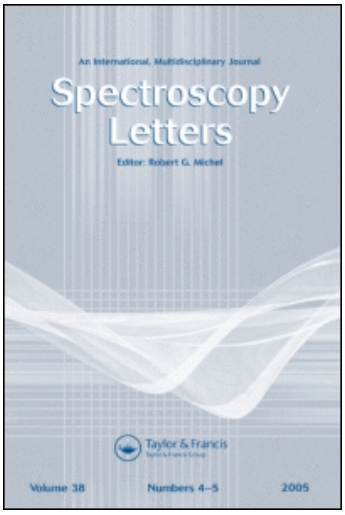


Spectroscopy Letters
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713597299

STRUCTURAL ELUCIDATION AND ^{1}H-NMR, ^{13}C-NMR, AND MASS SPECTROSCOPIC STUDY OF NOVEL 4-CHLORO-3-FORMYL-2(VINYL-1-OL) QUINOLINES AND 3-FORMYL-4-HYDROXY-2-METHYL QUINOLINES

R. Nandha Kumar[a]; T. Suresh[a]; P. S. Mohan[a]
[a] Department of Chemistry, Bharathiar University, Coimbatore, Tamil Nadu, India

Online publication date: 10 August 2002

To cite this Article Kumar, R. Nandha , Suresh, T. and Mohan, P. S.(2002) 'STRUCTURAL ELUCIDATION AND ^{1}H-NMR, ^{13}C-NMR, AND MASS SPECTROSCOPIC STUDY OF NOVEL 4-CHLORO-3-FORMYL-2(VINYL-1-OL) QUINOLINES AND 3-FORMYL-4-HYDROXY-2-METHYL QUINOLINES', Spectroscopy Letters, 35: 5, 741 — 750
To link to this Article: DOI: 10.1081/SL-120014944
URL: http://dx.doi.org/10.1081/SL-120014944

MARCEL DEKKER, INC. • 270 MADISON AVENUE • NEW YORK, NY 10016

SPECTROSCOPY LETTERS
Vol. 35, No. 5, pp. 741–750, 2002

STRUCTURAL ELUCIDATION AND ^{1}H-NMR, ^{13}C-NMR, AND MASS SPECTROSCOPIC STUDY OF NOVEL 4-CHLORO-3-FORMYL-2(VINYL-1-OL) QUINOLINES AND 3-FORMYL-4-HYDROXY-2-METHYL QUINOLINES

R. Nandha Kumar, T. Suresh, and P. S. Mohan*

Department of Chemistry, Bharathiar University
Coimbatore, 641 046, Tamil Nadu, India

ABSTRACT

The Vilsmeier Haack reaction upon 4-hydroxy-2-methyl quinolines yielded some unprecedented compounds. Elucidation of the structure of hitherto unknown novel 4-chloro-3-formyl-2(vinyl-1-ol)quinolines and 3-formyl-4-hydroxy-2-methyl quinolines by NMR and Mass Spectroscopic methods is reported.

Key Words: 4-Chloro-3-formyl-2(vinyl-1-ol)quinolines; 3-Formyl-4-hydroxy-2-methyl quinolines; Structural elucidation; ^{1}H-NMR; ^{13}C-NMR; Mass spectroscopy

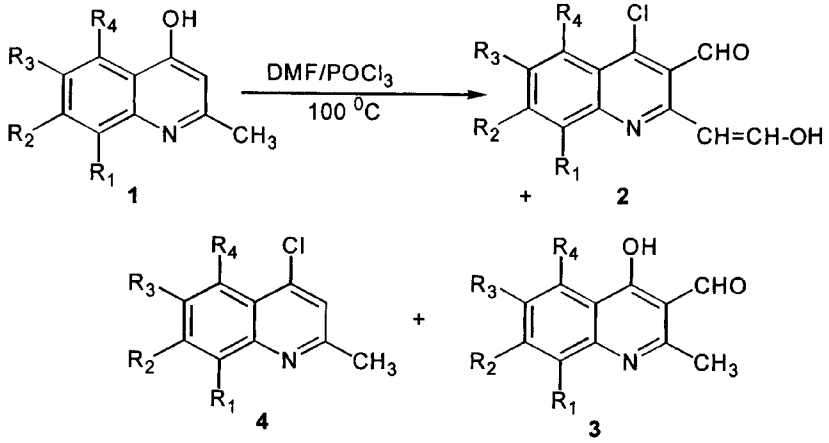
*Corresponding author. Fax : +91+0422-422387; E-mail: ps_mohan_in@yahoo.com

