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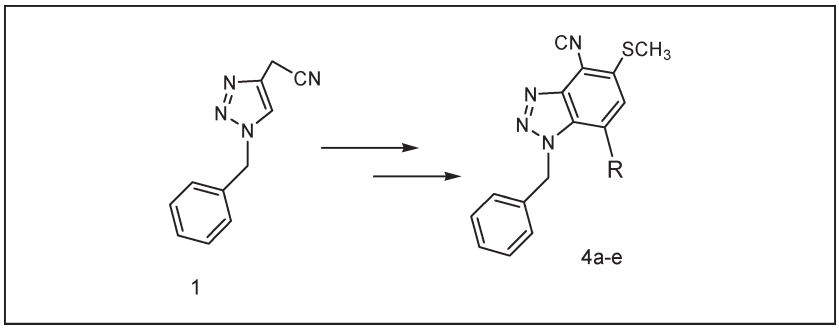

2-(1-Benzyl-1*H*–1,2,3-triazole-4-yl)-3-methylsulfanyl-5-oxo-5-substituted-*pent*-2-enenitrile **3a-e** were obtained in good yields by condensation of (1-benzyl-1*H*-1,2,3-triazole-4-yl)acetonitrile (**1**) with various α-oxoketene dithioacetals **2a-e** in the presence of sodium hydride. The intermediates **3a-e** underwent facile acid-induced cyclization in the presence of PTSA to afford the corresponding benzotriazoles **4a-e** in moderate yields.

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INTRODUCTION

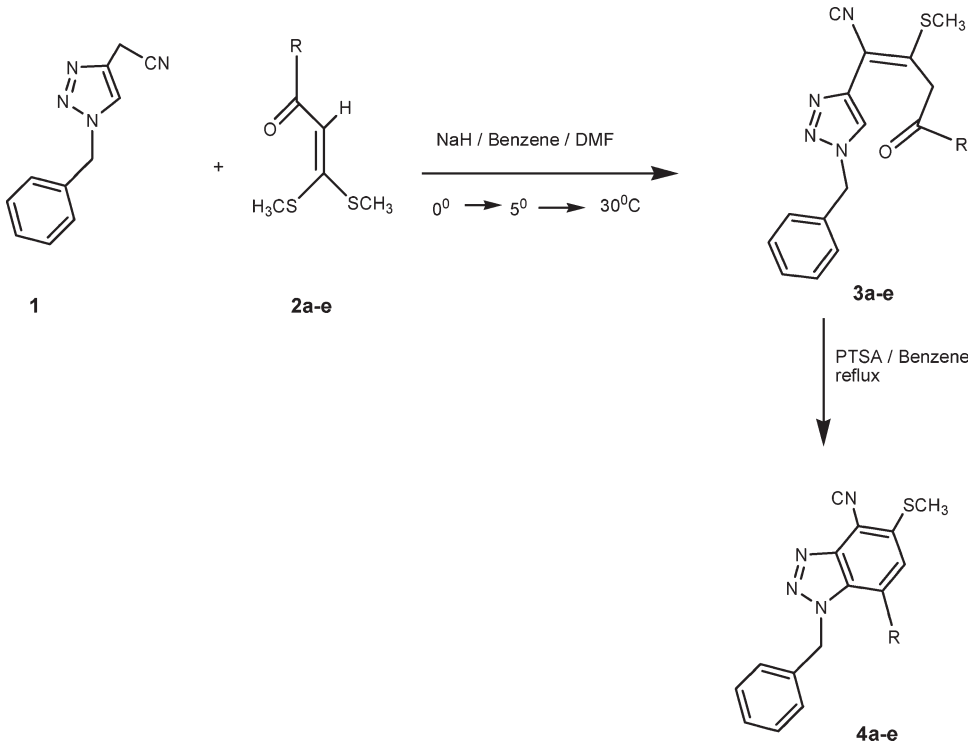
The α-oxoketene dithioacetals owe their potential synthetic application to their varied intrinsic chemical properties. The presence of carbonyl functionality and its position in conjugation with double bond carrying bis(alkylthio)group at the β-position place them among the versatile 1,3-dielectrophilic 3-carbon equivalents. The [3+3] benzoannulation methodologies involving the reaction of allyl anions with α-oxoketene dithioacetals, developed by Junjappa and coworkers [1–3], has emerged as a versatile method for the construction of a wide variety of aromatics, heteroaromatics, and benzoheterocycles. These benzoannulation methodologies have became the subject of intense investigation due to the easy availability of 1,3-dielectrophilic synthons, wide structural variants of allyl anions and a high degree of regiocontrol observed in these reactions.

