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Synthesis of some derivatives 4, 5-Di-Methyl $^{4}\Delta$ N-aryl Oxazoline-2-thione

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The 1,3-oxazoline-2-thiones are very important heterocyclic compounds in organic synthesis, in particular, the derivatives N-aryl oxazolines that presents an isomerism atropic around the C-N link between the carbon sp^2 of the aryl and nitrogen atom of the heterocyclic part. We obtained several derivatives of 4, 5-Di-Methyl $^{4}\Delta$ N-aryl oxazoline-2-thione by condensation followed by cyclization between isothiocyanate and acetoine.

Keyword: Atropoisomerie, Oxzoline, Stereo Electronic Parameters, Dihedral Angle.

1. Introduction

The cycle of oxazole is presented weakly in the natural products, the interest of the research on the derivatives oxazolines started in the fiveties, when to this time one believed that the penicillin is an oxazole derivative[1,2]. Different derivative oxazolines is used in the industry: as the 2,5-diaryl oxazolidine, used like solution in the liquid scintilators in the optic applications[3].

The formation of the cycle oxazole is generally analogous has the one of cycle furane but the more used method is the one of Rombinson-Gabriel, that is a cyclo - dehydration of the α-acylaminocétones[4,5]. The different developments of research in this axis especially moved in the changes of the varieties of the reaction Rombinson-

2. Materials and methods

2.1 General Procedures

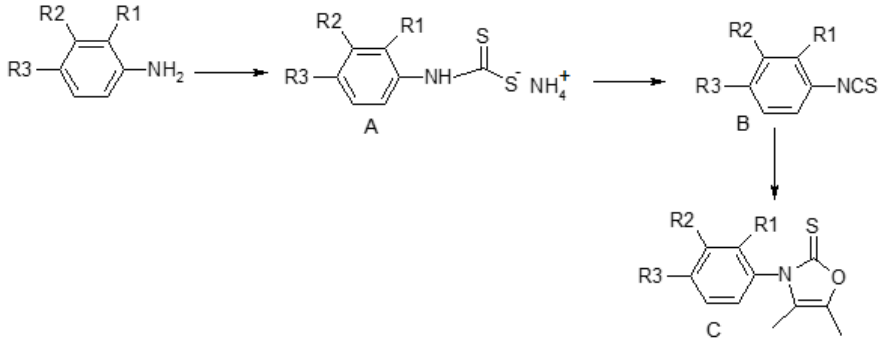
The IR spectra (*υmax*) were determined on a AVATAR 320 FT-IR spectrophotometer. The 1 D and 2 D NMR spectra were obtained on a Bruker Avance DRX 300 FT spectrophotometer operating at 300 MHz for ^{1}H NMR, and 125 MHz for ^{13}C NMR. For the ^{13}C NMR spectra. The LC system consisted of a liquid chromatography (Si-gel : 230-400 mesh (MerK) were used for column chromatography) operating at room temperature.

2.2 Preparation of ammonium N-aryl di-thiocarbamate (a):

The aromatic amine reacts with the carbone bisulfide in basic medium (ammoniac) under low temperature to give the ammonium N-aryl di-thiocarbamate as crystals or oil with a good yield[11-13].

2.3 Preparation of the aryl isothiocyanate (b):

The reaction of N-aryle ammonium dithiocarbamate with the lead nitrate under mechanical agitation give a brown color dough containing in its finally composition ; the lead sulfide, ammonium nitrate, nitric acid and aryle isothiocyanate, this last is isolated by a steam distillation[14,15].



R_1 = H	Me	OMe	OEt	H
R_2 = H	H	H	H	Cl
R_3 = H	H	H	H	H

Fig 1: Total synthesis of 4, 5-Di-Methyl $^4\Delta$ N-aryle oxzoline-2-thiones derivatives (a): CS_2, NH_4OH (b): $Pb(NO_3)_2$ c: acetoin)

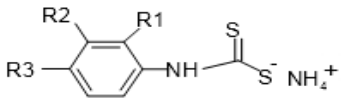
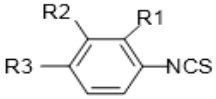
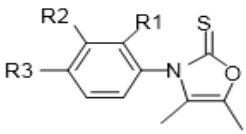
2.4 Synthesis of oxazoline Derivatives (c):

One carries to the ebb a mixture of 5 mM of N-aryl isothiocyanate and 4.5 mM of acetoine in 10 mL of pyridin during 16 hours. After the evaporation of the solvent the residual is carried to the ebb during 2 hours to do a reaction of dehydration in presence of diluted hydrochloric acid (HCl) as catalyst in the ethanol, the final products purified by liquid chromatography[16].

