Asian Journal of Chemistry; Vol. 26, No. 23 (2014), 8239-8242

ASIAN JOURNAL OF CHEMISTRY

http://dx.doi.org/10.14233/ajchem.2014.18098

A View of an Unusual Route for Certain Phosphorus Ylide

KHADIJAH M. AL-ZAYDI

Department of Chemistry, Science Faculty for Girls, King Abdulaziz University, Jeddah, P.O. Box 50918, Jeddah 21533, Kingdom of Saudi Arabia

Corresponding author: Tel.: +966 50 567 8718; E-mail: alzaydi_kh@yahoo.com; kalzaydi@kau.edu.sa

Received: 29 May 2014; *Accepted*: 12 August 2014; *Published online*: 15 November 2014; AJC-16333

An abnormal route for the synthesis of (5-(2-(2-cyanophenyl)hydrazono)-2,3-*bis*(methoxycarbonyl)-4-phenylcyclopent-2-enyl)triphenyl phosphonium (**5**) has been patented. The synthesis of compound (**5**) was performed by the reaction of 2-(2-(1,3-dioxo-1-phenylpropan-2-ylidene)hydrazinyl)benzonitrile with dimethylacetylene dicarboxylate in dichloromethane at room temperature for 2 h in order to yield a cyclic intermediate. The subsequent addition of triphenylphosphine afforded the desired product as interesting crystals suitable for X-ray crystallographic analysis. The synthesized compound was characterized based on (FT-IR, NMR, elemental analysis and single crystal X-ray diffraction studies). A possible mechanism for the synthesis was also reported.

Keywords: Phosphorus ylide.

INTRODUCTION

Phosphorus ylides are reactive systems which occur in a significant number of valuable reactions of organic synthesis[1-17]. The development of simple synthetic routes for widely used organic compounds from readily available reagents is one of the major tasks in organic chemistry. Cyclopentene derivatives are currently a matter of interest since many have been found to be of benefit in inhibiting and treating tumors[18].

Compound (5-(2-(2-aryl)hydrazono)-2,3-*bis*(methoxy-carbonyl)-4-phenylcyclo-pent-2-enyl)triphenylphosphonium (**1**) (Fig. 1) is an intermediate for the production of cyclo-pentene derivatives.

Literature survey shows that the major synthetic approach that was used previously to prepare phosphorus ylides is based on the treatment of the phosphonium salt (prepared *via* the reaction of the phosphine with alkyl halide) with base[2-4]. Furthermore, these compounds are generally prepared *via* the Michael addition of phosphorus nucleophiles to activated olefins[19].

It should be mentioned that (5-(2-(2-aryl)hydrazono)-2,3-*bis*(methoxy carbonyl)-4-phenylcyclopent-2-enyl)triphenyl-phosphonium derivatives have been previously synthesized and isolated with difficulty from a mixture of products[20-23]. Therefore, there is a necessity to synthesize this compound in pure form using a more straight forward method. It has been reported that the reaction of 2-(2-(1,3-dioxo-1-phenylpropan-2-ylidene)hydrazinyl)benzonitrile (**2**) with dimethyl-acetylene-dicarboxylate (**3**) in dichloromethane at room temperature gives the intermediate (A) (**Scheme-I**). The subsequent addition of triphenylphosphine resulted in two products[20].

After separation and identification of the obtained products by spectral data and elemental analyses, one of the products was identified as compound **4** (40 %), whereas the other one was identified as compound **5** (60 %), (**Scheme-I**)[20]. Whereas, it was found that one pot addition of reactants **2**, **3** and triphenyl-phosphine in dichloromethane as solvent at room temperature lead to the direct formation of compound (**4**) (**Scheme-I**)[24,25].

