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Reaction between thiocarbamidoalkyl naphthols and acetylenic esters: An interesting cyclocondensation reaction for the synthesis of new thiazolidin-4-one derivatives

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Abstract. This investigation was set to provide derivatives of thiazolidin-4-ones incorporated with aminoalkyl naphthols in a molecular frame work. For this purpose, a series of 1-thiocarbamidoalkyl-2-naphthols was prepared by the three component condensation of aromatic aldehydes, phenylthiourea and 2-naphthol. In the next step, these compounds underwent reaction with dialkyl acetylenedicarboxylates at ambient temperature in ethanol to afford the corresponding 4-thiazolidinones in high yields. Following the completion of the reaction, the products were solidified and isolated by filtration. The method is easy, inexpensive, chemoselective and environmentally benign and illustrates an interesting instance of click chemistry.

Keywords. Multi component reaction; cyclocondensation; 1-thiocarbamidoalkyl-2-naphthols; acetylenic esters; thiazolidin-4-ones.

1. Introduction

During the last two centuries, multicomponent reactions have been considered as a unique and versatile tool for the creation of diverse chemical libraries of pharmaceutical agents.[1] One instance of the MCRs is the synthesis of 1-amidoalkyl-2-naphthol derivatives. These compounds are a versatile class of intermediates in the synthesis of biologically active reagents such as 1, 3-oxazines and aminoalkyl naphthols. It is, therefore, not surprising that a considerable number of protocols for the synthesis of these compounds by three-component condensation of aldehydes, β-naphthol and acetonitrile or amides/carbamates or urea in the presence of different catalysts have been reported.[2–5] However, in consequence of the lower reactivity of the thio analogues of amide and urea, only limited published information regarding the replacement of amide with thioamide or thiourea are available in the literature.[6–9] The thioamido- and thiocarbamidoalkyl naphthols which were produced by these methods can be used as convenient building blocks in the synthesis of sulfur and nitrogen containing heterocyclic compounds.

Thiazolidinones are an important group of five membered heterocyclic rings. The 4-thiazolidinone scaffold has featured in a number of clinically prescribed drugs. They can be used as antibacterial,[10] anti-inflammatory,[11,12] anti-cancer,[13–15] antihistaminic,[16] anti-fungal,[17] anti-HIV[18] and anti-hypertensive[19] agents.

Due to the biological importance of these compounds, the development of efficient protocols for their preparation has received significant attention and several improved procedures have recently been reported. One of the most convenient and effective methods that has ever been designed is the reaction between thioamides and thiosemicarbazide derivatives with dialkyl acetylenedicarboxylates which provides 2-imino-5-alkoxycarbonyl-thiazolidin-4-ones.[20–22]

The current study was designed to afford derivatives of thiazolidin-4-ones incorporated with aminoalkyl naphthols in a molecular frame work.

2. Experimental

2.1 *Materials and Methods*

All chemicals were purchased from Merck and Fluka Chemical Companies and were used without further purification. Melting points were determined using an Electrothermal-9100 melting point apparatus and were uncorrected. IR spectra were run on a Bruker Tensor-27 FT-IR spectrometer. NMR spectra were recorded on a Bruker 400-MHz spectrometer using $CDCl_3$ as solvent. Carbon assignments for some of products were made based on DEPT 135 spectroscopy. Elemental analyses

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were performed on a Vario Macro CHNS Element Analyzer.

2.2 *General procedure for the preparation of thiazolidin-4-ones*

To a magnetically well stirred solution of 1-thiocarbamido-2-naphthol (1 mmol) in EtOH (5 mL), dimethyl acetylenedicarboxylate (DMAD) or diethyl acetylenedicarboxylate (DEAD), (1.2 mmol) was added at ambient temperature. The reaction mixture was then allowed to stir for an appropriate time. After the completion of reaction (as indicated by TLC, ethyl acetate: *n*-hexane, 30:70), the solid product was filtered off and washed thoroughly with cold ethanol.

