidines 2e-g are prepared, by heating to reflux ethanol (15 ml), 5 millimoles of 4-phosphopyrazoles 2 and 5 millimoles of dibenzoylmethane for 15 hours. The excess solvent is evaporated by vacuum distillation. 5 ml of light petroleum is added to precipitate pyrazolo (1,5-a) pyrimidines. After filtration, recrystallization is recrystallized in a mixture of benzene-light petroleum (80%-20%). The same reaction was tested with ethyl acetylacetate. 4-phospho-9-hydroxypyrazolo(1,5-a)pyrimidines 3 were obtained with good yields (68-74%) (Scheme 2)

## RESULTATS AND DISCUSSION

**Synthesis of 4-phosphopyrazolo (1,5-a)pyrimidines 2:** 5-amino-4-phosphopyrazoles type 1 are excellent substrates for the synthesis of phosphonitrogen bicyclic heterocycles.



Indeed, heated in 10 ml of reflux acetylacetone, these compounds lead directly to the expected 4-phosphopyrazolo (1,5-a) pyrimidines 2 (Schema-1).

### Experimental results of 4-phosphopyrazolo(1,5-a)pyrimidines 2a

White powder; Rdt = 90 %; F = 175°C ;  $\text{RMN-}^{31}\text{P}$  ( $\text{CDCl}_3$ ):  $\delta$  = 15.2  $\text{RMN-}^1\text{H}$  ( $\text{CDCl}_3$ ): d  $\delta$  = 1.34 (t,  $^3\text{J}_{\text{HH}} = 6.9$  Hz, 6H, P-O- $\text{CH}_2\text{-CH}_3$ ), 4.2 (qd,  $^3\text{J}_{\text{HP}} = 6.9$  Hz, 4H, P-O- $\text{CH}_2\text{-CH}_3$ ), 2.54 (s, C9- $\text{CH}_3$ ), 2.72 (s, C7- $\text{CH}_3$ ), 6.56 (s, 1 H, C=C-H), 6.94-7.73 (5H, arom-H), 8.97 (s, 1H, NH);  $\text{RMN-}^{13}\text{C}$  ( $\text{CDCl}_3$ ): 16.30 (d,  $^3\text{J}_{\text{CP}} = 6.9$  Hz,  $\text{CH}_2\text{-CH}_3$ ), 17.38 (C9- $\text{CH}_3$ ), 24.78 (C7- $\text{CH}_3$ ), 62.33 (d,  $^2\text{J}_{\text{CP}} = 4.8$  Hz,  $\text{CH}_2\text{-O-P}$ ), 77.25 (d,  $^1\text{J}_{\text{CP}} = 218.3$  Hz, C4), 149.98 (d,  $^2\text{J}_{\text{CP}} = 18.4$  Hz, C3), 159.18 (d,  $^2\text{J}_{\text{CP}} = 12.1$  Hz, C5), 108.61 (C8), 145.28 (C9), 161.0 (C7), 116.7-140.05 (arom-C) ;  $\text{C}_{18}\text{H}_{23}\text{N}_4\text{PO}_3$ : calculé: C 57.75; H 6.15; N 14.97. trouvé : C 57.06; H 6.11; N 14.77.

