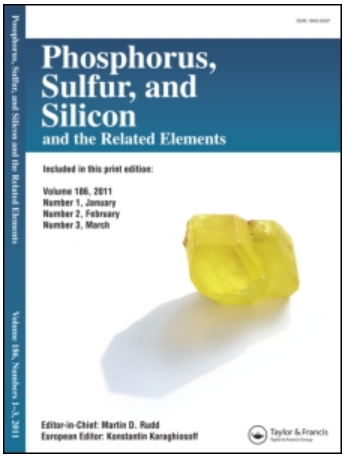

Phosphorus, Sulfur, and Silicon and the Related Elements
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713618290

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To cite this Article Frøyen, Paul(1991) 'NEW APPLICATIONS OF IMINOPHOSPHORANES. THE PREPARATION OF β-KETO CARBODIIMIDESAND THEIR REARRANGEMENTTO 2-AMINO-1,3-OXAZOLES', Phosphorus, Sulfur, and Silicon and the Related Elements, 60: 1, 81 — 84
To link to this Article: DOI: 10.1080/10426509108233928
URL: http://dx.doi.org/10.1080/10426509108233928

Phosphorus, Sulfur, and Silicon, 1991, Vol. 60, pp. 81–84
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NEW APPLICATIONS OF IMINOPHOSPHORANES. THE PREPARATION OF β-KETO CARBODIIMIDES AND THEIR REARRANGEMENT TO 2-AMINO-1,3-OXAZOLES

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(Received October 1, 1990)

β-Keto carbodiimides (**3**) have been synthesized by reacting 2-azido ketones (**1**) with triphenylphosphine in the presence of isocyanates/isothiocyanates; the former compounds (**3**) are readily transformed into 2-amino-1,3-oxazoles (**4**).

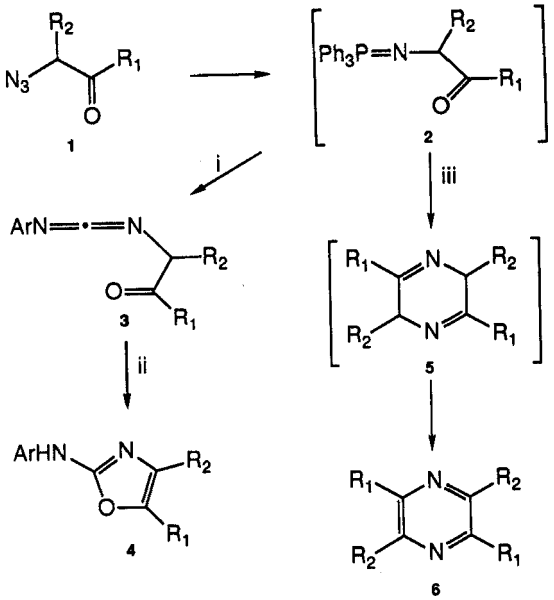
Key words: Synthesis; iminophosphoranes; β-keto cabodiimides; 2-arylamino-1,3-oxazoles.

Iminophosphoranes (**2**) have not been isolated. Attempts to prepare these compounds gave pyrazines (**6**) together with triphenylphosphine oxide in moderate yields.[1] Iminophosphoranes (**2**) were not detected in the reaction mixture, but it was assumed that the formation of pyrazines (**6**) involved the intermediacy of (**2**) which underwent a fast intermolecular aza-Wittig (Staudinger-Hauser[2]) reaction to yield dihydropyrazines (**5**), followed by aromatization of the latter to the appropriate pyrazine (**6**) (Scheme 1).

The proposed intermolecular reaction mechanism seems unlikely, but assuming that iminophosphoranes are initially formed in the Staudinger reaction of 2-azido ketones, it seemed possible that these elusive compounds could be intercepted by suitable reactants. Thus performing the Staudinger reaction in the presence of active carbonyl compounds, e.g., isocyanates, isothiocyanates, and ketenes should lead to some interesting heterocumulenic systems, potentially useful for the generation of a large variety of heterocycles. We now report an efficient synthesis of the previously unknown β-keto carbodiimides and their successive rearrangement to some novel 2-amino-1,3-oxazoles (**4**) in good yields (Table I).