EXPERIMENTAL

All melting points were measured on Gallenkamp electro-thermal melting point apparatus and are uncorrected. IR spectra were recorded on KBr disks using a Nicolet Magna 520 FTIR spectrophotometer. ^{1}H NMR and ^{13}C NMR spectra was recorded on a Bruker DPX400 spectrometer at 400 MHz with DMSO-d_6 as solvent and TMS as internal standards; chemical shifts are reported in δ units (ppm). Mass spectra were measured on a Shimadzu GCMS-QP1000 Ex mass spectrometer at 70 eV. Elemental analysis was measured by means of a Perkin Elmer 2400 CHN elemental analyzer flow chart. X-ray crystallography was carried out on a Kappa CCD Enraf Nonius FR 590 diffractometer, National Research Center, Dokki, Cairo, Egypt.

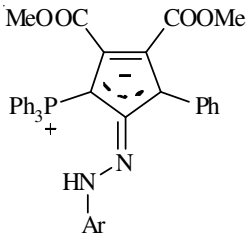
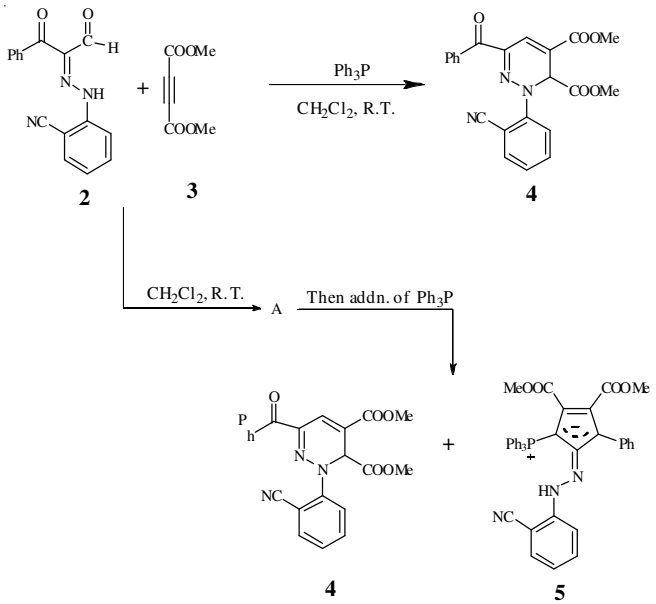


Fig. 1. Intermediate that is used for the production of cyclopentene derivatives



Scheme-I: Normal route for formation of compounds (**4**) and (**5**)

Synthesis of dimethyl 6-benzoyl-2-(2-cyanophenyl)-2,3-dihydropyridazine-3,4-dicarboxylate (4): Dimethylacetylenedicarboxylate (**3**) (0.14 g, 10 mmol) in 10 mL dichloroethane was added to a stirred solution of triphenylphosphine (0.26 g, 10 mmol) and 2-(2-(1,3-dioxo-1-phenylpropan-2-ylidene)hydrazinyl)benzonitrile (**2**) (0.28 g, 10 mmol) in 10 mL dichloroethane, then the reaction mixture was left at room temperature overnight. The solvent was removed and the residue cooled to deposit a solid, m.p. 205-206 ºC; IR (KBr, ν_{max}, cm^{-1}): 2221 (C=N), 1746, 1717 (2C=O ester) and 1673 (C=O ketone); ^{1}H NMR (DMSO-d_6, 400 MHz): δ 3.67, 3.76 (s, 3H, 2OCH_3), 6.61-7.32 (m, 9H, Ar-H) and 7.80 (s, 1H, pyridazine H-5); MS: 403 (M^+); Anal. Calcd. for $C_{22}H_{17}N_3O_5$ (403.39): C, 65.50; H, 4.25; N, 10.42; Found: C, 65.92; H, 4.08; N, 10.42 %.