**2b:** White powder; Rdt = 75 %; F = 167°C ;  $\text{RMN-}^{31}\text{P}$  ( $\text{CDCl}_3$ ):  $\delta$  = 15.14;  $\text{RMN-}^1\text{H}$  ( $\text{CDCl}_3$ ):  $\delta$  = 1.34 (t,  $^3\text{J}_{\text{HH}} = 7.0$  Hz, 6H, P-O- $\text{CH}_2\text{-CH}_3$ ), 4.23 (qd,  $^3\text{J}_{\text{HP}} = 7.35$  Hz, 4H, P-O- $\text{CH}_2\text{-CH}_3$ ), 2.55 (s, C9- $\text{CH}_3$ ), 2.72 (s, C7- $\text{CH}_3$ ), 6.57 (s,  $^1\text{H}$ , C=C-H), 8.93 (s,  $^1\text{H}$ , NH); 6.98-7.68 (m, 4H, arom-H) ;  $\text{RMN-}^{13}\text{C}$  ( $\text{CDCl}_3$ ):  $\square$  = 16.31 (d,  $^3\text{J}_{\text{CP}} = 6.8$  Hz,  $\text{CH}_2\text{-CH}_3$ ), 17.39 (C9- $\text{CH}_3$ ), 24.80 (C7- $\text{CH}_3$ ), 62.39 (d,  $^2\text{J}_{\text{CP}} = 4.6$  Hz,  $\text{CH}_2\text{-O-P}$ ), 77.17 (d,  $^1\text{J}_{\text{CP}} = 219.5$  Hz, C4), 149.94 (d,  $^2\text{J}_{\text{CP}} = 18.5$  Hz, C3), 159.17 (d,  $^2\text{J}_{\text{CP}} = 12.5$  Hz, C5), 108.65 (C8), 161.12 (C7), 145.27 (C9), 157.6 (d,  $^1\text{J}_{\text{FC}} = 257.20$  Hz, C4'F), 115.37 (d,  $^2\text{J}_{\text{FC}} = 22.3$  Hz, C3'F), 118.69 (d,  $^3\text{J}_{\text{FC}} = 7.5$  Hz, C2'F), 137.06 (C1'F) ;  $\text{RMN-}^{19}\text{F}$  ( $\text{CDCl}_3$ ): = 38.72 (tt,  $^3\text{J}_{\text{FH}} = 4.7$  Hz, 1F);  $\text{C}_{18}\text{H}_{22}\text{FN}_4\text{PO}_3$ : calculé : C 55.10; H 5.61; N 14.29. trouvé: C 55.35; H 5.32; N 14.63.

**2c:** White powder; Rdt= 79%; F = 220°C ;  $\text{RMN-}^{31}\text{P}$  (DMSO):  $\delta$  = 17.61;  $\text{RMN-}^1\text{H}$  (DMSO): 3.62 (d,  $^3\text{J}_{\text{HP}} = 12.07$ Hz, 6H, P-O- $\text{CH}_3$ ), 2.51 (s, C9- $\text{CH}_3$ ), 2.73 (S, C7- $\text{CH}_3$ ), 6.80 (s, 1H, C=C-H), 9.25 (s, 1H, NH); 6.90-7.651(m, 5H, arom-H);  $\text{RMN-}^{13}\text{C}$  (DMSO):  $\square$  = 16.89 (C9- $\text{CH}_3$ ), 24.30 (C7- $\text{CH}_3$ ), 51.8 (d,  $^2\text{J}_{\text{CP}} = 4.6$  Hz,  $\text{CH}_3\text{-O-P}$ ), 79.22 (d,  $^1\text{J}_{\text{CP}} = 214.8$  Hz, C4), 149.17 (d,  $^2\text{J}_{\text{CP}} = 17.4$  Hz, C3), 108.46 (C8), 146.5 (C9), 158.09 (d,  $^2\text{J}_{\text{CP}} = 12.1$  Hz, C5), 160.02 (C7), 116.7-140.05 (arom-C);  $\text{C}_{16}\text{H}_{19}\text{N}_4\text{PO}_3$ : calculé: C 55.49; H 5.49; N 16.18. trouvé: C 55.26; H 5.34; N 16.46.  $\text{C}_{16}\text{H}_{19}\text{N}_4\text{PO}_3$ : calculé: C 55.49; H 5.49; N 16.18. trouvé: C 55.26; H 5.34; N 16.46.  $\text{C}_{16}\text{H}_{19}\text{N}_4\text{PO}_3$ : calculé: C 55.49; H 5.49; N 16.18. trouvé: C 55.26; H 5.34; N 16.4

**2d:** yellow powder; Rdt = 85%; F = 205°C ;  $\text{RMN-}^{31}\text{P}$  (DMSO):  $\delta$  = 17.61;  $\text{RMN-}^1\text{H}$  (DMSO): 3.62 (d,  $^3\text{J}_{\text{HP}} = 11.77$  Hz, 6H, P-O- $\text{CH}_3$ ), 2.49 (s, C9- $\text{CH}_3$ ), 2.69 (s, C7- $\text{CH}_3$ ), 6.67 (s, 1 H, C=C-H), 9.27 (s, 1H, NH); 7.13-7.65 (m, 4H, arom-H);  $\text{RMN-}^{13}\text{C}$  (DMSO):  $\delta$  = 16.74 (C9- $\text{CH}_3$ ), 24.17 (C7- $\text{CH}_3$ ), 51.73 (d,  $^2\text{J}_{\text{CP}} = 4.8$  Hz,  $\text{CH}_3\text{-O-P}$ ), 78.92 (d,  $^1\text{J}_{\text{CP}} = 213.7$  Hz, C4), 108.01 (C8), 148.98 (d,  $^2\text{J}_{\text{CP}} = 17.3$  HZ, C3), 157.86 (d,  $^2\text{J}_{\text{CP}} = 12.3$  Hz, C5), 160.53 (C7), 145.33 (C9), 156.31 (d,  $^1\text{J}_{\text{FC}} = 221.7$  HZ, C4'F ), 115.39 (d,  $^2\text{J}_{\text{FC}} = 22.2$  Hz, C3'F ), 117.96 (d,  $^3\text{J}_{\text{FC}} = 7.6$  Hz, C2'F), 137.13 (C1'F);  $\text{RMN-}^{19}\text{F}$  (DMSO):