2.3 *Characterization data*

2a: IR (KBr): ν_{max} = 3430, 3062, 2955, 1731, 1684, 1644 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 9.81 (s, 1H, OH), 7.95 (d, J = 8.4 Hz, 1H), 7.75 (d, J = 7.6 Hz, 1H), 7.69 (d, J = 8.8 Hz, 1H), 7.64-7.54 (m, 3H), 7.50-7.46 (m, 1H), 7.43-7.40 (m, 2H), 7.36-7.21 (m, 6H), 7.09 (s, 1H), 7.08 (d, J = 9.2 Hz, 1H), 6.58 (s, 1H), 3.94 (s, 3H, OCH_3) ppm; ^{13}C NMR+DEPT (100 MHz, $CDCl_3$) δ: 166.4 (C), 164.0 (C), 154.7 (C), 153.6 (C), 140.6 (C), 139.7 (C), 133.5 (C), 131.6 (C), 130.0 (CH), 129.9 (CH), 129.8 (CH), 128.9 (CH), 128.8 (CH), 128.7 (C), 127.9 (CH), 127.8 (CH), 127.5 (CH), 127.0 (CH), 122.9 (CH), 121.4 (CH), 120.3 (CH), 117.6 (CH), 115.8 (C), 66.1 (CH), 52.9 (CH_3) ppm. Anal. Calc. for $C_{29}H_{22}N_2O_4S$: C 70.43, H 4.48, N 5.66, S 6.48%. Found: C 70.83, H 4.55, N 5.41, S 6.53%.

2b: IR (KBr): ν_{max} = 3439, 3072, 3007, 1725, 1705, 1649 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 9.15 (s, 1H, OH), 7.71 (d, J = 8.4 Hz, 1H), 7.65 (dd, J_1 = 11.6 Hz, J_2 = 8.8 Hz, 2H), 7.50-7.34 (m, 5H), 7.25-7.19 (m, 3H), 7.06 (d, J = 8.4 Hz, 1H), 7.00 (d, J = 8.8 Hz, 1H), 6.96 (s, 1H), 6.93 (dd, J_1 = 8.4 Hz, J_2 = 2 Hz, 1H), 6.75 (s, 1H), 3.79 (s, 3H, OCH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ: 166.3, 164.2, 155.1, 154.9, 139.8, 136.1, 134.6, 133.9, 133.4, 131.4, 131.2, 130.6, 129.9, 129.8, 129.6, 128.8, 128.7, 128.0, 127.9, 127.5, 123.3, 121.1, 120.0, 117.5, 115.2, 62.7, 52.9 ppm. Anal. Calc. for $C_{29}H_{20}Cl_2N_2O_4S$: C 61.82, H 3.58, N 4.97, S 5.69%. Found: C 61.99, H 3.55, N 4.69, S 6.69%.

2c: IR (KBr): ν_{max} = 3483, 3062, 2949, 1730, 1691, 1646 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 9.72 (s, 1H, OH), 7.88 (d, J = 8.4 Hz, 1H), 7.76 (d, J = 7.6 Hz, 1H), 7.70 (d, J = 9.2 Hz, 1H), 7.64-7.54 (m, 3H), 7.51-7.46 (m, 1H), 7.34-7.30 (m, 5H), 7.24 (td, J_1 = 8.4 Hz, J_2 = 2 Hz, 2H), 7.10 (s, 1H), 7.07 (d, J = 9.2 Hz, 1H), 6.54 (s, 1H), 3.94 (s, 3H, OCH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ: 166.4, 163.9, 154.7, 154.0, 139.4, 139.1, 133.8, 133.4, 131.4, 130.2, 129.9, 129.1, 128.9, 128.8, 128.7, 127.7, 127.1, 123.1, 121.2, 120.3, 117.8, 115.3, 65.3, 53.0 ppm. Anal. Calc. for $C_{29}H_{21}ClN_2O_4S$: C 65.84, H 4.00, N 5.30, S 6.06%. Found: C 66.30, H 3.90, N 4.88, S 6.51%.

2d: IR (KBr): ν_{max} = 3477, 3145, 3062, 2949, 1726, 1709, 1631 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 9.35 (s, 1H, OH), 7.88 (d, J = 8.4 Hz, 1H), 7.77-7.72 (m, 2H), 7.59-7.42 (m, 5H), 7.34-7.31 (m, 3H), 7.25 (dd, J_1 = 8.0 Hz, J_2 = 1.2 Hz, 1H), 7.18 (dt, J_1 = 8.0 Hz, J_2 = 1.6 Hz, 1H), 7.11 (d, J = 8.8 Hz, 1H), 7.07 (d, J = 6.8 Hz, 1H), 7.05 (s, 1H), 6.92 (s, 1H), 3.90 (s, 3H, OCH_3) ppm; ^{13}C NMR+DEPT (100 MHz, $CDCl_3$) δ: 166.3 (C), 164.2 (C), 154.9 (C), 154.7 (C), 140.0 (C), 137.4 (C), 133.5 (C), 133.2 (C), 131.6 (C), 130.3 (CH), 130.2 (CH), 129.9 (CH), 129.8 (CH), 129.7 (CH), 129.4 (CH), 128.8 (CH), 128.7 (C), 127.9 (CH), 127.7 (CH), 127.3 (CH), 123.2 (CH), 121.4 (CH), 120.0 (CH), 117.3 (CH), 115.7 (C), 63.3 (CH), 52.8 (CH_3) ppm. Anal. Calc. for: $C_{29}H_{21}ClN_2O_4S$: C 65.84, H 4.00, N 5.30, S 6.06%. Found: C 65.75, H 4.10, N 5.32, S 6.56%.

