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A REGIOSPECIFIC SYNTHESIS OF 1-HETEROCYCLIC SUBSTITUTED 1,2,4-TRIAZOLES VIA ADDITION REACTION OF 1,2,4-TRIAZOLE WITH FUNCTIONALIZED CARBODIIMIDE

Ming-Wu Ding ^a , Gui-Ping Zeng ^a & Zhao-Jie Liu ^b

 $^{\rm a}$ Institute of Organic Synthesis , Central China Normal University , Wuhan, 430079, P.R. China

^b Institute of Organic Synthesis , Central China Normal University , Wuhan, 430079, P.R. China

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Ming-Wu Ding, Gui-Ping Zeng, and Zhao-Jie Liu*

Institute of Organic Synthesis, Central China Normal University, Wuhan, 430079, P.R. China

ABSTRACT

The reaction of 1,2,4-triazole with functionalized carbodiimide **2** or **6** under solid K_2CO_3 provide a convenient and regiospecific route to 1-(2-imidazolonyl)-1,2,4-triazole **4** or 1-(2-quinazolonyl)-1,2,4-triazole **8**.

Key Words: Triazoles; Iminophosphorane; Imidazolinones; Quinazolinones; Aza-Wittig reaction

Many 1-substituted 1,2,4-triazole compounds show good fungicidal activities and plant growth regulative activities. They are generally prepared by N-alkylations of 1,2,4-triazole with alkylating reagents, of which various types have been used, however, many of these reactions

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^{*}Corresponding author. E-mail: ding5229@yahoo.com.cn



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are limited by the simultaneous formation of the unwanted and biologically inactive 4-isomer.^[1] It was reported that 1,2,4-triazole derivatives can be regiospecifically synthesized by addition reactions of 1,2,4-triazole with aldehydes and this method was successfully utilized to prepare many novel triazole derivatives.^[2–5] However, there is no report about addition reaction of 1,2,4-triazole with carbodiimide. Recently we provided a facile synthesis of 2-substituted imidazolinones and quinazolinones via tandem aza-Wittig reaction.^[6–8] We now report a new regiospecific synthesis of 2-heterocyclic substituted 1,2,4-triazoles via base catalytic addition reaction of 1,2,4-triazole with functionalized carbodiimide.

The easily accessible vinyliminophosphorane 1 reacted with aromatic isocyanates to give carbodiimides 2. The direct reaction of 2 with 1,2,4-triazole at room temperature took place very slow for 2 did not disappear even after 5 days, however, when the reaction was carried out under solid $K_2CO_3(s)$, the reaction mixture was getting red quickly and then becoming yellow gradually within 15 min. The final product obtained was verified to be 1-(2-imidazolonyl)-1,2,4-triazole 4. No 4-isomer of 4 was formed during the reaction process. The structure of 4 has been characterized spectroscopically. For example, the ¹HNMR spectrum data in **4a** showed the signals of 3-H in triazole ring at 7.94 ppm as a single absorption and 5-H at 8.97 ppm as a single absorption. The use of a 10-fold of excess solid $K_2CO_3(s)$ gave better yields of 4. The best reaction time was 15 min, for the reaction mixture was getting dark gradually after 15 min due to side reactions (Table 1). The formation of 4 can be rationalized in terms of an initial nucleophilic addition of 1,2,4-triazole under potassium carbonate to give the intermediate 3 which directly cyclized to give 4 (Sch. 1).

The above method was also successively applied to synthesize 1-(2-quinazolonyl)-1,2,4-triazole **8**, which having been found to show fungicidal activities.^[9] Iminophosphorane **5** reacted with aromatic isocyanates to give carbodiimides **6**, which was allowed to react with 1,2,4-triazole under solid potassium carbonate to give **8** (Sch. 2). Good yields of **8** were obtained when catalytic solid potassium carbonate was used with overnight stirring (Table 1). The structure of **8** has been characterized spectroscopically. For example, the ¹H NMR spectrum data in **8a** showed the signals of 3-H in triazole ring at 8.14 ppm as a single absorption and 5-H at 8.60 ppm as a single absorption. The formation of **8** can be rationalized in terms of an initial nucleophilic addition of 1,2,4-triazole under potassium carbonate to give **8**.

