Asian Journal of Chemistry Vol. 20, No. 4 (2008), 2491-2496

Synthesis and Characterization of Some Derivatives of 4,5-Dimethyl-Δ^4-N-aryl-N-ethylimidazoline-2-thione

N. Belboukhari*, A. Cheriti, A. Djafri† and C. Roussel‡
Phytochemistry & Organic Synthesis Laboratory
University of Bechar, 08000, Bechar, Algeria
Fax: (213)(49)815244; E-mail: nasser.belboukhari.inv14@univ-cezanne.fr

The azoline compounds which are the derivatives of imidazole possess many applications such as raw materials in the industrial chemistry, in polymers and pharmaceutical chemistry. A large number of natural products containing in nitrogenous heterocyclic compounds have some biological properties. The nucleic acids (ADN, ARN) which are responsible for genetic heritage and essential element of cellular core, are formed of basis of imidazoline (*e.g.*, guanine, adenine and cytosine). In pursuiance of present research works on the set of the azolines, we intend to synthesize some derivatives of N-aryl imidazole (**d**) through condensation between the thiourea (**c**) derivatives and the acetone by refluxation in pyridine. The synthesized azolines have been characterized by infrared, UV and NMR.

Key Words: Imidazole, Heterocyclic compounds, Atropic isomers.

INTRODUCTION

The methods of synthesis of the heterocyclic azoles depend on the relative position of the hetero-atoms. Among the various general methods, the follo-wing methods were adopted:

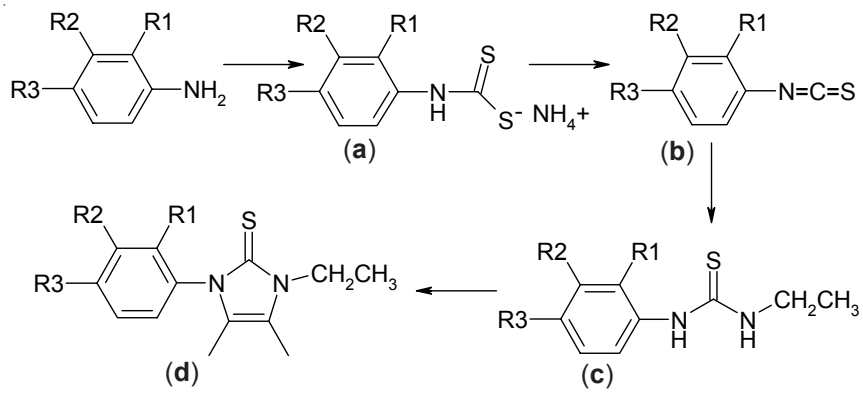
When the two hetero-atoms are in position 1,2, the reaction makes itself by condensation of a derivative β-di-functional compounds with a reagent that brings the two hetero atoms as the hydrazine or the diazoalcanes for the pyrazoles, the hydroxylamine or oxide of nitrile for the preparation of the oxazoles[1].

When the two hetero-atoms are in position 1,3, several methods are possible: one of the most used methods is Hantzsch method that consists in condensing it a derivative halo-carbonyl on an amide for obtaining the imidazoles[2].

†Synthesis Organic Applied Laboratory, University of Oran Are Senia, Algeria.
‡Laboratorie de Stéréochimie Dynamique et Chiralité CNRS UMR 6180, Université Paul Cézanne AIX Marseille III, France.

The present work has been achieved for a chromatographic separation survey on phase chiral of some derivatives N-aryl thiazoline-2-thiones and the corresponding imino compounds[3-6].

The publications available in literature for the synthesis of the azoles derivatives shows that it n' doesn't have a general method of synthesis allowing the access these compounds there. For it we chose according to the retro synthetic plan, a method to do a study on the synthesis of some derivatives of 4,5-dimethyl-Δ^4-N-aryl-N-ethylimidazoline-2-thione (**d**) from the aromatic amino compound (**a**)[7].



