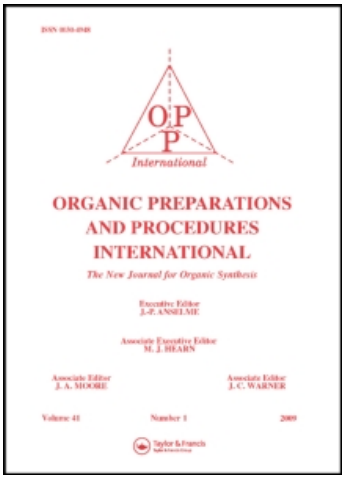


Organic Preparations and Procedures International
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t902189982

SYNTHESIS OF 2-CYANO-3-DIMETHYLAMINO-*N*-PHENYLACRYLAMIDES USING THE VILSMEER REACTION

S. Selvi[a]; P. T. Perumal[a]
[a] Organic Chemistry Division, Central Leather Research Institute, Chennai, INDIA

To cite this Article Selvi, S. and Perumal, P. T.(2001) 'SYNTHESIS OF 2-CYANO-3-DIMETHYLAMINO-*N*-PHENYLACRYLAMIDES USING THE VILSMEER REACTION', Organic Preparations and Procedures International, 33: 2, 194 — 198
To link to this Article: DOI: 10.1080/00304940109356589
URL: http://dx.doi.org/10.1080/00304940109356589

20. J. Morey and A. Frontera, *J. Chem. Ed.*, **72,** 63 (1995).

21. J. Morey, J. M. Saa, *Tetrahedron*, **49**, 105 (1993).

22. F. Toda and T. Shigemasa, *J. Chem. Soc., Perkin Trans., I*, 209 (**1989**).

23. F. Toda, H. Takumi and M. Akehi, *J. Chem. Soc., Chem. Commun.*, 1270 (**1990**).

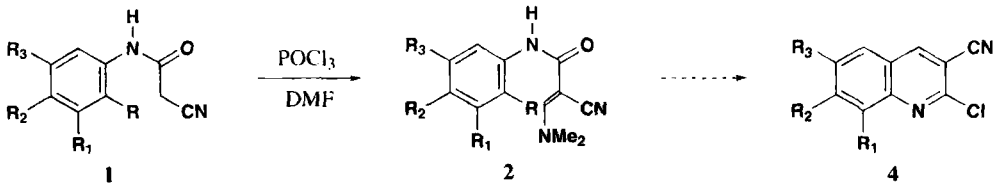
****

SYNTHESIS OF 2-CYANO-3-DIMETHYLAMINO-*N*-PHENYLACRYLAMIDES USING THE VILSMEIER REACTION

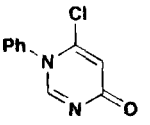
Submitted by S. Selvi and P. T. Perumal*
(12/05/00)

Organic Chemistry Division
Central Leather Research Institute, Adyar, Chennai - 600 020, INDIA
Fax No:91-044-491 1589;E-Mail:ptperumal@hotmail.com

The Vilsmeier reaction involves the electrophilic substitution of halomethyleniminium salts, on suitable carbon nucleophiles such as electron-rich aromatic compounds,[1] alkene derivatives,[2] activated methyl or methylene compounds.[3] Our group has been exploiting the Vilsmeier reaction as the main route or one of the steps in the synthesis of heterocyclic and carbocyclic compounds.[4] During the course of our work, we required 2-chloro-3-cyanoquinolines (**4**) for some fungicidal activity studies related to leather. A search of the literature revealed that 2-cyano-3-(dimethylamino)-*N*-phenylacrylamides (**2**) are excellent precursors to cyanoquinolines.[5,6] Such compounds have been prepared by the action of Vilsmeier reagent or triethyl orthoformate on cyanoacetanilides (**1**). The first method involving the reaction of cyanoacetanilide with DMF/$POCl_3$ at 90° for 5 h. gave a very low overall yield (< 26%) of (**2a**) together with 12% yield of pyrimidine derivative (**3**) thus making this route unattractive.[7] The second method reported by Adams and Adams[6] involves the reaction of a mixture of triethyl orthoformate and DMF with cyanoacetanilides in the presence of catalytic amount of *p*-toluenesulfonic acid at 120° for 20 h. In an effort to find milder conditions for this purpose, we carried out the Vilsmeier reaction on cyanoacetanilides using DMF/$POCl_3$ at various temperatures as the temperature plays a very important role in determining the nature of the products and yields. We envisaged that better yields of cyanoacrylamides could be obtained by conducting the Vilsmeier reaction on cyanoacetanilides at lower temperature rather than heating at 100°.



