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A ONE-STEP SYNTHESIS OF 4,4'-(METHYLENEDI-4,1-PHENYLENE)BIS-[5-(2-THIENYLMETHYL)-2,4-DIHYDRO-3H-1,2,4-TRIAZOL-3-ONE]

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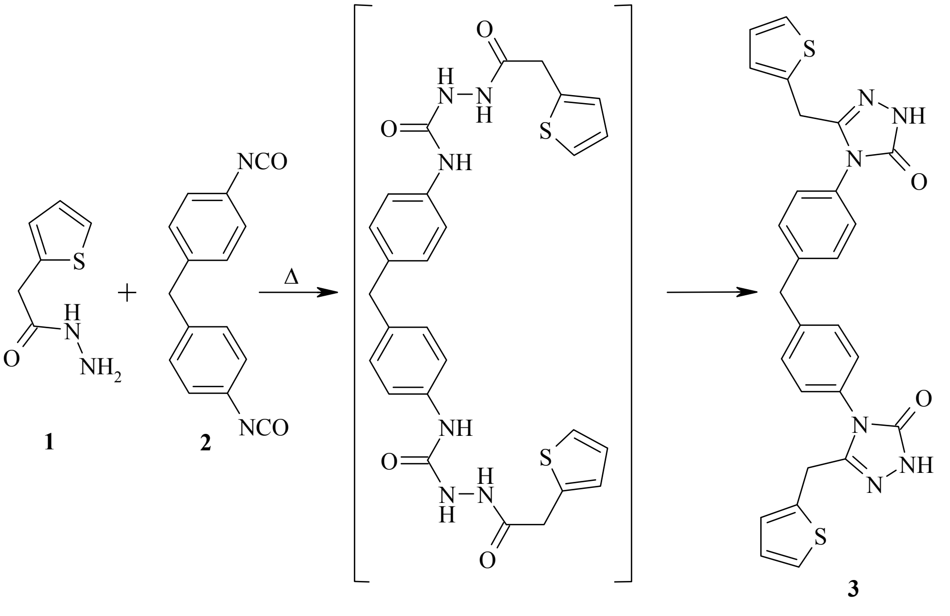
Heterocyclic rings have played an important role in medicinal chemistry, serving as the key templates central to the development of numerous important therapeutic agents. Among the numerous five-membered heterocycles studied, 1,2,4-triazoles have been identified as active core structures in antimicrobial [1], antitumor [2], anticonvulsant, and antiviral agents [3, 4]. One of the methods for the synthesis of these derivatives is the cyclization reaction of acetylsemicarbazides in alkaline medium [5–7].

Here I report a simple, one-step procedure for the synthesis of 4,4'-(methylenedi-4,1-phenylene)bis-[5-(2-thienylmethyl)-2,4-dihydro-3H-1,2,4-triazol-3-one] (**3**) in good yield.



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The title compound **3** was obtained by heating a mixture of the 2-thienylacetic acid hydrazide (**1**) with 4,4'-diphenylmethane diisocyanate (**2**). The process was carried out by heating the substrates in an oil bath at 100°C. The reaction is complete within 10 h. The results of elemental analysis and the spectral data indicate that the reaction leads to the formation of a cyclic five-membered ring system. The course of this reaction probably includes the formation of an intermediate semicarbazide derivative that spontaneously undergoes a cyclization reaction to the 1,2,4-triazole ring. The reaction mechanism will be the subject of further research. The method presented is more simple (two reagents), faster (one stage), and cheaper (less reagents) than the traditional cyclization method of semicarbazide derivatives.

Hydrazide **1** was prepared in our laboratory by a method described earlier [8]. IR spectra were recorded in KBr using a Specord IR-75 spectrophotometer. The ^{1}H and ^{13}C NMR spectra were recorded on a Bruker Avance 300 spectrometer (300 MHz) in DMSO-d$_6$ with TMS as internal standard. Purity was checked on Aluminum oxide 60 F$_{254}$ TLC plates in $CHCl_3$–EtOH, 10:1, solvent system with UV visualization.

4,4'-(Methylenedi-4,1-phenylene)bis[5-(2-thienylmethyl)-2,4-dihydro-3H-1,2,4-triazol-3-one] (3). A mixture of the hydrazide **1** (1.4 g, 20 mmol) and diisocyanate **2** (2.5 g, 10 mmol) was heated at 100–110ºC for 15 h. The product was washed with ether to remove the unreacted isocyanate, dried, and crystallized from ethanol. Yield 4.43 g (85%); mp 220ºC. IR spectrum, ν, cm^{-1}: 3185 (NH); 3069 (CH Ar); 2927, 1715 (C=O); 1448 (CH). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 4.03 (6H, s, 3CH$_2$); 6.56 (2H, d, *J* = 3.4, H thiophene); 6.79 (2H, dd, *J* = 5.1, *J* = 3.5, H thiophene); 7.12–7.36 (10H, m, H Ar); 11.76 (2H, s, 2NH). ^{13}C NMR spectrum, δ, ppm: 33.01 (CH$_2$); 38.36 (CH$_2$); 117.36, 123.64, 125.05, 125.29, 127.47 (CH Ar); 133.84, 135.29, 136.02, 153.96 (C Ar); 167.81 (C=O). Found, %: C 61.81; H 4.41; N 15.79. $C_{27}H_{22}N_6O_2S_2$. Calculated, %: C 61.58; H 4.21; N 15.96.

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