DOI: 10.1081/SL-120014944 0038-7010 (Print); 1532-2289 (Online)

INTRODUCTION

The Vilsmeier Haack reagent is an important synthetic tool of organic chemistry, which provides a facile entry in to large number of heterocyclic systems. The reactive species in the above case is the *in situ* generation of the halomethyleniminium salts derived from the action of acid chlorides on *N,N*-disubstituted formamides.[1,2] Besides the formylation of the reactive aromatic and hetero aromatic substrates,[3] by this Vilsmeier Haack reagent, their versatility has been widely acknowledged as an activating agent for acylhalo addition[4] and ring annulation.[5–8] A wide spectrum of newer heterocycles of interesting biological importance have been synthesized by the application of this potential reagent have been reported.[9–15]

Our endeavours, ended up with some active intermediates 4-chloro-3-formyl-2(vinyl-1-ol)quinolines and 3-formyl-4-hydroxy-2-methylquinolines by applying this Vilsmeier Haack reaction on 4-hydroxy-2-methyl quinolines[16] (Scheme I). These active and unprecedented intermediates paves a path for the construction of newer heterocycles and their biological screening are of future interest. Hence, the structural elucidation of **2** and **3**



2,3 & 4 a. $R_1 = R_2 = R_3 = R_4 = H$
b. $R_2 = R_3 = R_4 = H$, $R_1 = CH_3$
c. $R_1 = R_3 = R_4 = H$, $R_2 = CH_3$
d. $R_1 = R_2 = R_4 = H$, $R_3 = Cl$
e. $R_2 = R_3 = H$, $R_2 = R_4 = CH_3$

Scheme I.

Table 1. ^{1}H-NMR Spectra of Compounds **2(a–e)**

Compound	Chemical Shift, δ/ppm (J, Hz)						
2a	C_8-H	C_7-H	C_6-H	C_5-H	C_3-CHO	C_2-vinylic protons	C_2-vinylic –OH
	7.6 d, J = 8.1	7.7 t, J = 8.3	7.9 t, J = 7.3	8.2 d, J = 8.3	9.2 s	9.4 & 9.6 2s	16.5 bs
2b	C_8-CH_3	C_7-H	C_6-H	C_5-H	C_3-CHO	C_2-vinylic protons	C_2-vinylic –OH
	2.8 s,	7.7 d, J = 7.16	7.5 t, J = 7.92	8.1 d, J = 8.24	9.2 s	9.4 & 9.5 2s	16.5 bs
2c	C_8-H	C_7-CH_3	C_6-H	C_5-H	C_3-CHO	C_2-vinylic protons	C_2-vinylic –OH
	7.8 s	2.6 s	7.6 d, J = 7.56	8.1 d, J = 8.16	9.2 s	9.3 & 9.5 2s	16.5 bs
2d	C_8-H	C_7-H	—	C_5-H	C_3-CHO	C_2-vinylic protons	C_2-vinylic –OH
	7.5 d, J = 7.96	7.3 d, J = 7.68	—	8.1 s	9.2 s	9.3 & 9.5 2s	16.5 bs
2e	C_8-CH_3	C_5-CH_3	C_6-H	C_7-H	C_3-CHO	C_2-vinylic protons	C_2-vinylic –OH
	2.6 s		7.6 d, J = 7.46	7.9 d, J = 7.96	9.3 s	9.4 & 9.5 2s	16.5 bs

Table 2. ^{1}H-NMR Spectra of Compounds **3(a–e)**

Compound	Chemical Shift, δ/ppm (J, Hz)						
3a	C_8-H	C_7-H	C_6-H	C_5-H	C_3-CHO	C_2-CH_3	C_4-OH
	7.3	7.5	7.7	8.2	9.4	2.4	14.1
	d, J = 7.84	t, J = 7.58	t, J = 7.6	d, J = 8.28	s	s	bs
3b	C_8-CH_3	C_2-CH_3	C_6-H	C_5-H	C_3-CHO	C_7-H	C_4-OH
	2.6 s		7.4	8.0	9.3	7.6	15.3
			t, J = 7.6	d, J = 8.24	s	d, J = 7.28	bs
3c	C_7-CH_3	C_2-CH_3	C_6-H	C_5-H	C_3-CHO	C_8-H	C_4-OH
	2.5 s		7.6	8.0	9.4	7.8	15.1
			d, J = 7.14	d, J = 8.20	s	s	bs
3d	C_8-H	C_7-H	—	C_5-H	C_3-CHO	C_2-CH_3	C_4-OH
	7.7	7.4	—	8.2	9.4	2.5	14.2
	d, J = 7.64	d, J = 8.76		s	s	s	bs
3e	C_8-CH_3	C_5-CH_3	C_2-CH_3	C_7-H	C_3-CHO	C_6-H	C_4-OH
		2.7		7.7	9.2	7.5	14.5
		s		d, J = 7.68	s	d, J = 7.84	bs

