

Chemistry of cyclopropenones: synthesis of new pyrrolo[2,1-*b*]-1,3,4-oxadiazoles

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Abstract

2,3-Diphenylcyclopropenone (**1**) reacts with ylidene-*N*-phenylhydrazine-carbothioamides **2a–e** to form the pyrrolo[2,1-*b*]-1,3,4-oxadiazoles **5a–e**.

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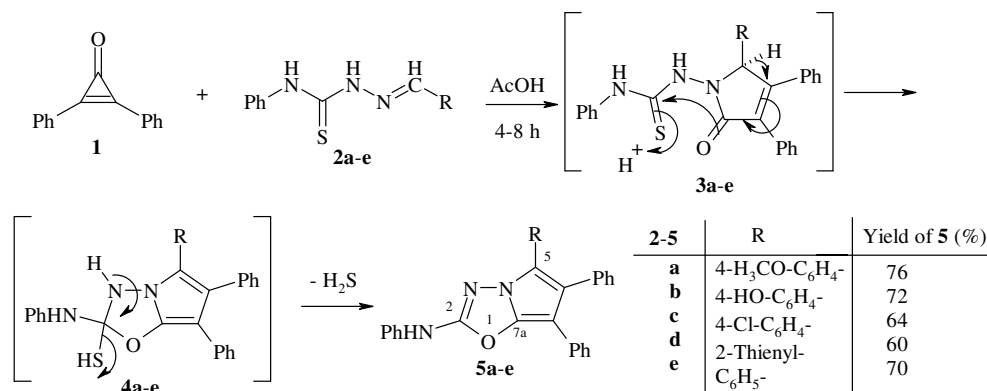
Keywords: Ylidene-*N*-phenylhydrazine-carbothioamides; 2,3-Diphenylcyclopropenone; [2+3] Cycloaddition; Pyrrolo[2,1-*b*]-1,3,4-oxadiazoles

2,3-Diphenylcyclopropenone (**1**) has been found to react with a wide range of imines and other compounds containing the C=N moiety, usually to form pyrrolinones via formal [2+3] cycloaddition reactions.^{1–8} Whilst investigating the utility of compound **1** in heterocycle synthesis, we have reported the synthesis of pyridazinethiones and 1,2,4-triazolo[4,3-*b*]pyridazine-thiones from the reaction of thiosemicarbazides with **1**.⁹ Additionally, we have shown that **1** reacts with *N*-imidoylthioureas to form pyrimidin-4(3*H*)-ones.¹⁰ We also noted that *N*-[2-(4'-[2.2]paracyclophanyl)-ethylidene]methylamine *N*-oxide reacted with 2,3-diphenylcyclopropenones to produce [2.2]paracyclophane-based pyrrole(-2-one, -thione and -ylidene-malononitrile) in good yields via formal [3π+3π] cycloaddition.¹¹ As part of our research to synthesize heterocyclic compounds, we recently synthesized a series of 1,3-thiazines by reactions of *N*-aroylsubstituted thioureas with ethyl propiolate, dimethyl but-2-ynedioate and (*E*)-1,4-diphenylbut-2-ene-1,4-dione.¹² Recent literature¹³ has shown the utility of 1,3,4-oxadiazole derivatives as ancillary ligands for highly efficient OLEDs.¹³ In this letter, we report the cycloadditions of

substituted ylidene-*N*-phenylhydrazine-carbothioamides with 2,3-diphenylcyclopropenone (**1**), possibly followed by further in situ cyclization of the adducts. Thus, on adding glacial acetic acid solutions of **1**¹⁴ to ylidene-*N*-phenylhydrazine-carbothioamides **2a–e** (**2a**,¹⁵ **2b**,¹⁶ **2c**,¹⁷ **2d**¹⁸ and **2e**¹⁹) in the same solvent, the reaction proceeds to give 2,5,6,7-tetrasubstituted-pyrrolo[2,1-*b*](1,3,5-oxadiazolyl)-2-amines **5a–e** in 60–76% yields²⁰ (Scheme 1). We chose compounds **2a–e** having aryl groups with electron donating and withdrawing substituents on the benzene ring, in order to examine their reactivity. Moreover, we chose the thienyl derivative **2d** in order to generalize the idea beyond benzenoid aromatics, to heterocycle-substituted starting materials. The structural proof of **5a–e** was based upon the mass, ¹H NMR, ¹³C NMR and IR spectra as well as elemental analyses. For example, mass spectrometry and elemental analysis proved the molecular formula of **5a** as C₃₀H₂₃N₃O₂. The IR spectrum did not reveal any absorptions due to C=S or OH groups. However, a sharp band appeared at ν_{max} = 3290 cm^{−1} due to the presence of an amino group. An absorption band at ν_{max} = 1080 cm^{−1} was assigned to C–O stretching. In the ¹H NMR spectrum of **5a**, the aromatic protons resonated as two double doublets and four multiplets, respectively. Distinctive ¹³C NMR signals of **5a** appeared at δ = 156.4, 142.0, 122.2,