Synthesis of (5-(2-(2-cyanophenyl)hydrazono)-2,3-*bis*(methoxycarbonyl)-4-phenylcyclopent-2-enyl)triphenylphosphonium (5): A mixture of (0.28 g, 10 mmol) of 2-(2-(1,3-dioxo-1-phenylpropan-2-ylidene)hydrazinyl)-benzonitrile (**3**) and (0.14 g, 10 mmol) dimethylacetylenedicarboxylate (**4**) in 25 mL CH_2Cl_2 was stirred for 2 h at room temperature. Then, triphenylphosphine (0.26 g, 10 mmol) was added and stirring was maintained at room temperature overnight. After evaporating to dryness under vacuum, the resulting solid product was collected by filtration, washed with ethanol, dried and recrystallized from ethanol to give compound **6** as orange crystals: yield (0.59 g, 91 %). m.p. 175-176 ºC; IR (KBr, ν_{max}, cm^{-1}): 3416 (NH), 2229 (C=N), 1746 (C=O, ester); ^{1}H NMR (DMSO-d_6, 400 MHz): δ 2.75 (d, 1H, *J* = 14.4 Hz, cyclopentane H), 3.70 (s, 3H, OCH_3), 3.77 (s, 3H, OCH_3), 6.16-7.92 (m, 24H, Ar-H), 11.22 (s, 1H, NH, D_2O exchangeable). ^{13}C NMR (DMSO-d_6, 100 MHz): δ 45.3, 49.0, 50.6, 50.81, 100.3, 111.5, 113.0, 117.6, 117.6, 121.6, 123.6, 124.3, 126.9, 128.5, 128.6, 132.8, 133.5, 136.5, 142.2, 147.8, 150.5, 116.5 (CN), 165.1, 171.2 (C=O); MS: 650 (M^+); Anal. Calcd. for $C_{40}H_{33}N_3O_4P$ (650.68): C, 73.83; H, 5.11; N, 6.46. Found: C, 73.92; H, 5.08; N, 6.40 %.

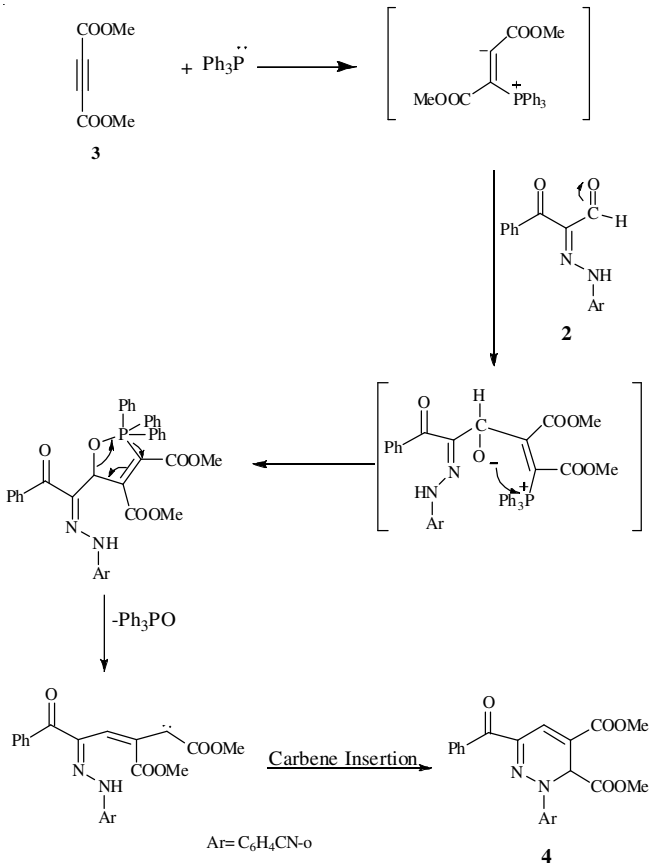
RESULTS AND DISCUSSION

As an extension of our studies, compound **4** was synthesized according to the previously mentioned method[24], and the structure of **4** was confirmed by X-ray diffraction analysis (Table-1 for crystal's data) of a suitable crystal, Fig. 2[26]. The proposed reaction mechanism is described in **Scheme-II**[24].

