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ORIGINAL ARTICLE

$TiCl_4$: An efficient catalyst for one-pot synthesis of 1,2-dihydro-1-aryl-naphtho-[1,2-*e*][1,3]oxazin-3-one derivatives and their drug score analysis

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One-pot reaction;
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Abstract Multi-component, economical and efficient synthesis of 1,2-dihydro-1-aryl-naphtho[1,2-*e*][1,3]-oxazin-3-one derivatives (**4a**–**k**) with an excellent yield is described through a one-pot condensation of β-naphthol, aromatic aldehydes and urea in presence of catalytic amount of $TiCl_4$ (10 mol%) under conventional heating and microwave irradiation. The role of catalyst in the conversion of reactants to the final compounds is described. All the compounds have been characterized by spectral (IR, ^1H, ^{13}C NMR and Mass) and analytical data. The pharmacological parameters of title compounds were also analyzed for their bioavailability by Osiris property explorer.

1. Introduction

The naphthalene nucleus is commonly found in the compounds of commercial importance. A number of pharmaceutical and agricultural agents have a naphthalene framework. Therefore, the synthesis of aromatic condensed naphthoxazinone derivatives has received considerable attention because of their broad spectrum of biological properties (Patel et al., 1999; EI-Shafei and Badr Eldin, 1994; Girgis, 2000; Waxman and Darke, 2000). Particularly, naphthalene condensed 1,3-oxazin-3-one derivatives have exhibited antibacterial properties (Latif et al., 1982). In spite of their importance from biological and synthetic points of view, relatively few methods describe the synthesis of naphthalene condensed 1,3-oxazin-3-one derivatives (Latif et al., 1982; Ikeda et al., 1980) including condensation of aminoalkylnaphthols as precursors with phosgene in the presence of triethylamine (Szatmari et al., 2004). Carbonyl diimidazole was used instead of phosgene for the preparation of these

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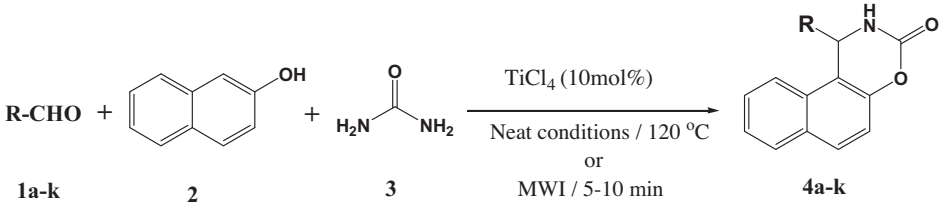
compounds (Cimarelli et al., 2004). Also, it can be synthesized by the multicomponent condensation of aldehyde, β-naphthol and urea in the presence of PTSA as a catalyst (Dabiri et al., 2007). Even though various procedures are reported, disadvantages *viz*., low yields, use of excess of reagents, catalysts and use of toxic organic solvents existed. Therefore, it is necessary to develop an alternative route for the synthesis of naphthalene condensed-1,3-oxazin-3-one derivatives.

In recent years, a tremendous upsurge of interest in various chemical transformation processes by catalysts under mild conditions has offered important advantages in organic synthesis. One of those acidic catalysts is $TiCl_4$ which has been explored as powerful catalyst for various organic transformations such as synthesis of α-amino phosphonates (Thirupathi Reddy et al., 2007), Biginelli reaction (Valizadeh et al., 2008), olefination of aldehydes (Basavaiah and Rao, 2002) and synthesis of imidazo [1,2-*a*]pyridine derivatives (Cai et al., 2006). The reported route is an efficient, convenient and novel method for the condensation of β-naphthol with aldehyde and urea in the presence of $TiCl_4$ (10 mol%) to afford condensed 1,3-oxazin-3-one derivatives in good yields (Scheme 1).