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Scheme 1. Mechanism for the formation of pyrrolo[2,1-b]-1,3,4-oxadiazoles **5a-e**.

120.0, 117.0 and 51.0 corresponding to C-2, NH-Ph C, C-7, C-5, C-7a and OCH₃, respectively. Four carbon signals of the thiophene moiety were assigned in the ¹³C NMR spectrum of **5d** at δ = 136.6, 126.8, 125.6 and 124.2 corresponding to thiophene-C-2, thiophene-C-3-H, thiophene-C-5-H and thiophene-C-4-H, respectively. The structure of the products obtained (Scheme 1) supports the formal [2+3] cycloaddition pathway proposed by Eicher¹⁻⁴ to form adducts **3a-e**. Thereafter, cyclization of **3a-e** together with aromatization of the pyrrole ring is proposed to furnish intermediates **4a-e**. Ultimately, intermediates **4a-e** lose a molecule of hydrogen sulfide to form the stable heterocycles **5a-e** (Scheme 1).

In conclusion, yliden-*N*-phenylhydrazine-carbothioamides react with 2,3-diphenylcyclopropenone by way of an initial [2+3] cycloaddition followed by a cyclization process.

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- General procedure: To a 250 cm³ two-necked round-bottomed flask containing a solution of **2a-e** (2 mmol) in glacial acetic acid (100 mL), a solution of **1** (0.412 g, 2 mmol) in glacial acetic acid (10 mL) was added dropwise with stirring. The mixture was stirred at room temperature for 1 h, and then at reflux for 4–8 h (the reaction was monitored by TLC). The solvent was evaporated under vacuum and the solid residue was dissolved in dry acetone (30 mL) and the solution was chromatographed on thin layer plates (silica gel) using toluene/ethyl acetate (10:1). The mobile phases containing products **5a-e** were extracted and the obtained products were recrystallized from the stated solvents.
- [6,7-Diphenyl-5-(4'-methoxyphenyl)-pyrrolo[2,1-b]oxadiazolyl]-2-phenylamine (**5a**). Orange crystals (0.70 g, 76%), mp 222 °C (ethanol). ¹H NMR (400 MHz, CDCl₃): δ = 8.82 (s, 1H, NH), 7.90 (dd, 2H, *J* = 8.00, 1.0 Hz, Ar-H), 7.50–7.20 (m, 9H, Ph-H), 7.00–6.84 (m, 6H, Ph-H), 6.72 (dd, 2H, *J* = 8.0, 1.0 Hz, Ar-H), 3.90 (s, 3H, OCH₃). ¹³C NMR (400 MHz, CDCl₃): δ = 156.4 (C-2), 152.0 (Ar-C-O), 142.0 (NH-Ph C), 136.2 (O-Ph C), 134.8 (O-Ph 2CH), 134.4 (C-7, Ph C), 132.6 (C-6, Ph C), 132.0, 128.0 (*ortho*-2Ph CH), 127.2, 127.0, 126.6 (*meta*-Ph 2CH), 125.8 (O-Ph 2CH), 123.8, 123.6, 123.4 (*para*-Ph CH), 123.0 (C-6), 122.2 (C-7), 120.8 (C-2, NH-Ph 2CH), 120.0 (C-5), 117.0 (C-7a), 51.0 (OCH₃). IR (KBr): ν_{max} = 3290 (m, NH), 3080–3008 (w, Ar-CH), 2980–2860 (m, aliph.-CH), 1612 (s, C=N), 1590 (m, C=C), 1080 (s, C-O) cm⁻¹. λ_{max} (CH₃CN, lg ϵ , nm): 440 (4.2). MS (EI): *m/z* (%) = 457 [M⁺] (100), 440 (64), 380 (24), 338 (22), 302 (24), 279 (14), 220 (18), 178 (68), 152 (24), 119 (34), 85 (24), 77 (30). Anal. Calcd for C₃₀H₂₃N₃O₂ (457.54): C, 78.76; H, 5.07; N, 9.18. Found: C, 78.86; H, 5.10; N, 9.10.