TABLE-1
CRYSTAL DATA AND STRUCTURE REFINEMENT FOR **4**

Empirical formula	$C_{21}H_{17}N_3O_5$	
Formula weight	391.383	
Temperature	298 K	
Wavelength	0.71073 Å	
Crystal system	Prismatic	
Space group	$C_{2/c}$	
Unit cell dimensions	a = 10.1935 (6) Å	α = 90.00°
	b = 16.9076 (11) Å	β = 98.402 (3)°
	c = 23.211 (2) Å	γ = 90.00°
Volume	3957.4 (5) $Å^3$	
Z	8	
Density (calculated)	1.314 Mg/m^3	
Absorption coefficient	0.10 mm^{-1}	
Δ/σ_{max}	0.039	
$\Delta\rho_{max}$	0.25e$Å^{-3}$	
$\Delta\rho_{min}$	-0.25e$Å^{-3}$	
Theta range for data collection	2.910-18.499°.	
Index ranges	-9 < = h < = 9, -15 < = k < = 15, -20 < = l < = 20	
Reflections collected	2778	
Independent reflections	1073 [R(int) = 0.029]	
Completeness to θ = 18.49°	99.5 %	
Absorption correction	Multi-scan	
Refinement method	Full-matrix least-squares on F^2	
Data/restraints/parameters	1073/0/271	
Goodness-of-fit on F^2	1.001	
Final R indices [I > 3σ(I)]	R1 = 0.033, wR2 = 0.068	
R indices (all data)	R1 = 0.063, wR2 = 0.153	
Absolute structure parameter	Not determined	

Efforts have been directed towards the development of convenient synthetic approaches for the construction of some heterocyclic compounds[22,27]. The method for the synthesis of (5-(2-(2-cyanophenyl)hydrazono)-2,3-*bis*(methoxycar-bonyl)-4-phenylcyclopent-2-enyl)triphenyl phosphonium (**5**) was modified. In this case, the reaction of 2-(2-(1,3-dioxo-1-phenylpropan-2-ylidene)hydrazinyl)benzonitrile (**2**) with dimethylacetylene dicarboxylate (**3**) in dichloromethane was performed at room temperature for 2 h in order to yield a cyclic intermediate.