2a) R = R_1 = R_2 = R_3 = H
2b) R = R_1 = R_3 = H; R_2 = CH_3
2c) R = R_3 = CH_3; R_1 = R_2 = H
2d) R = C_2H_5; R_1 = R_2 = R_3 = H
2e) R = R_2 = R_3 = H; R_1 = OCH_3
2f) R = R_1 = R_3 = H; R_2 = OCH_3
2g) R = R_1 = R_3 = H; R_2 = Cl
2h) R = R_2 = R_3 = H; R_1 = Cl
2i) R = R_1 = R_3 = H; R_2 = NO_2
2j) R = R_1 = R_2 = R_3 = H; R = COOH
2k) R = R_1 = R_3 = H; R_2 = Cl; R = COOH



3

Various *N*-arylcyanoacetamides (**1**) required for this study were prepared by heating ethyl cyanoacetate with substituted anilines for about 4-5 h. in oil bath at 100° and were then subjected to Vilsmeier reaction at room temperature, 45° and 60°. Higher yields of cyanoacrylamides (**2**) were obtained by stirring the reaction mixture at room temperature for 3-4 h. rather than at elevated temperature. At 90°, low yields (below 24%) resulted. This method does not require any drastic experimental conditions and appears to be very simple compared to other methods.[5,6] The results are summarized in the Table.

EXPERIMENTAL SECTION

Mps are uncorrected. Infrared spectra were recorded as KBr pellets on a Nicolet Impact 400 spectrometer. Nuclear magnetic resonance spectra were determined on a Brucker spectrometer, at 300 MHz (PMR) and at 75 MHz (^{13}C NMR). Mass spectra were obtained on a Hewlett Packard 5890 Series II with an HP 5971A mass selective detector.

Table. Yields, mps, Analyses and NMR Spectral Data of **2a-k**

Cmpd[a]	Yield (%)	mp (°C)	Analysis (Found) C	H	N	^{1}H NMR	^{13}C NMR
2a	84	154-156	66.96 (66.72)	6.09 (6.01)	19.52 (19.69)	7.87 (s, 1H), 7.64 (s, 1H), 7.52 (d, *J* = 7.8 Hz, 2H),7.31 (t, *J* = 7.6 Hz, 2H), 7.09(t, *J* = 7.3 Hz, 1H), 3.36 (s, 3H), 3.21 (s, 3H)	162.96, 156.66, 137.99, 128.88, 123.98, 120.06, 119.72, 71.24, 47.50, 38.49
2b	90	174-177	68.10 (68.32)	6.59 (6.93)	18.33 (18.01)	7.85 (s, 1H), 7.59 (s, 1H), 7.39 (d, *J* = 7.8 Hz, 2H), 7.11 (d, *J* = 7.8 Hz, 2H), 3.35 (s, 3H), 3.20 (s, 3H), 2.31 (s, 3H)	162.92, 156.63, 135.48, 133.64, 129.44, 120.15, 119.86, 71.29, 47.53, 38.53, 20.84

Table. Continued...