- [6,7-Diphenyl-5-(2'-hydroxyphenyl)-pyrrolo[2,1-b]oxadiazolyl]-2-phenylamine (**5b**). Orange plates (0.64 g, 72%), mp 240–242 °C (methanol). ¹H NMR (400 MHz, CDCl₃): δ = 9.50 (s, 1H, OH), 8.80 (s, 1H, NH), 7.56 (d, 1H, *J* = 1.0 Hz, *ortho*-OHAr-H), 7.45–7.30 (m, 4H, Ph-H), 7.20–7.00 (m, 9H, Ph-H), 6.80–6.60 (m, 5H, Ph-H). ¹³C NMR (100.6 MHz, CDCl₃): δ = 156.0 (C-3), 141.6 (NH-Ph C), 140.2 (HO-Ar-C-4'), 136.2 (HO-Ar-C-1'), 134.0 (C-7, Ph C), 132.6 (C-6, Ph C), 132.4 (*ortho*-HOAr 2CH), 131.6, 127.8, 127.0 (*ortho*-2Ph CH), 127.0, 126.8, 126.4 (*meta*-Ph 2CH), 124.2, 124.0, 123.6 (*para*-Ph CH), 123.4 (C-6), 122.5 (C-7), 120.6 (C-2, NH-Ph 2CH), 120.2 (C-5), 117.4 (C-7a). IR (KBr): ν_{max} = 3465 (m, OH), 3280 (m, NH), 3080–3012 (w, Ar-CH), 1610 (s, C=N), 1594 (m, C=C), 1450 (s), 1075 (m, C-O) cm⁻¹. λ_{max} (CH₃CN, lg ϵ , nm): 460 (4.4). MS (EI): *m/z* (%) = 444 [M+1] (40),

443 [M⁺] (100), 426 (38), 412 (22), 380 (24), 330 (26), 192 (40), 118 (26), 94 (36), 77 (30). Anal. Calcd for C₂₉H₂₁N₃O₂ (443.51): C, 78.54; H, 4.77; N, 9.47. Found: C, 78.40; H, 4.70; N, 9.38.

[6,7-Diphenyl-5-(4'-chlorophenyl)-pyrrolo[2,1-b]oxadiazolyl]-2-phenylamine (**5c**). Orange crystals (0.59 g, 64%), mp 298 °C (acetonitrile). ¹H NMR (400 MHz, CDCl₃): δ = 8.85 (s, 1H, NH), 7.46–7.22 (m, 9H, Ph-H), 6.90–6.70 (m, 8H, Ph-H), 6.50 (dd, 2H, J = 8.0, 1.0 Hz, Ar-H). ¹³C NMR (100.6 MHz, CDCl₃): δ = 156.0 (C-2), 141.5 (NH-Ph C), 133.4 (C-7, Ph C), 131.4 (C-6, Ph C), 130.0 (C-5, Ph C), 128.2, 128.0, 127.8 (*ortho*-2Ph CH), 127.0, 126.8, 126.4 (*meta*-Ph 2CH), 126.0 (Cl-Ar C), 123.8, 123.6, 123.0 (*para*-Ph CH), 122.6 (C-6), 122.0 (C-7), 121.8, 121.4 (Cl-Ar 2CH), 120.4 (C-5), 118.0 (C-7a). IR (KBr): ν_{max} = 3286 (m, NH), 3060–3000 (w, Ar-CH), 1610 (s, C=N), 1592 (m, C=C), 1070 (s, C-O), cm⁻¹. λ_{max} (CH₃CN, lg ε, nm): 442 (4.3). MS (EI): m/z (%) = 463 [M+2] (34), 461 [M⁺] (100), 448 (24), 439 (64), 342 (26), 340 (32), 278 (14), 276 (18), 220 (18), 178 (60), 152 (20), 134 (30), 120 (34), 114 (32), 118 (34), 112 (34), 77 (26). Anal. Calcd for C₂₉H₂₀ClN₃O (461.96): C, 75.40; H, 4.36; Cl, 7.67; N, 9.10. Found: C, 75.30; H, 4.30; Cl, 7.60; N, 9.12.

