J. Braz. Chem. Soc., Vol. 16, No. 2, 179-189, 2005.
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0103 - 5053 $6.00+0.00

Article

Synthesis and Tautomeric Studies of Enamines from 1-(*n*-Hexyl)-3-methyl-2-pyrazolin-5-one

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1-(*n*-Hexil)-3-metil-2-pirazolin-5-ona foi acilada com cloretos de acidos e a condensação com aminas primárias forneceu uma série de enaminas. De acordo com os dados de RMN de ^{1}H e ^{13}C, os derivados acilas têm principamente uma estrutura 4-acilpirazol-5-ol com ligação de hidrogênio intramolecular e os derivados 4-aminometilenos existem predominantemente na forma de enamina estabilizada também por este tipo de interação.

1-(*n*-Hexyl)-3-methyl-2-pyrazolin-5-one was acylated with acid chlorides. Condensation of acyl derivatives with primary amines afforded enamines. According to the ^{1}H and ^{13}C NMR data, the acyl derivatives have mainly a 4-acylpyrazol-5-ol structure with intramolecular hydrogen bond, and the 4-aminomethylene derivatives exist predominantly in the enamine form stabilized by the same type of interaction.

Keywords: pyrazolones, alkylpyrazolones, acylation, acylpyrazolones, enamines

Introduction

Transition metals coordination complexes using a variety of polydentate ligands are very important in several fields of science and technology.[1-4] They can give a wide variety of model compounds, to mimic, simulate, or modify biological and physical properties.[5,6] An important number of the ligands that have been reported to date are Schiff bases[7-10] or β-ketoenamines[11,12] that are usually obtained from salicylaldehyde or β-dicarbonyl compounds.[12,13] Other reagents have been almost completely neglected.

4-Aminomethylene derivatives of pyrazolin-5-ones (Figure 2D) have been known for almost a century[14] and have been used as ligands to obtain metal complexes.[15] They are not as well known as metal complexes of acylpyrazolones though.[16] Pyrazolone derivatives usually reported do not have good solubility in solvents such as hexane, ethyl acetate, chloroform, acetone, tetrahydrofurane and ethanol, because in most cases they have a phenyl ring at N-1. In order to find better applications for these kinds of compounds, solubility must be improved. Attaching an alkyl chain at position 1 rather than an aryl ring would help to overcome this drawback. This approach faces the facts that very few alkylhydrazines are commercially available and that there is a lack of convenient procedures[17] to synthesize them. Despite of these problems, alkylation of 3-methyl-[18] and 3-phenyl-[19] pyrazol-5-one has been reported. These 1-alkylpyrazolones underwent acylation,[18] benzoylation[20] and nitrosation[21] in a similar way to their 1-phenyl homologues. Since little information on 4-aminomethylene derivatives of alkylpyrazolones is available, it was decided to study them. In this paper, besides the synthetic procedures, the structural features that have been found on characterizing these compounds are reported. In order to save time and chemicals, attention was focused on changing the acyl group and the amines, leaving the alkyl chain at N-1 unchanged; this procedure does not restrain the conclusions of this work. Therefore, 4-acyl-(1-*n*-hexyl)-3-methyl-5-pyrazolones and bidentate, tridentate and tetradentate 4-aminomethylene derivatives, some of them including a chiral center, are reported herein.

Results and Discussion

The synthesis is outlined in Scheme 1. As previously described,[18] alkylation of 3-methylpyrazol-5-one (**1**) takes place at N-1 to give 1-(*n*-hexyl)-3-methyl-2-pyrazolin-5-

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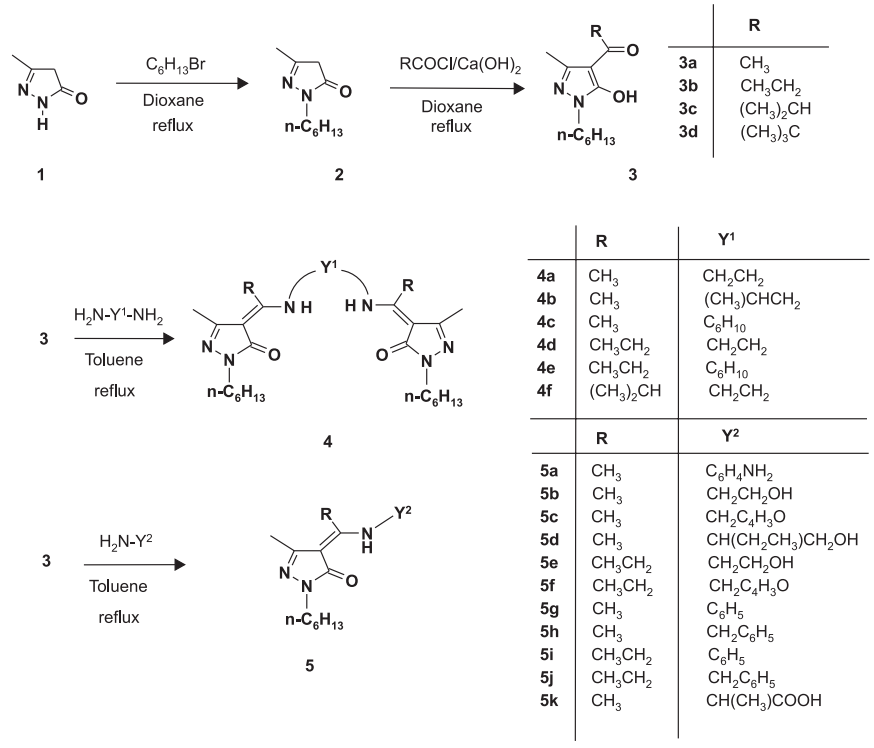


	R
3a	CH_3
3b	CH_3CH_2
3c	$(CH_3)_2CH$
3d	$(CH_3)_3C$

	R	Y^1
4a	CH_3	CH_2CH_2
4b	CH_3	$(CH_3)CHCH_2$
4c	CH_3	C_6H_{10}
4d	CH_3CH_2	CH_2CH_2
4e	CH_3CH_2	C_6H_{10}
4f	$(CH_3)_2CH$	CH_2CH_2

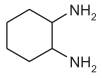
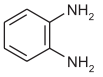
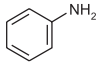
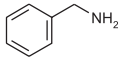
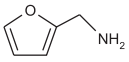
	R	Y^2
5a	CH_3	$C_6H_4NH_2$
5b	CH_3	CH_2CH_2OH
5c	CH_3	$CH_2C_4H_3O$
5d	CH_3	$CH(CH_2CH_3)CH_2OH$
5e	CH_3CH_2	CH_2CH_2OH
5f	CH_3CH_2	$CH_2C_4H_3O$
5g	CH_3	C_6H_5
5h	CH_3	$CH_2C_6H_5$
5i	CH_3CH_2	C_6H_5
5j	CH_3CH_2	$CH_2C_6H_5$
5k	CH_3	$CH(CH_3)COOH$

Scheme 1. Synthesis.

one (**2**). This compound was acylated with acyl halides in alkaline medium[22,23] yielding 4-acyl-1-(*n*-hexyl)-3-methylpyrazol-5-ol (**3**). The yields of 4-acyl derivatives **3** were 70% (**3a**), 68% (**3b**) and 40 % (**3c**). Acylation with pivaloyl chloride afforded 1-(*n*-hexyl)-3-methyl-4-pivaloylpyrazol-5-ol (**3d**) only in a modest 10%, despite of the prolonged reaction time. Compounds **3** were used to prepare 4-aminomethylene derivatives. Thus, condensation with diamines afforded compounds **4**, while condensation with monoamines afforded compounds **5**. Compounds **4** are tetradentate ligands and compounds **5** are either tridentate or bidentate. In addition 1,2-diaminopropane and *trans*-1,2-diaminocyclohexane are chiral. However, they were used as racemic mixtures. Regarding the monoamines, a variety of them was used. Some of them were aliphatic, aromatics, aminoacids or aminoalcohols. Among them DL-alanine and *l*-(-)-2-aminobutanol were chiral. Table 1 summarizes reaction times and yields for 4-aminomethylene compounds **4** and **5**. As it could be expected, in most cases yields were higher with monoamines than with diamines. It was also observed that yields diminished when the NH_2 was bonded to a secondary carbon, for instance **4c** and **4e**. A sharp reduction in the yield of compound **4** resulted as ramification in the acyl group increased, for example **4a**, **4d** and **4f**. No aminomethylene product was isolated from pivaloylpyrazolone (**3d**) under the same conditions. The reaction of compound **3a** with *o*-phenylenediamine afforded compound **5a** resulting from the condensation of just one amino group. The remaining amino group of compound **5a** would become less nucleophilic. Compound **5a** was treated with an extra equivalent of **3a**, being recovered unchanged. With respect to the yields achieved in reactions with monoamines, they were not only a consequence of the nucleophilicity but of the reagents and products solubility in the reacting medium. When DL-alanine was used, the yield of reaction was very low indeed, probably due to the scarce solubility of the aminoacid in the reaction solvent. Compounds **5b** and **5c** separated easily as a solid material from the reacting mixture, being recovered in higher yields. The effect of increasing hindrance was also observed in the yields of compounds **5**.

