Azinoiminophosphorane Mediated Synthesis of 5*H*,7*H*-1,2,4-Triazolo[1,5-*c*][1,3]benzoxazepin-7-ones and 6*H*,8*H*-1,2,4-Triazolo-[1,5-*c*][1,3]oxazepin-6-ones

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The aza-Wittig reactions of benzophenone-, acetophenone- and benzaldehyde 1-[(triphenylphosphoranylidene)amino]ethylidenehydrazones (**4**) with phthalic anhydride, 2,3-dimethylmaleic anhydride and 7-oxabicyclo[2,2,1]hept-5-ene-2,3-dicarboxylic anhydride (**5a**) provide a new route to 5*H*,7*H*-1,2,4-triazolo[1,5-*c*]-[1,3]benzoxazepin-7-ones **8a-c** or 6*H*,8*H*-1,2,4-triazolo[1,5-*c*][1,3]oxazepin-6-ones **8d-h** *via* the thermal reaction of the expected azinoimine lactones **6**.

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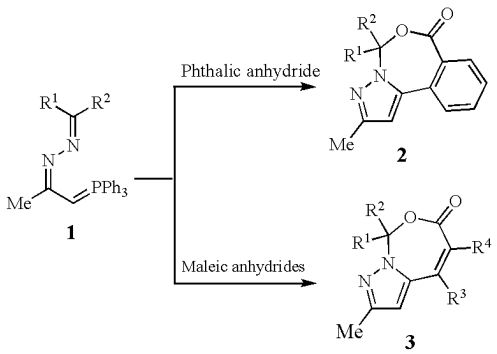
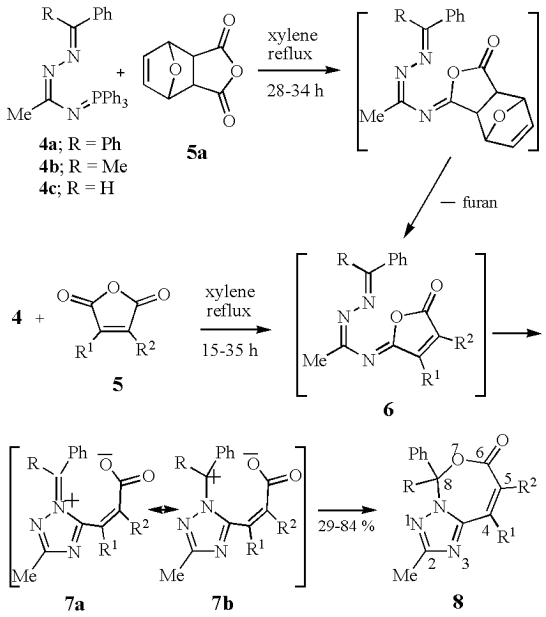
In recent years, there has been a significant interest in the chemistry of iminophosphoranes because of their utility in the synthesis of a wide variety of nitrogen heterocycles, and many interesting heterocyclization reactions involving functionalized iminophosphoranes have been reviewed [1]. Also, we reported that aza-Wittig reactions of azinoiminophosphoranes **4** with aromatic aldehydes gave some trisubstituted 1,2,4-triazoles by thermal rearrangement of intermediate azinoimines [2]. In addition, Schweizer and co-workers reported that the reactions of azine ylides **1** with phthalic anhydride and maleic anhydride derivatives would give the 5*H*,7*H*-pyrazolo[1,5-*d*][2,4]benzoxazepin-7-ones **2** [3] and 6*H*,8*H*-pyrazolo[1,5-*c*][1,3]oxazepin-6-ones **3** [4], respectively (Scheme I).

Scheme I



With their results in mind, we tried to apply this methodology to the synthesis of 5*H*,7*H*-1,2,4-triazolo[1,5-*c*][1,3]-benzoxazepin-7-ones **8a-c** and 6*H*,8*H*-1,2,4-triazolo[1,5-*c*][1,3]oxazepin-6-ones **8d-h** by the reaction of azinoiminophosphoranes **4** with phthalic anhydride, maleic anhydride and 2,3-dimethylmaleic anhydride (Scheme II). Some of reports in the literature have shown that on reacting stabilized aza-ylides with cyclic carboxylic acid anhydrides imine lactones occur successfully with the ring closed species being the predominant result [5].