In continuation of our studies on JI annulation and Heteroaromatic annulation reaction [4] on triazole chemistry [5] and in view of the pharmacological significance of benzotriazoles [6–9], we became interested in the corresponding benzotriazole group of compounds and found that the method developed by Junjappa and Ila to construct an aromatic ring over the preconstructed triazole ring would be an efficient route for the synthesis of benzotriazole. Interestingly, the literature survey revealed that entire benzotriazole chemistry has been confined to construct a triazole ring over the appropriately substituted benzene ring [10–13]. We therefore deemed it interesting to attempt the construction of benzotriazoles from the preconstructed triazole ring with required substitution. We have successfully achieved this goal and present our results in this communication.

DISCUSSION

The required α-oxoketene dithioacetals **2a-e** were prepared as described in the literature [14,15] and (1-benzyl-1*H*-1,2,3-triazol-4-yl]acetonitrile **1** was prepared from 1-benzyl-4-chloromethyl-1*H*-1,2,3-triazole [16]. The reaction of (1-benzyl-1*H*-1,2,3-triazol-4-yl)-acetonitrile **1** with various α-oxoketene dithioacetals **2a-e** in the presence of sodium hydride in dry dimethyl formamide and benzene mixture (50:50) afforded the corresponding 2-(1-benzyl-1*H*-1,2,3-triazol-4-yl]-3-methylsulfanyl-5-oxo-5-substituted-*pent*-2-enenitrile **3a-e** in good yields (60–75%) (Scheme 1). Evolution of methanethiol (MeSH) was observed during the course of the reaction. Formation of this conjugate adduct was ascertained by spectral and analytical data. The presence of a sharp band in the region 1675–1746 cm^{-1} due to the carbonyl group and a sharp band around 2200 cm^{-1}, due to cyano group supports the formation of the adduct. The ^1H NMR spectra exhibited two sets of characteristic methylene

Scheme 1. a, R = Ph; b, R = *p*BrPh; c, R = *p*ClPh; d, R = *p*CH_3Ph; and e, R = 1-Naphthyl.



protons as singlets in the region δ 4.9–5.1 and δ 5.4–5.6 for $COCH_2$ and N—CH_2 respectively depending upon the alkyl/aryl substituents. The C5—H of the triazole ring in all the synthesized intermediates resonated around δ 7.6. The ^{13}C NMR spectra of the compound **3** also confirmed the formation of the intermediates, where characteristic carbonyl carbon resonated in the region δ 180.2 and the adjacent methylene carbon at around δ 44.07. These intermediates **3a-e** underwent facile acid-induced cyclization in presence of PTSA to furnish corresponding 1-benzyl-5-methylsulfanyl-7-substituted-1*H*-1,2,3-benzotriazole-4-carbonitrile **4a-e** in moderate yields (40–60%). The absence of carbonyl band in IR spectra, C5—H of triazole and carbonyl-methylene protons in ^1H NMR spectra confirms the cyclization. Similarly the carbonyl carbon and one of methylene carbon also disappeared in ^{13}C NMR spectra, confirming the formation of cyclized product **4**. Its application for functionally substituted benzotriazoles and other heterocycles is in progress.

EXPERIMENTAL

Melting points were determined in open capillaries and are uncorrected. IR spectra were recorded on Nicolet Impact-410 FT-IR spectrophotometer, using KBr pellet technique. ^1H NMR and ^{13}C NMR experiments were performed at 300 MHz on Bruker AC-300F spectrometer (TMS as internal standard). Mass spectra were recorded on EI-70 EV instrument. Elemental analyses were carried out using Heraus CHN rapid analyzer.