Scheme-II: Proposed mechanism for the formation of compound **4**

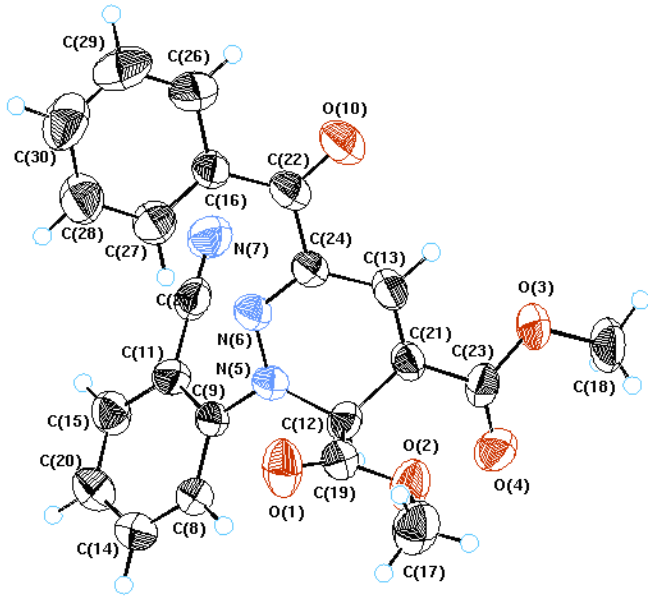
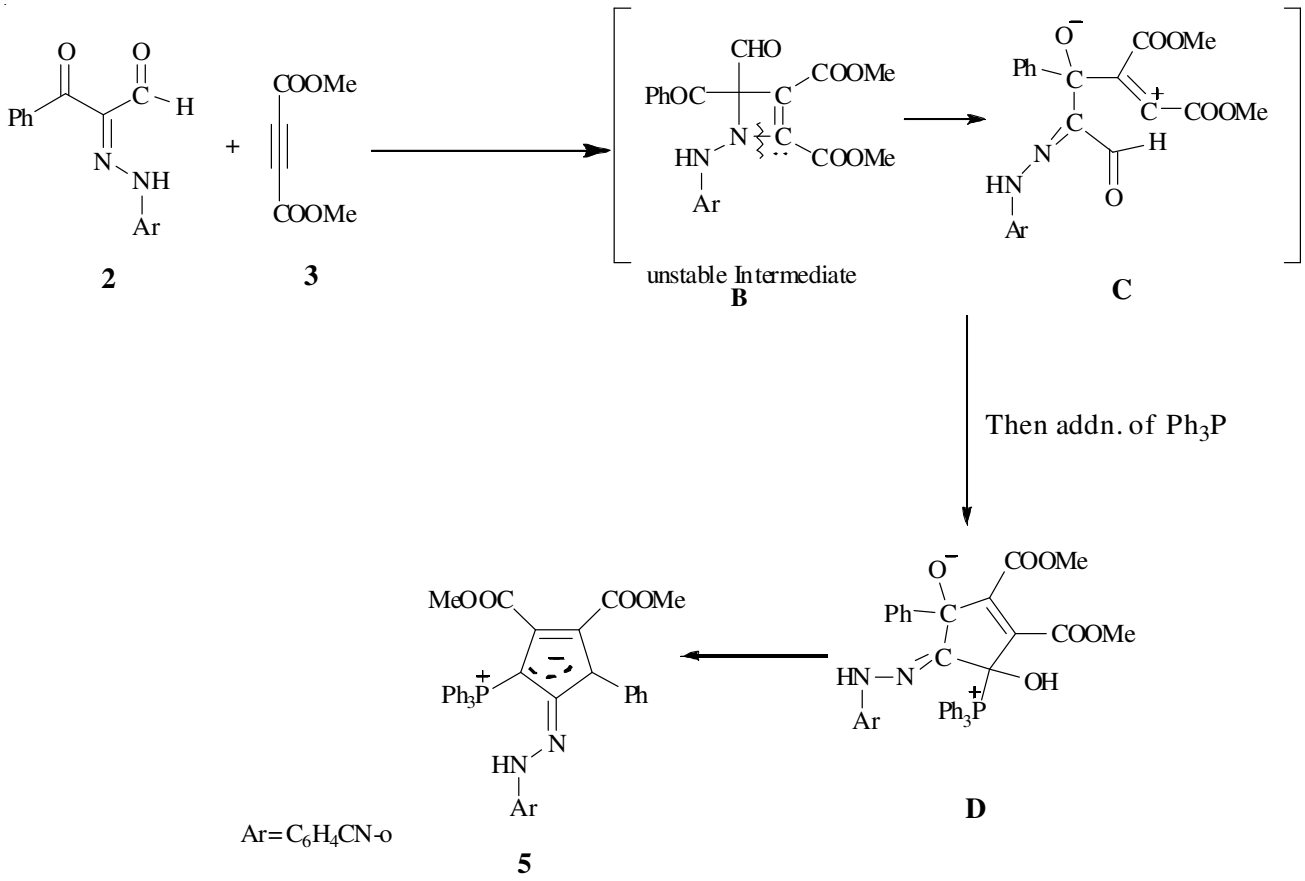


Fig. 2. Ortep of dimethyl 6-benzoyl-2-(2-cyanophenyl)-2,3-dihydropyridazine-3,4-dicarboxylate (**4**)

Afterwards, the addition of triphenylphos-phine to the reaction mixture afforded compound **5** as the sole product (**Scheme-III**).