2. Results and discussion

During the course of our investigation, we first explored the effect of solvents and catalysts on a typical condensation of aldehyde (**1a**), β-naphthol (**2**) and urea (**3**) to afford oxazin-3-one derivative (**4a**). It can be emphasized that all the catalysts and solvents used could promote the reaction to a certain extent except $FeSO_4{\cdot}7H_2O$ and $CuSO_4{\cdot}5H_2O$. Although $FeCl_3{\cdot}6H_2O$, $NiCl_2{\cdot}6H_2O$ and $SnCl_4{\cdot}5H_2O$ have exhibited good catalytic activity, the water insoluble solids or salts formed from these catalysts when treated with water make the work-up procedure more complicated. It is obvious that $TiCl_4$ demonstrated superior catalytic activity and was the best catalyst among those examined. However, the reaction could be completed in a short time and afforded the desired product in excellent yield when it was carried out under the solvent free condition. In order to further evaluate the influence of $TiCl_4$, this reaction was carried out using different amounts of $TiCl_4$ (mol%) under neat conditions at 120 °C. Therefore, maximum yield (75%) was possible when titanium chloride was used as a catalyst in the neat condition and the remaining catalysts have exhibited moderate to least activity. It was observed that the reaction hardly proceeded in the absence of $TiCl_4$. The increase in the amount of $TiCl_4$ (mol%) afforded higher yield. When the amount of catalyst increased to 10 mol%, the yield was significantly increased up to 95%. However, an excess of $TiCl_4$ did not help to increase the yield. On the contrary, more than 10 mol% of catalyst resulted in slightly lower yield.

These optimization results prompted us to select 10 mol% of $TiCl_4$ for further study. Moreover, application of microwave irradiation has opened a new prospective in synthetic organic chemistry, not only in terms of high yield and selectivity but also ease of reaction conditions and rate of acceleration (Verma, 2003). Hence, microwaves have been applied to accelerate reaction rates for a variety of chemical transformations. In this line, to our surprise it was observed that, when 4-flourobenzaldehyde (**1b**) was irradiated with β-naphthol (**2**) and urea (**3**) in the presence of $TiCl_4$ (10 mol%) under microwave irradiation, the reaction was completed within 5 min followed by simple work-up to afford 1,2-dihydro-1-aryl-naphtho[1,2-*e*][1,3]-oxazin-3-one (**4b**) (96% of yield) (Table 1).



Scheme 1 Three component coupling reaction of aromatic aldehyde, β-naphthol and urea to yield the title compounds **4a–k.**

Table 1 Synthesis of 1,2-dihydro-1-aryl-naphtho [1, 2-*e*] [1, 3]-oxazin-3-ones **4a–k** in the presence of $TiCl_4$ (10 mol%).

Entry	R1	Method A Time (min)	Yield (%)	Method B Time (min)	Yield (%)	MP (°C)
4a	4-$CH_3C_6H_4$-	55	95	4	96	168–170
4b	4-F-C_6H_4-	55	85	5	96	202–204[#]
4c	3-F-C_6H_4-	60	80	6	86	259–251
4d	C_6H_5-	50	75	5	85	220–222[#]
4e	$CH_2O_2C_6H_3$-	55	72	8	82	232–234
4f	4-OH-C_6H_4-	50	85	10	90	181–183[#]
4g	4-Cl-C_6H_4-	58	70	5	85	210–212[#]
4h	3-Cl-C_6H_4-	62	68	6	82	193–195
4i	4-NO_2-C_6H_4-	70	60	9	80	188–190
4j	2-NO_2-C_6H_4-	65	86	8	78	195–197
4k	4-OCH_3-C_6H_4-	55	75	4	85	186–188[#]

[#] Ikeda et al. (1980).

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In comparison to the solvent free conventional method the yield of the reaction under microwave irradiation is higher and the reaction time is shorter. Therefore, we employed the above conditions for the conversion of various aldehydes (**1a–k**) with β-naphthol **(2)** and urea (**3**) to the corresponding 1,2-dihydro-1-aryl-naphtho[1,2-*e*][1,3]-oxazin-3-one derivatives (**4a–k**) in the presence of $TiCl_4$ (10 mol%) using both the methods. We have also observed that the presence of electron donating or electron withdrawing groups on the aromatic ring of aldehydes did not make any obvious difference in terms of yields of 1,3-oxazin-3-one derivatives. However, the electron withdrawing group $-NO_2$ requires longer time to achieve the yield (Table 1).

The ^1H NMR and ^{13}C NMR spectroscopic data, as well as IR spectra are in good agreement with the proposed structure. The ^1H NMR spectrum of (**4a**) in $CDCl_3$ showed a doublet at δ 6.03 for CH proton and a singlet at δ 6.55 for NH proton along with characteristic multiplets for the aromatic protons at δ 7.87–7.17 which account for the 10 protons. The ^{13}C NMR spectrum of **4a** exhibited 19 signals in agreement with the proposed structure. Also, the mass spectral analyses of all the compounds are consistent with their molecular mass.