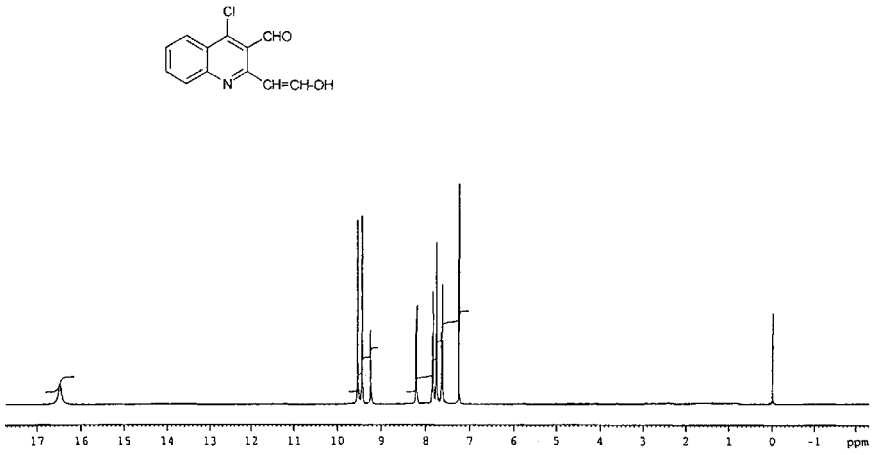


Figure 1. ^{1}H-NMR spectrum of 4-chloro-3-formyl-2(vinyl-1-ol)quinoline (400 MHz).

and their derivatives should gain much more importance. This paper describes the study and structural elucidation of **2(a–e)** and **3(a–e)** by ^{1}H-NMR, ^{13}C-NMR and Mass spectroscopy.

EXPERIMENTAL

Reagent grade ethylacetoacetate, aniline, diphenylether, phosphorous oxychloride and dimethylformamide were used after usual purification methods. Similarly, the solvents such as petroleum ether, ethyl acetate, benzene were purified by standard reported procedures. The reactions are performed under dry condition at 100°C for stipulated period of time. Reaction sequences were inferred through thin layer chromatography techniques.

^{1}H-NMR spectra of all the products obtained were recorded in a AMX-400 MHz spectrometer in $CDCl_3$ solution; Chemical shifts are expressed in ppm (δ) relative Tetra methyl silane (TMS), coupling constants (J) in Hz and signal multiplicities are represented by bs (broad singlet), s (singlet), d (doublet) and t (triplet). ^{13}C-NMR were also recorded on the same AMX-400 MHz spectrometer with Tetra methyl silane (TMS) as internal standard. The mass spectra were recorded on a Jeol JMS-D-300 mass spectrometer.