The structure of compound **5** was confirmed by elemental analysis, spectral data, and X-ray crystallography (Fig. 3)[26]. Single crystal X-ray diffraction of compound **5** adds strong



Scheme-III: Proposed mechanism of the formation of compound **5**

TABLE-2
CRYSTAL DATA AND STRUCTURE REFINEMENT FOR **5**

Empirical formula	$C_{40}H_{30}N_3O_4P$	
Formula weight	647.671	
Temperature	298 K	
Wavelength	0.71073 Å	
Crystal system	Prismatic	
Space group	$P_{21/c}$	
Unit cell dimensions	a = 9.1133 (11) Å	α = 90.00°
	b = 20.945 (3) Å	β = 105.010 (2)°
	c = 17.994 (3) Å	γ = 90.00°
Volume	3317.5 (8) $Å^3$	
Z	4	
Density (calculated)	1.297 Mg/m^3	
Absorption coefficient	0.13 mm^{-1}	
Δ/σ_{max}	0.041	
$\Delta\rho_{max}$	0.71e $Å^{-3}$	
$\Delta\rho_{min}$	-0.96e $Å^{-3}$	
θ range for data collection	2.910-19.980 °.	
Index ranges	-8 <= h <= 8, -20 <= k <= 20, -17 <= l <= 17	
Reflections collected	8620	
Independent reflections	1149 [R(int) = 0.101]	
Completeness to θ = 19.98°	99.3 %	
Absorption correction	Multi-scan	
Refinement method	Full-matrix least-squares on F^2	
Data/restraints/parameters	1149/0/433	
Goodness-of-fit on F^2	1.001	
Final R indices [I>3σ(I)]	R1 = 0.050, wR2 = 0.100	
R indices (all data)	R1 = 0.181, wR2 = 0.164	
Absolute structure parameter	Not determined	
Largest diff. peak and hole	0.71 and -0.96e. $Å^{-3}$	

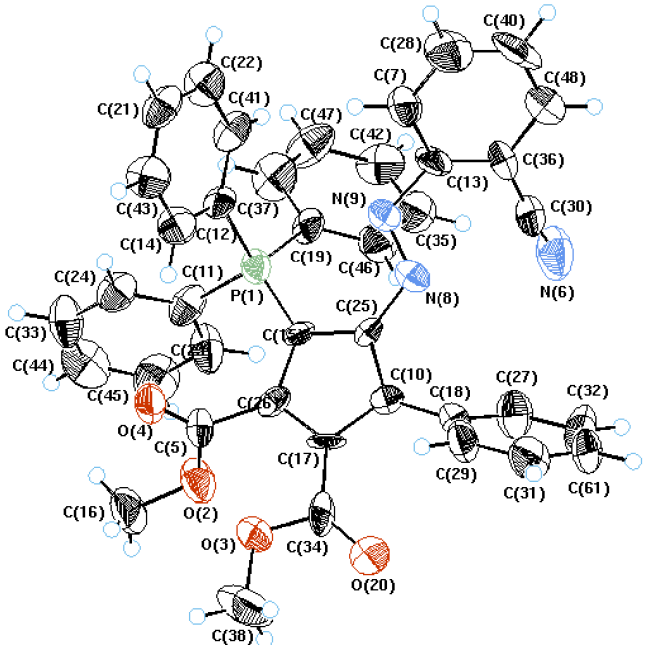


Fig. 3. Ortep of (5-(2-(2-cyanophenyl)hydrazono)-2,3-*bis*(methoxycarbonyl)-4-phenylcyclopent-2-enyl)triphenylphosphonium (**5**)

evidence for the proposed structure (Table-2 for crystal's data). Formation of compound **5** was assumed to proceed *via* cycloaddition of compounds **2** to **3**, which gives the unstable four-membered ring (**B**) that subsequently rearrange to give intermediate (**C**). The nucleophilic attack of triphenylphosphine to the aldehydic group in (**C**), followed by the addition and finally deoxygenation of compound **D** yielded the new polyfunctional phosphacyclopentane **5** (**Scheme-III**). This synthesis is superior to the former methods as it supplies a higher yield and simplifies the separation process.

Conclusion

Changing the mode of addition of reactants, resulted in an efficient, facile pathway for the synthesis of an important phosphourus ylide in pure form.