Prototropic tautomerism has been widely studied in 1-arylpyrazolones and derivatives[24-26] but not in 1-alkyl homologues. Specifically the tautomerism of 1-aryl-4-acylpyrazolones has been the subject of various studies.[27-35] Based upon ^{1}H- and ^{13}C-NMR studies, Kurkovskaya[30] *et al*. concluded that in $CDCl_3$ solution, and at low temperature, 4-acetyl- and 4-benzoyl derivatives are mainly present in the associated OH form (**A'**) (Figure 1) with a minor portion of NH form (**B**). They also found that electronegative groups, at position 3 in the heterocycle, favors the free OH form (**A**).[30] In the case of 4-acyl-(1-*n*-hexyl)-3-methyl-5-pyrazolones (**3**), the possible tautomers are the same as those shown in Figure 1. Relevant ^{1}H-NMR and ^{13}C-NMR chemical shifts of compounds **3a-d** are summarized in Table 2. Data agrees with the existence

Table 1. Synthesis of enamines: reaction time and yields.

Amine	R-CO-C4	Yield (%)	time (h)	Compound
$H_2NCH_2CH_2NH_2$	CH_3CO	70	6	**4a**
	CH_3CH_2CO	50	7	**4d**
	$(CH_3)_2CHO$	15	10	**4f**
$H_2NCH_2CH(CH_3)NH_2$	CH_3CO	60	6	**4b**
	CH_3CO	15	10	**4c**
	CH_3CH_2CO	12	10	**4e**
	CH_3CO	58	10	**5a**
	CH_3CO	77	7	**5g**
	CH_3CH_2CO	60	8	**5i**
	CH_3CO	71	7	**5h**
	CH_3CH_2CO	55	8	**5j**
	CH_3CO	97	8	**5c**
	CH_3CH_2CO	50	8	**5f**
$HOCH_2CH_2NH_2$	CH_3COCH_3	88	6	**5b**
	CH_2CO	85	8	**5e**
$CH_3CH_2CH(NH_2)CH_2OH$	CH_3CO	57	8	**5d**
$CH_3CH(NH_2)COOH$	CH_3CO	25	8	**5k**

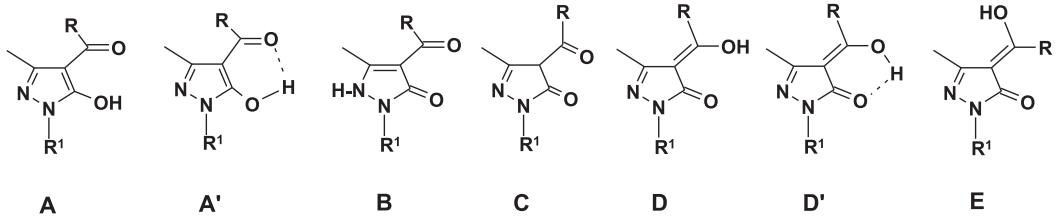
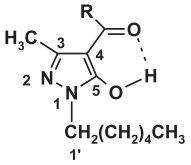


Figure 1. Tautomers of compounds **3**.

Table 2. Selected ^1H and ^{13}C NMR chemical shifts of compounds **3a, 3b, 3c** and **3d**



Compound	R	$\delta(^1H)$			$\delta(^{13}C)$				
		C3-CH_3	CH_2 1'	OH	C1'	C4	C3	C5	C=O
3a	CH_3	2.38	3.87	11.14	45.6	102.8	146.3	159.0	195.0
3b	CH_3CH_2	2.13	3.61	12.01	44.9	101.9	145.7	158.7	197.8
3c	$(CH_3)_2CH$	2.22	3.70	11.53	45.3	100.9	145.4	159.6	201.9
3d	$(CH_3)_3C$	2.32	3.69	12.71	45.1	100.6	144.8	161.1	204.5

of mainly one tautomeric form. ^{13}C signals for the carbonyl carbons (195.0-204.5 ppm),[36] clearly correspond to a ketone structure. These values are very close to those already reported by other authors,[30] showing that the hydroxymethylene form (**D, D', E**) can be excluded.

^{1}H NMR chemical shifts for the hydroxyls (11.14-12.71) and the absence of electronegative groups in the heterocycle rule out the OH free form (**A**).[30] The presence of a CH form (**C**) is not likely because it is known that proton transfer between pyrazole C4 and OH or NH is usually slow.[30,37] This form requires an additional signal set (approximately 4 ppm),[38] that was not observed. Consequently, in $CDCl_3$ solution at 28 ºC, 4-acyl-(1-*n*-hexyl)-3-methyl-5-pyrazolones (**3a-d**) exist mainly as 4-acylpyrazol-5-ols with intramolecular hydrogen bond (**A'**), in agreement with other reports.[30,31,39,40] Additionally, ^{1}H and ^{13}C NMR spectra in acetone-d_6 and DMSO-d_6 were obtained for compounds **3a** and **3c**, observing same pattern as with chloroform solutions.

The information obtained from IR spectroscopy did not provided new evidence to the tautomers structure. However, it is noteworthy that the spectra for neat samples and $CHCl_3$ solutions, for compounds **3**, show a broad absorption band around 3150 cm^{-1}, (OH stretching) and a peak between 1626 and 1619 cm^{-1} (C=O stretching).

Possible tautomers for compounds **4** and **5** are presented in Figure 2. It has been shown that, based upon low temperature NMR spectra,[14] 4-aminomethylene derivatives of 1-aryl-4-acyl-5-pyrazolones exist predominantly as a **D'** structure, that is stabilized by an intramolecular hydrogen bond. Increasing the temperature shifts the equilibrium towards the NH form (**B**).

^{1}H NMR signals at 11.6 ppm for compounds **4** and **5** can be associated with a NH. This chemical shift value rules out the NH (**B**) tautomer, since in this case a chemical shift of 6 ppm should be expected.[14] In some cases a splitting due to a coupling between the NH and the α-CH or the $\alpha\beta$-CH_2 is observed. For compounds **4c, 5d** and **5k** a doublet is observed, whereas a multiplet is observed for compound **4b** (Table 3). Besides, a doublet around 4.6 ppm is observed for the $CH_2\alpha$ to the NH in compounds **5c**, **5f**, **5h** and **5j**, the coupling constant being ^{3}J 6.0-6.1 Hz. A similar value is reported by Braibante *et al.*[41] for 3-amino substituted-5,5-dimethylcyclohexen-2-en-1-ones (**6b**). The behavior of compounds **4** and **5** could be explained if the major tautomer in the solution is an enamine. Further evidence comes from the ^{15}N (INEPT,[42] ^{1}J 95 Hz, $CDCl_3$) spectrum for compound **4b**. Two signals at 247.6 and 261.4 ppm, corresponding to two different NH units, were observed in this spectrum. Therefore, the OH (**A**, **A'**) and CH (**C**) tautomers can be dismissed because they do not have a NH group. Although the splitting for the NH is not well resolved in the other homologues, the same structure should exist because they have the same chemical shifts stated above.