Scheme II



	R	R^1	R^2
8a	Ph	−CH=CH−CH=CH−	
8b	Me	−CH=CH−CH=CH−	
8c	H	−CH=CH−CH=CH−	
8d	Ph	Me	Me
8e	Me	Me	Me
8f	H	Me	Me
8g	Ph	H	H
8h	Me	H	H

The known key iminophosphoranes **4** were easily prepared by the reaction of a mixture of triphenylphosphine and iodine with benzophenone-, acetophenone- or benzaldehyde 1-aminoethylidenehydrazone, respectively [2,6]. The aza-Wittig reactions of **4** with phthalic anhydride or 2,3-dimethylmaleic anhydride in xylene at reflux temperature [7] led directly to 29-84 % yields of the hitherto unknown 5*H*,7*H*-1,2,4-triazolo[1,5-*c*][1,3]benzoxazepin-7-ones **8a-c** or 6*H*,8*H*-1,2,4-triazolo[1,5-*c*][1,3]-oxazepin-6-ones **8d-f**. However, aza-Wittig reaction of **4**

with maleic anhydride led to an indistinct complex reaction mixture as indicated by thin layer chromatography. The product **8g** or **8h** could be produced by allowing the azinoiminophosphorane **4a** or **4b** to react with the Diels-Alder adduct of maleic anhydride and furan, 7-oxabicyclo[2,2,1]hept-5-ene-2,3-dicarboxylic anhydride (**5a**) [8] followed by a retro-Diels-Alder reaction [4,9]. A reasonable mechanism for the transformation of **4** into **8** is shown in the Scheme II. The presumed intermediate azinoimine lactones **6** were too unstable to isolate under the reaction condition, so the thermal reactions of **6** would give the resonance-stabilized azomethine imines **7a** or **7b** followed by cyclization to afford compounds **8**.

Structural elucidation of **8** was accomplished on the basis of spectral data. The ^{13}C nmr spectra showed a characteristic peak at δ = 163.85-166.89 for the lactone carbonyl carbon, and two triazole carbons resonated in the δ = 150.60 to 153.99 region and δ = 159.37 to 161.20 region. The ^{1}H nmr spectra showed that the C4-methyl protons and C5-methyl protons in **8d-f** are two pairs of singlets with deuterochloroform as solvent. The C4-methyl protons in **8d** are found at 1.77(1) and 1.77(4) ppm, the C5-methyl protons at 2.11(0) and 2.11(4) ppm. In **8e**, C4-methyl protons are found at 1.75(5) and 1.75(8) ppm, C5-methyl protons absorbed at 2.02(2) and 2.02(5) ppm; in **8f**, 2.16(9) and 2.17(1) ppm for C4-methyl protons, 2.34(8) and 2.35(1) ppm for C5-methyl protons. Thus, a 1:1 mixture of the two conformational isomers exist for **8d-f** as shown by the ^{1}H nmr ratio of C4-methy peaks [10]. The infrared spectra showed absorption for carbonyl band (1700-1728 cm^{-1}). The mass spectral data of **8a-c** showed characteristic decomposition peaks at m/z = 185 (M^+-PhCOR), 157 (M^+-PhCOR-CO), 129 and those of **8d-h** showed all a decomposition peak at m/z = M^+-CO and slightly different decomposition patterns depending on the R substituents (Table 1).

In conclusion, we have shown that reactions of the azinoiminophosphoranes **4** with phthalic anhydride, 2,3-dimethylmaleic anhydride and 7-oxabicyclo[2,2,1]hept-5-ene-2,3-dicarboxylic anhydride giving 5*H*,7*H*-1,2,4-triazolo[1,5-*c*][1,3]benzoxazepin-7-ones **8a-c** or 6*H*,8*H*-1,2,4-triazolo[1,5-*c*][1,3]oxazepin-6-ones **8d-h**.

EXPERIMENTAL

All reagents and solvents were reagent grade or were purified by standard methods before use and the reactions were routinely carried out under an inert atmosphere. Silica gel 60 (70-230 mesh ASTM) used for column chromatography was supplied by E. Merck. Analytical thin layer chromatography (tlc) was performed on silica gel with fluorescent indicator coated on aluminium sheets. Melting points were taken using an Electrothermal melting point apparatus and are uncorrected. Microanalyses were obtained using a Carlo Erba EA 1180 element analyzer. Mass spectra were obtained using a ThermoQuest Polaris Q mass spectrometer operating at 70 eV. The ^{1}H and ^{13}C nmr spectra were measured on a Gemini 300 spectrometer. All chemical shifts are reported in parts per million (δ) relative to tetramethylsilane.