2.1. Role of catalyst

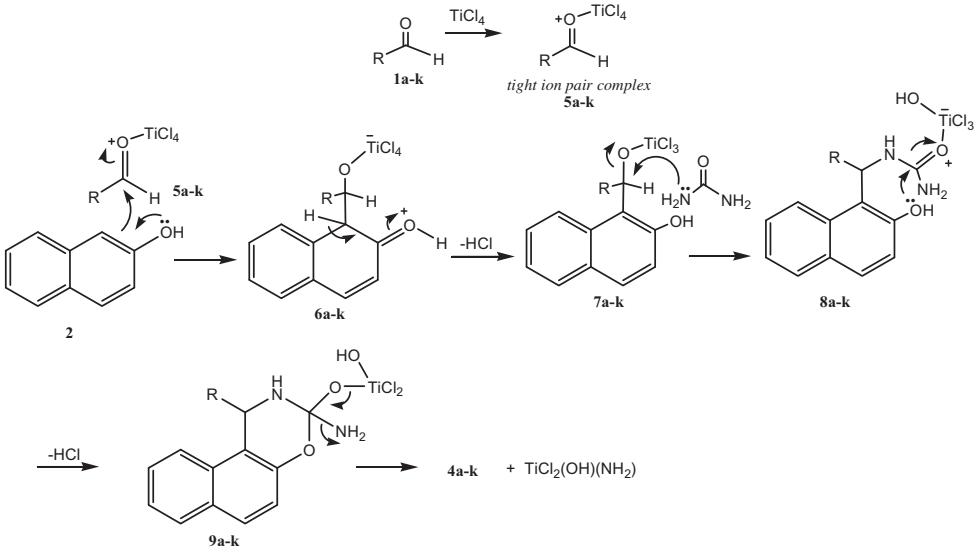
It is evident that the Lewis acids form the tight ion complex with the oxygen atoms of the carbonyl groups (Kattimani et al., 2011). Hence, the reaction initially involves the formation of '*tight ion pair complex*' **5a–k** between $TiCl_4$ (due to electron deficient titanium atom) and non-bonded electrons on the oxygen of the carbonyl group of the aldehyde **1a–k**. Therefore, carbon of the carbonyl group becomes more electrophilic toward nucleophile for the attack by π electrons of β-naphthol **1**. Hence, the attack of π electrons of β-naphthol occurs more readily to form adduct **6a–k** which loses HCl and results in intermediate **7a–k** which further experiences nucleophilic attack of NH_2 of urea to form adduct **8a–k**. Once again the '*ion pair complex*' formed due to the co-ordination of Ti and oxygen of the amide carbonyl favors the nucleophilic attack of electrons on the phenolic OH group and results into the formation of the title compounds **4a–k** in excellent yield, depicted in Scheme 2.

3. Molecular Osiris properties

For a new molecule to qualify as a drug candidate, it has to be analyzed for the parameters set by Lipinski's rule of five using Osiris property explorer (Lipinski, 2004; Taj et al., 2011). Lipinski's rule of five is the thumb rule to evaluate drug score or to determine if chemical compound with a certain pharmacological or biological activity has properties that would make it a likely orally active drug in humans. Interestingly, the title compounds do not violate the Lipinski rule and they fall well in the range as mentioned when evaluated by the Osiris property explorer, and also the drug likeliness in the range −17.62 to −12.28 and drug score of 0–0.24 which will surely lead us to evaluate the compounds experimentally (Table 2). Promising results were shown for compounds **4d**, **4f**, and **4k** with the drug score of 0.20. All the title compounds were shown as safe drugs without any tumorigenic, irritability and reproductive effects as evaluated in Osiris property explorer. However, all the compounds have shown slight mutagenicity.

