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Oxidative aromatization of 1,3,5-trisubstituted 4,5-dihydro-1*H*-pyrazoles efficiently by H_5IO_6/KI, as a novel reagent under solvent free conditions

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ABSTRACT

Oxidation of 1,3,5-trisubstituted 4,5-dihydro-1H-pyrazoles to the corresponding pyrazoles has been achieved by utilizing H_5IO_6/KI, in solvent free under mild reaction and conventional thermal condition at room temperature with excellent yields.

KEYWORDS

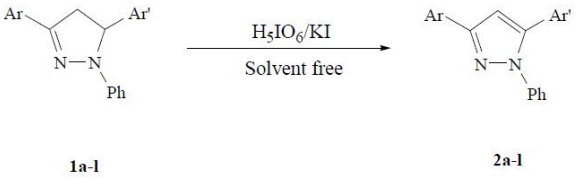
H_5IO_6/KI;
2-Pyrazoles;
Oxidation;
Solvent-free condition.

INTRODUCTION

Many five-membered heterocycles including pyrazoles[1] are considered as important class of heterocyclic compounds possessing interesting biologica[1,2] and pharmacological properties as anti-inflammatory,[3] anti-cancer,[4] anti-bacterial,[5] anti-viral,[6] anti-diabetic,[7] anti-microbial,[8] and anti-fungal agents[9]. Some pyrazoles possess fluorescence characteristics[10], display agrochemical properties[11] (i.e., herbicidal and soil fungicidal activity) and have applications as pesticides and insecticides[12]. Pyrazolines obtained by cyclization of chalcones with arylhydrazines,[13] can be easily oxidized to pyrazoles. A variety of oxidizing agents have been previously reported to convert pyrazolones to pyrazoles including $Zr(NO_3)_4$,[14] carbon-activated oxygen,[15] Pd/C/AcOH,[16] Co(II)/O_2,[17] iodobenzenediacetate,[18] $Pb(OAc)_4$,[19] MnO_2,[20] $KMnO_4$,[21] $Ag(NO_3)_2$,[22] HgO,[23] *N*-hydroxyphthalimide (NHPI)[24] and I_2O_5/KBr[25]. Many, however, impose certain disadvantages such as longer reaction times, low yields of products and toxicity due to the presence of some metallic ions embodied in these reagents. Such limitations necessitate further demand to develop other environmentally benign and easily accessible reagents for conversion of 2-pyrazolines to pyrazoles. The presence of some metallic ions embodied in these reagents. Such limitations necessitate further demand to develop other environmentally benign and easily accessible reagents for conversion of 2-pyrazolines to pyrazoles.

RESULTS AND DISCUSSION

As part of our ongoing efforts to search for more robust protocols for aromatization of various heterocycles including pyrazolines,[26] we have successfully examined in this article the application of ortho-



1a-l 2a-l

Scheme 1 : Oxidation of 2-pyrazolines by H_5IO_6/KI

TABLE 1 : Oxidative aromatization of 2-pyrazolines 1a-l to the corresponding pyrazoles 2a-l with H_5IO_6/KI in solvent free at r.t.

Entry	Product	Ar	Ar'	Time(min)	Yelde(%)	M.P(°c)
1	3a	Ph	Ph	4	96	137-139
2	3b	Ph	4-Cl	6	92	110-112
3	3c	Ph	4-OMe	7	93	95-97
4	3d	4-OMe	Ph	8	92	75-77
5	3e	4-OMe	4-Cl	6	96	125-127
6	3f	4-OMe	4-OMe	7	94	134-136
7	3g	4-OMe	4-Br	9	93	122-124
8	3h	2-Naphtyl	Ph	3	95	98-100
9	3i	2-Naphtyl	4-Cl	5	97	140-142
10	3j	2-Naphtyl	4-OMe	6	90	149-150
11	3k	2-Naphtyl	4-Br	10	95	70-72
12	3l	2-Naphtyl	4-Me	9	93	93-95

a) All the products are known, characterized by IR, NMR spectral analysis and compared with the authentic samples b) Isolated yields. c) Melting points of compounds are consistent with reported values.

periodic acid/ potassium iodide (H_5IO_6/KI), in a solvent free condition as a new and efficient system for aromatization of 1,3,5-trisubstituted 4,5-dihydro-1H-pyrazoles (1a-l) to the corresponding pyrazoles (2a-l) Scheme 1, TABLE 1.