Cmpd[a]	Yield (%)	mp (°C)	Analysis (Found) C	H	N	^{1}H NMR	^{13}C NMR
2c	82	139-141	69.11 (69.17)	7.04 (7.07)	17.27 (17.23)	7.85 (s, 1H), 7.71 (s, 1H), 7.54 (s, 1H), 7.05 (d, J = 7.6 Hz, 1H), 6.86 (d, J = 7.6 Hz, 1H), 3.34 (s, 3H), 3.18 (s, 3H) 2.31 (s, 3H), 2.24 (s, 3H)	162.79, 156.35, 136.32, 136.23, 129.86, 125.61, 125.55, 122.91, 119.74, 71.17, 58.42, 38.63, 21.02, 17.58
2d	60	101-103	69.11 (69.19)	7.04 (7.14)	17.27 (17.21)	7.86 (s, 1H), 7.84 (s, 1H), 7.22 (t, J = 8.6 Hz, 1H), 7.19 (t, J = 6.0 Hz, 1H), 7.08 (d, J = 7.1 Hz, 2H), 3.34 (s, 3H), 3.18 (s, 3H) 2.62 (q, J = 7.4 Hz, 2H), 1.87 (t, J = 7.4 Hz, 3H)	163.02, 156.49, 135.33, 134.71, 128.51, 126.54, 124.91, 122.94, 119.81, 71.30, 47.41, 38.49, 24.34, 13.82
2e	87	150-154	63.66 (63.61)	6.16 (6.20)	17.13 (17.09)	8.41 (s, 1H), 8.31 (d, J = 6.8 Hz, 1H), 7.84 (s, 1H), 7.04-6.86 (m, 3H), 3.89 (s, 3H), 3.34 (s, 3H), 3.20 (s, 3H)	162.77, 156.49, 148.25, 128.06, 123.34, 120.92, 119.59, 119.48, 109.97, 71.96, 55.87, 47.51, 38.54
2f	82	168-170	63.66 (63.62)	6.16 (6.18)	17.13 (17.14)	7.86 (s, 1H), 7.55 (s, 1H), 7.41 (d, J = 8.6 Hz, 2H), 6.86 (d, J = 8.6 Hz, 2H), 3.78 (s, 3H), 3.36 (s, 3H), 3.21 (s, 3H)	162.94, 156.51, 156.30, 131.04, 122.10, 119.82, 114.07, 71.16, 55.42, 47.45, 38.48
2g	78	196-197	57.72 (57.64)	4.84 (4.80)	16.83 (16.72)	7.83 (s, 1H), 7.60 (s, 1H), 7.44 (d, J = 8.6 Hz, 2H), 7.14 (d, J = 8.6 Hz, 2H), 3.35 (s, 3H), 3.20 (s, 3H)	163.00, 156.73, 136.63, 129.42, 128.91, 121.29, 119.62, 71.14, 47.60, 38.57
2h	75	166-170	57.72 (57.81)	4.84 (4.82)	16.83 (16.79)	7.86 (s, 1H), 7.68 (s, 1H), 7.05-7.23 (m, 4H), 3.37 (s, 3H), 3.20 (s,3H)	163.08, 156.84, 139.19, 134.55, 129.84, 124.01, 120.17, 119.55, 117.98, 71.08, 47.64, 38.59

Table. Continued...

Cmpd[a]	Yield (%)	mp (°C)	Analysis (Found) C	H	N	^{1}H NMR	^{13}C NMR
2i	40	198-200	55.38 (55.19)	4.65 (4.54)	21.53 (21.68)	8.56 (s, 1H), 8.23 (s, 1H), 8.12 (d, J = 8.4 Hz, 2H, 7.81(d, J = 8.4 Hz, 2H), 3.30 (s, 3H), 3.18 (s, 3H)	164.21, 157.02, 145.96, 124.77, 119.37, 118.72, 109.89, 71.34, 47.10, 38.17
2j	45	204-206	60.23 (60.02)	5.05 (5.14)	16.21 (16.34)	11.57 (s, 1H), 8.57 (m, 2H), 7.76 (t, J = 7.5 Hz, 2H), 7.34-7.40 (m, 2H), 3.37 (s, 3H), 3.24 (s,3H)	161.32, 158.66, 155.39, 147.70, 136.76, 128.04, 125.99, 125.28, 117.35, 114.98, 69.92, 47.67, 38.60
2k	50	229-230	53.16 (53.01)	4.12 (4.23)	14.31 (14.48)	11.65 (s, 1H), 8.05 (s, 1H), 7.74 (s, 1H), 7.67 (s, 1H),7.55 (d, J = 9.0 Hz, 1H), 7.12 (d, J = 9.0 Hz, 1H), 3.23 (s, 3H), 3.11(s, 3H)	160.12, 157.11, 154.89, 145.86, 136.0, 128.88, 126.65, 126.20, 116.65, 115.72, 68.93, 47.0, 38.25

a) All were isolated as yellow crystalline solid.