2e: IR (KBr): ν_{max} = 3473, 3193, 3071, 2972, 1724, 1707, 1688, 1648 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 9.36 (s, 1H, OH), 8.25 (d, J = 2.0 Hz, 1H), 8.09 (dd, J_1 = 8.0 Hz, J_2 = 1.2 Hz, 1H), 7.93 (d, J = 8.4 Hz, 1H), 7.79 (d, J = 7.6 Hz, 1H), 7.74 (d, J = 8.8 Hz, 1H), 7.66-7.51 (m, 5H), 7.41 (t, J = 8.0 Hz, 1H), 7.38-7.34 (m, 3H), 7.11 (s, 1H), 7.09 (d, J = 8.8 Hz, 1H), 6.67 (s, 1H), 3.93 (s, 3H, OCH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ: 166.3, 163.9, 154.7, 148.4, 142.8, 133.4, 131.4, 130.6, 130.0, 129.9, 129.1, 128.8, 127.7, 127.5, 123.3, 122.9, 122.1, 120.3, 118.2, 65.9, 53.0 ppm. Anal. Calc. for $C_{29}H_{21}N_3O_6S$; C 64.55, H 3.92, N 7.79, S 5.94%. Found: C 64.03, H 4.21, N 7.54, S 5.66 %.

2f: IR (KBr): ν_{max} = 3480, 3062, 2953, 1715, 1691, 1642 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 9.51 (s, 1H, OH), 8.12 (td, J_1 = 9.2 Hz, J_2 = 2.0 Hz, 2H), 7.89 (d, J = 8.4 Hz, 1H), 7.78 (d, J = 7.2 Hz, 1H), 7.73 (d, J = 8.8 Hz, 1H), 7.65-7.49 (m, 7H), 7.36- 7.33 (m, 3H), 7.11 (s, 1H), 7.08 (d, J = 8.8 Hz, 1H), 6.66 (s, 1H), 3.93 (s, 3H, OCH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ: 166.3, 163.8, 154.7, 154.6, 147.8, 147.7, 147.3, 139.2, 133.3, 131.3, 130.6, 130.0, 129.9, 129.1, 128.8, 128.2, 127.7, 127.4, 124.1, 123.3, 121.0, 120.3, 118.2, 64.6, 53.0 ppm. Anal. Calc. for $C_{29}H_{21}N_3O_6S$; C 64.55, H 3.92, N 7.79, S 5.94%. Found: C 64.55, H 4.40, N 7.39, S 5.55%.

2g: IR (KBr): ν_{max} = 3386, 3061, 2949, 1730, 1690, 1643 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 9.87 (s, 1H,

OH), 7.91 (d, J = 8.4 Hz, 1H), 7.74 (d, J = 7.6 Hz, 1H), 7.68 (d, J = 8.8 Hz, 1H), 7.63-7.53 (m, 3H), 7.49-7.45 (m, 1H), 7.35-7.30 (m, 5H), 7.09 (s, 1H), 7.07 (d, J = 8.8 Hz, 1H), 6. 80 (td, J_1 = 8.8 Hz, J_2 = 2 Hz, 2H), 6.53 (s, 1H), 3.94 (s, 3H, OCH_3), 3.74 (s, 3H, OCH_3) ppm; ^{13}C NMR+DEPT (100 MHz, $CDCl_3$) δ: 166.4 (C), 163.9 (C), 159.1 (C), 154.6 (C), 153.2 (C), 139.7 (C), 133.5 (C), 132.8 (C), 131.5 (C), 129.9 (CH), 129.8 (CH), 128.9, 128.8 (CH), 128.7 (CH), 127.8 (CH), 127.0 (CH), 122.9 (CH), 121.4 (CH), 120.3 (CH), 117.5 (CH), 115.9 (C), 114.2 (CH), 65.7 (CH), 55.2 (CH_3), 52.9 (CH_3) ppm. Anal. Calc. for $C_{30}H_{24}N_2O_5S$: C 68.69, H 4.61, N 5.34, S 6.11%. Found: C 68.36, H 4.99, N 5.70, S 6.27%.