According to the experimental results shown in TABLE 1, more efficient conversion of 2-pyrazolines occurs under room temperature in solvent free to yield the corresponding pyrazoles in shorter reaction times and higher yields (90-97%).

EXPERIMENTAL

Chemicals were obtained from Merck and Fluka chemical companies. The IR spectra were recorded on a Shimadzu 435-U-04 spectrophotometer (KBr pellets) and NMR spectra were obtained in $CDCl_3$ using a 400 MHz JEOL FT NMR spectrometer. All melting points were determined on an Electro Thermal 9100 melting point apparatus.

GENERAL PROCEDURE: OXIDATION OF 2-PYRAZOLINES (1A-L) BY H_5IO_6/KI

To a magnetically stirred suspension of KI (1.2 mmol, 199 mg), a solution of H_5IO_6 (1.2 mmol, 273 mg) in H_2O (5 ml) and 2-pyrazoline 1a-l (1 mmol) were added to a mortar and the mixture was pulverized with a pestle. The resulting reaction mixture was stirred at room temperature for an appropriate time TABLE 1. After the complete conversion of the substrate in 3-10 min. as monitored by TLC using acetone/ n-hexane (4:1), the reaction mixture was quenched with aqueous sodium bicarbonate solution (5%) and extracted with ethyl ether (10 mL). The organic layer was then dried over anhydrous sodium sulphate and concentrated to leave the crude solids 2a-l in 90-97 % yield TABLE 1. The products were further purified by recrystallization from ethanol (96%).

CONCLUSION

We have developed a new and mild procedure for oxidation of 2-pyrazolines to 2-pyrazoles utilizing ortho-periodic acid/potassium iodide (H_5IO_6/KI),

as a highly efficient, inexpensive, ecologically safe and easily recoverable reagent which acts under solvent free condition at room temperature.

REFERENCES

[1] F.A.Amer, M.Hammouda, A.A.S.El-Ahl, B.F.Abdol-Wahab; *J.Chin.Chem.Soc.*, ***54***, 1543 **(2007)**; (b) A.O.Abdolhamid, A.H.El-Ghandour, A.A.M.El-Reedy; *J.Chin.Chem.Soc.*, ***55***, 406 **(2008)**.

[2] M.Zia-ul-Hag, M.Arshad, R.Saeed-ur-Rehman; *J.Chin.Chem.Soc*., ***48***, 45 **(2001)**.

[3] S.Rapposelli, A.Lapucci, F.Minutolo, E.Orlandini, G.Ortore, M.Pinza, A.Balsamo; *Farmaco*, ***59***, 25 **(2004)**.

[4] (a) K.D.Shin, M.Y.Lee, D.Shin, S.Lee, K.H.Son, S.Koh, Y.K.Paik, B.M.Kwon, D.C.Han; *J.Biol.Chem*., **280**, 41439 **(2005)**; (b) C.Rochais, J.S.Santos, O.de, P.Dallemagne, S.Rcult; *Heterocycles*., **68**, 2063 **(2006)**.

[5] P.Cali, L.Naerum, S.Mukhija, A.Hjelmencrantz; *Bioorg.Med.Chem.Lett.*, **14**, 5997 **(2004)**; (b) M.A.El-Maghraby, A.K.Khalafaliah, M.E.Hassan, H.A.Soleiman; *J.Chin.Chem.Soc*., ***35***, 53 **(1988)**.

[6] M.Sechi, L.Sannia, F.Carta, M.Palomba, R.Dallocchio, A.Dessi, M.Derudas, Z.Zawahir, N.Neamati; *Antiviral Chem.Chemother*., **16**, 41 **(2005)**.

[7] B.Cottineau, P.Toto, C.Marot, A.Pipaud, J.Chenault; *Bioorg.Med.Chem.Lett*., **12**, 2105 **(2002)**.