^{13}C spectra for compounds **4** and **5** show four down

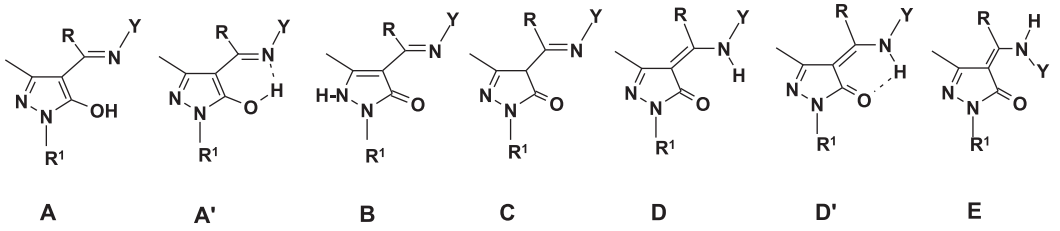
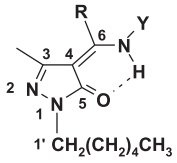


Figure 2. Tautomers of compounds **4** and **5**.

Table 3. Selected ^{1}H and ^{13}C NMR chemical shifts of compounds **4b**, **4c**, **5d** and **5k**



Compound	$\delta(^{1}H)$			$\delta(^{13}C)$				
	C3-CH_3	NH	J_{NH-CH}	C1'	C4	C3	C6	C=O
4b	3.63	11.64	m	43.6	98.5	144.8	164.5	165.3
4c	3.72	11.82	8.9	44.0	99.9	144.7	162.8	166.2
5d	3.71	11.32	8.9	44.0	98.0	145.2	165.2	165.5
5k	3.77	11.57	7.6	44.0	98.7	145.9	164.4	165.4

Table 4. Selected IR values (cm^{-1}) of compounds **4a-4d**, **4f**, **5g** and **5h**

Compound	KBr			$CHCl_3$		
	N-H	C-Hsat.	C=O	N-H	C-Hsat.	C=O
4a	3447	2927, 2859	1623		2933, 2865	1620
4b	3436	2928, 2860	1625	3436	2935, 2865	1619
4c	3365	2927, 2856	1622	3365	2948, 2864	1620
4d	3430	2927, 2861	1619	3407	2936, 2865	1616
4f	3456	2927, 2859	1607		2934, 2866	1608
5g	3400	2921, 2858	1625		2963, 2863	1619
5h	3436	2925, 2859	1624		2963, 2864	1619

field signals, namely 166 (C5), 164 (C1), 145 (C3) and 99 (C4) ppm, supporting the idea of one predominant tautomer. The 166 ppm signal can be associated with an amide, implying that C5 is a C=O and, hence, the tautomer is an enamine.

IR spectra for compounds **4** and **5** in KBr discs show broad absorption bands at 3400 cm^{-1} (N-H stretching[43]) and 1620 cm^{-1} (C=O stretching). Spectra in chloroform were also recorded, without finding any significant difference between the frequencies. Therefore, it follows that the same tautomer exists in the solid and in the solution (Table 4).

In conclusion, compounds **4** and **5** exist largely as an unique tautomer. This tautomer corresponds to the enamine structure stabilized by an intramolecular hydrogen bond (**D'**). This result agrees whit the previous report.[14,20] Other tautomeric forms cannot be excluded, since they might be present at very low concentrations, being undetectable by NMR. Even more, a rapid equilibrium between some tautomers might occur, detecting an average signal instead. Theoretical studies are being carried out to explain the preference towards the aminomethylene tautomer.

Experimental

Chemicals were obtained from Merck, Sigma, Aldrich and J. T. Baker. 1,2-Diaminopropane, *trans*-1,2-diaminocyclohexane and alanine were used as racemic mixtures; an optically pure sample of *l*-(-)-2-aminobutanol was used. Butyryl chloride[44] and 3-methyl-5-pirazolone[45] were prepared as usual. Dioxane was purified and dried with sodium by heating to reflux during 14 hours before use. Compounds were characterized by FTIR (Nicolet Magna 550), ^{13}C, ^{1}H and ^{15}N NMR (Bruker AC 250P; 62.9, 250 and 17.8 MHz, respectively, $SiMe_4$ as internal standard, and CH_3NO_2 for ^{15}N, operating temperature 28ºC). ^{13}C-^{1}H correlation and DEPT spectra were also used to assign the signals. Melting points were obtained on a Kofler microscope and are uncorrected. To complete characterization C, H, N analyses were obtained (Fisons EA 1108). The numbering that was followed for signal assignment is shown in Figure 3.

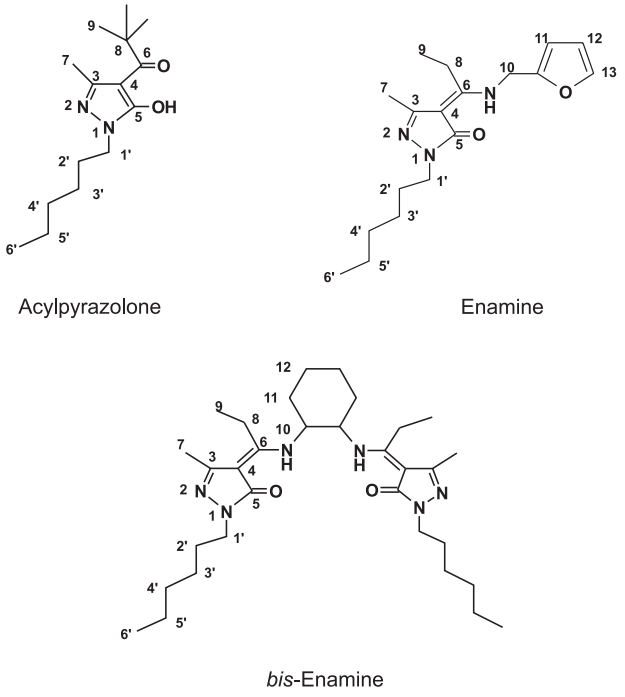


Figure 3. Numbering used for signal assignment.

1-(n-Hexyl)-3-methyl-2-pyrazolin-5-one[18] ***(2)***

To a stirred solution of 3-methylpyrazol-5-one (**1**) (9.80 g, 100.0 mmol) in dioxane (300 mL), *n*-hexylbromide (14 mL, 100.0 mmol) was added and the mixture was heated at reflux for 48 h. The solvent was then evaporated in a rotary evaporator, and water (50 mL) was added. The mixture was neutralized with $NaHCO_3$ and three times extracted with ether. The organic extracts were dried over Na_2SO_4, filtered and concentrated and the remaining material distillated under reduced pressure (115ºC, 0.15 mm Hg) to give **2** as a pale yellow solid (12.74 g, 70%); IR ν_{max}/cm^{-1}: 3400, 2929, 2862, 1554 (neat); IR ν_{max}/cm^{-1} 2938, 2863, 1691 ($CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 0.88 (t, *J* 6.6 Hz, 3H, CH_3 6'), 1.31 (m, 6H, CH_2 3', 4', 5'), 1.60 (m, 2H, CH_2 2'), 2.10 (s, 3H, CH_3),

3.19 (s, 2H, CH_2), 3.61(t, *J* 7.2 Hz, 2H, CH_2); ^{13}C NMR ($CDCl_3$) δ 13.9 (C6'), 16.9 (C6), 22.5, 26.3, 28.3, 31.4 (C5', C4', C2', C3'), 41.7 (C4), 40.0 (C1'), 155.2 (C3), 172.0 (C=O, C5). Anal. Calc. for $C_{10}H_{18}N_2O$: C, 65.89; H, 9.95%. Found: C, 65.84; H, 10.14%.

*Synthesis of compounds **3**. General procedure*

The literature procedure,[18,22,23] with some modifications in the reaction time and work up, was followed. In a two necked round bottomed flask with magnetic stirrer, a reflux condenser and a dropping funnel, compound **2** (16.60 g, 80.0 mmol) was dissolved in dry dioxane (100 mL), and then $Ca(OH)_2$ (11.90 g, 160.0 mmol) was added. Acid chloride (100.0 mmol) was added dropwise to the stirring mixture. The reaction mixture was heated to reflux and then it was cooled to room temperature. The mixture was treated with 2N HCl (200 mL) and stirred until all the solid material was dissolved, and then transferred to a separating funnel. The organic phase was separated, and the aqueous phase was extracted with ether. The organic extracts were collected and washed with brine until neutral pH and then dried over Na_2SO_4. The solution was filtered and concentrated and the remaining material distillated under reduced pressure to give **3** as yellow oil.