2h: IR (KBr): ν_{max} = 3374, 3061, 2949, 1731, 1690, 1644 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 10.0 (s, 1H, OH), 7.90 (d, J = 8.4 Hz, 1H), 7.74 (d, J = 7.2 Hz, 1H), 7.68 (d, J = 8.8 Hz, 1H), 7.57-7.44 (m, 4H), 7.32-7.29 (m, 3H), 7.25 (td, J_1 = 8.8 Hz, J_2 = 2.8 Hz, 2H), 7.09 (s, 1H), 7.06 (d, J = 8.8 Hz, 1H), 6.69 (td, J_1 = 8.8 Hz, J_2 = 2.8 Hz, 2H), 6.51 (s, 1H), 5.68 (s, 1H, OH), 3.94 (s, 3H, OCH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ: 166.5, 164.0, 155.5, 154.4, 153.3, 139.8, 133.4, 132.6, 131.5, 129.9, 128.9, 128.8, 128.7, 127.7, 127.0, 123.0, 121.5, 120.2, 117.6, 115.9, 115.7, 65.7, 53.0 ppm. Anal. Calc. for $C_{29}H_{22}N_2O_5S$: C 68.22, H 4.34, N 5.49, S 6.28%. Found: C 68.11, H 4.18, N 5.47, S 5.56%.

2i: IR (KBr): ν_{max} = 3456, 3141, 3071, 1726, 1680, 1639 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 9.84 (s, 1H, OH), 7.94 (d, J = 8.8 Hz, 1H), 7.75 (d, J = 7.2 Hz, 1H), 7.69 (d, J = 9.2 Hz, 1H), 7.63-7.54 (m, 3H), 7.50-7.40 (m, 3H), 7.35-7.30 (m, 4H), 7.27-7.21 (m, 2H), 7.09 (s, 1H), 7.07 (s, 1H), 6.58 (s, 1H), 4.39 (q, J = 7.2 Hz, 2H, O**C**H_2CH$_3$), 1.41 (t, J = 7.2 Hz, 3H, OCH$_2$**C**H_3) ppm; ^{13}C NMR+DEPT (100 MHz, $CDCl_3$) δ: 166.0 (C), 164.0 (C), 154.7 (C), 153.8 (C), 140.6 (C), 139.4 (C), 133.5 (C), 131.6 (C), 130.0 (CH), 129.9 (CH), 129.8 (CH), 128.9 (CH), 128.8 (CH), 128.7 (C), 127.9(CH), 127.8 (CH), 127.5 (CH), 127.0 (CH), 122.9 (CH), 121.4 (CH), 120.3 (CH), 118.1 (CH), 115.8 (C), 66.1 (CH), 62.2 (CH_2), 14.2 (CH_3) ppm; Anal. Calc. for $C_{30}H_{24}N_2O_4S$: C 70.85, H 4.76, N 5.51, S 6.30%. Found: C 70.37, H 4.87, N 5.42, S 6.58%

2j: IR (KBr): ν_{max} = 3437, 3070, 2993, 1727, 1698, 1651 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 9.28 (s, 1H, OH), 7.82 (d, J = 8.8 Hz, 1H), 7.78-7.73 (m, 2H), 7.60-7.44 (m, 5H), 7.35-7.30 (m, 3H), 7.16 (d, J = 8.4 Hz, 1H), 7.11 (d, J = 8.8 Hz, 1H), 7.05 (s, 1H), 7.03 (dd, J_1 = 8.8 Hz, J_2 = 2.0 Hz, 1H), 6.86 (s, 1H), 4.34 (q, J = 7.2 Hz, 2H, OCH_2CH$_3$), 1.37 (t, J = 7.2 Hz, 3H, OCH$_2$**C**H_3) ppm.; ^{13}C NMR (100 MHz, $CDCl_3$) δ: 165.8, 164.2, 155.3, 154.9, 139.4, 136.1, 134.6, 133.9, 133.5, 131.4, 131.2, 130.6, 129.9, 129.8, 129.6, 128.8, 128.7, 128.0, 127.9, 127.5, 123.3, 121.1, 120.0, 118.1, 115.3, 62.7, 62.1, 14.2 ppm; Anal. Calc. for $C_{30}H_{22}Cl_2N_2O_4S$; C 62.40, H 3.84, N 4.85, S 5.55. Found: C 62.74, H 3.77, N 4.48, S 5.35%.