The Staudinger reactions were performed in methylene chloride at ambient temperature by addition of triphenylphosphine to an equimolecular mixture of azidoketone (**1**) and isothiocyanate/isocyanate, respectively. It is believed that the mechanism, after the initial Staudinger phosphorylation of the azidoketone (**1**), involve a normal aza-Wittig reaction to give the β-keto carbodiimide (**3**). This assumption is supported by the isolation of the intermediate carbodiimide (**3a**) from the reaction of (**1a**) with triphenylphosphine and phenyl isothiocyanate in ether at the lowest possible temperature for the Staudinger reaction to occur (10–12°C). The isolated carbodiimide (**3a**, strong infrared absorption at 2100 cm-1) rearranged on standing to the 2-amino-oxazole (**4a**). A reasonable pathway for the formation of (**4**) is visualized in Scheme 2.

Presumably, the ring closure is initiated by a nucleophilic attack of the carbonyl

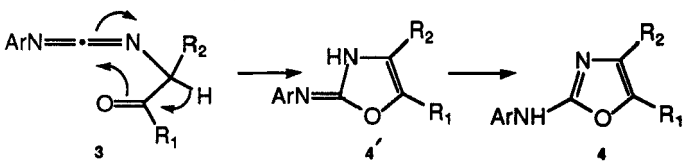


SCHEME 1. Reagents and conditions: i, ArNCO or ArNCS, CH_2Cl_2, room temp.; ii, Oxalic acid, dioxane, 60–70°C; iii, Benzene, reflux, 5–6 h.

TABLE I

Yields of 2-amino-1,3-oxazoles (**4**)

Compound	Ar	R_1	R_2	% yield
4a	Ph	Ph	Me	96
4b	Ph	Ph	H	85
4c	Ph	Me	H	92
4d	1-Naphtyl	Me	H	83
4e	Ph	t-Bu	H	90
4f	Ph	4-MeOC$_6$H$_4$	H	85



SCHEME 2

oxygen on the sp-hybridized carbon atom of the carbodiimide moiety, accompanied by a hydrogen shift from C-1 to nitrogen. Whether this is a concerted process or a two-step reaction is not clear at the moment. It is reasonable to suppose, however, that the reaction proceeds through an aromatic transition state where the bonding hydrogen orbital overlap simultaneously with orbitals on C-1 and the neighboring N-atom. This kinetically controlled reaction would lead to the intermediate (**4'**),

which subsequently isomerizes to the thermodynamically stable 2-amino-1,3-oxazole (**4**). An alternative stepwise mechanism, where the cyclization of (**3**) is assisted by protonation at the more basic N-atom, would likewise account for the observed products. We are uncertain about the role of the oxalic acid, however, since the ring closure as judged by the disappearance of the infrared absorption at about 2100 cm^{-1}, is completed in a few minutes even without any added acid. This indicates that the main effect of the oxalic acid addition could be just an easier product separation due to protonation of the forming oxazole. Thus it is noteworthy that the oxazoles (**4a–b**) and (**4f**) crystallize from the reaction mixture as the oxalic acid salts.

EXPERIMENTAL

The commercially available ketones were converted into the 2-azido ketones by bromination followed by treatment with sodium azide in dimethyl sulfoxide.

Preparation of 2-arylamino-1,3-oxazoles (**4a–f**). The Staudinger reactions were performed at room temperature by the addition of triphenylphosphine (0.66 g, 2.5 mmol) to an equimolecular mixture (2.5 mmol) of azidoketone (**1**) and the appropriate isocyanate or isothiocyanate in 3 ml dry methylene chloride. The reaction went to completion in a few minutes, whereafter stirring was continued for half an hour. A solution of oxalic acid in dioxane was thereafter added, and the reaction mixture was heated to 60–70°C for a couple of minutes. The oxazoles (**4**) crystallized on cooling and could be filtered off. The compounds (**4a–b**) and (**4f**) crystallized from the reaction mixture as oxalates. The salts were dissolved in water and converted into the 2-amino-1,3-oxazoles by treatment with sodium carbonate. After extraction with chloroform the compounds (**4a–b**) and (**4f**) were purified by recrystallization from ethanol.