*4-Acetyl-1-(n-hexyl)-3-methylpyrazol-5-ol (**3a**)*

The procedure described above was followed. The reflux time was 30 min. (12.54 g, 70% yield), bp 98-99 ºC (0.10 mm Hg); IR ν_{max}/cm^{-1}: 3200, 2930, 2863, 1626 (neat); IR ν_{max}/cm^{-1}: 3201, 2942, 2864, 1623 ($CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.87 (t, *J* 6.7 Hz, 3H, CH_3 6'), 1.30 (m, 6H, CH_2 3', 4', 5'), 1.78 (m, 2H, CH_2 2'), 2.38 (s, 6H, $2CH_3$), 3.87 (t, *J* 7.2 Hz, 2H, CH_2), 11.14 (s, 1H, OH); ^1H NMR (acetone-d_6) δ 0.86 (t, *J* 6.9 Hz, 3H, CH_3 6'), 1.30 (m, 6H, CH_2 3', 4', 5'), 1.77 (m, 2H, CH_2 2'), 2.39 (s, 6H, $2CH_3$), 3.85 (t, *J* 7.0 Hz, 2H, CH_2), 6.8 (s, 1H, OH); ^1H NMR (DMSO-d_6) δ 0.86 (t, *J* 6.8 Hz, 3H, CH_3 6'), 1.26 (m, 6H, CH_2 3', 4', 5'), 1.67 (m, 2H, CH_2 2'), 2.34 (s, 6H, $2CH_3$), 3.76 (t, *J* 7.0 Hz, 2H, CH_2), 6.6 (s, 1H, OH); ^{13}C NMR($CDCl_3$) δ 13.8 (C6'), 15.2 (C7), 22.3, 26.0 (C5', C4'), 27.1 (C8), 28.7, 31.1 (C2', C3'), 45.6 (C1'), 102.8 (C4), 146.3 (C3), 159.0 (C5), 195.0 (C=O C6); ^{13}C NMR(acetone-d_6) δ 13.1 (C6'), 14.1 (C7), 22.0, 25.7 (C5', C4'), 26.4 (C8), 28.7, 30.8 (C2', C3'), 44.8 (C1'), 102.4 (C4), 146.0 (C3), 158.7 (C5), 194.5 (C=O C6); ^{13}C NMR(DMSO-d_6) δ 13.8 (C6'), 14.3 (C7), 21.9, 25.6 (C5', C4'), 28.2 (C-8), 28.4, 30.7 (C2', C3'), 43.8 (C1'), 103.9 (C4), 147.1 (C3), 158.3 (C5), 192.5 (C=O C6). Anal. Calc. for $C_{12}H_{20}N_2O_2$: C, 64.26; H, 8.99%. Found: C, 64.36; H, 9.10%.

*1-(n-Hexyl)-3-methyl-4-propionylpyrazol-5-ol (**3b**)*

The procedure described above was followed. The reflux time was 2 h (12.95 g, 68% yield), bp 120 ºC (0,15 mm Hg); IR ν_{max}/cm^{-1}: 3147, 2930, 2863, 1623 (neat); ^1H NMR ($CDCl_3$) δ 0.6 (t, *J* 6.3 Hz, 3H, CH_3 6'), 0.91 (t, *J* 7.3 Hz, 3H, CH_3), 1.02 (m, 6H, CH_2 3', 4', 5'), 1.52 (m, 2H, CH_2 2'), 2.13 (s, 3H, CH_3), 2.47 (q, *J* 7.3 Hz, 2H, CH_2), 3.61(t, *J* 7.2 Hz, 2H, CH_2), 12.01 (s, 1H, OH); ^{13}C NMR ($CDCl_3$) δ 7.3 (C9), 13.3 (C6'), 14.7 (C7), 21.9, 25.6, 28.3, 30.7 (C5', C4', C2', C3'), 32.5 (C8), 44.9 (C1'), 101.9 (C4), 145.7 (C3), 158.7 (C5), 197.8 (C=O, C6). Anal. Calc. for $C_{13}H_{22}N_2O_2$: C, 65.52; H, 9.30; N, 11.75%. Found: C, 65.86; H, 9.26; N, 11.46%.

*1-(n-Hexyl)-4-isobutyryl-3-methylpyrazol-5-ol (**3c**)*

The procedure described above was followed. The reflux time was 12 h. (8.10 g, 40% yield), bp 122 ºC (0,15 mm Hg); IR ν_{max}/cm^{-1}: 3145, 2931, 2864, 1619 (neat); ^1H NMR ($CDCl_3$) δ 0.68 (t, *J* 6.4 Hz, 3H, CH_3 6'), 1.01 (d, *J* 6.9 Hz, 6H, $2CH_3$), 1.12 (m, 6H, CH_2 3', 4', 5'), 1.60 (m, 2H, CH_2 2'), 2.22 (s, 3H, CH_3), 2.96 (m, 1H, CH), 3.70 (t, *J* 7.1 Hz, 2H, CH_2), 11.53 (s, 1H, OH); ^1H NMR (acetone-d_6) δ 0.87 (t, *J* 6.6 Hz, 3H, CH_3 6'), 1.16 (d, *J* 6.8 Hz, 6H, $2CH_3$), 1.30 (m, 6H, CH_2 3', 4', 5'), 1.75 (m, 2H, CH_2 2'), 2.36 (s, 3H, CH_3), 3.20 (m, 1H, CH), 3.86 (t, *J* 7.0 Hz, 2H, CH_2), 8.80 (s, 1H, OH); ^1H NMR (DMSO-d_6) δ 0.89 (t, *J* 6.6 Hz, 3H, CH_3 6'), 1.05 (d, *J* 6.8 Hz, 6H, $2CH_3$), 1.30 (m, 6H, CH_2 3', 4', 5'), 1.68 (m, 2H, CH_2 2'), 2.34 (s, 3H, CH_3), 3.57 (m, 1H, CH), 3.80 (t, *J* 7.1 Hz, 2H, CH_2), 6.50 (s, 1H, OH); ^{13}C NMR ($CDCl_3$) δ 13.6 (C9), 15.0 (C6'), 18.4 (C7), 22.1, 25.8, 28.5, 30.9 (C5', C4', C2', C3'), 36.1 (C8), 45.3 (C1'), 100.9 (C4), 145.4 (C3), 159.6 (C5), 201.9 (C=O, C6); ^{13}C NMR (acetone-d_6) δ 13.3 (C9), 14.4 (C6'), 18.0 (C7), 22.2, 25.9, 28.9, 31.0 (C5', C4', C2', C3'), 36.1 (C8), 45.0 (C1'), 100.9 (C4), 145.5 (C3), 159.6 (C5), 201.7 (C=O, C6); ^{13}C NMR (DMSO-d_6) δ 13.8 (C9), 14.1 (C6'), 18.5 (C7), 21.9, 25.6, 28.2, 30.7 (C5', C4', C2', C3'), 35.7 (C8), 45.0 (C1'), 102.4 (C4), 147.5 (C3), 159.2 (C5), 199.4 (C=O, C6). Anal. Calc. for $C_{14}H_{24}N_2O_2$: C, 66.63; H, 9.59; N, 11.10%. Found: C, 66.40; H, 9.47; N, 11.30%.

*1-(n-Hexyl)-3-methyl-4-pivaloylpyrazol-5-ol (**3d**)*

The procedure described above was followed. The reflux time was 18 h. (2.13 g, 10% yield), bp 130 ºC (0,15 mm Hg); IR ν_{max}/cm^{-1}: 3156, 2933, 2866, 1605 (neat); ^1H NMR ($CDCl_3$) δ 0.66 (t, *J* 6.4 Hz, 3H, CH_3 6'), 1.11 (m, 6H, CH_2 3', 4', 5'), 1.47 (s, 9H, $3CH_3$), 1.58 (m, 2H, CH_2 2'), 2.32 (s, 3H, CH_3), 3.69 (t, *J* 7.2 Hz, 2H, CH_2), 12.71 (br, s,

1H, OH); ^{13}C NMR ($CDCl_3$) δ 13.6 (C6'), 18.0 (C7), 22.1, 25.9 (C5', C4'), 26.2 (C9), 28.4, 30.9 (C2', C3'), 42.0 (C8), 45.1 (C1'), 100.6 (C4), 144.8 (C3), 161.1 (C5), 204.5 (C=O, C6). Anal. Calc. for $C_{15}H_{26}N_2O_2$: C, 67.63; H, 9.84; N, 10.52%. Found: C, 67.23; H, 9.90; N, 10.60%.