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

EXPERIMENTAL

IR spectra (ν_{max}) 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, multiplicities were determined by a polarization transfer (DEPT) experiment. The LC system consisted of a liquid chromatography (Si-gel : 230-400 mesh (MerK) were used for column chromatography)operating at room temperature.

Preparation of N-aryl dithiocarbamate: In a ball tricole of 1 L kept in an ice bath, added 43 mL (0.71 mol) of CS_2 and 90 mL (1.3 mol) of the ammonia. Under mechanical agitation, 0.6 mol of the aromatic amino compounds was added, after an agitation the dithiocarbamates of ammonium appeared as crystals or oil[8,9].

Preparation of N-aryl isothiocyanate: In a reactor tricole of 1500 mL provided with a mechanical agitator, the dithiocarbamate of ammonium

(dissolves in 800 mL of distilled water), 400 mL of concentrated solution of lead nitrate (200 g dissolves in 400 mL of distilled water) were added. The reaction mixture is subjected to an agitation for 30 to 40 min. The extraction of the isothiocyanate is possible by steam distillation. On decantion, a yellow oil is obtained and dried with calcium chloride. The pure isothiocyanate is obtained after filtration[10-12].

Preparation of thiourea: The isothiocyanate (5 mmol) reacted with ethylamine (5 mmol) in organic solvent (ethanol or propanol-2) at low temperature (0 °C) to obtain the thiourea (yield 30-70 %) after the purification by recrystallization with the absolute ethanol[13-16].

Synthesis of imidazoline: 5 mmol of the thiourea and 5 mmol of the acetone were added in 10 mL butanol. After the evaporation of the solvent, the residue was purified on chromatography column. The eluent is the *n*-hexane or benzene and the silica frost as stationary phase. The obtained product is recrystallized in absolute ethanol[17,18].

Phenyl isothiocyanate (b-1): C_6H_5NCS, T_f = -21°C, T_b = 221°C, d = 1.13, R_f = 0.217, ^{1}H NMR ($CDCl_3$, ppm): 7.35 (m, 5H, H-arom).

2-Methylphenyl isothiocyanate (b-2): C_7H_7NCS, T_f = 107°C, T_b = 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-Methoxyphenyl isothiocyanate (b-3): C_7H_7ONCS, Yield 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 ($CDCl_6$, ppm): 3.899 (s, 3H), 6.878 (m, H-5, H-3), 6.9181 (m, H-2), 7.121 (m, H-4).

2-Ethoxyphenyl isothiocyanate (b-4): C_8H_9ONCS, Yield 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-Chlorophenyl isothiocyanate (b-5): C_6H_4NCSCl, Yield 14 %, T_f = 132 °C, T_b = 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).

4-Chlorophenyl isothiocyanate (b-6): C_6H_4NCSCl, Yield 11 %, T_f = 129°C, R_f = 0.39. ^{1}H NMR ($CDCl_3$, ppm): 6.84 (d, H-3, H-5), 7.14 (d, H-2, H-6).

N-Phenyl-N-ethyl thiourea (c-1): $C_9H_{12}N_2S$, Yield 69 %, T_f = 88, R_f = IR (KBr, cm^{-1}) : 3136, 2987, 1601, 1526, 1425, 1210, 1206, 1080, 801. ^{1}H NMR ($CDCl_3$, ppm): 1.189 (t, 3H), 3.67 (q, 2H), 6.03, 7.25, 7.45 (m, H-arom), 8.00 (s, NH).

N-(2-Methylphenyl)-N-ethyl thiourea (c-2): $C_{10}H_{14}N_2S$, Yield 71 %, T_f = 150°C, R_f = 0.64, IR (KBr, cm^{-1}): 3335, 2955, 1579, 1498, 1290, 1211, 756, 479. ^{1}H NMR ($CDCl_3$, ppm): 1.4 (t, 3H), 4.05 (q, 2H), 6.00 (s, NH), 6.9 (m, 2H, H-3, H-5), 7.25 (m, 2H, H-2, H-4).