(**4a**): m.p. 213°C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 2.34 (s, 3H, 4-Me), 6.93–6.98 (m, 1H, H_{arom}), 7.25–7.35 (m, 3H, H_{arom}), 7.44–7.55 (m, 4H, H_{arom}), 7.65–7.68 (m, 2H, H_{arom}), 10.23 (s, 1H, NH); ^{13}C NMR (75.4 MHz, DMSO-d_6) δ 116.62 (N-Ph-o), 121.05 (N-Ph-p), 123.81 (5-Ph-o), 126.25 (5-Ph-p), 128.80 (N-Ph-m and 5-Ph-m), 129.01 (5-Ph-i), 131.61 (C-4), 137.69 (C-5), 139.43 (N-Ph-i), 155.01 (C-2); MS (70 eV): m/z (%) 250 (100, M^+), 180 (41.2, M-C_3H_4NO), 104 (46.5); IR (film) ν 3380 (br.), 3020, 1660, 1640, 1575, 1490, 1320, 1025 cm^{-1}.

(**4b**): m.p. 175–176°C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 6.97 (t, 1H, N-Ph-p), 7.26–7.49 (m, 6H, Ph-m and 4-H, 7.62 (d, 2H, N-Ph-o), 7.68 (d, 2H, 5-Ph-o), 10.35 (s, 1H, NH); ^{13} C NMR (75.4 MHz, DMSO-d_6) δ 116.59 (N-Ph-o), 121.14 (N-Ph-p), 122.48 (C-4 and 5-Ph-o), 126.98 (5-Ph-p), 128.04 (5-Ph-i), 128.85 (N-Ph-m and 5-Ph-m), 139.35 (N-pH-i), 143.64 (C-5), 156.46 (C-2); MS (70 eV): m/z (%) 236 (100, M^+), 207 (11.7), 180 (18.5), 105 (25.9), 104 (34.8), 78 (12.1), 77 (58.8); IR (film) ν 3300 (br.), 3020, 1670, 1550, 1490, 1320, 1070, 1025 cm^{-1}.

(**4c**): m.p. 154-156°C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 2.22 (s, 3H, 5-Me), 6.57 (S, 1H, 4-H), 6.90 (t, 1H, Ph-p), 7.27 (t, 2H, Ph-m), 7.58 (d, 2H, Ph-o); ^{13}C NMR (75.4 MHz, DMSO-d_6) δ 10.38 (5-Me), 116.37 (Ph-o), 120.76 (C-4), 121.52 (Ph-p), 128.90 (Ph-m), 139.94 (Ph-i), 141.15 (C-5), 155.75 (C-2); MS (70 eV): m/z (%) 174 (100, M^+), 173 (20, M-H), 145 (4.1, M-HCO), 131 (9.9, M-CH_3CO), 119 (5.4, M-C_3H_5N), 104 (63.1, M-C_3H_4NO); IR (KBr) ν 3400, 1690, 1595, 1500, 1400, 1320, 1020, 980, 855, 830, 740, 710, 695 cm^{-1}.

(**4d**): m.p. 178°C; ^{1} H NMR (300 MHz, DMSO-d_6) δ 2.26 (s, 3H, 5-Me), 6.62 (s, 1H, 4-H), 7.44–7.59 (m, 4H, H_{arom}), 7.89–7.92 (m, 1H, H_{arom}), 8.12–8.15 (m, 1H, H_{arom}), 8.32–8.35 (m, 1H, H_{arom}); ^{13}C NMR (75.4 MHz, DMSO-d_6) δ 114.52, 121.27, 122.01, 122.06, 125.14, 125.30, 125.85, 128.07, 133.78, 135.08, 141.52, 156.54; MS (70 eV): m/z (%) 224 (100, M), 223 (41.9), 181 (23.3, M-CH_3CO), 154 (48.4, M-C_3H_5NO), 153 (30), 127 (28.2); IR (film) ν 3000–3500, 2920, 2950, 1690, 1630, 1600, 1560, 1315, 1225, 1150 cm^{-1}.