(6,7-Diphenyl-5-thiophen-2'-yl-pyrrolo[2,1-b]oxadiazolyl)-2-phenylamine (**5d**). Orange plates (0.52 g, 60%), mp 180 °C (methanol). ¹H NMR (400 MHz, CDCl₃): δ = 8.86 (s, 1H, NH), 7.66–7.52 (m, 7H, Ph-H), 7.50 (dd, 1H, J = 7.6, 1.0 Hz), 7.30 (dd, 1H, J = 7.6, 1.0 Hz), 7.20–6.90 (m, 8H, Ph-H), 6.84 (t, 1H, J = 7.6 Hz). ¹³C NMR (100.6 MHz, CDCl₃): δ = 156.8 (C-2), 141.8 (NH-Ph C), 136.6

(2-thiophene C), 133.6 (C-7, Ph C), 132.8 (C-6, Ph C), 128.6, 128.2, 127.8 (*ortho*-2Ph-CH), 127.6, 127.4, 127.0 (*meta*-2Ph-CH), 126.8 (3-thiophene-CH), 126.4, 126.0, 125.8 (*para*-Ph-CH), 125.6 (5-thiophene-CH), 124.2 (4-thiophene-CH), 123.6 (C-7), 122.8 (C-6), 120.4 (C-5), 118.0 (C-7a). IR (KBr): ν_{max} = 3320 (s, NH), 3170–3020 (w, Ar-CH), 1610 (s, C=N), 1586 (s, C=C), 1120 (C-S), 1070 (s, C-O), cm⁻¹. λ_{max} (CH₃CN, lg ε, nm): 466 (3.6). MS (EI): m/z = 433 [M⁺] (60), 350 (100), 304 (34), 226 (30), 192 (26), 118 (24), 92 (34), 124 (20), 77 (46). Anal. Calcd for C₂₇H₁₉N₃OS (433.54): C, 74.80; H, 4.42; N, 9.69; S, 7.40. Found: C, 74.67; H, 4.50; N, 9.60; S, 7.30.

(5,6,7-Triphenyl-pyrrolo[2,1-b]-1,3,4-oxadiazolyl)-2-phenylamine (**5e**). Orange crystals (0.60 g, 70%), mp 250 °C (ethyl acetate). ¹H NMR (400 MHz, DMSO-*d*₆): δ = 8.90 (s, 1H, NH), 7.60–7.30 (m, 10H, Ph-H), 7.10–6.90 (m, 5H, Ph-H), 6.80–6.74 (m, 5H, Ar-H). ¹³C NMR (100.6 MHz, DMSO-*d*₆): δ = 156.0 (C-2), 142.0 (NH-Ph C), 134.0 (C-7, Ph C), 132.4 (C-6, Ph C), 132.0 (C-5, Ph C), 128.6, 128.0, 127.6, 127.4 (*ortho*-2Ph CH), 127.0, 126.6, 126.4, 126.2 (*meta*-Ph 2CH), 125.6, 124.8, 124.4, 123.8 (*para*-Ph CH), 123.5 (C-7), 122.6 (C-6), 120.6 (C-5), 118.2 (C-7a). IR (KBr): ν_{max} = 3295 (m, NH), 3080–3008 (w, Ar-CH), 1612 (s, C=N), 1590 (m, C=C), 1450 (s), 1072 (m, C-O) cm⁻¹. λ_{max} (CH₃CN, lg ε, nm): 438 (4.4). MS (EI): m/z (%) = 427 [M⁺] (100), 410 (20), 350 (34), 324 (22), 274 (34), 256 (18), 220 (18), 178 (68), 152 (24), 118 (40), 77 (36). Anal. Calcd for C₂₉H₂₁N₃O (427.51): C, 81.48; H, 4.95; N, 9.83. Found: C, 81.30; H, 4.90; N, 9.76.