= 43.44 (tt,  $^3J_{\text{FH}} = 4.8$  Hz);  $\text{C}_{16}\text{H}_{18}\text{FN}_4\text{PO}_3$ : calculé: C 52.75; H 4.95; N 15.38. trouvé :C 52.95; H 4.91; N 15.30.

**2e**: White powder; Rdt = 78%; F = 215°C; RMN- $^{31}\text{P}$  ( $\text{CDCl}_3$ ):  $\delta = 19.64$ ; RMN- $^1\text{H}$  ( $\text{CDCl}_3$ ): 3.70 (d, 6H,  $^3J_{\text{HP}} = 11.37$  Hz, P-O-CH $_3$ ), 6.50 (s, 1H, C=C-H), 9.23 (s, 1H, NH); 6.90-7.97(m, 15H, arom-H); RMN- $^{13}\text{C}$  ( $\text{CDCl}_3$ ):  $\delta = 52.04$  (d,  $^2J_{\text{CP}} = 4.6$  Hz CH $_3$ -O-P), 79.22 (d,  $^1J_{\text{CP}} = 218.8$  Hz, C4), 149.17 (d,  $^2J_{\text{CP}} = 17.4$  Hz, C3), 107 (C8), 158.09 (d,  $^2J_{\text{CP}} = 12.1$  Hz, C5), 160.0 (C7), 147.6 (C9) 117.53-141.02 (arom-C);  $\text{C}_{26}\text{H}_{23}\text{N}_4\text{PO}_3$ : calculé : C 66.38; H 4.89; N 11.91. trouvé :C 66.27; H 5.01; N 11.76.

**2f**: Poudre blanche; Rdt = 71%; F = 208°C; RMN- $^{31}\text{P}$  (DMSO):  $\delta = 17.75$  RMN- $^1\text{H}$  ( $\text{CDCl}_3$ ): 3.70 (d, 6H,  $^3J_{\text{HP}} = 11.37$  Hz, P-O-CH $_3$ ), 6.50 (s, 1H, C=C-H), 9.23 (s, 1H, NH); 6.90-7.97(m, 15H, arom-H); RMN- $^{13}\text{C}$  ( $\text{CDCl}_3$ ):  $\delta = 52.04$  (d,  $^2J_{\text{CP}} = 4.6$  Hz CH $_3$ -O-P), 79.22 (d,  $^1J_{\text{CP}} = 218.8$  Hz, C4), 149.17 (d,  $^2J_{\text{CP}} = 17.4$  Hz, C3), 107 (C8), 158.09 (d,  $^2J_{\text{CP}} = 12.1$  Hz, C5), 160.0 (C7), 147.6 (C9) 117.53-141.02 (arom-C);  $\text{C}_{26}\text{H}_{23}\text{N}_4\text{PO}_3$ : calculé : C 66.38; H 4.89; N 11.91. trouvé : C 66.27; H 5.01; N 11.76.H 4.48; N 11.38.