*Synthesis of compounds **4** and **5**. General procedure*

The reaction was carried out using magnetic stirrer in a flask provided with a Dean Stark to separate the water produced during the reaction. Compound **3** and the corresponding amine were dissolved in toluene and heated to reflux. The solution was then washed with brine until neutral pH and then dried over Na_2SO_4. After filtration, the solution was concentrated in a rotary evaporator and the remaining material was crystallized, affording the enamines as crystalline solids.

*N,N'-Bis-{[1-(n-hexyl)-3-methyl-5-oxo-2-pyrazolin-4-ylethyliden]-1-yl}ethylenediamine (**4a**)*

Compound **3a** (20.00 g, 89.3 mmol) and ethylenediamine (3.0 mL, 44.7 mmol) in toluene (30 mL) were used. Reflux time was 6 h. The crude product was crystallized from a hexane-ethyl acetate mixture to give **4a** (14.75 g, 70%), mp 144 ºC; IR ν_{max}/cm^{-1}: 3447, 2927, 2859, 1623 (KBr); IR ν_{max}/cm^{-1}: 2933, 2865, 1620 ($CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 0.87 (t, *J* 6.6 Hz, 6H, $2CH_3$ 6'), 1.30 (m, 12 H, $2CH_2$ 3', $2CH_2$ 4', $2CH_2$ 5'), 1.70 (m, 4H, $2CH_2$ 2'), 2.28, 2.32 (ss, 12 H, $4CH_3$), 3.74 (m, 8H, $4CH_2$), 11.62 (s, 2H, 2N-H); ^{13}C NMR ($CDCl_3$) δ 13.8 (C6'), 15.1, 17.1 (2C7, 2C8), 22.3, 26.3, 28.9, 31.3 (2C5', 2C4', 2C2', 2C3'), 42.7 (2C1'), 43.6 (2C9), 98.9 (2C4), 144.9 (2C3), 164.6 (2C6), 165.4 (2C=O, C5). Anal. Calc. for $C_{26}H_{44}N_6O_2$: C, 66.06; H, 9.38%. Found: C, 66.13; H, 9.35%.

*N,N'-Bis-{[1-(n-hexyl)-3-methyl-5-oxo-2-pyrazolin-4-ylethyliden]-1-yl}-1,2-diaminopro-pane (**4b**)*

Compound **3a** (30.00 g, 134.0 mmol) and 1,2-diaminopropane (5.7 mL, 67.0 mmol) in toluene (70 mL) were used. Reflux time was 6 h. The crude product was crystallized from a hexane-ethyl acetate mixture to give **4b** (19.54 g, 60%), mp 93 ºC; IR ν_{max}/cm^{-1}: 3436, 2928, 2860, 1625 (KBr); IR ν_{max}/cm^{-1}: 3436, 2935, 2865, 1619 ($CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 0.78 (t, *J* 6.3 Hz, 6H, $2CH_3$ 6'), 1.19 (m, 12H, $2CH_2$ 3', $2CH_2$ 4', $2CH_2$ 5'), 1.34 (d, *J* 6.4 Hz, 3H, CH_3), 1.60 (m, 4H, $2CH_2$ 2'), 2.13 (s, 6H, $2CH_3$), 2.16, 2.20 (ss, 6H, 2 CH_3), 3.46 (m, 2H, CH_2), 3.63 (t, *J* 7.1 Hz, 4H, $2CH_2$), 3.95 (m, 1H, CH), 11.64 (m, 2H, 2N-H); ^{13}C NMR ($CDCl_3$) δ 13.8 (2C6'), 15.0, 15.1 (2C8), 17.0 (2C7), 19.0 (C10), 22.3, 26.2, 28.8, 31.2 (8C, 2C5', 2C4', 2C2', 2C3'), 43.6 (2C1'), 48.8, 49.4 (2 C9), 98.5, 98.8 (2C4), 144.8 (2C3), 163.8, 164.5 (2C6), 165.3 (2C=O, C5); ^{15}N NMR ($CDCl_3$) δ 247.6 (HN-CH(CH_3)), 261.4 (HN-CH_2). Anal. Calc. for $C_{27}H_{46}N_6O_2$: C, 66.63; H, 9.53; N, 17.27%. Found: C, 66.40; H, 9.30; N, 17.20%.

*N,N'-Bis-{[1-(n-hexyl)-3-methyl-5-oxo-2-pyrazolin-4-ylethyliden]-1-yl}-trans-1,2-diaminocyclohexane (**4c**)*

Compound **3a** (24.00 g, 107.1 mmol) and *trans*-1,2-diaminocyclohexane (6.6 mL, 53.6 mmol) in toluene (35 mL) were used. Reflux time was 10 h. The crude product was crystallized from a hexane-ethyl acetate mixture to give **4c** (4.23 g, 15%), mp 140 ºC; IR ν_{max}/cm^{-1}: 3365, 2927, 2856, 1622 (KBr); IR ν_{max}/cm^{-1}: 3365, 2948, 2864, 1620 ($CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 0.86 (t, *J* 6.5 Hz, 6H, $2CH_3$ 6'), 1.31 (m, 12H, $2CH_2$ 3', $2CH_2$ 4', $2CH_2$ 5'), 1.59 (m, 4H, $2CH_2$ 11), 1.71 (m, 4H, $2CH_2$ 2'), 1.90 (m, 4H, $2CH_2$ 10), 2.32 (s, 12H, $4CH_3$ 7, 8), 3.72 (t, *J* 7.4 Hz, 4H, $2CH_2$ 1'), 3.94 (m, 2H, 2CH 9), 11.82 (d, *J* 8.9 Hz, 2H, 2N-H); ^{13}C NMR ($CDCl_3$) δ 13.8 (2C6'), 15.4 (2C8), 17.3 (2C7), 21.9 (2C11), 22.5, 26.6, 29.0 (2C5', 2C4', 2C2'), 29.7 (2C10), 31.5 (2C3'), 44.0 (2C1'), 53.7 (2C9), 99.9 (2C4), 144.7 (2C3), 162.8 (2C6), 166.2 (2C=O, C5). Anal. Calc. for $C_{30}H_{50}N_6O_2$: C, 68.40; H, 9.57; N, 15.95%. Found: C, 68.10; H, 9.60; N, 16.10%.

*N,N'-Bis-{[1-(n-hexyl)-3-methyl-5-oxo-2-pyrazolin-4-ylpropyliden]-1-yl}ethylenediamine (**4d**)*

Compound **3b** (8.00 g, 33.6 mmol) and ethylenediamine (1.1 mL, 16.8 mmol) in toluene (20 mL) were used. Reflux time was 7 h. The crude product was crystallized from a hexane-ethyl acetate mixture to give **4d** (4.20 g, 50%), mp 95-96 ºC; IR ν_{max}/cm^{-1}: 3430, 2927, 2861, 1619 (KBr); IR ν_{max}/cm^{-1}: 3407, 2936, 2865, 1616 ($CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 0.87 (t, *J* 6.6 Hz, 6H, $2CH_3$ 6'), 1.31 (m, 18H, $2CH_2$ 3', $2CH_2$ 4', $2CH_2$ 5', $2CH_3$), 1.71 (m, 4H, $2CH_2$ 2'), 2.31 (s, 6H, $2CH_3$), 2.68 (q, *J* 7.7 Hz, 4H, $2CH_2$), 3.74 (m, 8H, $4CH_2$), 11.60 (s, 2H, 2N-H); ^{13}C NMR ($CDCl_3$) δ 12.6 (2C9), 13.9 (2C6'), 16.6 (2C7), 21.7 (2C5'), 22.4 (2C8), 26.4, 29.0, 31.4 (2C4', 2C2', 2C3'), 42.4 (2C1'), 43.9 (2C10), 97.8 (2C4), 144.6 (2C3), 166.0 (2C6), 169.7 (2C=O, C5). Anal. Calc. for $C_{28}H_{48}N_6O_2$: C, 67.16; H, 9.66; N, 16.78%. Found; C, 66.76; H, 9.70; N, 16.80%.