2k: IR (KBr): ν_{max} = 3434, 3068, 2985, 1726, 1699, 1652 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 9.74 (s, 1H, OH), 7.88 (d, J = 8.4 Hz, 1H), 7.76 (d, J = 8.0 Hz, 1H), 7.70 (d, J = 8.8 Hz, 1H), 7.64-7.54 (m, 3H), 7.50-7.46 (m, 1H), 7.35-7.30 (m, 5H), 7.25 (td, J_1 = 8.4 Hz, J_2 = 2.4 Hz, 2H), 7.10 (s, 1H), 7.07 (d, J = 8.8 Hz, 1H), 6.55 (s, 1H), 4.39 (q, J = 7.2 Hz, 2H, O**C**H_2CH$_3$), 1.41(t, J = 7.2 Hz, 3H, OCH$_2$CH_3) ppm; ^{13}C NMR+DEPT (100 MHz, $CDCl_3$) δ: 166.0 (C), 164.0 (C), 154.7 (C), 154.2 (C), 139.2 (C), 139.1 (C), 133.7 (C), 133.4 (C), 131.4 (C), 130.2 (CH), 129.9 (CH), 129.1 (CH), 128.9 (CH), 128.8 (CH), 128.7 (C), 127.7 (CH), 127.1 (CH), 123.1 (CH), 121.2 (CH), 120.3 (CH), 118.3 (CH), 115.4 (C), 65.3 (CH), 62.2 (CH_2), 14.2 (CH_3) ppm; Anal. Calc. for $C_{30}H_{23}ClN_2O_4S$; C 66.35, H 4.27, N 5.16, S 5.90%. Found: C 66.55, H 4.15, N 5.03, S 5.61%.

2l: IR (KBr): ν_{max} = 3430, 3065, 2983, 1726, 1697, 1637 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 9.36 (s, 1H, OH), 7.88 (d, J = 8.4 Hz, 1H), 7.76 (d, J = 8.4 Hz, 1H), 7.73 (d, J = 8.8 Hz, 1H), 7.59-7.46 (m, 4H), 7.42 (dd, J_1 = 8.0 Hz, J_2 = 0.8 Hz, 1H), 7.34-7.30 (m, 3H), 7.25 (dd, J_1 = 7.6 Hz, J_2 = 1.6 Hz, 1H), 7.18 (dt, J_1 = 8.0 Hz, J_2 = 1.6 Hz, 1H), 7.11 (d, J = 8.8 Hz, 1H), 7.07 (dd, J_1 = 7.6 Hz, J_2 = 1.2 Hz, 1H), 7.04 (s, 1H), 6.91 (s, 1H), 4.34 (q, J = 7.2 Hz, 2H, OCH_2CH$_3$), 1.37 (t, J = 7.2 Hz, 3H, OCH$_2$CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ: 165.8, 164.3, 154.9, 154.8, 139.7, 137.5, 133.5, 133.2, 131.6, 130.3, 130.2, 129.9, 129.8, 129.7, 129.4, 128.8, 128.7, 127.9, 127.7, 127.3, 123.2, 121.4, 120.0, 117.9, 115.7, 63.3, 62.0, 14.2 ppm; Anal. Calc. for $C_{30}H_{23}ClN_2O_4S$: C 66.35, H 4.27, N 5.16, S 5.90%. Found: C 66.88, H 4.27, N 5.03, S 5.75%.

2m: IR (KBr): ν_{max} = 3516, 3078, 2978, 1732, 1697, 1652 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 9.39 (s, 1H, OH), 8.25 (t, J = 2.0 Hz, 1H), 8.11-8.08 (m, 1H), 7.93 (d, J = 8.4 Hz, 1H), 7.79 (d, J = 7.6 Hz, 1H), 7.74 (d, J = 8.8 Hz, 1H), 7.66-7.51 (m, 5H), 7.41 (t, J = 8.0 Hz, 1H) 7.38-7.34 (m, 3H), 7.11 (s, 1H), 7.09 (d, J = 8.8 Hz, 1H), 6.67 (s, 1H), 4.39 (q, J = 7.2 Hz, 2H, OCH_2CH$_3$), 1.40 (t, J = 7.2 Hz, 3H, OCH$_2$CH_3) ppm; ^{13}C NMR+DEPT (100 MHz, $CDCl_3$) δ: 165.8 (C), 164.0 (C), 155.3 (C), 154.8 (C), 154.7 (C), 148.4 (C), 142.8 (C), 138.8 (C), 133.4 (CH), 131.4 (C), 130.6 (CH), 130.0 (CH), 129.9 (CH), 129.1 (CH), 128.8 (C), 127.7 (CH), 127.5 (CH), 123.3 (CH), 122.9

(CH), 122.1 (CH), 120.9 (CH), 120.3 (CH), 118.8 (CH), 64.2 (CH), 62.3 (CH_2), 14.2 (CH_3) ppm; Anal. Calc. for $C_{30}H_{23}N_3O_6S$; C 65.09, H 4.19, N 7.59, S 5.79%.Found: C 65.16, H 4.38, N 7.52, S 5.43%.