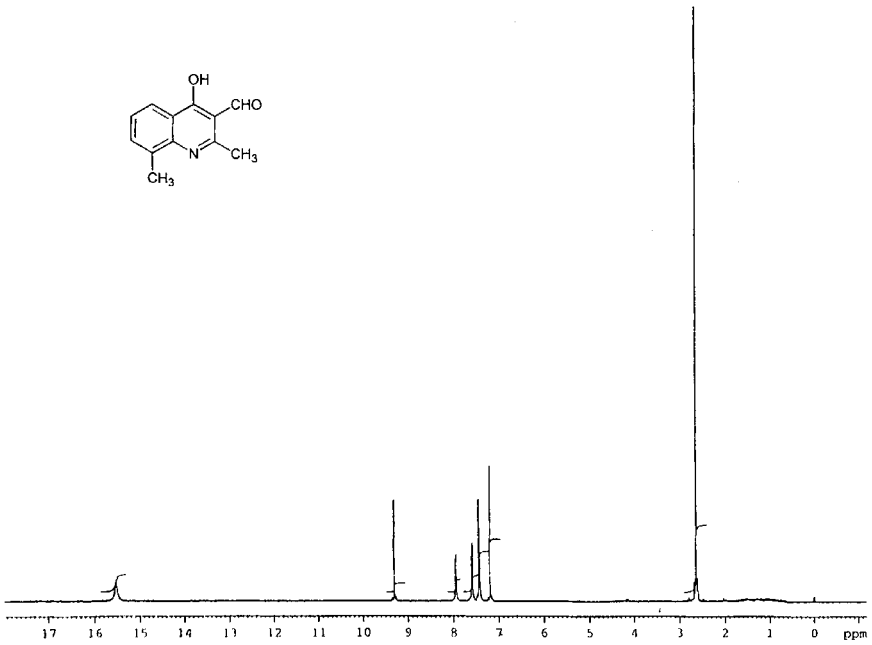


Figure 2. ^{1}H-NMR spectrum of 3-formyl-4-hydroxy-2,8-dimethylquinolines (400 MHz).

RESULTS AND DISCUSSION

The exclusive products **2(a–e)** and **3(a–e)** have been characterized by analytical and spectroscopic data. The ^{1}H-NMR spectra of the compound **2a** revealed a fine singlet at δ 9.2 for the formyl group. A broad singlet was observed down the field at δ 16.5 due to the vinylic hydroxy group. The very interesting fact here to be inferred is the sharp absorption peaks for the two vinylic protons exhibited two singlets at δ 9.4 and δ 9.6, each of two-proton integration. This may be a second order spectra on observation of the peaks. Hence the two doublets merged to form two singlets of higher intensities and also there might be a rapid proton exchange between the two vinylic protons. The assignment of chemical shifts of the aromatic protons with their respective J values are shown below,

δ 8.2 (d, C_5-H, J = 8.3 Hz)

δ 7.9 (t, C_6-H, J = 7.3 Hz)

δ 7.7 (t, C_7-H, J = 8.3 Hz)
δ 7.6 (d, C_8-H, J = 8.1 Hz)

The following are the chemical shifts (δ/ppm) assigned from the ^{13}C-NMR spectra of compound

Ar-CHO	:	192.41
Vinyl Carbons	:	189.33 & 189.08
Aryl Carbons (C_2, C_3, C_4, C_5, C_6 C_7, C_8, C_9, C_{10})	:	146.24, 137.30, 135.90, 133.32, 126.93, 125.21, 122.61, 119.32 & 118.99

Mass spectrum of the compound registered a molecular ion peak at m/e 234 (16.5%) (M+), m/e 236 (5.2%) (M+2) and fragment ions at m/e 206 (66.7%), 164 (36.5%) and the base peak at m/e 189 (100%) well attests our assignment. Further, the IR and CHN analysis well corroborated the NMR and Mass spectral data. These above spectral details established the compound **2a** as 4-chloro-3-formyl-2(vinyl-1-ol)quinolines.

The ^{1}H-NMR spectra of the compound **3a** furnished a fine and sharp singlet at δ 9.4 for the C_3–formyl group. A broad singlet down the filed at δ

Table 3. ^{13}C-NMR Spectra of Compound **2(a–e)**

	Chemical Shift, (δ/ppm)			
Compound	Aryl–CHO	Vinylic Carbons	Aryl Carbons	Substituted Groups
2a	192.41	189.33, 189.08	146.24, 137.30, 135.90, 133.32, 126.93, 125.21, 122.61, 119.32, 118.99	—
2b	192.35	189.45, 189.01	147.22, 136.94, 133.95, 130.23, 126.61, 126.39, 122.99, 121.96, 118.59	C_8-$\underline{C}H_3$ 18.45
2c	192.28	189.41, 189.09	145.26, 135.68, 134.06, 131.22, 126.28, 126.05, 122.75, 122.34, 119.70	C_7-$\underline{C}H_3$ 19.52
2d	192.27	189.26, 189.08	133.90, 133.21, 129.80, 129.04, 124.41, 121.13, 120.86, 199.87, 118.34	—
2e	192.34	189.38, 189.07	144.34, 136.38, 133.86, 130.95, 127.54, 126.01, 123.11, 122.45, 118.60	C_8- & C_5-$\underline{C}H_3$ 19.80, 18.95

14.1 accounts for the C_4—hydroxyl group. This may be due to the intramolecular hydrogen bonding between the hydroxy moiety and the formyl moiety. There exhibits a fine singlet of three-proton integration at δ 2.4 for the C_2—methyl group. The chemical shift assignment for the aromatic protons with respective J values are shown below,