3.1. Structure activity relationship (SAR) studies

Activity of the molecules obtained from molecular Osiris property explorer was correlated with the structure of the molecule (SAR) (Taj et al., 2011). All the molecules have not shown toxicity risks such as tumorigenicity, effect on the reproductive system and irritability property. However, a slight mutagenic property is observed for all the compounds. Highest penetrative effect (Clog*P*) was shown by the compounds **4a, 4g–i** having the *chloro* group at *ortho* and *meta* positions, *nitro* at *para* position respectively. Compound **4h** having the hydroxyl group at *para* position has exhibited the least penetrative effect. Maximum drug likeliness was exhibited by compound **4g** having the *chloro* group at *para* position and minimum by compound **4c** having the *fluoro* group at *meta* position.



Scheme 2 Proposed mechanism for the formation of title compounds **4a–k** under the influence of $TiCl_4$.

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Table 2 Osiris property explorer for the bioavailability of 1,2-dihydro-1-aryl-naphtho [1, 2-*e*] [1, 3]-oxazin-3-ones (**4a**–**k**).

Entry	Toxicity risks				*ClogP*	Dug likeliness	Drug score
	Mutagenicity	Tumorigenicity	Reproductive effect	Irritability			
4a	+	−	−	−	5.04	−15.80	0.20
4b	+	−	−	−	4.7	−14.62	0.21
4c	+	−	−	−	4.78	−17.62	0.16
4d	+	−	−	−	4.72	−15.80	0.22
4e	+	−	−	−	4.82	−14.26	0.19
4f	+	−	−	−	4.42	−14.03	0.24
4g	+	−	−	−	5.33	−12.80	–
4h	+	−	−	−	5.33	−14.92	0.17
4i	+	−	−	−	5.02	−14.12	0.17
4j	+	−	−	−	4.45	−17.50	0.20
4k	+	−	−	−	4.61	−14.25	0.22

+ mild, + + medium, + + + high, − no toxicity.

Compound **4f** having the hydroxyl group at *para* position showed effective drug score and least activity was shown by compound **4g** *chloro* at *para* position.

4. Conclusions

In the present work $TiCl_4$ as an efficient catalyst is described which converts the starting materials (multi component) into title compounds by using only 10 mol% of the catalyst. The catalyst coordinates with the oxygen atoms of the carbonyl group of aldehyde as well as that of the amide hence supporting the nucleophilic attack as evidenced by the mechanism proposed in Scheme 2. We believe that the above used catalyst in the present methodology addresses the current drive toward synthetic chemistry due to the cheap and easily available substrate, simple workup, high yield, easy handling, non-toxicity and economy of the catalyst.

5. Experimental

The infrared spectra were recorded on a Nicolet impact – 410 FTIR spectrometer using the KBr pellet technique. The NMR spectra were recorded on a Varian 300 MHz spectrometer and chemical shifts are reported in ppm, whereas electron impact mass spectra (EIMS) were recorded on a MI Ver 14 on UIC 002002 EI-70 eV spectrometer and elemental analysis was carried out in Heraus CHN rapid analyzer. Microwave irradiation was carried out using an oven (BPL, 800T model).

*5.1. Synthesis of 1-(aryl)-1,2-dihydro-naphtho[1,2-e][1,3]-oxazin-3-one (**4a**–**k**)*

5.1.1. Method A

A mixture of aldehyde (1 mol), β-naphthol (1 mol), urea (1 mol) and $TiCl_4$ (10 mol%) was heated at 120 °C for the appropriate time according to Table 1. The progress of the reaction was monitored by thin layer chromatography. After completion of the reaction, the reaction mass was cooled to 25 °C, and water was added. The resultant product was collected by filtration, washed with water which was recrystallized from ethyl acetate:hexane (1:3).

5.1.2. Method B

A mixture of aldehyde (1 mol), β-naphthol (1 mol), urea (1 mol) and $TiCl_4$ (10 mol%) was kept in a microwave oven (BPL, 800T model) and irradiated at 450 W for the appropriate time according to Table 1. The progress of the reaction was monitored by thin layer chromatography. After completion of the reaction, the reaction mass was cooled to 25 °C and water was added. The precipitate was filtered off and washed with water; pure product was isolated by recrystallization with ethyl acetate: hexane (1:3).