The benzophenone-, acetophenone- and benzaldehyde 1-[(triphenylphosphoranylidene)amino]ethylidenehydrazones (**4a-c**) [2,6] and 7-oxabicyclo[2,2,1]hept-5-ene-2,3-dicarboxylic anhydride (**5a**) [8] were prepared following the literature procedures.

5*H*,7*H*-1,2,4-Triazolo[1,5-*c*][1,3]benzoxazepin-7-ones **8a-c** and 6*H*,8*H*-1,2,4-Triazolo[1,5-*c*][1,3]oxazepin-6-ones **8d-8h**. General Procedure.

To a solution of iminophosphorane **4** (1.5 mmoles) in 15 ml of xylene was added cyclic carboxylic acid anhydride (2.25 mmoles) and this solution was stirred at reflux temperature for

Table 1

5*H*,7*H*-1,2,4-Triazolo[1,5-*c*][1,3]benzoxazepin-7-ones **8a-c** and 6*H*,8*H*-1,2,4-Triazolo[1,5-*c*][1,3]oxazepin-6-ones **8d-h**

	Reaction Time (h)	Yield (%)	MP (°)	Molecular Formula	Analysis (%) Calcd./Found C	H	N	Mass Spectra m/z (%)
8a	24	68	192-193	$C_{23}H_{17}N_3O_2$	75.19	4.66	11.44	367 (M^+, 0.5), 186 (14), 185 (100), 157 (8),
				(367.40)	75.01	4.45	11.20	129 (25), 105 (14), 88 (12)
8b	20	57	133-134	$C_{18}H_{15}N_3O_2$	70.81	4.95	13.76	305 (M^+, 0.6), 186 (15), 185 (100),
				(305.33)	70.58	4.88	13.47	157 (10), 129 (29), 88 (9)
8c	15	48	135-137	$C_{17}H_{13}N_3O_2$	70.09	4.50	14.42	291 (M^+, 2), 186 (56), 185 (100),
				(291.30)	69.81	4.40	14.15	157 (13), 129 (58), 88 (28)
8d	30	84	161-163	$C_{21}H_{19}N_3O_2$	73.03	5.54	12.17	345 (M^+, 33), 317 (100), 300 (45), 163 (79),
				(345.39)	72.78	5.30	11.82	135 (51), 105 (94), 77 (47)
8e	35	64	84-85	$C_{16}H_{17}N_3O_2$	67.83	6.05	14.83	283 (M^+, 17), 255 (15), 241 (100), 213 (78),
				(283.33)	67.64	5.81	14.57	163 (77), 135 (42), 106 (58), 77 (16)
8f	20	45	157-158	$C_{15}H_{15}N_3O_2$	66.90	5.61	15.60	269 (M^+, 2), 241 (2), 163 (100), 135 (23),
				(269.30)	66.65	5.50	15.28	107 (24), 106 (34), 77 (7)
8g	34	31	211-213	$C_{19}H_{15}N_3O_2$	71.91	4.76	13.24	317 (M^+, 6), 289 (9), 212 (20), 182 (100),
				(317.34)	71.73	4.70	1311	181 (80), 135 (4), 105 (69), 77 (20)
8h	28	29	oil	$C_{14}H_{13}N_3O_2$	65.87	5.13	16.46	255 (M^+, 0.6), 227 (9), 226 (55), 213 (35),
				(255.27)	65.60	5.02	16.19	184 (23), 135 (58), 105 (100), 77 (29)