REFERENCES

1. K.M. Al-Zaydi, Method for Making Phosphorus Yilide, US Patent 8,278,477 B2, October 2 (2012).
2. D.E.C. Cobridge, Phosphorus: An Outline of the Chemistry, Biochemistry and Uses, Elsevier, Amsterdam, edn 5 (1955).
3. R. Engel, Synthesis of Carbon-Phosphorus Bonds, CRC Press: Boca Raton (1988).
4. J.I.G. Cadogan, Organophosphorus Reagents in Organic Synthesis, Academic Press: New York (1979).
5. A.W. Johnson, Ylides and Imines of Phosphorus, Wiley, New York (1993).
6. A.W. Johnson, Ylide Chemistry, Academic Press, New York (1966).
7. E. Zbiral, *Synthesis*, 775 (1974).
8. K.B. Becker, *Tetrahedron*, **36**, 1717 (1980).
9. P. Ferrer, C. Avendaño and M. Söllhuber, *Liebigs Ann. Chem*., **1995**, 1895 (1995).
10. O.I. Kolodiazhnyi, *Russ. Chem. Rev*., **66**, 225 (1997).
11. H.J. Bestmann and O. Vostrowsky, *Top. Curr. Chem*., **109**, 85 (1983).
12. H.J. Bestmann and R. Zimmermann, *Top. Curr. Chem*., **20**, 1 (1971).
13. M. Zakarianejad, H. Ghasempour, S.M. Habibi-Khorassani, M.T. Maghsoodlou, B. Makiabadi, M. Nassiri, Z. Ghahghayi and A. Abedi, *ARKIVOC*, 171 (2013).
14. Y.-T. Lee, Jang, Syu, Chou, Lee and Lin, *Chem. Commun.*, **48**, 8135 (2012).
15. R. Azhakar, S.P. Sarish, H.W. Roesky, J. Hey and D. Stalke, *Organometallics*, **30**, 2897 (2011).
16. D.R. Gautam, K.E. Litinas, K.C. Fylaktakidou and D.N. Nicolaides, *Phosphorus Sulfur Silicon Relat. Elem*., **178**, 1851 (2003).
17. M.K. Gurjar, R.D. Wakharkar, G.R. Desiraju, A. Nangia, J.S. Yadav, A.C. Burman, R. Mukherjee, H.B.R. Borate, S. Chandrasekhar, M. Jaggi, A.T. Singh, K. Kapoor, S. Sarkhel and K.V.V.M. Sairam, US Patent 7,179,937 (2007).
18. J.L. Methot and W.R. Roush, *Adv. Synth. Catal*., **346**, 1035 (2004).
19. K.M. Al-Zaydi, *J. Saudi Chem. Soc*., **6**, 477 (2002).
20. K.M. Al-Zaydi, *Heterocycles*, **78**, 2003 (2009).
21. K.M. Al-Zaydi, *Ultrason. Sonochem.*, **16**, 805 (2009).
22. K.M. Al-Zaydi, R.M. Borik and M.H. Elnagdi, *Molecules*, **8**, 910 (2003).
23. Al-Zaydi and R.M. Borik, *Molecules*, **12**, 2061 (2007).
24. K.M. Al-Zaydi, E.A. Hafez and M.H. Elnagdi, *J. Chem. Res*., **154**, 0510 (2000).
25. Crystallographic data for compounds (5) and (**6**) reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publications CCDC 698609, 698616 respectively these data can be obtained free of charge *via* www.ccdc.cam.ac.uk/conts/retrieving.html (or from the CCDC, 12 Union Road, Cambridge, CB2 1EZ, UK; Fax: +44 1223 336033; E-mail: deposit@ccdc.cam.ac.uk).
26. M. Freytag, S. Ito and M. Yoshifuji, *Chem. Asian J*., **1**, 693 (2006).
27. K.M. Al-Zaydi, R.M. Borik and M.H. Elnagdi, *Ultrason. Sonochem*., **16**, 660 (2009).