*5.1.2.1. 1-(p-Tolyl)-1,2-dihydro-naphtho[1,2-e][1,3]oxazin-3-one (**4a**).* mp 168 °C; IR (KBr, cm^{-1}): 3262, 3152, 3076, 1721, 1632, 1595, 1517; ^{1}H NMR: 2.41 (s, CH_3), 6.03 (d, J = 2.6, 1H, CH), 6.55 (s, 1H, NH), 7.16–7.87 (m, 10H, Ar–H); ^{13}C NMR ($CDCl_3$): 23.7, 54.1, 114.8, 117.7, 124.0, 125.9, 127.1, 128.2, 128.4, 129.5, 129.7, 131.1, 131.3, 139.0, 140.2, 148.3, 150.1. MS (EI): *m*/*z* 321 [M+]; Anal. Calcd. for $C_{19}H_{15}NO_2S$: C, 71.00; H, 4.70; N, 4.36. Found: C, 69.80; H, 4.67; N, 4.38.

*5.1.2.2. 1-(4-Fluorophenyl)-1,2-dihydro-naphtho[1,2-e][1,3]-oxazin-3-one (**4b**).* mp 202 °C; IR (KBr, cm^{-1}): 3233, 3063, 2978, 1715, 1605, 1455, 1466; ^{1}H NMR (300 MHz, DMSO-d_6), 6.39 (s, 1H, CH), 6.87 (s, 1H, NH), 6.95–7.89 (m, 10H, Ar–H); ^{13}C NMR (DMSO-d_6): 52.5, 115.0, 1165, 116.8, 116.9, 124.0, 126.5, 128.5, 129.6, 130.2, 131.4, 139.3, 145.9, 154.2, 160.8, 164.0; MS (EI): *m*/*z* 293 [M+]; Anal. Calcd. for $C_{18}H_{12}NFO_2$: C, 73.71; H, 4.12; N, 4.78. Found: C, 73.68; H, 4.14; N, 4.80.

*5.1.2.3. 1-(3-Fluorophenyl)-1,2-dihydro-naphtho[1,2-e][1,3]-oxazin-3-one (**4c**).* mp 259 °C; IR (KBr, cm^{-1}): 3238, 3143, 3063, 2918, 1710, 1598; ^{1}H NMR δ_H (300 MHz, DMSO-d_6), 6.25 (s, 1H, CH), 6.62 (s, 1H, NH), 6.92–7.91 (m, 10H, Ar–H); MS (EI): *m*/*z* 293 [M+]; Anal. Calcd. for $C_{18}H_{12}NFO_2$: C, 73.71; H, 4.12; N, 4.78. Found: C, 73.75; H, 4.10; N, 4.82.

5.1.2.4. 1-Benzo[1,3]dioxol-5-yl-1,2-dihydro-naphtho[1,2-e]-[1,3]oxazin-3-one (4e). mp 232 °C; IR (KBr, cm^{-1}): 3429, 3400, 3060, 2962, 1723, 1603, 1573, 1552, 1487; ^{1}H NMR δ_H (300 MHz, DMSO-d_6), 5.96 (s, CH_2), 6.14 (s, 1H, CH), 6.73–

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8.10 (m, 9H, Ar–H), 8.83 (s, 1H, NH); ^{13}C NMR (DMSO-d_6): 54.3, 102.1, 108.2, 109.1, 114.9, 117.7, 121.2, 124.0, 125.9, 128.2, 129.1, 129.5, 131.1, 131.3, 137.7, 147.8, 148.2, 148.4, 153.7. MS *m*/*z* 319 [M+]; Anal. Calcd. for $C_{19}H_{13}NO_4$: C, 71.47; H, 4.10; N, 4.39. Found: C, 71.45; H, 4.12; N, 4.42.

*5.1.2.5. 1-(3-Chlorophenyl)-1,2-dihydro-naphtho[1,2-e][1,3]-oxazin-3-one (**4h**)*. mp 193 °C; IR (KBr, cm^{-1}): 3210, 3130, 3065, 2958, 1719, 1630, 1509, 1465, 1422; ^{1}H NMR δ_H (300 MHz, DMSO-d_6), 6.28 (s, 1H, CH), 6.84–8.02, (m, 9H, Ar–H), 8.96 (s, 1H, NH); ^{13}C NMR (DMSO-d_6): 54.0, 114.2, 117.7, 123.9, 126.1, 126.4, 127.9, 128.4, 128.9, 129.5, 129.7, 131.3, 131.4, 131.9, 134.3,146.0, 148.4, 150.0; MS (EI): *m*/*z* 311 [M^{2+}], 309 [M^+]; Anal. Calcd. for $C_{18}H_{12}NClO_2$: C, 69.80; H, 3.90; N, 4.52. Found: C, 69.82; H, 3.87; N, 4.55.