2n: IR (KBr): ν_{max} = 3434, 3069, 2981, 1728, 1698, 1649 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ: 9.54 (s, 1H, OH), 8.14-8.10 (m, 2H), 7.90 (d, J = 8.4 Hz, 1H), 7.78 (d, J = 7.6 Hz, 1H), 7.73 (d, J = 8.8 Hz, 1H), 7.65-7.50 (m, 6H), 7.37-7.32 (m, 3H), 7.11 (s, 1H), 7.08 (d, J = 8.8 Hz, 1H), 6.66 (s, 1H), 4.39 (q, J = 7.2 Hz, 2H, OCH_2CH$_3$), 1.40 (t, J = 7.2 Hz, 3H, OCH$_2$CH_3) ppm; ^{13}C NMR+DEPT (100 MHz, $CDCl_3$) δ: 165.9 (C), 163.9 (C), 155.3 (C), 154.7 (C), 147.7 (C), 147.4 (C), 138.8 (C), 133.3 (C), 131.3 (C), 130.6 (CH), 130.1 (CH), 130.0 (CH), 129.1 (CH), 128.8, 128.2 (CH), 127.7 (CH), 127.4 (CH), 124.1 (CH), 123.3 (CH), 120.9 (CH), 120.3 (CH), 118.7 (CH), 115.0 (C), 64.6 (CH), 62.3 (CH_2), 14.2 (CH_3) ppm; Anal. Calc. for $C_{30}H_{23}N_3O_6S$: C 65.09, H 4.19, N 7.59, S 5.79%. Found: C 65.25, H 4.28, N 7.59, S 5.74%.

2o: IR (KBr): ν_{max} = 3437, 3066, 2998, 1729, 1691, 1646 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ: 9.89 (s, 1H, OH), 7.91 (d, J = 8.8 Hz, 1H), 7.74 (d, J = 7.6 Hz, 1H), 7.68 (d, J = 8.8 Hz, 1H), 7.63-7.54 (m, 3H), 7.49-7.44 (m, 1H), 7.35-7.30 (m, 5H), 7.09 (s, 1H), 7.07 (d, J = 8.8 Hz, 1H), 6.80 (dt, J_1 = 8.8 Hz, J_2 = 2.8 Hz, 2H), 6.54 (s, 1H), 4.40 (q, J = 7.2 Hz, 2H, OCH_2CH$_3$), 3.75 (s, 3H, OCH_3), 1.41 (t, J = 7.2 Hz, 3H, OCH$_2$CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ: 166.0, 164.0, 159.1, 154.6, 153.4, 139.4, 133.5, 132.8, 131.5, 129.9, 129.8, 129.7, 128.9, 128.8, 128.7, 127.8, 126.9, 122.9, 121.4, 120.3, 118.0, 115.9, 114.2, 65.7, 62.1, 55.2, 14.2 ppm; Anal. Calc. for $C_{31}H_{26}N_2O_5S$: C 69.13, H 4.87, N 5.20, S 5.95%. Found: C 69.62, H 4.95, N 5.22, S 6.35%.

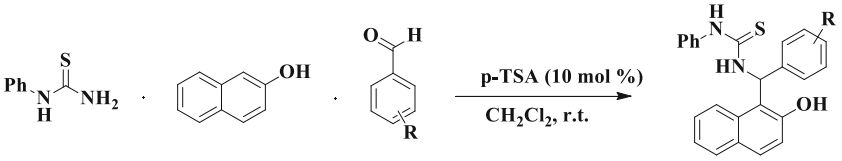
2p: IR (KBr): ν_{max} = 3418, 3067, 2983, 1733, 1689, 1642 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ: 10.07 (s, 1H, OH), 7.89 (d, J = 8.4 Hz, 1H), 7.74 (d, J = 7.6 Hz, 1H), 7.68 (d, J = 8.8 Hz, 1H), 7.56-7.43 (m, 4H), 7.32-7.29 (m, 3H), 7.24 (td, J_1 = 8.4 Hz, J_2 = 2.8 Hz, 2H), 7.08 (s, 1H), 7.06 (d, J = 8.8 Hz, 1H), 6.67 (td, J_1 = 8.4 Hz, J_2 = 2.8 Hz, 2H), 6.51 (s, 1H), 5.54 (s, 1H, OH), 4.39 (q, J = 7.2 Hz, 2H, OCH_2CH$_3$), 1.41 (t, J = 7.2 Hz, 3H, OCH$_2$CH_3) ppm; ^{13}C NMR+DEPT (100 MHz, $CDCl_3$) δ: 166.1 (C), 164.0 (C), 155.5 (C), 154.3 (C), 153.5 (C), 139.5 (C), 133.4 (C), 132.6 (C), 131.5 (C), 129.9 (CH), 128.9 (CH), 128.8 (CH), 128.7 (C), 127.7 (CH), 127.0 (CH), 123.0 (CH), 121.5 (CH), 120.2 (CH), 118.1 (CH), 116.0 (C), 115.7 (CH), 65.7 (CH), 62.3 (CH_2), 14.2 (CH_3) ppm; Anal. Calc. for $C_{30}H_{24}N_2O_5S$; C 68.69, H 4.61, N 5.34, S 6.11%. Found: C 68.81, H 4.66, N 5.48, S 6.41%.