(1-Benzyl-1*H*-1,2,3-triazole-4-yl)acetonitrile (1). A mixture of 1-benzyl-4-chloromethyl-1*H*-1,2,3-triazole (20.9 g, 0.1 mol) [16] and sodium cyanide (0.3 mol) in aq. ethanol (85%, 120 mL) was refluxed for 12 h (TLC). The reaction mixture was cooled, poured into water (200 mL), and extracted twice with benzene (100 mL). The benzene extract was washed thrice with water (200 mL), dried over anhydrous sodium sulfate and passed through silica bed. The filtrate was concentrated under reduced pressure to yield residual golden yellow oil in good yield (75%), which solidifies on cooling as needles. Pale brown solid, Yield 60%, mp 65–67°C; ir (KBr) ν cm^{-1}: 3066, 2922, 2229, 1412, 1129, 710; ^1H NMR (300 MHz, $CDCl_3$) δ: 3.86 (s, 2H, CH_2CN), 5.54(s, 2H, CH_2-N), 7.28–7.53(m, 5H, Ar-H), 7.30(s, 1H, C5—H of triazole); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 17.5, 52.8, 112.6, 125.5, 128.4, 128.6, 129.2, 134.7. Anal. calcd for $C_{11}H_{10}N_4$: C, 66.65; H, 5.08; N, 28.26. Found: C, 66.61; H, 5.01; N, 28.29%

General procedure for the preparation of 2-(1-benzyl-1*H*-1,2,3-triazole-4-yl)-3-methylsulfanyl-5-oxo-5-substituted-*pent*-2-enenitrile (3a-e). To a suspension of NaH (60%, 0.88 g, 22 mmol) in dry benzene (20 mL) and dry DMF (20 mL) under stirring, a solution of (1-benzyl-1*H*-1,2,3-triazol-4-yl) acetonitrile **1** (2 g, 10 mmol) in dry benzene (10 mL) was added at 0°C over a period of 15 minutes and further stirred at 0–5°C for 15 min. Solution of α-oxoketene dithioacetal **2a-e** (10 mmol) in dry DMF (10 mL) was added slowly over 10 min to this mixture with stirring at 0–5°C. The reaction mixture was stirred at room temperature for 4–5 h. The solution was poured into aqueous ammonium chloride solution (8%, 200 mL), and extracted twice with benzene (50 mL). The collective benzene extract was washed thrice with water

(100 mL), dried over anhydrous sodium sulfate, passed through a silica bed and concentrated. After standing for 2 h, the crystallized material was separated by filtration and washed with a mixture of benzene and hexane (1:1) to afford **3a-e**.

2-(1-Benzyl-1H-1,2,3-triazole-4-yl)-3-methylsulfanyl-5-oxo-5-phenyl-*pent*-2-enenitrile (3a). Colorless solid, yield 70%, mp 114–116°C; ir (KBr) ν cm^{-1}: 3136, 2930, 2214, 1680, 1610, 1574, 1471; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.55 (s, 3H, SCH_3), 5.46 (s, 2H, NCH_2), 5.03 (s, 2H, $COCH_2$), 7.03–7.84 (m, 11H, C5—H of triazole, ArH); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 15.4, 44.07, 61.20, 96.3, 119.7, 127.8, 128.4, 128.6, 130.2, 132.4, 142.0, 165.4, 190.2. Anal. calcd for $C_{21}H_{18}N_4OS$: C, 67.36; H, 4.85; N, 14.96. Found: C, 67.24; H, 4.79; N, 14.99%.

2-(1-Benzyl-1H-1,2,3-triazole-4-yl)-5-(4-bromophenyl)-3-methylsulfanyl-5-oxo-*pent*-2-enenitrile (3b). Colorless solid, yield 75%, mp 140–142°C; ir (KBr) ν cm^{-1}: 3143, 2925, 2213, 1680, 1677, 1610, 1579, 1492; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.58 (s, 3H, SCH_3), 5.40 (s, 2H, NCH_2), 4.95 (s, 2H, $COCH_2$), 7.37–7.90 (m, 10H, C5—H of triazole, ArH); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 14.8, 46.6, 58.8, 107.0, 125.5, 125.7, 127.5, 128.4, 128.6, 129.2, 129.4, 130.8, 136.4, 144.3, 163.4, 184.5. Anal. calcd for $C_{21}H_{17}BrN_4OS$: C, 55.64; H, 3.78; N, 12.36. Found: C, 55.58; H, 3.65; N, 12.45%.