**2g**: White powder; Rdt = 84 %; F = 187°C; RMN- $^{31}\text{P}$  ( $\text{CDCl}_3$ ):  $\delta = 15.17$ ; RMN- $^1\text{H}$  ( $\text{CDCl}_3$ ):  $\delta = 1.31$  (t,  $^3J_{\text{HH}} = 7.0$  Hz, 6H, P- O-CH $_2$ -CH $_3$ ), 4.18 (qd,  $^3J_{\text{HP}} = 7.3$  Hz, 4H, P-O-CH $_2$ -CH $_3$ ), 6.58 (s, C=C-H), 9.15 (s, 1H, NH), 6.98-7.75 (m, 15H, arom-H); RMN- $^{13}\text{C}$  ( $\text{CDCl}_3$ ):  $\delta = 16.24$  (d,  $^3J_{\text{CP}} = 6.9$  Hz, P-O-CH $_2$ -CH $_3$ ), 62.41 (d,  $^2J_{\text{CP}} = 4.9$  Hz, P-O-CH $_2$ -CH $_3$ ), 77.35 (d,  $^1J_{\text{CP}} = 218.4$  Hz, C4), 149.78 (d,  $^2J_{\text{CP}} = 18.4$  Hz, C3), 159.17 (d,  $^2J_{\text{CP}} = 12.5$  Hz, C5), 108.65 (C8), 161.12 (C7), 145.27 (C9), 117.4-140.01 (arom-C).  $\text{C}_{28}\text{H}_{27}\text{N}_4\text{PO}_3$ : calculé : C 68.29; H 5.49; N 11.38. trouvé :C 67.79; H 5.24; N 11.22. Nuclear magnetic resonance data from the proton confirm the formation of 4-phosphopyrazolo(1,5-a)pyrimidines. We note on the spectra the disappearance of the signals relating to the protons of the NH $_2$  and N-H motif of the pyrazolic ring and the appearance, on the other hand, of the new signals corresponding to the protons of the methyl and phenyl groups of  $\alpha,\beta$ -diketones. There is also a proton signal of the pyrimidine ring C = C-H between 6.5 and 6.9 ppm. Nuclear magnetic resonance data from the proton confirm the formation of 4-phosphopyrazolo(1,5-a)pyrimidines. We note on the spectra the disappearance of the signals relating to the protons of the NH $_2$  and N-H motif of the pyrazolic ring and the appearance, on the other hand, of the new signals corresponding to the protons of the methyl and phenyl groups of  $\alpha,\beta$ -diketones. There is also a proton signal of the pyrimidine ring C = C-H between 6.5 and 6.9 ppm. In nuclear magnetic resonance of phosphorus, the phosphorus atom in 4-phosphopyrazolo(1,5-a)pyrimidines 2 resonates in the region of chemical displacement between 15.2 and 19.62 ppm (Table 1).

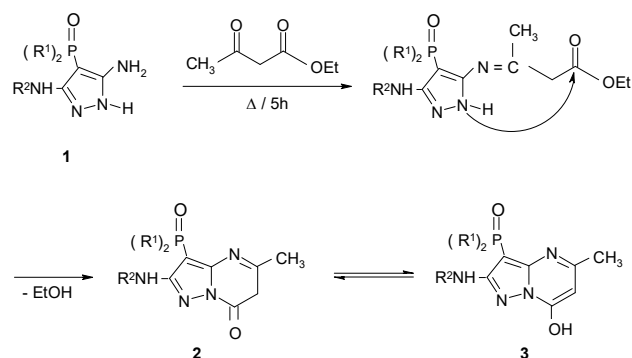
**Tableau 1.  $^{31}\text{P}$  en ppm pour les 4-phosphopyrazolo(1,5-a)pyrimidines 2**

Composé	2a	2b	2c	2d	2e	2f	2g
$\delta^{31}\text{P}$	15.2	5.14	17.61	17.8	19.64	17.75	15.17

Analysis of the data in Table 1 shows that the  $^{31}\text{P}$  core of compounds 2c - f comprising the unit (CH $_3$ O) 2P (O) is significantly more deshielded ( $\delta = 17.61 - 19.64$  ppm) than that of compounds 2a, 2b, 2g comprising the unit (C $_2$ H $_5$ O) 2P

(O) ( $\delta = 15.14 - 15.2$  ppm). Such deshielding can be attributed to the electroattractor effect of the methoxy group (CH $_3$ O) more intense than that of the ethoxy group (C $_2$ H $_5$ O). The NMR spectra of  $^{13}\text{C}$  are consistent with the structure of 4-phosphopyrazolo(1,5-a)pyrimidines. We note, in fact, the signals of the various types of carbon and in particular those corresponding to the pyrimidine ring.