δ 7.3 (d, 1H, C_8-H, J = 7.84 Hz)

δ 7.5 (t, 1H, C_7-H, J = 7.58 Hz)

δ 7.7 (t, 1H, C_6-H, J = 7.6 Hz)

δ 8.2 (d, 1H, C_5-H, J = 8.28 Hz)

The mass spectrum of the compound registered its molecular ion peak at m/e 187. The IR spectra and the CHN analysis well supported the exclusive results obtained from the NMR and mass spectra studies. The

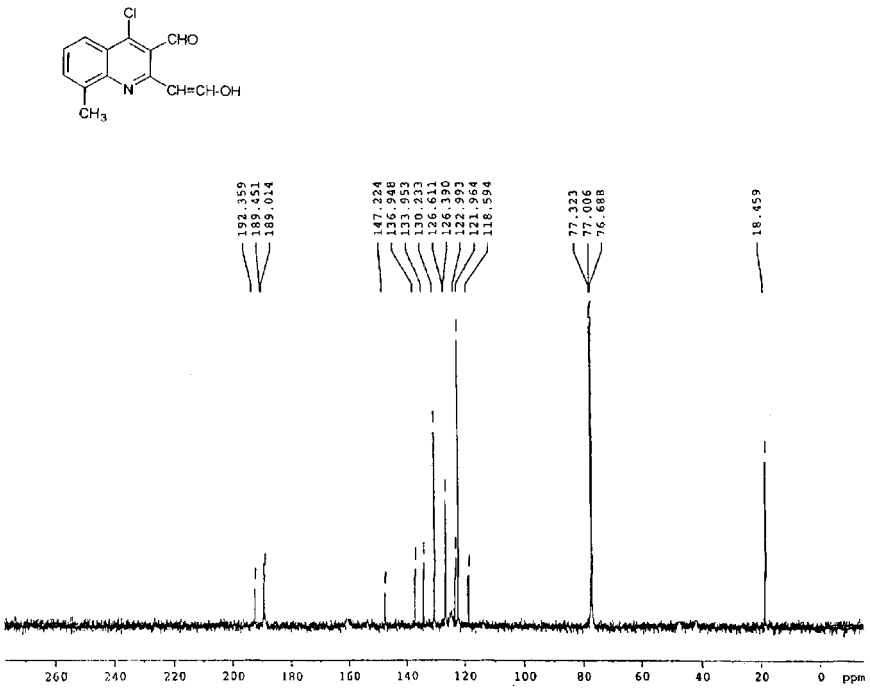


Figure 3. ^{13}C-NMR spectrum of 4-chloro-3-formyl-8-methyl-2(vinyl-l-ol)quinoline (400 MHz).

above spectroscopic details accredited the compound **3a** as 3-formyl–4-hydroxy–2-methylquinoline.

Tables 1 and 2 list the ^{1}H-NMR spectral data of **2(a–e)** and **3(a–e)** respectively with the assignment of chemical shifts. Figures 1 and 2 show the ^{1}H-NMR spectra for compounds **2a** and **3b** respectively. Table 3 lists the ^{13}C-NMR spectral data of **2(a–e)** Fig. 3 shows the ^{13}C – NMR spectra for the compound **2b**.

ACKNOWLEDGMENTS

One of the authors (RNK) thanks Bharathiar University for the award of University Research Fellowship. SIF, Indian Institute of Science, Bangalore and Central Drug and Research Institute, Lucknow supported the spectral details.