(**4e**): m.p. 176°C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.25 (s, 9H, t-Bu), 6.54 (s, 1H, 4-H), 6.87–6.92 (t, 1H, Ph-p), 7.23–7.29 (m, 2H, Ph-m), 7.59 (d, 2H, Ph-o); ^{13}C NMR (75.4 MHz, DMSO-d_6) δ 28.40 (Me), 30.57 (5-C), 116.20 (Ph-o), 118.29 (C-4), 120.56 (Ph-p), 128.69 (Ph-m), 139.79 (Ph-i), 152.91 (C-5), 155.47 (C-2); MS (70 eV): m/z (%) 216 (28.2, M^+), 201 (100, M-Me), 77 (16), 55 (13.9), 44 (18.6); IR (film) ν 3000–3550, 2960, 2940, 1685, 1635, 1590, 1500, 1315, 1215 cm^{-1}.

(**4f**): m.p. 163–165°C; ^{1}H NMR (300 MHz, DMSO-d_6 δ 3.79 (s, 3H, Me), 6.95 (t, 1H, N-Ph-p), 7.25 (d, 2H, 5-Ph-m), 7.30–7.33 (m, 2H, N-Ph-m), 7.35 (s, 1H, 4-H), 7.54 (d, 2H, 5-Ph-o), 7.67 (d, 1H, n-Ph-p), 10.26 (s, 1H, NH); ^{13}C NMR (75.4 MHz, DMSO-d_6) δ 55.14 (Me), 114.47 (5-Ph-o), 116.47 (N-Ph-o), 120.52 (N-Ph-p), 120.86 (5-Ph-i), 120.96 (C-4), 124.14 (5-Ph-m), 128.81 (N-Ph-m), 139.50 (N-Ph-i), 143.74 (C-5), 155.92 (C-2); MS (70 eV): m/z (%) 266 (100, M^+), 252 (16.9), 251 (45.3, M-Me), 210 (12.3), 135 (15.3), 133 (10.9), 104 (10.5), 92 (13.1); IR (film) ν 3380 (br.), 3020, 1670, 1600, 1585, 1500, 1390, 1315, 1250, 1150, 1030 cm^{-1}.

(**3a**) In the case of 2-azido-1-phenyl-1-propanone (**1a**), an attempt was made to isolate the intermediate carbodiimide (**3a**) from the reaction of this azide with triphenylphosphine and phenyl isothiocyanate. To a stirred solution of 1.0 mmol of (**1a**) in 1 ml of ether was added 1.0 mmol of phenyl isothiocyanate and 1.0 mmol of triphenylphosphine. The reaction mixture was held at 10–12°C during the reaction. Triphenylphosphine sulfide was filtered off and the solvent evaporated under nitrogen. The resulting oily product was washed with pentane and dried under vacuum. A good analysis could not be obtained for this substance due to its instability, but its structure could be deduced from the IR spectrum (strong absorption at 2100 cm^{-1}) and the rearrangement to 4-methyl-2-phenylamino-1,3-oxazole (**4a**).

ACKNOWLEDGEMENT

This work was performed during a stay at the Dept. of Chemistry, University of Oslo. I am grateful to Dr. J. Skramstad for his continued interest in my work, and for the generous provision of research chemicals.

REFERENCES

1. E. Zbiral and J. Stroh, *Ann. Chem.*, **727**, 231 (1969).
2. H. Staudinger, and E. Hauser, *Helv. Chim. Acta*, **4**, 861 (1921).