3. Results and Discussion

In this research work, the use of 1-thiocarbamidoalkyl-2-naphthol derivatives **1** as precursors in the synthesis of new 4-thiazolidinones is described. The eight required substrates (**1a**-**1h**) were synthesized according to a previously reported method[8] via three component reaction of 2-naphthol, phenylthiourea and aromatic aldehydes, containing electron-donating and electron-withdrawing groups at various positions of aromatic ring, in the presence of *p*-TSA (10 mol %) as catalyst at ambient temperature in dichloromethane (scheme 1).

After synthesizing a series of 1-thiocarbamidoalkyl-2-naphthols, we turned our attention on the synthesis of thiazolidin-4-one derivatives via reaction of thiocarbamidoalkyl naphthols with acetylenic esters. In an initial study, the reaction of 1-((2-hydroxynaphthalen-1-yl) (phenyl) methyl)-3-phenylthiourea (**1a**) with DMAD was examined in different solvents. As table 1 shows, using of ethanol as solvent gave best results, so ethanol was chosen as the solvent for this reaction.

In the first experiment, the reaction of 1-((2-hydroxynaphthalen-1-yl) (phenyl) methyl)-3-phenylthiourea (**1a**, 1 mmol) with dimethyl acetylenedicarboxylate (1.2 mmol) as representative, was performed at room temperature with reaction time 1 h. After completion of the reaction, the mixture was filtered and the precipitate washed thoroughly with cold ethanol. The pure solid product was isolated without need to further purification, because the excess of unreacted DMAD is soluble in EtOH and could easily be removed from the reaction mixture. In addition, the reaction profile is very



R= 1a: H, 1b: 2,4 $(Cl)_2$, 1c: 4-Cl, 1d: 2- Cl, 1e: 3-NO_2 , 1f: 4- NO_2, 1g: 4- OCH_3, 1h: 4-OH

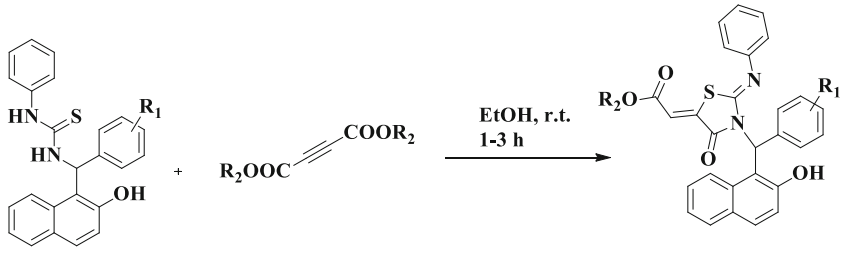
Scheme 1. Preparation of 1-thiocarbamidoalkyl-2-naphthols.

Table 1. Effect of solvents on product formation.

Entry	Solvent	Time (min)	Yield (%)
1	CH_2Cl_2	180	0
2	$CHCl_3$	180	0
3	THF	180	80
4	EtOH	60	90
5	1, 4-Dioxane	180	60
6	CH_3CN	120	75

Table 2. Synthesis of thiazolidin-4- ones from thiocarbamidoalkyl naphthols.