N-(2-Methoxyphenyl)-N-ethyl thiourea (c-3): $C_{10}H_{14}N_2OS$, Yield 45 %, TF = 76°C, R_f = 0.64, IR (KBr, cm^{-1}) : 3360, 2960, 1545, 1491, 1394, 1197, 731, 457. ^1H NMR ($CDCl_3$, ppm): 2.286 (s, 3H), 1.156 (t, 3H), 3.65 (q,2H), 5.57 (s,NH), 7.26 (m, H-aroma), 7.99 (s, H-arom).

N-(2-Ethoxyphenyl)-N-ethyl thiourea (c-4): $C_{11}H_{16}N_2OS$, Yield 33 %, T_f = 85°C, R_f = 0.635, IR (KBr, cm^{-1}) :3337, 2928, 1602, 1449, 1269, 1177, 757, 464. ^1H NMR ($CDCl_3$, ppm): 1.185 (t, 3H), 3.67 (q, 2H), 6.05 (s, NH), 7.25 (m, 2H), 7.45 (m, 2H), 8.25 (s, NH).

(3-Chlorophenyl)-N-ethyl thiourea (c-5): $C_9H_{11}N_2SCl$, Yield 31 %, T_f = 91 °C, R_f = 0.665, IR (KBr, cm^{-1}): 3338, 2956, 1576, 1441, 1289, 1145, 794, 599. ^1H NMR ($CDCl_3$, ppm): 1.12 (t, 3H), 3.7 (q, 2H), 5.06 (s, NH), 7.3 (m, 4H), 8.1 (s, NH).

(4-Chloro-phenyl)-N-ethyl thiourea (c-6): $C_9H_{11}N_2SCl$, Yield 22 %, T_f = 97°C, R_f = 0.645, IR (KBr, cm^{-1}): 3339, 2940, 1536, 1445, 1338, 1210, 788, 462. ^1H NMR ($CDCl_3$, ppm): 1.423 (t, 3H), 6.909 (m, 2H), 5.11 (s, NH), 7.243 (m, 2H), 8.16 (NH).

4,5-Dimethyl-N-phenyl-N-ethyl-Δ^4-imidazoline-2-thione (d-1): $C_{13}H_{16}N_2S$, Yield 21 %, T_f = 177°C, R_f = 0.817, IR (KBr, cm^{-1}): 3094, 3022, 2920, 1602, 1578, 1506, 1482, 1419, 1332, 1311, 1275, 1254, 912, 801, 765, 714, 696, 678 and 573, ^1H NMR ($CDCl_3$, ppm): 1.368 (t, 2H), 1.795 (s, 3H), 2.10 (s, 3H), 4.1 (q, 2H), 7.26 (m, H-3, H-5), 7.36 (m, H-2, H-4, H-6).

4,5-Dimethyl-N-(2-methylphenyl)-N-ethyl-Δ^4-imidazoline-2-thione (d-2): $C_{14}H_{18}N_2S$, Yield 23 %, T_f = 239, R_f = 0.815, IR (KBr, cm^{-1}): 3100, 3016, 2926, 1578, 1506, 1479, 1416, 1323, 1290, 1251, 1146, 1101, 1089, 912, 795, 777, 720, 684 and 585. ^1H NMR ($CDCl_3$, ppm): 1.34 (t, 3H), 1.73 (t, 3H), 2.09 (s,3H), 2.19 (s,3H), 4.16 (q,2H), 7.25 (m,H-arom), ^{13}C NMR ($CDCl_3$, ppm): 9.27, 9.41, 13.978, 17.74, 40.155, 120.7, 121.31, 127.11, 128.62, 129.2, 135.93, 136.65, 160.91.