*5.1.2.6. 1-(4-Nitrophenyl)-1,2-dihydro-naphtho[1,2-e][1,3]-oxazin-3-one (**4i**)*. mp 188 °C; IR (KBr, cm^{-1}): 3203, 3115, 3020, 2930, 1695, 1610; ^{1}H NMR δ_H (300 MHz, DMSO-d_6), 6.35 (s, 1H, CH), 8.50 (s, 1H, NH), 6.95–8.00 (m, 10H, Ar–H); MS (EI): *m*/*z* 320 [M^+]; Anal. Calcd. for $C_{18}H_{12}N_2O_4$: C, 67.50; H, 3.78; N, 8.75. Found: C, 67.53; H, 3.76; N, 8.76.

*5.1.2.7. 1-(2-Nitrophenyl)-1,2-dihydro-naphtho[1,2-e][1,3]-oxazin-3-one (**4j**)*. mp 195 °C; IR (KB, cm^{-1}): 3210, 3040, 2925, 1702, 1600; ^{1}H NMR δ_H (300 MHz, DMSO-d_6), 6.31 (s, 1H, CH), 8.42 (s, 1H, NH), 6.90–8.21 (m, 10H, Ar–H); MS (EI): *m*/*z* 320 [M^+]; Anal. Calcd. for $C_{18}H_{12}N_2O_4$: C, 67.50; H, 3.78; N, 8.75. Found: C, 67.51; H, 3.80; N, 8.73.

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References

Basavaiah, D., Rao, A.J., 2002. Synth. Commun. 32, 195.
Cai, L., Brouwer, C., Sinclair, K., Cuevas, J., Victor Pike, V.W., 2006. Synthesis 1, 133.
Cimarelli, C., Palmieri, G., Volpini, E., 2004. Can. J. Chem. 82, 1314.
Dabiri, M., Delbari, A.S., Bazgir, A., 2007. Synlett 5, 821.
El-Shafei, H.A., Badr Eldin, S.M., 1994. Egypt J. Microbiol. 27, 353.
Girgis, A.S., 2000. Pharmazie, 466.
Ikeda, K., Morimoto, T., Sekia, M., 1980. Chem. Pharm. Bull., 1178.
Kattimani, P.P., Raikar, S.V., Kamble, R.R., Kariduraganavar, M.Y., Hunnur, R.K., 2011. Main Group Chem. 10, 165.
Latif, N., Mishriky, N., Assad, F.M., 1982. Aust. J. Chem. 35, 1037.
Lipinski, C.A., 2004. Drug Discov. Today Technol. 1, 337.
Patel, M., McHugh J Jr., R., Cordova, C., Labe, R.M., Erickson, V.S., Trainor, G.L., Ko, S.S., 1999. Bioorg. Med. Chem. Lett. 9, 3221.
Szatmari, I., Hetenyi, A., Lazar, L., Fulop, F., 2004. J. Heterocycl. Chem. 41, 367.
Taj, T., Kamble, R.R., Gireesh, T.M., Hunnur, R.K., Marganko p, S.B., 2011a. Eur. J. Med. Chem. 46, 4366. http://dx.doi.org/10.1016/j.ejmech.2011.07.007.
Taj, T., Raikar, S.V., Kamble, R.R., 2011b. Arabian J. Chem.. http://dx.doi.org/10.1016/j.arabjc.2011.01.029.
Thirupathi Reddy, Y., Narsimha Reddy, P., Sunil Kumar, B., Rajput, P., Sreenivasulu, N., Rajitha, B., 2007. Phosphorus, Sulfur Silicon Relat. Elem. 182, 161.
Valizadeh, H., Gholipur, H., Zarrebin, R., Amiri, M., Sabzi, M.R., 2008. Phosphorus, Sulfur Silicon Relat. Elem. 183, 1552.
Verma, R.S., 2003. Advances in Green Chemistry: Chemical Synthesis Using Microwave Irradiation. Astra Zeneca Research Foundation India, Bangalore.
Waxman, L., Darke, P.L., 2000. Antiviral Chem. Chemother. 11, 1.

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