2-(1-Benzyl-1H-1,2,3-triazole-4-yl)-5-(4-chlorophenyl)-3-methylsulfanyl-5-oxo-*pent*-2-enenitrile (3c). Colorless solid, yield 65%, mp 152–154°C; ir (KBr) ν cm^{-1}: 3139, 2923, 2209, 1678, 1587, 1468; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.48 (s, 3H, SCH_3), 5.55 (s, 2H, NCH_2), 5.00 (s, 2H, $COCH_2$), 6.72–7.76 (m, 10H, C5—H of triazole, ArH); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 15.2, 47.1, 61.5, 99.7, 119.0, 125.5, 128.4, 128.6, 129.2, 129.4, 130.0, 135.5, 137.7, 142.0, 164.8, 190.0. Anal. calcd for $C_{21}H_{17}ClN_4OS$: C, 61.68; H, 4.19; N, 13.70. Found: C, 61.56; H, 4.10; N, 13.82%.

2-(1-Benzyl-1H-1,2,3-triazole-4-yl)-5-(4-methylphenyl)-3-methylsulfanyl-5-oxo-*pent*-2-enenitrile (3d). Colorless solid, yield 60%, mp 139–141°C; ir (KBr) ν cm^{-1}: 3129, 2914, 2210, 1673, 1570, 1260; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.53 (s, 3H, SCH_3), 5.46 (s, 2H, NCH_2), 4.99 (s, 2H, $COCH_2$), 7.07–7.72 (m, 10H, C5—H of triazole, ArH); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 15.3, 20.5, 46.9, 59.8, 109.1, 125.5, 128.4, 128.5, 128.7, 129.2, 129.4, 134.4 137.7, 165.4, 190.0. Anal. calcd for $C_{22}H_{20}N_4OS$: C, 68.02; H, 5.19; N, 14.42. Found: C, 67.93; H, 5.09; N, 14.54%.

2-(1-Benzyl-1H-1,2,3-triazole-4-yl)-3-methylsulfanyl-5-(1-naphthyl)-5-oxo-*pent*-2-enenitrile (3e). Colorless solid, yield 65%, mp 146–148°C; ir (KBr) ν cm^{-1}: 3142, 2932, 2219, 1668, 1574, 1460; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.42 (s, 3H, SCH_3), 5.35 (s, 2H, NCH_2), 4.90 (s, 2H, $COCH_2$), 7.06–8.74 (m, 13H, C5—H of triazole, ArH); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 15.7, 47.7, 62.0, 102.3, 123.7, 125.5, 126.6, 127.6, 128.2, 128.4, 128.6, 129.9, 134.4, 144.9, 164.0, 186.5. Anal. calcd for $C_{25}H_{20}N_4OS$: C, 70.73; H, 4.75; N, 13.20. Found: C, 70.61; H, 4.68; N, 13.31%.

General procedure for the preparation of 1-benzyl-5-methylsulfanyl-7-substituted-1*H*-1,2,3-benzotriazole-4-carbonitrile (4a-e). A solution of 2-(1-benzyl-1*H*-1,2,3-triazol-4-yl)-3-methylsulfanyl-5-oxo-5-substituted-*pent*-2-enenitrile 3a-e (2.5 mmol) and PTSA (1 g, 5.3 mmol) in benzene was refluxed for 4–6 h. The reaction mixture (monitored by TLC) was concentrated and dissolved in chloroform and poured into aqueous sodium bicarbonate solution (6%, 150 mL). The organic layer was separated, washed thrice with water (100 mL) and dried over anhydrous sodium sulfate. The solvent was removed under reduced pressure to yield the greenish yellow oil, which was purified by column chromatography using a benzene-hexane mixture (45:55–80: 20v/v) as eluent to furnish 4a-e.