3. Results and Discussions

The electronic specters of the compounds 4, 5-Di-Methyl $^4\Delta$ N-aryl Oxazoline-2-thiones present three absorption bands: a very intense band assigned to the transition electronic π-π* of the grouping aryle that appears for all the compounds oxazolines toward 214-223 nm, a characteristic band of heterocycle corresponds to the transition electronic π-π* toward 232-235 nm and a band of average intensity that appear toward 268-277 nm is assigned to a state excited of the function thione (C=S)[17].

Table 1: structures of all prepared and synthesized derivatives (a: N-aryle dithiocarbamate, b: N-aryle isocyanate, c: N-aryle oxazolinethione-2)

structure	N	R1	R2	R3
	1a	H	H	H
	2a	Me	H	H
	3a	OMe	H	H
	4a	OEt	H	H
	5a	H	Cl	H
	1b	H	H	H
	2b	Me	H	H
	3b	OMe	H	H
	4b	OEt	H	H
	5b	H	Cl	H
	1c	H	H	H
	2c	Me	H	H
	3c	OMe	H	H
	4c	OEt	H	H
	5c	H	Cl	H

The protons that characterize the derivatives 4, 5-Di-Methyl $^4\Delta$ N-aryle Oxazoline-2-thione are: the protons of Methyl's in position 4 and 5, the aromatic protons and the protons of the substituting. The atom of oxygen by its electronegative effect decreases the electronic density to the level of the carbon in position 5 in relation to the sulfur atom what provokes a unarmored of methyl's 4 and 5 in the oxazolines. The chemical shifts of the protons of methyl's 4 and 5 appear in all ^{1}H NMR specters as singular. The chemical shift that is in the strong fields corresponds to the protons armored of the Methyl 4. The methyl 4 protons are armored more that methyl 5 protons because the current aryl effect, what shows that the molecule possesses an atropic isomerism due to the blockage of the free rotation between the carbon sp2 of aryl and nitrogen atom of oxazole so that the methyl is in the armor zone of the aryl part[18] .

The plan that carries the aryl forms with the plan of the heterocycle a dihedral angle that varies according to the attractions of aryl and thione function (C=S), as between the aryl and the methyl in position 4.

The chemical shifts of the aromatic protons matched as the signals complicated in the interval: 6.9-7.5 ppm[19] .

The quaternary carbons 2, 4 and 5 are more unarmored because anisotropy effect of heterocyclic copounds. The plan structure of molecule favorite the electronic transition effects of a core to the other, the most interesting poles are those that are sensitive to the electronic variations, of this fact the ^{13}C NMR can give us a lot more information than the ^{1}H NMR.

Phenyl isothiocyanate (**1b**) **:** C_6H_5NCS , Tf = -21°C, Tb = 221°C, d=1.13, R_f = 0.20 ; ^{1}H NMR ($CDCl_3$, ppm) : 7.35(m,5H, Harom)

2-Me-Phenyl isothiocyanate (**2b**) **:** C_7H_7NCS , Tf=107°C , Tb=239°C , d=1.115, R_f=0.47 , ^{1}H NMR ($CDCl_3$, ppm) : 2.3(s,3H) , 7.251(m,H-3, H-5) ,7.25158(dd, H-4) , 7.269(d, H-2)

2-Methoxy-Phenyl isothiocyanate (**3b**) **:** C_7H_7ONCS, 37°/, R_f=0.087, IR (KBr, cm^{-1}): 3250, 2990, 2960, 2945, 2550, 2190, 1600, 1500, 1450, 1430, 1250, 1225, 1200, 1100, 1050, 780, 700 and 585. ^{1}H NMR ($CDCl_3$, ppm): 3.899(s,3H), 6.878(m,H-5,H-3) , 6.9181(m,H-2) , 7.121(m,H-4).

2-Ethoxy-Phenyl isothiocyanate(**4b**) : C_8H_9ONCS ,32% , R_f=0.087 . ^{1}H NMR ($CDCl_3$, ppm) : 1.5 (t, CH_3) , 4.1 (q,CH_2) , 6.85 (m,H-5, H-3) , 7.16(m, H-2,H-4).