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Table 1. Preparation of 1-(2-Imidazolonyl)-1,2,4-triazole **4** and 1-(2-Quinazolonyl)-1,2,4-triazole **8**

Compds.	Ar ¹	Ar ²	Ar	Reaction Time (h)	K ₂ CO ₃ (s)	Yield (%)*
4a	Ph	Ph		0.25	10 equiv	82
				1	10 equiv	38
				24	10 equiv	11
				0.25	0.1 equiv	22
				0.25	1 equiv	45
4b	Ph	4-Cl-Ph		0.25	10 equiv	72
4c	Ph	3-Cl-Ph		0.25	10 equiv	68
4d	4-Cl-Ph	4-Cl-Ph		0.25	10 equiv	87
4 e	3-Cl-Ph	Ph		0.25	10 equiv	80
4f	3-Cl-Ph	4-Cl-Ph		0.25	10 equiv	76
8a			Ph	24	0.1 equiv	74
8b			4-Cl-Ph	24	0.1 equiv	70
8c			3-Cl-Ph	24	0.1 equiv	71

*isolated yields based on iminophosphoranes.



EXPERIMENTAL

Melting points were uncorrected. MS were measured on a HP5988A spectrometer. IR were recorded on a Shimadzu IR-408 infrared spectrometer. NMR were taken on a Varian XL-200 spectrometer.

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General Preparation of 1-(2-Imidazolonyl)-1,2,4-triazole 4

To a solution of vinyliminophosphorane 1 (5 mmol) in dry methylene dichloride (15 mL) was added aromatic isocyanate (5 mmol) under nitrogen at room temperature. After the reaction mixture was stirred for $4 \sim 6$ h, the solvent was removed off under reduced pressure and ether/petroleum ether (1:2, 20 mL) was added to precipitate triphenylphosphine oxide. Filtered, the solvent was removed to give carbodiimide 2, which was used directly without further purification. To the solution of 2 prepared above in CH₃CN (15 mL) was added 1H-1,2,4-triazole (0.34 g, 5 mmol) and excess solid K₂CO₃ (6.9 g, 50 mmol). The mixture was stirred for 15 min vigorously at room temperature and filtered, the filtrate was condensed and the residual was recrystallized from methylene dichloride/petroleum ether or purified by a short silica gel column to give 1-(2-imidazolonyl)-1,2,4-triazole 4.

4a: yellow crystals, m.p. $160 \sim 162^{\circ}$ C, ¹H NMR (CDCl₃, 200 MHz) δ 8.97 (s, 1H, triazolyl-5-H), 7.94 (s, 1H, triazolyl-3-H), 8.21 ~ 7.18 (m, 11H, Ar–H and =CH); IR (cm⁻¹), 1722, 1640, 1560, 1476; MS (*m/z*), 315 (M⁺, 100%), 171 (42%), 144 (14%), 117 (76%).

4b: yellow crystals, m.p. $197 \sim 199^{\circ}$ C, ¹H NMR (CDCl₃, 200 MHz) δ 9.06 (s, 1H, triazolyl-5-H), 7.94 (s, 1H, triazolyl-3-H), 8.20 \sim 7.12 (m, 10H, Ar–H and =CH); IR (cm⁻¹), 1728, 1636, 1562, 1474; MS (*m*/*z*), 349 (M⁺, 100%), 351 (33%), 205 (25%), 151 (40%), 116 (20%).

4c: yellow crystals, m.p. $152 \sim 154^{\circ}$ C, ¹H NMR (CDCl₃, 200 MHz) δ 9.08 (s, 1H, triazolyl-5-H), 7.94 (s, 1H, triazolyl-3-H), 8.22 ~ 7.14

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(m, 10H, Ar–H and =CH); IR (cm⁻¹), 1725, 1638, 1558, 1475; MS (m/z), 349 (M⁺, 100%), 351 (34%), 205 (23%), 151 (28%), 116 (19%).

4d: yellow crystals, m.p. $197 \sim 199^{\circ}$ C, ¹H NMR (CDCl₃, 200 MHz) δ 9.10 (s, 1H, triazolyl-5-H), 7.90 (s, 1H, triazolyl-3-H), 8.20 \sim 7.10 (m, 9H, Ar–H and =CH); IR (cm⁻¹), 1730, 1638, 1550, 1478, MS (*m/z*), 383 (M⁺, 100%), 385 (62%), 387 (11%), 205 (47%), 151 (30%).

4e: yellow crystals, m.p. $176 \sim 178^{\circ}$ C, ¹H NMR (CDCl₃, 200 MHz) δ 9.06 (s, 1H, triazolyl-5-H), 7.92 (s, 1H, triazolyl-3-H), 8.21 \sim 7.12 (m, 10H, Ar–H and =CH); IR (cm⁻¹), 1728, 1640, 1552, 1478; MS (*m*/*z*), 349 (M⁺, 100%), 351 (33%), 205 (27%), 151 (36%).