**Synthesis of 4-phospho-9-hydroxypyrazolo(1,5-a)pyrimidines 3**: The same reaction was tested with ethyl acetylacetae. 4-phospho-9-hydroxypyrazolo(1,5-a)pyrimidines 3 were obtained with good yields (Scheme 2). We could not isolate the intermediate resulting from the attack of the ketone carbonyl group by the NH $_2$  motif of 4-phospho-5-aminopyrazole. This intermediate must cycle rapidly as it is formed, by action of the doublet of the amine N-H of the pyrazolic ring on the ester function. The unstable 4-phosphopyrazolo(1,5-a)pyrimidin-9-one 3', tautomeristically driven to 4-phospho-9-hydroxypyrazolo(1,5-a)pyrimidine 3.



Experimental results of products 3. **3a**: Brown powder; Rdt = 68 %; F = 202°C. RMN- $^{31}\text{P}$  ( $\text{CDCl}_3$ ):  $\delta = 15.54$ ; RMN- $^1\text{H}$  ( $\text{CDCl}_3$ ):  $\delta = 3.78$  (d, 6H,  $^3J_{\text{HP}} = 11.8$  Hz, CH $_3$ O-P); 2.36 (s, 3H, CH $_3$ ), 5.79 (s, 1H, OH), 6.55 (s, 1H, C=C-H), 9.5 (s, 1H, NH), 6.95-7.60 (m, 4H, arom-H); RMN- $^{13}\text{C}$  ( $\text{CDCl}_3$ ):  $\delta = 19.54$  (C7-CH $_3$ ), 52.94 (d,  $^2J_{\text{CP}} = 4.8$  Hz, CH $_3$ -O-P), 77.20 (d,  $^1J_{\text{CP}} = 222.7$  Hz, C4), 147.61 (C7), 100.13 (C8), 150.8 (d,  $^2J_{\text{CP}} = 18.8$  Hz, C3), 155.44 (C9), 158.56 (d,  $^2J_{\text{CP}} = 12.0$  Hz, C5), 159.04 (d,  $^1J_{\text{FC}} = 258.04$  Hz, C4'F), 115.48 (d,  $^2J_{\text{FC}} = 22.6$  Hz, C3'F), 118.56 (d,  $^3J_{\text{FC}} = 7.7$  Hz, C2'F), 135.99 (C1'F); RMN- $^{19}\text{F}$  ( $\text{CDCl}_3$ ):  $\delta = 40.45$  (tt,  $^3J_{\text{FH}} = 4.7$  Hz, 1F);  $\text{C}_{15}\text{H}_{16}\text{FN}_4\text{PO}_4$ : calculé: C 49.18; H 4.37; N 15.30. trouvé: C 49.05; H 4.42; N 15.22.

**3b**: White powder; Rdt = 72 %; F = 215 °C; RMN- $^{31}\text{P}$  (DMSO):  $\delta = 19.48$ ; RMN- $^1\text{H}$  (DMSO):  $\delta = 3.50$  (d,  $^3J_{\text{HP}} = 11.8$  Hz, 6H, CH $_3$ O-P), 2.34 (s, CH $_3$ ), 5.70 (s, 1H, OH), 6.7 (s, 1H, C=CH), 8.78 (s, 1H, NH), 6.9-7.88 (m., 5 arom-H); RMN- $^{13}\text{C}$  (DMSO):  $\delta = 51.40$  (d,  $^2J_{\text{CP}} = 4.6$  Hz, P-O-CH $_3$ ), 18.75 (C7-CH $_3$ ), 99.7 (C8), 78.62 (d,  $^1J_{\text{CP}} = 212.5$  Hz, C4), 151.64 (d,  $^2J_{\text{CP}} = 18$  Hz, C3), 152.23 (d,  $^2J_{\text{CP}} = 12.3$  Hz, C5), 149.85 (C7), 154.8 (C9), 116.16-141.5 (Carom); (Carom);  $\text{C}_{15}\text{H}_{17}\text{N}_4\text{PO}_4$ : calculé : C 51.72; H 4.88; N 16.09. trouvé : C 51.52; H 4.80; N 16.01. **3c**: White powder; Rdt = 71 %; F = 240°C; RMN- $^{31}\text{P}$  ( $\text{CDCl}_3$ ):  $\delta = 12.3$ . RMN- $^1\text{H}$  ( $\text{CDCl}_3$ ): 1.37 (t,  $^2J_{\text{HH}} = 7.0$  Hz, 6H, P-O-CH $_2$ -CH $_3$ ), 4.20 (qd,  $^2J_{\text{HH}} = 7.0$  Hz, 4H, P-O-CH $_2$ -CH $_3$ ), 2.36 (s, CH $_3$ ), 6.60 (s, 1H, C=C-H), 9.6 (s, 1H, NH), 5.77 (s, 1H, OH), 6.98-7.64 (m, 5H, arom-H); RMN- $^{13}\text{C}$  ( $\text{CDCl}_3$ ):  $\delta = 16.30$  (d,  $^3J_{\text{CP}} = 6.7$  Hz, P-O-CH $_2$ -CH $_3$ ), 19.50 (C7-CH $_3$ ), 62.73 (d,  $^2J_{\text{CP}} = 4.8$  Hz, P-O-CH $_2$ -CH $_3$ ), 100.03 (C8), 74.3 (d,  $^1J_{\text{CP}} = 223.2$  Hz, C4), 146.7 (d,  $^2J_{\text{CP}} = 20.0$  Hz, C3), 153.82 (d,  $^2J_{\text{CP}} = 11.5$  Hz,

