FACILE SYNTHESIS OF 5-ARYL-FURAN-2-ALDEHYDE AND 5-ARYL-FURAN-2-CARBOXYLIC ACID USING CERIC AMMONIUM NITRATE

K Subrahmanya Bhat and B Shivarama Holla*
Department of Chemistry, Mangalore University,
Mangalagangotri-574199, INDIA
*E-mail: hollabs@rediffmail.com

Abstract: A new method for the synthesis of furan-2-carboxaldehyde and 5-(substituted-phenyl)-furan-2-carboxylic acids using ceric ammonium nitrate (CAN) is reported.

Introduction: Nitrofuran and arylfuran derivatives are reported to possess varied biological activities (1-4). The widely used nitrofuran heterocycles are now known to have toxic side effects, which demand safer new drugs (5-7). In this attempt nitro group in nitrofuran heterocycles were replaced by nitrophenyl moiety. A useful starting material for the introduction of furan moiety into other heterocycles is 5-substitutedphenyl-furan-2-aldehyde and 5-substitutedphenyl-furan-2-carboxylic acids. This intermediate is synthesized so far by Meerwein reaction (8). This reaction involves diazotization of aniline and coupling of diazonium ion with furan-2-aldehyde or 2-furoic acid. However this reaction is very slow and requires stirring for 12-14h, under catalytic influence of cupric chloride. Recently, wide applicability of ceric ammonium nitrate in organic synthesis was explored by various research groups (9-14). In this communication we report the utility of ceric ammonium nitrate (CAN) in the coupling of diazonium chloride with furan-2-aldehyde and 2-furoic acid.

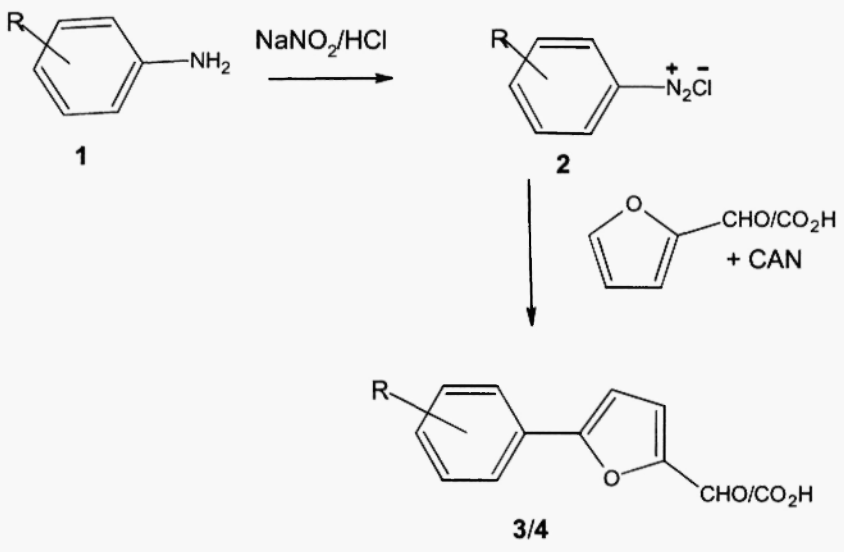
Experimental:

Melting points are determined by open capillary method and are uncorrected. IR spectra were recorded in KBr pellets on a Perkin - Elemer 157 IR spectrophotometer. ^{1}H NMR spectra were recorded in DMSO-d_6 on EM-390 (300MHz) NMR spectrometer. The purity of compounds was checked by TLC on silica gel plates using a hexane: dioxan (10:1) solvent system and iodine was used as a visualizing agent.

Syntheses of 5-aryl-furan-2-aldehyde (3a-g): A mixture of substituted aniline(100 mmol), hydrochloric acid(15%, 60ml) and water (90ml) was heated until a clear solution was obtained, cooled to 0-5^{0}C, diazotized with aqueous sodium nitrite (30%), 24 ml) and filtered. To the filtered solution, water (50ml) and furfural (9.6g, 100 mmol) were added. Aqueous solution of ceric ammonium nitrate (4g in 10 ml of water) was added dropwise and stirred for 2h at room temperature and kept aside for 5h. The resulting solid was filtered off, suspended in water and purified by recrystallization from a mixture of dimethyl formamide and ethanol. The melting points of compounds **3a-g** are in conformity with that of literature values (15) (**Table I**).

Syntheses of 5-aryl-furan-2-carboxylic acid (4a-d): The procedure is similar to that for 5-aryl-furan-2-aldehyde. Instead of furan-2-aldehyde, furan-2-carboxylic acid is used. The physicochemical data of the synthesized compounds **4a-d** are in agreement with that of literature values (15) (**Table II**).