Product	R_1	R_2	Yield (%)	Time (min)	M.p.(°C)
2a	H	CH_3	90	60	243–245
2b	2,4-dichloro	CH_3	85	60	212–213
2c	4-Chloro	CH_3	91	90	187–189
2d	2-Chloro	CH_3	92	75	146–148
2e	3-NO_2	CH_3	86	120	132–133
2f	4-NO_2	CH_3	93	120	143–145
2g	4-OCH_3	CH_3	89	75	203–204
2h	4-OH	CH_3	90	60	224–226
2i	H	CH_2CH_3	81	180	171–172
2j	2,4-dichloro	CH_2CH_3	82	170	210–211
2k	4-Chloro	CH_2CH_3	86	180	189–190
2l	2-Chloro	CH_2CH_3	84	165	121–122
2m	3-NO_2	CH_2CH_3	80	180	201–202
2n	4-NO_2	CH_2CH_3	85	180	229–231
2o	4-OCH_3	CH_2CH_3	86	165	203–205
2p	4-OH	CH_2CH_3	81	150	223–225



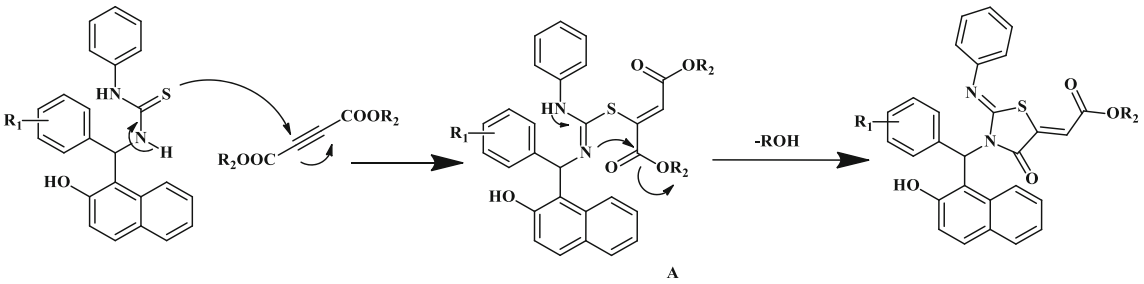
Scheme 2. Reaction of thiocarbamidoalkyl naphthols with DMAD and DEAD.

clean and no by product is formed. Encouraged by these excellent results, we examined the scope of this method for reactions of the other synthesized thiocarbamidoalkyl naphthols with DMAD. In every case, the reaction was accomplished in a short time and the corresponding product was obtained in high yield. It is pertinent to note, since some of the compounds such as **1e** and **1f** are less soluble in ethanol, longer reaction time (about 2 h) was needed for the reaction to be completed. The difference in the product yields is mainly due to the different solubility of thiocarbamidoalkyl naphthols in ethanol which is a result of different substituents on the phenyl ring.

In a similar fashion, the reactions of thiocarbamidoalkyl naphthols with diethyl acetylenedicarboxylate have been investigated. It was found that these reactions gave lower yields of products and needed longer times to completion (2–3 h) due to the low reactivity of DEAD compared to DMAD. The results are summarized in table 2 (scheme 2).

A plausible mechanism for the synthesis of thiazolidin-4-one derivatives has been proposed in scheme 3. This reaction begins by addition of the sulfur atom onto the acetylene triple bond which is susceptible to nucleophilic attack. Subsequently the intermediate (A) undergoes intramolecular cyclization to afford deliberated thiazolidin-4-one.

All the synthesized thiazolidin-4-ones have been characterized on the basis of elemental and spectral studies.



Scheme 3. A plausible mechanism for the formation of thiazolidin-4- ones.

The FT-IR spectrum of **2a** revealed a broad band at 3430 cm^{-1} due to the absorption of OH group. Two strong absorption bands were also revealed at 1731 and 1684 cm^{-1} due to carbonyl groups. The ^1H NMR spectrum of **2a** showed singlets at 3.94 and 6.58 ppm, which are due to the methyl and vinyl protons. The singlet at 7.09 ppm was assigned to aliphatic hydrogen of aminoalkyl naphthol moiety (CH) and the signal observed at 9.81 ppm corresponds to the OH proton. Also, the ^1H NMR of **2a** revealed signals between 7.08 and 7.95 with the integration of 16 protons which was consistent with protons of naphthyl ring and two phenyl rings. The ^{13}C NMR of this compound showed two characteristic peaks at 164.0 and 166.4 ppm for carbonyl groups. The peaks at 52.9 and 66.1 ppm correspond to the methyl and methine carbons of compound. The other signals in the range of 115.8–154.7 ppm belong to the other sp^2 carbons in the molecule.

4. Conclusion

In conclusion, an efficient, facile and environmentally benign synthesis of novel functionalized thiazolidin-4-ones has been achieved by the reaction of 1-thiocarbamidoalkyl-2-naphthols with dialkyl acetylenedicarboxylates in ethanol. The attractive features of this procedure are the mild reaction conditions, short reaction times, absence of any catalyst, high yields and simple isolation of products.

Supplementary Information

Supplementary Information associated with this article is available at www.ias.ac.in/chemsci.

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