[8] (a) E.Takabatake, R.Kodama, Y.Tanaka, R.Dohmori, H.Tachizawa, T.Naito; *Chem.Pharm.Bull*., **16**, 1900 **(1979)**; (b) S.S.Parmar, B.R.Pandy, C.Dwivedic, R.D.Harbinson; *J.Pharm.Sci*., **63**, 1152 **(1974)**; (c) S.Shinde, W.Jadhav, R.Pawar, S.Bhusare; *J.Chin.Chem.Soc*., **51**, 775 **(2004)**.

[9] F.Al-Omran, A.A.El-Khair; *J.Heterocycl.Chem.*, **41**, 327 **(2004)**; (b) H.A.Soleiman, A.K.Khalafallah, H.M.Abdelzaher, *J.Chin.Chem.Soc*., **47**, 1267 **(2000)**.

[10] M.A.Raslan, R.M.AbdEl-Aal, M.E.Hassan, N.A.Ahmed, K.U.Sadek; *J.Chin.Chem.Soc*., **48**, 91 **(2001)**.

[11] Z.Yan-Wu, C.Ling-Hua; *J.Chin.Chem.Soc*., **55**, 385 **(2008)**.

[12] (a) Y.Li, H.Q.Zhang, J.Liu, X.P.Yang, Z.J.Liu; *J.Agric.Food Chem*., **54**, 3636 **(2006)**; (b) T.L.Siddall, D.G.Ouse, Z.L.Benko, G.M.Garvin, J.L.Jackson, J.M.McQuiston, M.J.Ricks, T.D.Thibault, J.A.Turner, J.C.Van Heertum, M.R.Weimer; *Pest Manage.Sci.*, **58**, 1175 **(2002)**; (c) C.Lamberth; *Heterocycles.*, **71**, 1467 **(2007)**.

[13] D.Azarifar, M.Shaebanzadeh; *Molecules*, **7**, 885 **(2002)**; (b) D.Azarifar, H.Ghasemnejad; *Molecules*, **8**, 642 **(2003)**; (c) D.Azarifar, B.Maleki; *J.Heterocycl.Chem*., **42**, 157 **(2003)**.

[14] G.Sabitha, G.S.K.Kumar Reddy, Ch.S.Reddy, N.Fatima, J.Yadav; S.*Synthesis*, 1267 **(2003)**.

[15] N.Nakamichi, Y.Kawashita, M.Hayashi; *Synthesis*, 1015 **(2004)**.

[16] N.Nakamichi, Y.Kawashita, M.Hayashi; *Org.Lett*., **4**, 3955 **(2002)**.

[17] J.N.Shah, C.K.Shah; *J.Org.Chem*., **43**, 1266 **(1978)**.

[18] S.P.Singh, D.Kumar, O.Prakash, R.P.Kapoor; *Synth.Commun*., **27**, 2683 **(1997)**.

[19] W.A.F.Gladstone, R.O.C.Norman; *J.Chem.Soc*., *Chem.Commun*., 1536 **(1966)**.

[20] I.Bhatnage, M.V.George; *Tetrahedron*, **24**, 1293 **(1968)**.

[21] L.I.Smith, K.L.Howard; *J.Am.Chem.Soc*., **65**, 159 **(1943)**.

[22] R.P.Dodwadmath, T.S.Wheeler; *Proc.Ind.Acad.Sci*., **2A**, 438 **(1935)**.

[23] K.Auwers, P.Heimke; *Liebigs Ann*., **458**, 186 **(1927)**.

[24] B.Han, Z.Liu, Q.Liu, L.Yang, Z.Li-Liu, W.Yu; *Tetrahedron*., **62**, 2492 **(2006)**.

[25] F.L.Chai, Y.Zhao, O.Sheng, Z.O.Liu; *Tetrahedron Lett*., **47**, 9283 **(2006)**.

[26] (a) H.Ghasemnejad-Bosra, M.Faraje, S.Habibzadeh, F.Ramzaniyan-Lehmali, *J.Serb.Chem.Soc*., **75**, 299 **(2010)**. (b) D.Azarifar, H.Ghasemnejad-Bosram; *Synthesis*, 1123 **(2006)**; (c) H.Ghasemnejad-Bosra, M.Haghdadi, I.Gholampour-Azizi; *Heterocycles*, **75**, 391 **(2008)**.