*N,N'-Bis-{[1-(n-hexyl)-3-methyl-5-oxo-2-pyrazolin-4-ylpropyliden]-1-yl}-trans-1,2-diaminocyclohexane (**4e**)*

Compound **3b** (10.00 g, 42.0 mmol) and *trans*-1,2-diaminocyclohexane (2.6 mL, 21.0 mmol) in toluene (35

mL) were used. Reflux time was 10 h. The crude product was crystallized from a hexane-ethyl acetate mixture to give **4e** (1.40 g, 12%), mp 200 ºC; IR ν_{max}/cm^{-1}: 3419, 2933, 2860, 1620 (KBr); ^{1}H NMR (DMSO-d$_6$) δ 0.94 (t, *J* 6.3 Hz, 6H, 2CH$_3$ 6'), 1.27 (t, *J* 7.6 Hz, 6H, 2CH$_3$ 9), 1.34 (m, 12H, 2CH$_2$ 3', 2CH$_2$ 4', 2CH$_2$ 5'), 1.66 (m, 4H, 2CH$_2$ 2'), 1.79 (m, 4H, 2CH$_2$ 12), 2.00, 2.15 (mm, 4H, 2CH$_2$ 11), 2.30 (s, 6H, 2CH$_3$ 7), 2.75, 3.05 (mm, 4H, 2CH$_2$ 8), 3.67 (t, *J* 7.0 Hz, 4H, 2CH$_2$ 1'), 3.95 (m, 2H, 2CH 10), 11.47 (d, *J* 10.0 Hz, 2H, 2N-H); ^{13}C NMR (DMSO-d$_6$) δ 13.0 (2C9), 13.8 (2C6'), 16.4 (2C7), 21.6 (2C8), 22.0 (2C5'), 23.5 (2C12), 25.9, 28.5 (2C4', 2C2'), 30.9 (2C3'), 32.6 (2C11), 42.7 (2C1'), 53.1 (2C10), 96.8 (2C4), 143.7 (2C3), 165.6 (2C6), 169.9 (2C=O, C5). Anal. Calc. for $C_{32}H_{54}N_6O_2$: C, 69.28; H, 9.81; N, 15.15%. Found: C, 68.90; H, 9.90; N, 15.20%.

*N,N'-Bis-{[1-(n-hexyl)-3-methyl-5-oxo-2-pyrazolin-4-ylisobutyryliden]-1-yl}ethylenediamine (**4f**)*

Compound **3c** (5.00 g, 19.8 mmol) and ethylenediamine (0.7 mL, 10.0 mmol) in toluene (20 mL) were used. Reflux time was 10 h. The crude product was crystallized from a hexane-ethyl acetate mixture to give **4f** (0.78 g, 15%), mp 128 ºC; IR ν_{max}/cm^{-1}: 3456, 2927, 2859, 1607 (KBr); IR ν_{max}/cm^{-1}: 2934, 2866, 1608 ($CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 0.85 (t, *J* 6.7 Hz, 6H, 2CH$_3$ 6'), 1.30 (m, 12H, 2CH$_2$ 3', 2CH$_2$ 4', 2CH$_2$ 5'), 1.40 (d, *J* 7.4 Hz, 12H, 4CH$_3$), 1.70 (m, 4H, 2CH$_2$ 2'), 2.31 (s, 6H, 2CH$_3$), 3.51 (septet, *J* 7.4 Hz, 2H, 2CH), 3.74 (t, *J* 7.4 Hz, 4H, 2CH$_2$), 3.85 (m, 4H, 2CH$_2$), 11.95 (s, 2H, 2N-H); ^{13}C NMR ($CDCl_3$) δ 14.0 (2C6'), 17.8 (2C7), 19.2 (4C9), 22.5, 26.5, 29.0 (2C5', 2C4', 2C2'), 29.7 (C8), 31.5 (2C3'), 44.0 (2C1'), 44.7 (2C10), 98.0 (2C4), 144.3 (2C3), 166.1 (2C6), 172.6 (2C=O, C5). Anal. Calc. for $C_{30}H_{52}N_6O_2$: C, 68.14; H, 9.91; N, 15.89%. Found: C, 67.90; H, 9.90; N, 15.90%.

*4-[1-(2-Aminophenyl)aminoethylidene]-1-(n-hexyl)-3-methyl-2-pyrazolin-5-one (**5a**)*

Compound **3a** (10.00 g, 44.6 mmol) and *o*-phenylenediamine (2.40 g, 22.3 mmol) in toluene (40 mL) were used. Reflux time was 10 h. The crude product was crystallized from hexane to give **5a** (4.06 g, 58%), mp 115 ºC; IR ν_{max}/cm^{-1}: 3417, 3326, 3218, 3068, 3033, 2925, 2858, 1625 (KBr); ^{1}H NMR ($CDCl_3$) δ 0.81 (t, *J* 6.8 Hz, 3H, CH$_3$ 6'), 1.26 (m, 6H, CH$_2$ 3', 4', 5'), 1.69 (m, 2H, CH$_2$ 2'), 2.19 (s, 3H, CH$_3$), 2.28 (s, 3H, CH$_3$), 3.73 (t, *J* 7.3 Hz, 2H, CH$_2$), 3,92 (s, 2H, NH$_2$), 6.72-7.08 (m, 4H, C$_6$H$_4$), 12.45 (s, 1H, N-H); ^{13}C NMR ($CDCl_3$) δ 13.9 (C6'), 16.2 (C8), 17.2 (C7), 22.4, 26.4, 29.0, 31.4 (C5', C4', C2', C3'), 43.8 (C1'), 99.7 (C4), 116.0, 118.2, 122.1, 127.5, 128.9 (2C10, 2C11, C12, phenyl ring), 142.6 (C9), 145.4 (C3), 164.8 (C6), 165.8 (C=O, C5). Anal. Calc. for $C_{18}H_{26}N_4O$: C, 68.76; H, 8.33; N, 17.82%. Found: C, 68.50; H, 8.40; N, 17.80%.

*1-(n-Hexyl)-4-[1-(2-hydroxyethyl)aminoethylidene]-3-methyl-2-pyrazolin-5-one (**5b**)*

Compound **3a** (1.30 g, 5.8 mmol) and ethanolamine (0.4 mL, 5.8 mmol) in toluene (10 mL) were used. Reflux time was 6 h. The crude product was crystallized from a hexane-ethyl acetate mixture to give **5b** (1.36 g, 88%), mp 94 ºC; IR ν_{max}/cm^{-1}: 3425, 3205, 2926, 2861, 1620 (KBr); ^{1}H NMR ($CDCl_3$) δ 0.83 (t, *J* 6.3 Hz, 3H, CH$_3$ 6'), 1.26 (m, 6H, CH$_2$ 3', 4', 5'), 1.66 (m, 2H, CH$_2$ 2'), 2.25 (s, 3H, CH$_3$), 2.30 (s, 3H, CH$_3$), 3.53 (t, *J* 5.0 Hz, 2H, CH$_2$), 3.70 (t, *J* 7.3 Hz, 2H, CH$_2$), 3.82 (t, *J* 5.0 Hz, 2H, CH$_2$), 4.80 (s, 1H, O-H), 11.36 (s, 1H, N-H); ^{13}C NMR ($CDCl_3$) δ 14.0 (C6'), 15.7 (C8), 17.3 (C7), 22.5, 26.5, 29.1, 31.5 (C5', C4', C2', C3'), 43.9 (C1'), 45.6 (C9), 60.6 (C10), 98.2 (C4), 145.3 (C3), 165.2 (C6), 165.7 (C=O, C5). Anal. Calc. for $C_{14}H_{25}N_3O_2$: C, 62.89; H, 9.42; N, 15.72%. Found: C, 62.49; H, 9.45; N, 15.32%.