REFERENCES

1. Meth-Cohn, O.; Stanforth, S.P. In *Comprehensive Organic Synthesis*; Trost, Fleming, B.M. I., Eds.; Vol. 2, Heathlock, C.H. Vol. Ed.; Pergamon: Oxford, 1991; 777.
2. Ram, S. Singh; Radhey, M. Singh. Synthesis of 4-(N,N-dimethylaminomethylene)-2-alkyl-2-oxazolin-5-ones via Vilsmeier Haack Reagent and their reactions with Various N- and O-nucleophiles. Ind. J. Chem. **2000**, *39B*, 688–693.
3. A) Meth-Cohn, O.; Bramha Narine. A Versatile New Synthesis of Quinolines, Thienopyridines and Related Fused Pyridines. Tet. Lett. **1978**, *23*, 2045–2048. B) Khalid, A. Khan; Aboo Shoeb. Chemistry of Carbostyril: Part-I – Oxidation Reactions of 4-hydroxy-1-methyl-2(1H)-quinolines. Ind. J. Chem. **1985**, *24B*, 62–66. C) Lawrence Bell, H.; Micheal, McGuire; Andrew Freeman, G. Chemistry of 5-pyrimidine carboxyaldehydes. J. Heterocyclic Chem. **1983**, *20*, 41–44.
4. Tamotsu Fujisawa; Sachio Iida; Toshio Sato. A Convenient Method for the Transformation of Alcohols to Alkyl Chlorides using N,N-Diphenylchlorophenylmethyleniminium Chloride. Chemistry Letters **1984**, *27B*, 1173–74.
5. Venugopal, M.; Perumal, P.T. A New Method for the Synthesis of Chloroindenes by Vilsmeier reagent. Synth. Comm. **1991**, *21*, 515–519.
6. Vattoly, J. Majo; Paramasivan, T. Perumal. Intramolecular Cyclization of Azides by Iminium Species. A Novel Method for the Construction of Nitrogen Heterocyles under Vilsmeier Conditions. J. Org. Chem. **1998**, *63*, 7136–7142.

7. David, R.; Adams; Jose, N. Dominguez; Julio, A. Perez. Synthesis of Quinolines by Reaction of Anilinobutenoates with Vilsmeier Reagent. Tet. Lett. **1983**, *24* (5), 517–518.
8. Suresh Chander Roa, M.; Krishna Rao, G.S. Vilsmeier Reaction on some 1-Alkyl-1laryl allyl alcohols: Benzannulation Heading to Biphenyl-mono & Dicarboxaldehydes. Ind. J. Chem. **1998**, *27B*, 213–216.
9. Parameswara Reddy, M.; Krishna Rao, G.S. Applications of Vilsmeier Reaction. 13. Vilsmeier Approach to Polycyclic Aromatic Hydrocarbons. J. Org. Chem. **1981**, *46*, 5371–5373.
10. Alan Katritzky, R.; Charles, M. Marson. Synthesis of a Dodocahydro-18,21-dioxoniakekulene. J. Am. Chem. Soc. **1983**, *105*, 3279–3283.
11. A) Barnela, S.B.; Seshadri, S. Studies in Vilsmeier-Haack Reaction: Part XIX – Synthesis pf Isoxazolo[3,2-b]quinazolone from 2-hydroxy-3-methyl-4-quinazolone. Ind. J. Chem. **1986**, *25B*, 709–711. B) Agnes Horvath; Istan Hermecz; Benjamin Podanyi; Zoltan Meszaros. Nitrogen Bridgehead Compounds, Part 50. Vilsmeier-Haack Acylation of 6,7,8,9-Tetrahydro-4H-pyrido[1,2-a]pyrimidin-4-ones, Part 5. J. Heterocyclic Chem. **1985**, *22*, 593–599.
12. Nohara, A.; Umetani, T.; Sanno, A. Studies on Antinaphylactic Agents-I: A Facile Synthesis of 4-oxo-4H-1-Benzopyran-3-carboxaldehydes by Vilsmeier Reagents. Tetrahedron **1974**, *30*, 3553–3561.
13. Egle Beccalli, M.; Alessandro, Marchesina; Henriette, Molanari. The Vilsmeier Reaction with 3,4-Disubstituted Isozaldin-5-ones. A New Synthesis of 1,3-oxazin-6-ones and 1,3-oxazine-2,6-Diones. Tet. Lett., **1986**, *27* (5), 627–630.
14. Ram Singh, S.; Radhey Singh, M. Synthesis of 4-(N,N-dimethylaminomethylene)-2-alkyl-2-oxazolin-5-ones via Vilsmeier Haack Reagent and their Reactions with Various N- and O-Nucleophiles. Ind. J. Chem. **2000**, *39B*, 688–693.
15. Ali Tasneem, M.M.; Rajanna, K.C.; Sai Prakash, P.K. An Efficient and Facile Synthesis of 2-chloro-3-formyl Quinolines from Acetanilides in Micellar Media by Vilsmeier–Haack Cyclisation. Synlett **2001**, *2*, 251–253.
16. Nandha Kumar, R.; Suresh, T.; Mohan, P.S. Utility of Vilsmeier Haack Reaction: A Novel and Potential Intermediate for the Construction of Newer Nitrogen Heterocycles. Synthetic Communications. **2001** (unpublished results).

Received June 10, 2002
Accepted June 27, 2002