4,5-Dimethyl-N-(2-methoxy-phenyl)-N-ethyl-Δ^4-imidazoline-2-thione (d-3): $C_{14}H_{18}N_2OS$, Yield 17 %, T_f = 229, R_f = 0.814, IR (KBr, cm^{-1}): 3148, 3106, 3022, 1605, 1575, 1509, 1473, 1446, 1422, 1320, 1278, 1254, 1198, 1152, 1101, 1020, 912, 771, 732 and 684. ^1H NMR ($CDCl_3$, ppm): 1.778 (s, 3H), 2.084 (s, 3H), 2.19 (s, 3H), 1.351 (t, 3H), 4.18 (q, 2H), 7.1 (m, Harom). ^{13}C NMR ($CDCl_3$, ppm): 9.3, 9.44, 14.00, 17.77, 40.165, 120.74, 121.39, 127.11, 128.6, 129.4, 131.18, 135.95, 136.58, 161.014.

4,5-Dimethyl-N-(2-ethoxyphenyl)-N-ethyl-Δ^4-imidazoline-2-thione (d-4): $C_{15}H_{20}N_2OS$, Yield 13 %, T_f = 219 °C, R_f = 0.814, IR (KBr, cm^{-1}): 2997, 1605, 1551, 1425, 1335, 1245, 1150, 675 and 575. ^1H NMR ($CDCl_3$, ppm): 1.78 (s,3H), 2.09 (s, 3H), 1.35 (t, 3H), 4.17 (q, 2H), 7.28 (m, H-arom). ^{13}C NMR ($CDCl_3$, ppm): 9.32, 9.43, 14.00, 17.67, 40.163, 120.75, 121.40, 127.11, 128.64, 129.22, 135.95, 136.61, 161.00.

4,5-Dimethyl-N-(3-chlorophenyl)-N-ethyl-Δ^4-imidazoline-2-thione (d-5): $C_{13}H_{15}N_2SCl$, Yield 12.5 %, T_f = 162, R_f = 0.80. IR (KBr, cm^{-1}): 3160, 1605, 1590, 1488, 1458, 1437, 1323, 1257, 1233, 1077, 774, 705, 687 and 669. ^1H NMR ($CDCl_3$, ppm): 1.83 (s, 3H), 2.16 (s, 3H), 1.3 (t, 3H), 4.18 (q, 2H), 7.37 (m, H-arom). ^{13}C NMR ($CDCl_3$, ppm): 9.33, 9.46, 17.67, 40.17, 120.81, 121.79, 126.18, 128.7, 135.02, 135.73, 161.01.

4,5-Dimethyl N-(4-chlorophenyl)-N-ethyl-Δ^4-imidazoline-2-thione (d-6): $C_{13}H_{15}N_2SCl$, Yield 11 %, T_f = 227°C, R_f = 0.83. IR (KBr, cm^{-1}): 3154, 3112, 3028, 1578, 1500, 1476, 1419, 1320, 1284, 1269, 1251, 1089, 912, 837, 756, 741 and 573. ^1H NMR ($CDCl_3$, ppm): 1.80 (s, 3H), 2.12 (s, 3H), 1.17 (t, 3H), 4.1 (q, 2H), 6.878 (m, 2H, H-3, H-5), 7.121 (m, 2H, H-2, H-6).

RESULTS AND DISCUSSION

One of the signals is observed as a singular more armored than the other. This armor explains itself by the electronic current effect creates by the phenyl and that the protons of the methyl at position 4 are in the zone of armor (electro-negative zone of anisotropic orientation)[19,20].

This armor also showed that this molecule represent an isomerism so-called atropo isomerism, which is due to the blockage of the free rotation around N-aryl. This blockage brings the structure to a dihedral angle, between the heterocyclic part and the phenyl group. This angle will be calculated theoretically by the methods quantum and as experimentally determined by RX spectroscopy[21,22].

In this configuration one can explain the variations of the chemical displacements of the protons of methyl at position 4 also for the whole set of the studied imidazoline derivatives. The protons of ($^aCH_3$-$CH_2{}^b$-N) present two signals of resonance appear toward the same zone of sweep of the electromagnetic field with two signals, one is a triplet and the other is a quadruplet. The protons (a) have are armored more that the protons (b), it explains itself by the electronic effect of nitrogen[23].