Results and Discussion: In the meerwien reactions often the yields are lower due to the decomposition of diazonium chloride. Moreover it requires longer reaction times of 14-18h. The catalysis by cupric ion often



Scheme1

Table I Physicochemical data of 5-Substitutedphenyl-furan-2-carboxaldehyde (**3a-g**)

Compd No.	R	Mol. formula	Yield (%)	M.P(^{0}C)
3a	2-Cl-	$C_{11}H_7ClO_2$	68	70
3b	4-Cl-	$C_{11}H_7ClO_2$	72	130
3c	2,4-Cl_2-	$C_{11}H_6Cl_2O_2$	70	72
3d	4-Br-	$C_{11}H_7BrO_2$	76	156-58
3e	2-NO_2-	$C_{11}H_7NO_4$	68	97-98
3f	3-NO_2-	$C_{11}H_7NO_4$	65	155
3g	4-NO_2-	$C_{11}H_7NO_4$	76	205-07

Table II Physicochemical data of 5-Substitutedphenyl-furan-2-carboxylic acids (**4a-d**)

Compd No.	R	Mol. formula	Yield (%)	M.P(^{0}C)
4a	4-Cl-	$C_{11}H_7ClO_3$	72	198
4b	2-NO_2-	$C_{11}H_7NO_5$	65	152-54
4c	4-NO_2-	$C_{11}H_7NO_5$	70	227-30
4d	4-Br-	$C_{11}H_7BrO_3$	76	182-84

leads to unwanted side products. It is expected that the reaction could be carried out under the influence of ceric ions, which would follow the similar pattern. Ceric ammonium nitrate is easily available, cheap and stable compound. Ceric ions are highly effective in bringing about the diazo coupling reaction. The compounds **3a-g** and **4a-d** were synthesized by modified meerwein reaction in 65-76% yield. Formation of these compounds is confirmed to be same by an alternate synthesis (6). The ^{1}H NMR spectrum of compound **3g** showed two distinct doublets in the range ä 7.58 to 7.73 integrating for two protons was due to the presence of furan ring. Two doublets observed in the range ä 8.12 – 8.38 was due to para substituted aromatic protons. A sharp peak at ä 9.69 was due to the presence of aldehydic proton. This proves that the compounds formed are same in both methods.

Conclusions: In short we have synthesized 5-Substituted-furan-2-aldehyde and 5-substituted-furan-2-carboxylic acids which can be used to build up different biologically active molecules. Ceric ammonium nitrate is cheap and stable reagent.

Acknowledgements: KSB is thankful to CSIR, New Delhi for the financial support in the form of Junior Research Fellowship.

References:

1. H.A. Burch, R.E. White, G. C. Wright and M. M. Goldenberg, J. Pharm. Sci, **69**, 107 (1980).
2. K. Hirauo, S. Yoshina, K. Okumura and I. Suzuka, Bull. Chem. Soc. Japan, **40**, 2229 (1967).
3. B. S. Holla and M. K. Shivananda, Farmaco., **51**, 785(1996).
4. B.S. Holla, M. K. Shivananda, M. S. Shenoy and G. Antony, Farmaco., **53**, 531(1998).
5. T. Novinson, R. Hanson, M.K. Dimmit, L. N. Simon, R.K Robins and D. E. O'Brien, J. Med. Chem., **17**, 645 (1974).
6. R. P. Rao, R.K Robins and D. E. O'Brien, J. Heterocycl. Chem., **10**, 1021 (1973).
7. J. Kobe, R.K Robins and D. E. O'Brien, J. Heterocycl. Chem., **11**, 199 (1974).
8. C. S. Rondestvedt, Org. React., **24**, 225 (1976).
9. G. A. Molander, Chem. Rev., **92**, 29 (1992).
10. V.A.J. Moreno, I. Robina, B.F.G. Fernindez and J. Fuentes, Tetrahederon Lett., **39**, 9271 (1998).
11. S. Poigny, M. Guyot and M. Samadi, Tetrahederon, **54**, 14791 (1998).
12. A.B. Paolobelli, R. Ruzziconi, P. Lupattelli, P. Scafato and C. Spezzacatena, J. Org. Chem., **64**, 3364 (1999).
13. J.R. Hwu, S.S. Shiao, J. Org. Chem., **60**, 856 (1995).
14. L. Grossi and S. Strazzari, J. Org. Chem., **65**, 2748 (2000).
15. H. Akashi and K. Oda, Rep. Inst. Chem. Res., Kyoto Univ., **19**, 93(1949); Chem. Abstr. **45**, 7519h (1951).

Received on June 19, 2003.