Table 2

IR and NMR Data of Compounds **8**

	IR ν (cm^{-1}) (KBr)	^{1}H NMR δ (ppm) (Deuterochloroform)	^{13}C NMR δ (ppm) (Deuterochloroform)
8a	1724, 1514, 1448, 1320, 1277, 1227, 1083, 900	2.42 (s, 3H), 7.12-7.36 (m, 11H), 7.50-7.55 (m, 1H), 7.86 (d, 1H, J = 7.9 Hz), 8.05 (d, 1H, J = 7.9 Hz)	14.14 (d), 94.66, 125.74, 127.60, 128.29, 129.24, 130.28, 132.65, 132.43, 133.38, 133.60, 138.55, 153.68, 159.74, 166.16
8b	1712, 1510, 1444, 1413, 1297, 1250, 1095, 959	2.36 (s, 3H), 2.57 (s, 3H), 6.85-6.88 (m, 2H), 7.11-7.13 (m, 3H), 7.32 (t, 1H, J = 7.6 Hz), 7.47 (t, 1H, J = 7.3 Hz), 7.84 (d, 1H, J = 7.9 Hz), 7.94 (d, 1H, J = 7.9 Hz)	14.01 (d), 31.12, 92.25, 124.57, 125.33, 128.23, 128.78, 129.56, 130.50, 132.39, 132.63, 133.23, 140.24, 153.31, 160.19, 166.52
8c	1720, 1502, 1421, 1293, 1234, 1087, 1044, 885	2.44 (s, 3H), 7.04 (s, 1H), 7.43 (m, 5H), 7.62 (t, 1H, J = 7.6 Hz), 7.75 (t, 1H, J = 7.9 Hz), 8.11 (d, 2H, J = 7.6 Hz)	14.08, 83.83 (d), 125.36, 127.18, 127.64, 128.39, 128.73, 129.04, 130.26, 131.49, 133.25, 133.59, 153.46, 161.20, 166.49
8d	1720, 1502, 1448, 1401, 1366, 1293, 1203, 1176, 1067, 900	1.77(1) and 1.77(4) (s, 3H), 2.11(0) and 2.11(4) (s, 3H), 2.36 (s, 3H), 7.11-7.13 (m, 4H), 7.34-7.40 (m, 6H)	14.10, 17.21 (d), 18.10 (d), 93.76, 127.28 (d), 128.34 (d), 129.36 (d), 131.08, 133.07, 138.65, 153.99, 159.37, 166.46
8e	1700, 1506, 1429, 1382, 1304, 1273, 1223, 1149, 1099, 990	1.75(5) and 1.75(8) (s, 3H), 2.02(2) and 2.02(5) (s, 3H), 2.26 (s, 3H), 2.51 (s, 3H), 6.86-6.88 (m, 2H), 7.29-7.32 (m, 3H)	13.91 (d), 13.99 (d), 17.25 (d), 17.71 (d), 30.58, 91.28, 123.92, 128.85, 130.47, 133.27, 140.91, 153.60, 159.76, 166.89
8f	1712, 1499, 1429, 1308, 1203, 1091, 1044, 885, 741	2.16(9) and 2.17(1) (s, 3H), 2.34(8) and 2.35(1) (s, 3H), 2.38 (s, 3H), 6.92 (s, 1H), 7.45-7.49 (m, 5H)	13.96 (d), 18.05, 18.14, 82.95 (d), 127.25, 128.71, 130.15, 131.46, 131.85, 132.37, 153.93, 160.72, 166.86
8g	1728, 1495, 1448, 1421, 1269, 1238, 1126, 1025, 834	2.38 (s, 3H), 6.25 (d, 1H, J = 12.2 Hz), 6.98 (d, 1H, J = 12.2 Hz), 7.04-7.06 (m, 4H), 7.34-7.42 (m, 6H)	14.03, 95.46, 126.69, 127.43, 127.74, 128.38, 129.72, 138.12, 151.18, 160.49, 163.85
8h	1712, 1499, 1421, 1281, 1242, 1184, 1095, 1033, 978, 831	2.30 (s, 3H), 2.53 (s, 3H), 6.20 (d, 1H, J = 12.2 Hz), 6.81-6.84 (m, 2H), 6.88 (d, 1H, J = 12.2 Hz), 7.29-7.33 (m, 3H)	13.89 (d), 30.94, 92.85, 124.81, 126.87, 127.10, 127.14, 129.10, 139.66, 150.60, 160.77, 164.09

the time indicated in Table 1. After cooling to room temperature the solvent was removed on a rotary evaporator. The residue was chromatographed on silica gel column eluting with hexane-ethyl acetate 3:1 to give the product **8**. Purification was achieved by crystallization from hexane.

The physical and spectral data of **8** prepared by this general method are listed in Table 1 and Table 2.

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