1-Benzyl-5-methylsulfanyl-7-phenyl-1H-1,2,3-benzotriazole-4-carbonitrile (4a). Yellow solid, yield 50%, mp 180–182°C; ir (KBr) ν cm^{-1}: 3140, 2923, 2219, 1572, 1498; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.58 (s, 3H, SCH_3), 5.40 (s, 2H, NCH_2), 7.06–7.82 (m, 11H, ArH); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 17.4, 61.1, 123.7, 125.5, 125.7, 126.4, 127.1, 127.6, 128.4, 128.6, 129.2, 129.4, 130.5, 130.7, 133.4, 139.0, 144.3. Anal. calcd for $C_{21}H_{16}N_4S$: C, 70.76; H, 4.52; N, 15.72. Found: C, 70.67; H, 4.67; N, 15.80%.

1-Benzyl-7-(4-bromophenyl)-5-methylsulfanyl-1H-1,2,3-benzotriazole-4-carbonitrile (4b). Green solid, yield 58%, mp 191–193°C; ir (KBr) ν cm^{-1}: 3134, 2924, 2211, 1583, 1486; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.50 (s, 3H, SCH_3), 5.65 (s, 2H, NCH_2), 7.02–7.94 (m, 10H, ArH); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 17.9, 61.7, 124.2, 124.4, 124.6, 126.1, 126.5, 127.8, 128.3, 128.6, 129.5, 131.5, 132.9, 139.7, 142.9. Anal. calcd for $C_{21}H_{15}BrN_4S$: C, 57.94; H, 3.47; N, 12.87. Found: C, 57.89; H, 3.35; N, 12.95%.

1-Benzyl-7-(4-chlorophenyl)-5-methylsulfanyl-1H-1,2,3-benzotriazole-4-carbonitrile (4c). Pale yellow solid, yield 60%, mp 187–189°C; ir (KBr) ν cm^{-1}: 3135, 2926, 2219, 1584, 1468; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.54 (s, 3H, SCH_3), 5.60 (s, 2H, NCH_2), 7.03–8.02 (m, 10H, ArH); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 16.5, 60.0, 108.4, 125.4, 125.6, 127.1, 128.2, 129.8, 132.0, 135.5, 137.4, 139.4. Anal. calcd for $C_{21}H_{15}ClN_4S$: C, 64.53; H, 3.87; N, 14.33. Found: C, 64.42; H, 3.78; N, 14.44%.

1-Benzyl-7-(4-methylphenyl)-5-methylsulfanyl-1H-1,2,3-benzotriazole-4-carbonitrile (4d). Pale yellow solid, yield 50%, mp 156–158°C; ir (KBr) ν cm^{-1}: 3132, 2920, 2214, 1580, 1466; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.48 (s, 3H, SCH_3), 5.41 (s, 2H, NCH_2), 7.05–7.69 (m, 10H, ArH); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 17.9, 60.5, 111.2, 123.9, 125.2, 125.4, 126.9, 127.1, 128.6, 137.0, 141.9. Anal. calcd for $C_{22}H_{18}N_4S$: C, 71.32; H, 4.90; N, 15,12. Found: C, 71.21; H, 4.80; N, 15.20%.

1-Benzyl-5-methylsulfanyl-7-(1-naphthyl)-1H-1,2,3-benzotriazole-4-carbonitrile (4e). Pale green solid, yield 40%, mp 170–172°C; ir (KBr) ν cm^{-1}: 3133, 2922, 2211, 1590, 1458; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.61 (s, 3H, SCH_3), 5.34 (s, 2H, NCH_2), 7.14–7.84 (m, 13H, ArH); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 16.4, 59.7, 114.4, 125.7, 127.1, 128.6, 129.2, 132.6, 137.3, 140.8. Anal. calcd for $C_{25}H_{18}N_4S$: C, 73.87; H, 4.46; N, 13.78. Found: C, 73.79; H, 4.51; N, 13.80%.

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