3-Chloro-Phenyl isothiocyanate(**5b**) : C_6H_4ClNCS , 14%, Tf=132°C , Tb=217°C , d=1.115, R_f=0.315. ^{1}H NMR ($CDCl_3$, ppm) : 7.37(m,H-3 , H-4 , H-5) , 7.83(s, H-2)

Synthèse des dérivés oxazoline-2-thione

4,5-Di-methylN-phenyl$^4\Delta$ Oxaazoline -2-thione (**1c**) : $C_{11}H_{11}ONS$, 13.4% , Tf=92°C, Rf=0.72 , IR(KBr) : 3045, 1603, 1589, 1370, 1211, 1127, 815, 703 cm^{-1} , ^{1}H NMR ($CDCl_3$, ppm) : 1.106(s,3H) , 1.41(s,3H) , 7.32(m,5H) ; RMN ^{13}C ($CDCl_3$, ppm) ,8.93 , 10.38,120.7 , 121.78, 126..27.

4, 5-Di-Methyl $^4\Delta$ N-(2-Me-phenyl) Oxazoline-2-thione (**2c**): $C_{12}H_{13}ONS$, 8.7% , Tf=81°C, Rf=0.89, IR(KBr) :3060, 1605, 1595, 1409, 1358, 1195, 1100, 807 cm^{-1} , ^{1}H NMR ($CdCl_3$) : 1.49(s,3H) , 1.71(s,3H), 1.94(s,3H) , 7.48(m, H_{arom})

4, 5-Di-Methyl $^4\Delta$ N-(2-Methoxy-phenyl) Oxazoline-2-thione (**3c**): $C_{12}H_{13}O_2NS$, 14.87%, Tf=109°C, Rf=0.94 , , IR(KBr) :3320, 3060, 1600, 1575, 1400, 1205, 1145, 1080, 790 cm^{-1} , ^{1}H NMR ($CDCl_3$, ppm) : 1.55(s,3H) , 1.71(s,3H) , 3.75(s,3H) , 6.99(m, H_{arom}).

4, 5-Di-Methyl $^4\Delta$ N-(2-Ethoxy-phenyl) Oxazoline-2-thione (**4c**): $C_{13}H_{15}O_2NS$, 14.00% , Tf=124°C, Rf=0.78, IR(KBr) : 3300, 3050, 1600, 1580, 1420, 1200, 1145, 1070, 805 cm^{-1} , ^{1}H NMR ($CDCl_3$, ppm) : 1.97(s,3H), 2.5(s,3H) , 1.45(t,3H) , 4.62(q,2H) , 7.34(m,H_{arom}) , ^{13}C NMR ($CDCl_3$, ppm) : 8.91(4-CH_3) , 10.38 (5-CH_3) , 16.97 (2'-CH_3) , 39.67 (2'-CH_2) , 120.76 (C-3') , 121.83 (C-5'), 126.17(C-6'), 128.15 (C-4), 129.15 (C-1'), 130.00 (C-2'), 130.00 (C-4), 130.84 (C-5), 163.23 (C=S).

4, 5-Di-Methyl $^4\Delta$ N-(3-Chloro-phenyl) Oxazoline-2-thione (**5c**): $C_{11}H_{10}ONS$, 9.47%, Tf=137, Rf=0.77 , , IR (KBr) : 3038, 1600, 1500, 1380, 1320, 1200, 1100, 805,683,570 cm^{-1} , ^{1}H NMR ($CDCl_3$, ppm) : 1.797 (s,3H), 2.175 (s,3H) , 7.25 (m, H_{arom}) , ^{13}C NMR ($CDCl_3$, ppm) : 8.94 (4-CH_3) , 10.39 (5-CH_3) , 120.78 (3'-C), 121.86 (1'-C), 126.17 (2'-C, 4'-C), 128.15 (6'-C), 129.01 (5'-C), 130.00 (C-4), 130.84 (C-5), 163.11 (C=S).

4. Conclusion

The synthesis of oxazolic compounds was largely possible by Robinson-Gabriel methods, that generally we obtained the oxazolkine derivatives with variable yields, this method that allowed us to avoid in a certain number of case the difficulty in separation of final products. The 4, 5-Di-Methyl $^4\Delta$ N-aryle Oxazoline-2-thiones present an atropic isomerism showed by ^{1}H NMR. The oxazolinthione atropoisomers may be separate by HPLC methods on chiral stationary phases.

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