Typical Experimental Procedure for Compounds 2a-h.- To a solution of an *N*-aryl cyanoacetamide (0.005 mol) in 6 mL DMF and kept in ice cold condition was added 1.4 mL of $POCl_3$ (0.015 mol) slowly with stirring. The reaction mixture was allowed to attain room temperature and stirred for 3-4 h. The residue was then poured into crushed ice, and neutralized with 10% sodium hydroxide. The crude product obtained was collected, washed with water and dried. The compounds were purified by recrystallization from an ethyl acetate and petroleum ether mixture.

Acknowledgement: One of the authors (S.S) is thankful to Council of Scientific and Industrial Research, New Delhi for financial support.

REFERENCES

1. G. Jones and S. P. Stanforth, *Org. React.*, **49**, 1 (1997).

2. C. Jutz, in *"Advances in Organic Chemistry"* ,Vol. 9, p.225, E. C. Taylor, Ed., John Wiley & Sons, New York, 1976.

3. C. M. Marson, *Tetrahedron*, **48**, 3659 (1992).

4. a) V. J. Majo and P. T. Perumal, *J. Org. Chem.*, **63**, 7136 (1998); b) S. Selvi and P. T. Perumal, *Indian J. Chem. Sec. B*, **39B**, 163 (2000); c) M. Venugopal, B. Balasundaram and P. T. Perumal, *Synth. Commun.*, **23**, 2593 (1993); d) V. J. Majo and P. T. Perumal, *J. Org. Chem.*, **61**, 6523 (1996).

5. O. Meth-Cohn, B. Narine and B. Tarnowski, *J. Chem. Soc. Perkin Trans. I*, 1537 (**1981**).

6. D. R. Adams and C. Adams, *Synth. Commun.*, **20**, 469 (1990).

7. a) T. Hirota, T. Koyama, T. Nanba and M. Yamato, *Chem. Pharm. Bull.*, **25**, 2838 (1977); b) T. Koyama, T. Hirota, Y. Shinohara, M. Yamato and S. Ohmori, *ibid.*, **23**, 497 (1975).

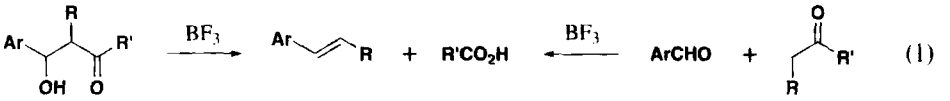
****

BORON TRIFLUORIDE MEDIATED, ONE-POT SYNTHESIS OF 3-METHYL-1,2-DIHYDRONAPHTHALENES

Submitted by Rama R. Malladi and George W. Kabalka*
(11/06/00)

Departments of Chemistry and Radiology
The University of Tennessee, Knoxville, TN 37996-1600

During the course of an investigation involving the stereoselective synthesis of 1,3-diols by reduction of β-hydroxyketones, a number of the prerequisite ketones were prepared *via* aldol condensations.[1] We discovered an unprecedented boron trifluoride initiated cleavage during this study when boron trifluoride was used as an aldol catalyst in non-ethereal solvents. The new cleavage reaction resulted in the formation of (*E*)-arylalkenes and carboxylic acids.[2,3] It was then found that this new boron trifluoride initiated Aldol-Grob reaction sequence could be carried out in a tandem fashion starting from aromatic aldehydes and ketones (*Eq. 1*).[4,5]



(1)

During the investigation of the new boron trifluoride catalyzed Aldol-Grob reaction, we discovered a novel reaction involving the addition of the starting aromatic aldehydes to the product styrenes in the presence of the acetic acid complex of boron trifluoride [6] followed by a Friedel-Crafts cycloalkylation (*Eq. 2*).[7-9]