4f: yellow crystals, m.p. $218 \sim 220^{\circ}$ C, ¹H NMR (CDCl₃, 200 MHz) δ 9.02 (s, 1H, triazolyl-5-H), 7.88 (s, 1H, triazolyl-3-H), 8.18 \sim 7.03 (m, 9H, Ar–H and =CH); IR (cm⁻¹), 1735, 1640, 1548, 1478; MS (*m*/*z*), 383 (M⁺, 88%), 385 (61%), 387 (11%), 205 (58%), 151 (58%).

General Preparation of 1-(2-Quinazolonyl)-1,2,4-triazole 8

To a solution of iminophosphorane **5** (2.12 g, 5 mmol) in dry methylene dichloride (15 mL) was added aromatic isocyanate (5 mmol) under nitrogen at $0 \sim 5^{\circ}$ C. After the reaction mixture was stand for $6 \sim 12$ h at $0 \sim 5^{\circ}$ C, the solvent was removed off under reduced pressure and ether/petroleum ether (1:2, 20 mL) was added to precipitate triphenylphosphine oxide. Filtered, the solvent was removed to give carbodiimide **6**, which was used directly without further purification. To the solution of **6** prepared above in CH₃CN (15 mL) was added 1H-1,2,4-triazole (0.34 g, 5 mmol) and catalytic solid K₂CO₃ (0.07 g, 0.5 mmol). The mixture was stirred overnight at room temperature and filtered, the filtrate was condensed and the residual was recrystallized from methylene dichloride/ petroleum ether or purified by a short silica gel column to give 1-(2-quinazolonyl)-1,2,4-triazole **8**.

8a: white crystals, m.p. $148 \sim 150^{\circ}$ C, ¹H NMR (CDCl₃, 200 MHz) δ 8.60 (s, 1H, triazolyl-5-H), 8.14 (s, 1H, triazolyl-3-H), 8.32 ~ 6.90 (m, 9H, Ar–H); IR (cm⁻¹), 1684, 1550, 1300; MS (*m*/*z*), 289 (M⁺, 100%), 221 (46%), 144 (14%), 77 (66%).

8b: white crystals, m.p. $156 \sim 158^{\circ}$ C, ¹H NMR (CDCl₃, 200 MHz) δ 8.68 (s, 1H, triazolyl-5-H), 8.16 (s, 1H, triazolyl-3-H), 8.36 \sim 6.92 (m, 8H, Ar–H); IR (cm⁻¹), 1686, 1552, 1306; MS (*m*/*z*), 323 (M⁺, 100%), 325 (32%), 255 (40%), 220 (12%), 144 (16%), 90 (71%).

8c: white crystals, m.p. $150 \sim 152^{\circ}$ C, ¹H NMR (CDCl₃, 200 MHz) δ 8.66 (s, 1H, triazolyl-5-H), 8.16 (s, 1H, triazolyl-3-H), 8.35 ~ 6.90 STA.

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(m, 8H, Ar–H); IR (cm⁻¹), 1685, 1550, 1302; MS (m/z), 323 (M⁺, 100%), 325 (33%), 255 (48%), 144 (24%), 90 (56%).

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REFERENCES

- Bentley, T.W.; Jones, R.V.H.; Wareham, P. J. Tetrahedron Lett. 1989, 30, 4013.
- Smith, K.; Hammond, M.E.W.; James, D.M.; Ellison, I.J.; Hutchings, Chem. Lett. 1990, 351.
- 3. Smith, K.; Small, A.; Hutchings, M.G. Synlett. 1991, 485.
- 4. Seele, R.; Goetz, N.; Brox, W.; Kober, R.; Ammermann, E.; Lorenz, G. EP449067 (1991).
- Seele, R.; Goetz, N.; Saupe, T.; Lorenz, G.; Ammermann, E. Ger. Offen. 4034352 (1992).
- 6. Ding, M.W.; Zeng, G.P.; Wu, T. J. Synth. Commun. 2000, 30, 1599.
- 7. Ding, M.W.; Xu, Z.F.; Wu, T. J. Synth. Commun. 1999, 29, 1171.
- 8. Ding, M.W.; Tu, H.Y.; Liu, Z. J. Synth. Commun. 1997, 27, 3657.
- 9. Green, D.E.; Percival, A. EP183458 (1986).

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