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Tetrahedron Letters 49 (2008) 4060–4062
Tetrahedron Letters

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

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Received 22 December 2007; revised 28 March 2008; accepted 10 April 2008
Available online 13 April 2008

**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**.


*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 literature[13] 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% yields[20] (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, $^1$H NMR, $^{13}$C NMR and IR spectra as well as elemental analyses. For example, mass spectrometry and elemental analysis proved the molecular formula of **5a** as $C_{30}H_{23}N_3O_2$. The IR spectrum did not reveal any absorptions due to C=S or OH groups. However, a sharp band appeared at $\nu_{max} = 3290\ cm^{-1}$ due to the presence of an amino group. An absorption band at $\nu_{max} = 1080\ cm^{-1}$ was assigned to C–O stretching. In the $^1$H NMR spectrum of **5a**, the aromatic protons resonated as two double doublets and four multiplets, respectively. Distinctive $^{13}$C NMR signals of **5a** appeared at $\delta = 156.4$, 142.0, 122.2,

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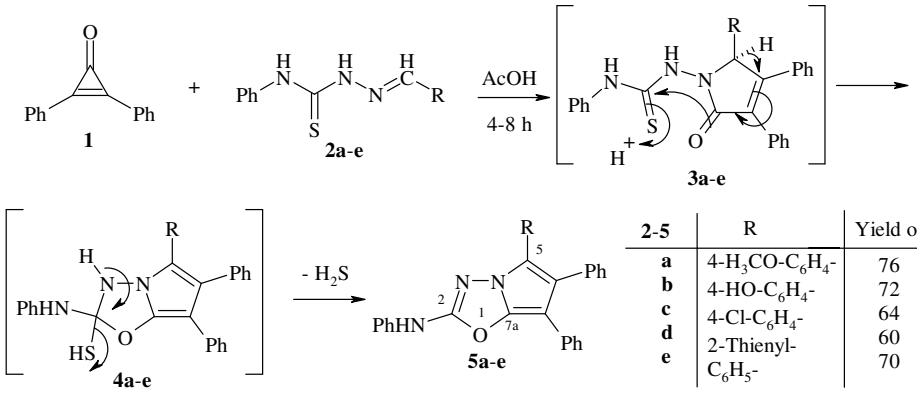
0040-4039/$ - see front matter © 2008 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2008.04.066




| 2-5 | R | Yield of **5** (%) |
|---|---|---|
| **a** | 4-$H_3CO$-$C_6H_4$- | 76 |
| **b** | 4-HO-$C_6H_4$- | 72 |
| **c** | 4-Cl-$C_6H_4$- | 64 |
| **d** | 2-Thienyl- | 60 |
| **e** | $C_6H_5$- | 70 |

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 O*C*$H_3$, respectively. Four carbon signals of the thiophene moiety were assigned in the $^{13}$C NMR spectrum of **5d** at $\delta = 136.6$, 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 Eicher[1–4] 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, ylidene-*N*-phenylhydrazine-carbothioamides react with 2,3-diphenylcyclopropenone by way of an initial [2+3] cycloaddition followed by a cyclization process.

## Acknowledgement

Professor Dr. Ashraf A. Aly thanks the DAAD foundation for financial support to stay in Germany, Braunschweig University, Institute for Organic Chemistry.

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20. General procedure: To a 250 $cm^3$ 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). $^1$H NMR (400 MHz, $CDCl_3$): $\delta = 8.82$ (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, $OCH_3$). $^{13}$C NMR (400 MHz, $CDCl_3$): $\delta = 156.4$ (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 ($OCH_3$). IR (KBr): $\nu_{max} = 3290$ (m, NH), 3080–3008 (w, Ar-CH), 2980–2860 (m, aliph.-CH), 1612 (s, C=N), 1590 (m, C=C), 1080 (s, C–O) $cm^{-1}$. $\lambda_{max}$ ($CH_3CN$, 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 $C_{30}H_{23}N_3O_2$ (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). $^1$H NMR (400 MHz, $CDCl_3$): $\delta = 9.50$ (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). $^{13}$C NMR (100.6 MHz, $CDCl_3$): $\delta = 156.0$ (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): $\nu_{max} = 3465$ (m, OH), 3280 (m, NH), 3080–3012 (w, Ar-CH), 1610 (s, C=N), 1594 (m, C=C), 1450 (s), 1075 (m, C–O) $cm^{-1}$. $\lambda_{max}$ ($CH_3CN$, 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 $C_{29}H_{21}N_3O_2$ (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). $^1$H NMR (400 MHz, $CDCl_3$): $\delta = 8.85$ (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). $^{13}$C NMR (100.6 MHz, $CDCl_3$): $\delta = 156.0$ (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): $\nu_{max} = 3286$ (m, NH), 3060–3000 (w, Ar-CH), 1610 (s, C=N), 1592 (m, C=C), 1070 (s, C–O), $cm^{-1}$. $\lambda_{max}$ ($CH_3CN$, lg $\varepsilon$, 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 $C_{29}H_{20}ClN_3O$ (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). $^1$H NMR (400 MHz, $CDCl_3$): $\delta = 8.86$ (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). $^{13}$C NMR (100.6 MHz, $CDCl_3$): $\delta = 156.8$ (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): $\nu_{max} = 3320$ (s, NH), 3170–3020 (w, Ar-CH), 1610 (s, C=N), 1586 (s, C=C), 1120 (C-S), 1070 (s, C–O), $cm^{-1}$. $\lambda_{max}$ ($CH_3CN$, lg $\varepsilon$, 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 $C_{27}H_{19}N_3OS$ (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). $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta = 8.90$ (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). $^{13}$C NMR (100.6 MHz, DMSO-$d_6$): $\delta = 156.0$ (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): $\nu_{max} = 3295$ (m, NH), 3080–3008 (w, Ar-CH), 1612 (s, C=N), 1590 (m, C=C), 1450 (s), 1072 (m, C–O) $cm^{-1}$. $\lambda_{max}$ ($CH_3CN$, lg $\varepsilon$, 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 $C_{29}H_{21}N_3O$ (427.51): C, 81.48; H, 4.95; N, 9.83. Found: C, 81.30; H, 4.90; N, 9.76.