The studied molecules possesses 11 to 13 carbons. In the NMR spectra, the resonance signals of hybridized carbons sp^2 of the phenyl appear at 120-130 ppm. The signal of the carbon in position 2 appears toward the weak fields, This carbon is unarmored by anisotropic effect of the double link C=S and the electronic effect of the sulfur atom and the 2 atoms of nitrogen, that brings weak carbon atom therefore in electron a strong unarmor defines by a chemical displacement, precisely to 170 ppm.

The resonance signals of the carbons of the 4 and 5 methyl's appear toward the weak fields to chemical displacements between 9 and 15 ppm. The armor of the methyl 4 carbon also explains itself by the anisotropy phenomenon of the phenyl group[24].

ACKNOWLEDGEMENTS

The authors are grateful to University of Bechar, Algeria for the financial support and SPI, Paul Cézanne University, Marseille, France for providing the necessary facilities.

REFERENCES

1. A.F. Pozharskii, A.D. Garnovskii and M. Siminov, *Rus. Chem. Rev.*, **35**, 122 (1966).
2. S.M. Elkhaws, M.A. Khalil and L. Chaaban, *IL Farmaco*, **44**, 415 (1989).
3. A. Djelloul, Master Thesis, Université d'Oran Es Senia, Algeria (1998).
4. M. Bouchekara, Thése de Magistere, Université d'Oran Es Senia (1993).
5. A. Djafri, Thése de doctorat, Université d'Oran Es Senia (1989).
6. A. Djafri, M. Bouchekara and F. Djafri, *J. Soc. Alger. Chim.*, **6**, 123 (1996).
7. C. Roussel, M. Adjimi, A. Chemlal and A. Djafri, *J. Org. Chem.*, **53**, 5076 (1988).
8. C. Roussel, R. Gallo, M. Chanon and J. Metzger, *Bull. Soc. Chim de France*, **5**, 1903 (1971).
9. G. Blatt, Organic Synthesis, John Wiley & Sons, Vol. 1, p. 447 (1941).
10. G. Brokent, V.V. Evreinov and E.K. Khodshasva, *Kinitika I Kataliz*, **13**, 314 (1972).
11. A. Renson and R.P. Tiger, *J. Chem. Soc, Perkin Trans II*, 2331 (1960).
12. R.P. Smith and L.S. Emerson, *J. Am. Chem. Soc.*, **70**, 6383 (1970).
13. A. Mayer, *Chem. Abstr.*, **36**, 5199 (1941).
14. S. Juin and Buu-Hoi, *Practical INST Pasteur*, **72**, 580 (1946).
15. A.I. Vogel, Practical Organic Chemistry, edn. 3, p. 442 (1967).
16. E.A. Werner, *J. Chem. Soc.*, **59**, 396 (1891).
17. C.J. Broan and A.R. Buther, *J. Chem. Soc. Perkin Trans II*, 731 (1989).
18. S. Jayakumar, M.P.S. Ishar and M.P. Mahajan, *Tetrahedron Lett.*, **39**, 6557 (1998).
19. N. Belboukhari and A. Cheriti, Com N° 21, 5ieme Congrés de la Soc.Alg.Chim; Bejaia (1999).
20. N. Belboukhari, Mémoire de Magistere, Université d'Oran Es Senia (2000).
21. N. Belboukhari and A. Cheriti, 5ieme Séme Int de Physique, SIPE 5, Béchar, Algeria (2000).
22. N. Belboukhari and A. Cheriti, 3ieme Col. int en chimie héterocyclique, Tlemcen (2004).
23. N. Belboukhari, A. Cheriti and A. Djafri, 5 ieme j. chim. théor, Mostaganem (2001).
24. N. Belboukhari, A. Cheriti and A. Djafri, 7 ieme j. chim. théor, novembre, Oran (2006).

(*Received*: 1 December 2006; *Accepted*: 18 December 2007) AJC-6139