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An efficient oxidation of 2-pyrazolines and isoxazolines by ceric ammonium nitrate (CAN) under solvent free conditions

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ABSTRACT

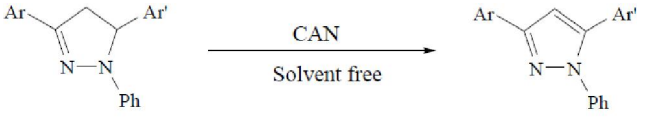
An efficient and simple procedure has been developed for the oxidation of 1,3,5-trisubstituted 4,5-dihydro-1*H*-pyrazoles to their corresponding aromatic derivatives promoted by ceric ammonium nitrate(CAN) under a solvent-free condition. The products 2-pyrazoles were produced in good to excellent 90-98 % yields.

KEYWORDS

Ceric ammonium nitrate (CAN);
2-Pyrazoles;
Oxidation;
Solvent-free condition.

INTRODUCTION

Pyrazolines have attracted much attention since they play important roles in synthetic organic over the years and are important bioactive compounds as anti-cancer,[1] anti-viral,[2] anti-inflammatory,[3] anti-diabetic,[4] anti-bacterial and antifungal agents.[5] In addition, a number of pyrazoles exhibit fluorescence characteristics and can act as agrochemical herbicides, soil fungicides, pesticides and insecticides.[6] Furthermore, pyrazoles are useful synthetic intermediates capable of undergoing various transformations and transition-metal catalyzed cross-coupling reactions, such as Heck, Stille, Suzuki, Sonogashira, and Negishi couplings.[7] Recently, transition-metal catalyzed coupling-cyclization reaction of functionalized allenes with organic halides for synthesis of pyrazoles has been reported.[8] These facts substantiate an obvious demand for development of new synthetic methods for pyrazoles due to their importance both as synthetic intermediates[9] and as pharmacological targets.[10] 2-pyrazoles can be easily obtained respectively from oxidation of and 2-pyrazolines.[10] Various efforts have been made previously in the oxidation of 2-pyrazolines with a variety of reagents including Pd/C/acetic acid,[11] carbon-activated oxygen,[12] cobalt soap of fatty acids,[13] lead tetraacetate,[14] mercury or lead oxide,[15] manganese dioxide,[16] potassium permanganate,[17, 18] silver nitrate,[19] iodobenzene diacetate,[20] zirconium nitrate,[21] nickel peroxide,[22] and tetrakispyridinenickel(II) dichromate.[23] However, many of these methods are subjected to certain drawbacks such as longer reaction times, low yields and toxicity due to the presence of some elements embodied in the reagents utilized. So still there is need of development of new catalysts which overcome all these drawbacks.



1a-l 2a-l

Scheme 1 : Oxidation of 2-pyrazolines by CAN

TABLE 1 : Oxidative aromatization of 2-pyrazolines 1a-l to the corresponding pyrazoles 2a-l by CAN in solvent free at r.t.

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

RESULTS AND DISCUSSION

To broaden the scope of our ongoing research on developing more convenient and robust methods for oxidative aromatization of different heterocycles,[24-26] herein we wish to introduce ceric ammonium nitrate (CAN), in this letter as a new and efficient reagent for conversion of 2-pyrazolines into their corresponding 2-pyrazoles under a solvent-free condition (Scheme **1**).

In this communication, CAN has been found to efficiently catalyze the aromatization of 2-pyrazolines **1a-l** at room temperature under a solvent-free condition within few minutes to afford the corresponding 2-pyrazoles **2a-l** in 90-98 % yields TABLE 1.

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.

OXIDATION OF 2-PYRAZOLINES (1A-L) WITH CAN; GENERAL PROCEDURE

To a magnetically stirred suspension of CAN (5% mol) 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 5-8 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 90-98 % yield TABLE 1. The products were further purified by recrystallization from ethanol (96%).

CONCLUSION

The present work offers a mild and simple procedure for oxidative aromatization of 2-pyrazolines promoted by CAN as a low cost and non-toxic reagent at room temperature under solvent free condition. Other advantages of this method are shorter re-

action times, high yields of the products, and use of solvent free as a green condition in the oxidation reactions.