*4-[1-(2-Furfuryl)aminoethylidene]-1-(n-hexyl)-3-methyl-2-pyrazolin-5-one (**5c**)*

Compound **3a** (1.00 g, 4.5 mmol) and furfurylamine (0.4 mL, 4.5 mmol) in toluene (10 mL) were used. Reflux time was 8 h. The crude product was crystallized from hexane to give **5c** (1.32 g, 97%), mp 113 ºC; IR ν_{max}/cm^{-1}: 3400, 3101, 2937, 2860, 1625 (KBr); ^{1}H NMR ($CDCl_3$) δ 0.84 (t, *J* 6.5 Hz, 3H, CH$_3$ 6'), 1.28 (m, 6H, CH$_2$ 3', 4', 5'), 1.69 (m, 2H, CH$_2$ 2'), 2.31 (s, 3H, CH$_3$ 7), 2.41 (s, 3H, CH$_3$ 8), 3.73 (t, *J* 7.4 Hz, 2H, CH$_2$ 1'), 4.56 (d, *J* 6.0 Hz, 2H, CH$_2$ 9), 6.32 (m, 2H, C$_4$H$_3$O 11, 12), 7.37 (m, 1H, C$_4$H$_3$O 13), 11.68 (s, 1H, N-H); ^{13}C NMR ($CDCl_3$) δ 13.9 (C6'), 15.3 (C8), 17.3 (C7), 22.4, 26.4, 29.0, 31.4 (C5', C4', C2', C3'), 40.0 (C9), 43.7 (C1'), 98.8 (C4), 108.1, 110.4, 142.8, 144.9 (C10, C11, C12 y C13, furan ring), 149.2 (C3), 164.2 (C6), 165.5 (C=O, C5). Anal. Calc. for $C_{17}H_{25}N_3O_2$: C, 67.30; H, 8.30; N, 13.85%. Found: C, 66.90; H, 8.40; N, 13.90%.

*1-(n-Hexyl)-4-[1-(1-hydroxymethylpropyl) aminoethylidene]-3-methyl-2-pyrazolin-5-one (**5d**)*

Compound **3a** (1.00 g, 4.0 mmol) and *l*-(-)-2-aminobutan-1-ol (0.4 mL, 4.5 mmol) in toluene (10 mL) were used. Reflux time was 8 h. The crude product was crystallized from a hexane-ethyl acetate mixture to give **5d** (0.67 g, 57%), mp 104 ºC; IR ν_{max}/cm^{-1}: 3418, 3226, 2926, 2861, 1618 (KBr); ^{1}H NMR ($CDCl_3$) δ 0.83 (t, *J* 6.5 Hz, 3H, CH$_3$ 6'), 0.95 (t, *J* 7.4 Hz, 3H, CH$_3$), 1.26 (m, 6H, CH$_2$ 3', 4',

5'), 1.53 (m, 2H, CH_2), 1.60 (m, 2H, CH_2 2'), 2.25 (s, 3H, CH_3), 2.33 (s, 3H, CH_3), 3.71 (m, 5H, $2CH_2$, CH), 4.51 (s, 1H, O-H), 11.32 (d, *J* 8.9 Hz, 1H, N-H); ^{13}C NMR ($CDCl_3$) δ 10.4 (C12), 14.0 (C6'), 16.0 (C7), 17.4 (C8), 22.5 (C5'), 24.8 (C11), 26.5, 29.2, 31.5 (C4', C2', C3'), 44.0 (C1'), 57.5 (C9), 65.0 (C10), 98.0 (C4), 145.2 (C3), 165.2 (C6), 165.5 (C=O, C5). Anal. Calc. for $C_{16}H_{29}N_3O_2$: C, 65.05; H, 9.89; N, 14.22%. Found: C, 65.30; H, 9.90; N, 14.30%.

*1-(n-Hexyl)-4-[1-(2-hydroxyethyl)aminopropylidene]-3-methyl-2-pyrazolin-5-one (**5e**)*

Compound **3b** (1.50 g, 6.3 mmol) and ethanolamine (0.4 mL, 6.3 mmol) in toluene (10 mL) were used. Reflux time was 8 h. The crude product was crystallized from a hexane-ethyl acetate mixture to give **5e** (1.50 g, 85%), mp 89 ºC; IR ν_{max}/cm^{-1}: 3269, 2932, 2860, 1620 (KBr); ^{1}H NMR ($CDCl_3$) δ 0.82 (m, 3H, CH_3 6'), 1.22 (m, 9H, CH_2 3', 4', 5' and CH_3), 1.66 (m, 2H, CH_2 2'), 2.26 (s, 3H, CH_3), 2.65 (q, *J* 7.6 Hz, 2H, CH_2), 3.53 (m, 2H, CH_2), 3.69 (t, *J* 7.3 Hz, 2H, CH_2), 3.82 (m, 2H, CH_2), 4.83 (s, 1H, O-H), 11.35 (s, 1H, N-H); ^{13}C NMR ($CDCl_3$) δ 10.8 (C9), 12.6 (C6'), 15.2 (C7), 20.5 (C8), 21.1, 25.1, 27.7, 30.1 (C5', C4', C2', C3'), 42.6 (C1'), 43.7 (C10), 59.2 (C11), 95.6 (C4), 143.3 (C3), 164.3 (C6), 169.0 (C=O, C5). Anal. Calc. for $C_{15}H_{27}N_3O_2$: C, 64.03; H, 9.67; N, 14.93%. Found: C, 63.70; H, 9.70; N, 14.95%.

*4-[1-(2-Furfuryl)aminopropylidene]-1-(n-hexyl)-3-methyl-2-pyrazolin-5-one (**5f**)*

Compound **3b** (1.50 g, 6.3 mmol) and furfurylamine (0.6 mL, 6.3 mmol) in toluene (10 mL) were used. Reflux time was 8 h. The crude product was crystallized from heptane to give **5f** (1.00 g, 50%), mp 60 ºC; IR ν_{max}/cm^{-1}: 3434, 3121, 2930, 2863, 1618 (KBr); ^{1}H NMR ($CDCl_3$) δ 0.85 (t, *J* 6.7 Hz, 3H, CH_3 6'), 1.30 (m, 9H, CH_2 3', 4', 5' and CH_3 9), 1.70 (m, 2H, CH_2 2'), 2.32 (s, 3H, CH_3 7), 2.76 (q, *J* 7.7 Hz, 2H, CH_2 8), 3.74 (t, *J* 7.4 Hz, 2H, CH_2 1'), 4.58 (d, *J* 6.1 Hz, 2H, CH_2 10), 6.32 (m, 2H, C_4H_3O 12, 13), 7.38 (m, 1H, C_4H_3O 14), 11.67 (s, 1H, N-H); ^{13}C NMR ($CDCl_3$) δ 12.6 (C9), 14.0 (C6'), 16.8 (C7), 21.8 (C8), 22.5, 26.5, 29.1, 31.5 (C5', C4', C2', C3'), 39.7 (C10), 43.9 (C1'), 97.6 (C4), 108.2, 110.6, 142.9, 144.5 (C11, C12, C13, C14, furan ring), 149.2 (C3), 166.1 (C6), 169.2 (C=O, C5). Anal. Calc. for $C_{18}H_{27}N_3O_2$: C, 68.11; H, 8.57; N, 13.24%. Found: C, 68.00; H, 8.60; N, 13.30%.

*1-(n-Hexyl)-3-methyl-4-[1-phenylaminoethylidene]-2-pyrazolin-5-one (**5g**)*

Compound **3a** (10.00 g, 44.6 mmol) and aniline (4.1 mL, 44.6 mmol) in toluene (20 mL) were used. Reflux time was 7 h. The crude product was crystallized from heptane to give **5g** (10.27 g, 77%), mp 59 ºC; IR ν_{max}/cm^{-1}: 3400, 3056, 2921, 2858, 1625 (KBr); IR ν_{max}/cm^{-1}: 2963, 2863, 1619 ($CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 0.90 (t, *J* 6.7 Hz, 3H, CH_3 6'), 1.34 (m, 6H, CH_2 3', 4', 5'), 1.77 (m, 2H, CH_2 2'), 2.38 (s, 6H, $2CH_3$), 3.82 (t, *J* 7.3 Hz, 2H, CH_2), 7.19, 7.33, 7.47 (m, 5H, Ph-H), 13.07 (s, 1H, N-H); ^{13}C NMR ($CDCl_3$) δ 14.0 (C6'), 16.8, 17.4; (C7, C8), 22.5, 26.5, 29.1, 31.5 (C5', C4', C2', C3'), 43.9 (C1'), 99.8 (C4), 125.5, 127.2, 129.4, 136.9 (phenyl ring), 145.4 (C3), 162.4 (C6), 165.6 (C=O, C5). Anal. Calc. for $C_{18}H_{25}N_3O$: C, 72.21; H, 8.42; N, 14.03%. Found: C, 72.00; H, 8.50; N, 14.00%.