C5), 147.37 (C7), 155.48 (C9), 117.64-139.95 (arom-C);  $C_{17}H_{21}N_4PO_4$ : calculé C 54.25; H 5.58; N 14.89. trouvé C 54.20; H 5.60; N 14.79.

**3d**: Brown power; Rdt = 74% ; F = 235 °C; RMN- $^{31}P$  ( $CDCl_3$ ):  $\delta$  = 13.48; RMN- $^1H$  ( $CDCl_3$ ):  $\delta$  = 1.36 (d,  $^3J_{HP}$  = 6.9 Hz, 6H, P-O-CH<sub>2</sub>-CH<sub>3</sub>), 4.23 (qd,  $^3J_{HH}$  = 6.9 Hz, 4H, P-O-CH<sub>2</sub>-CH<sub>3</sub>), 2.45 (s, CH<sub>3</sub>), 6.58 (s, 1H, C=C-H), 5.85 (s, 1H, OH), 9.78 (s, 1H, NH), 6.84-7.4 (m, 4H, arom-H); RMN- $^{13}C$  ( $CDCl_3$ ):  $\delta$  = 16.15 (d,  $^2J_{CP}$  = 6.8 Hz, P-O-CH<sub>2</sub>-CH<sub>3</sub>), 62.5 (d,  $^2J_{CP}$  = 4.9 Hz, P-O-CH<sub>2</sub>-CH<sub>3</sub>), 19.7 (C7-CH<sub>3</sub>), 74.48 (d,  $^1J_{CP}$  = 222.5 Hz, C4), 101.08 (C8), 147.5 (d,  $^2J_{CP}$  = 18.9 Hz, C3), 152.62 (d,  $^2J_{CP}$  = 11.4 Hz, C5), 148.54.0 (C7), 157(C9), 158.43 (d,  $^1J_{FC}$  = 240.1 Hz, C4'F); 116.6 (d,  $^2J_{FC}$  = 22.7 Hz, C3'F), 118.57 (d,  $3J_{FC}$  = 6.8 Hz, C2'F), 128.34 (C1'F); RMN- $^{19}F$  ( $CDCl_3$ ):  $\delta$  = 40,44 (tt,  $3J_{FH}$  = 4.8 Hz, 1F);  $C_{17}H_{20}FN_4PO_4$ : calculé C 51.77; H 5.07; N 14.21. trouvé : C 51.59; H 4.95; N 14.12. In  $^1H$  NMR, the disappearance of the large singlet relative to the protons of the NH<sub>2</sub> group of the starting pyrrole and the appearance of the new signals attributable to the protons C = C-H and OH resonating respectively around 6.6 ppm and 5.75 ppm allowed us to confirm the obtaining of 4-phospho-9-hydroxypyrazolo (1,5-a) pyrimidines 4b. NMR data from  $^{13}C$ ,  $^{31}P$ , and  $^{19}F$  confirm the purity and structure of the synthesized compounds.

## Conclusion

During this work, we showed that the action of  $\alpha,\beta$ -diketones and  $\alpha,\beta$ -cetoesters on 3,5-phosphopyrazoles provides 4-phosphopyrazolo (1,5-a)pyrimidines 3a and 4-phospho-9-hydroxypyrazolo (1,5-a)pyrimidines 3b. The spectroscopic IR and NMR data ( $^1H$ ,  $^{13}C$ ,  $^{19}F$ ,  $^{31}P$ ) that unambiguously confirmed the structure of these products are consistent with the data in the literature.

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