REFERENCES

[1] K.D.Shin, M.Y.Lee, D.S.Shin, S.Lee, K.H.Son, S.Koh, Y.K.Paik, B.M.Kwon, D.C.Han; *J.Biol.Chem.*, **280**, 41439 **(2005)**; (b) F.A.Amer, M.Hammouda, A.A.S.El-Ahl, B.F.Abdol-Wahab; *J.Chin.Chem.Soc.*, **54**, 1543 (**2007)**; (c) A.O.Abdolhamid, A.H.El-Ghandour, A.A.M.El-Reedy; *J.Chin.Chem.Soc.*, **55**, 406 (**2008)**.

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

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

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

[5] P.Cali, L.Naerum, S.Mukhija, A.Hjelmencrantz; *Bioorg.Med.Chem.Lett.*, **14**, 5997 (2004); (b) S.Shinde, W.Jadhav, R.Pawar, S.Bhusare; *J.Chin.Chem.Soc.*, **51**, 775 (**2004)**; (c) F.Al-Omran, A.A.El-Khair; *J.Heterocycl.Chem.*, **41**, 327 (**2004)**.

[6] Y.Li, H.Q.Zhang, J.Liu, X.P.Yang, Z.J.Liu; *J.Agric.Food Chem.*, **54**, (**2006)**; *Chin.Chem.Soc.*, **48**, 91 (**2001)**.

[7] G.M.Garvin, J.L.Jackson, J.M.McQuiston, M.J.Ricks, T.D.Thibault, J.A.Turner, J.C.VanHeertum, M.R.Weimer; *Pest Manage.Sci.*, **58**, 1175 (**2002)**.

[8] S.Ma; *Acc.Chem.Res.*, **36**, 701 **(2003)**; (b) X.Cheng, S.Ma; *Chem.Commun.*, 4263 **(2009)**; (c) J.D.Sieber, J.P.Morken; *J.Am.Chem.Soc.*, **128**, 74 (**2006)**.

[9] M.Schnürch, R.Flasik, A.F.Khan, M.Spina, M.D.Mihovilovic, P.Stanetty; *Eur.J.Org.Chem.*, 3283 (**2006)**.

[10] L.D.Nunno, A.Scilimati, P.Vitale; *Tetrahedron*, **58**, 2659 **(2002)**.

[11] D.Azarifar, H.Ghasemnejad; *Molecule.*, **8**, 642 **(2003)**; (b) D.Azarifar, B.Maleki; *J.Heterocycl.Chem.*, **42**, 157 (**2005)**.

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

[13] M.Hayashi, Y.Kawashita; *Lett.Org.Lett.*, **3**, 571 (**2006)**; (b) Y.Kawashita, C.Ueba, M.Hayashi; *Tetrahedron Lett.*, **47**, 4232 (**2006)**.(c) N.Nakamichi, Y.Kawashita, M.Hayashi; *Synthesis*, 1015 (**2004)**; (d) Y.Kawashita, N.Nakamichi, H.Kawabata, M.Hayashi; *Org.Lett.*, **5**, 3713 (**2003)**.

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

[15] W.A.F.Goldstone, R.O.C.Norman; *J.Chem.Soc.*, *Chem.Commun.*, 1537 (**1966)**.

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

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

[18] N.K.Kochetkov, S.D.Sokolov; "*Advances in Heterocyclic Chemistry*", Academic Press: New York, 420 (**1965)**.

[19] R.P.Dodwadmath, T.S.Wheeler; *Proc.Ind.Acad.Sci.*, **2A**, 438 (**1936)**.

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

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

[22] L.Bianchi, C.Dellerba, F.Grasparrini, M.Novi, C.Tavani; *Arkivoc.*, **10**, 142 (**2002)**.

[23] B.Wang, T.He, C.Li, H.Hu; *Chin.J.Org.Chem.*, **23**, 794 (**2003)**.

[24] H.Ghasemnejad-Bosra, M.Faraje, S.Habibzadeh, F.Ramzaniyan-Lehmali; *J.Serb.Chem.Soc.*, **75**, 299 (**2010)**.

[25] D.Azarifar, H.Ghasemnejad-Bosram; *Synthesis*, 1123 (**2006)**.

[26] H.Ghasemnejad-Bosra, M.Haghdadi, I.Gholampour-Azizi; *Heterocycles*, **75**, 391 (**2008)**.