*4-[1-Benzylaminoethylidene]-1-(n-hexyl)-3-methyl-2-pyrazolin-5-one (**5h**)*

Compound **3a** (11.00 g, 49.1 mmol) and benzylamine (5.4 mL, 49.1 mmol) in toluene (20 mL) were used. Reflux time was 7 h. The crude was crystallized from heptane to give **5h** (10.91 g**,** 71%), mp 81ºC; IR ν_{max}/cm^{-1}: 3436, 3033, 2925, 2859, 1624 (KBr); IR ν_{max}/cm^{-1}: 3050, 2963, 2864, 1619 ($CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 0.84 (t, *J* 6.7 Hz, 3H, CH_3 6'), 1.29 (m, 6H, CH_2 3', 4', 5'), 1.70 (m, 2H, CH_2 2'), 2.31 (s, 6H, $2CH_3$ 7, 8), 3.74 (t, *J* 7.4 Hz, 2H, CH_2 1'), 4.59 (d, *J* 6,0 Hz, 2H, CH_2 9), 7.33 (m, 5H, Ph-H 11, 12, 13), 11.80 (s, 1H, N-H); ^{13}C NMR ($CDCl_3$) δ 14.0 (C6'), 15.5, 17.4; (C7, C8), 22.5, 26.5, 29.1, 31.5 (C5', C4', C2', C3'), 43.8 (C1'), 46.9 (C9), 98.7 (C4), 126.9, 127.9, 129.0, 136.1 (phenyl ring), 144.9 (C3), 164.6 (C6), 165.6 (C=O, C5). Anal. Calc. for $C_{19}H_{27}N_3O$: C, 72.81; H, 8.68; N, 13.41%. Found: C, 72.70; H, 8.70; N, 13.10%.

*1-(n-Hexyl)-3-methyl-4-[1-phenylaminopropylidene]-2-pyrazolin-5-one (**5i**)*

Compound **3b** (1.00 g, 4.2 mmol) and aniline (0.4 mL, 4.2 mmol) in toluene (10 mL) were used. Reflux time was 8 h. The crude product was crystallized from heptane to give **5i** (0.79 g, 60%), mp 94 ºC; IR ν_{max}/cm^{-1}: 3449, 3041, 2923, 2858, 1622 (KBr); ^{1}H NMR ($CDCl_3$) δ 0.90 (t, *J* 6.3 Hz, 3H, CH_3 6'), 1.20 (m, 3H, CH_3), 1.35 (m, 6H, CH_2 3', 4', 5'), 1.75 (m, 2H, CH_2 2'), 2.38 (s, 3H, CH_3), 2.70 (q, *J* 7.6 Hz, 2H, CH_2), 3.82 (t, *J* 7.3 Hz, 2H, CH_2), 7.29, 7.38, 7.47 (m, 5H, Ph-H), 13.01 (s, 1H, N-H); ^{13}C NMR ($CDCl_3$) δ 13.4 (C9), 14.0 (C6'), 16.8 (C7), 22.0 (C8), 22.5, 26.5, 29.1, 31.5 (C5', C4', C2', C3'), 43.9 (C1'), 98.2 (C4), 126.1, 127.5, 129.5, 136.9 (phenyl ring), 144.8 (C3), 166.0 (C6), 168.6 (C=O, C5). Anal. Calc. for $C_{19}H_{27}N_3O$: C, 72.81; H, 8.68; N, 13.41%. Found: C, 72.70; H, 8.70; N, 13.50%.

*4-[1-Benzylaminopropylidene]-1-(n-hexyl)-3-methyl-2-pyrazolin-5-one (**5j**)*

Compound **3b** (1.00 g, 4.2 mmol) and benzylamine (0.5 mL, 4.2 mmol) in toluene (10 mL) were used. Reflux time was 8 h. The crude product was crystallized from heptane to give **5j** (0.76 g, 55%), mp 71 ºC; IR ν_{max}/cm^{-1}: 3438, 3026, 2929, 2860, 1611 (KBr); ^{1}H NMR ($CDCl_3$) δ 0.88 (t, *J* 6.6 Hz, 3H, CH_3 6'), 1.29 (m, 9H, CH_2 3', 4', 5' and CH_3 9), 1.74 (m, 2H, CH_2 2'), 2.35 (s, 3H, CH_3 7), 3.72 (q, *J* 7.7 Hz, 2H, CH_2 8), 3.77 (t, *J* 7.4 Hz, 2H, CH_2 1'), 4.64 (d, *J* 6.1 Hz, 2H, CH_2 10), 7.35 (m, 5H, Ph-H), 11.82 (s, 1H, N-H); ^{13}C NMR ($CDCl_3$) δ 12.5 (C9), 14.0 (C6'), 16.7 (C7), 21.9 (C8), 22.5, 26.5, 29.1, 31.5 (C5', C4', C2', C3'), 43.9 (C1'), 46.5 (C10), 97.5 (C4), 126.9, 128.0, 129.0, 136.2 (phenyl ring), 144.4 (C3), 166.1 (C6), 169.4 (C5, C=O). Anal. Calc. for $C_{20}H_{29}N_3O$: C, 73.36; H, 8.93; N, 12.83%. Found: C, 73.20; H, 8.90; N, 12.80%.

*4-[1-(1-Carboxyethyl)aminoethylidene]-1-(n-hexyl)-3-methyl-2-pyrazolin-5-one (**5k**)*

The same procedure was followed but the amino acid was added as a solution containing NaOH (0.60 g, 14.7 mmol) and water (15 mL). Compound **3a** (3.30 g, 14.7 mmol) and DL-alanine (1.30 g, 14.7 mmol) in toluene (50 mL) were used. Reflux time was 8 h. The reacting mixture was treated with 3M HCl (10 mL) and CH_2Cl_2 (20 mL). The aqueous phase was regulated to pH 4 with 5% aqueous $NaHCO_3$. The crude was crystallized from a heptane-ethyl acetate mixture to give **5k** (1.08 g, 25%), mp 137 ºC; IR ν_{max}/cm^{-1}: 3437, 2931, 2861, 1717, 1618 (KBr); ^{1}H NMR ($CDCl_3$) δ 0.83 (t, *J* 6.1 Hz, 3H, CH_3 6'), 1.25 (m, 6H, CH_2 3', 4', 5'), 1.60 (d, *J* 7.0 Hz, 3H, CH_3), 1.66 (m, 2H, CH_2 2'), 2.30 (s, 3H, CH_3), 2.34 (s, 3H, CH_3), 3.77 (t, *J* 7.2 Hz, 2H, CH_2), 4.36 (m, 1H, CH), 11.22 (s, 1H, O-H), 11.57 (d, *J* 7.6 Hz, 1H, N-H); ^{13}C NMR ($CDCl_3$) δ 14.0 (C6'), 15.9 (C7), 17.0 (C8), 18.7 (C11), 22.5, 26.4, 29.0, 31.4 (C5', C4', C2', C3'), 44.0 (C1'), 52.0 (C9), 98.7 (C4), 145.9 (C3), 164.4 (C6), 165.4 (C=O, C5), 172.0 (COOH, C10). Anal. Calc. for $C_{15}H_{25}N_3O_3$: C, 60.99; H, 8.53; N, 16.25%. Found: C, 60.70; H, 8.60; N, 15.85%.

Acknowledgements

This research was supported by Universidad de Concepción through a grant from Dirección de Investigación (PDI 203.023.032-1.0). The graduate scholarship for Mr. Fredy R. Pérez was provided by the MECESUP Program of the Chilean Government.

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Received: November 13, 2003
Published on the web: February 23, 2005