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REACTION OF 2-ARYL-5-R-5,6-DIHYDRO-7H-[1,2,4]-TRIAZOLO[5,1-*b*][1,3]THIAZIN-7-ONES WITH ARYL BROMOMETHYL KETONES AND BENZYL BROMIDE

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The products of the reaction of 2-aryl-5-R-5,6-dihydro-7H-[1,2,4]triazolo[5,1-b][1,3]thiazin-7-ones with aryl bromomethyl ketones are 2-aryl-7H-[1,2,4]triazolo[5,1-b][1,3]thiazin-7-ones and aryl methyl ketones or 2,5-diaryl[1,3]thiazolo[3,2-b][1,2,4]triazoles and 3-phenyl-2-propenoic acid, depending on the structure of R. The reaction of 2-aryl-5-R-5,6-dihydro-7H-[1,2,4]triazolo[5,1-b][1,3]thiazin-7-ones with benzyl bromide yields 5-aryl-3-benzylthio-4H-1,2,4-triazoles and 3-aryl-2-propenoyl bromide.

Keywords: aryl bromomethyl ketones, 2-aryl-5-R-5,6-dihydro-7H-[1,2,4]triazolo[5,1-*b*][1,3]thiazin-7-ones, 2-aryl-7H-[1,2,4]triazolo[5,1-*b*][1,3]thiazin-7-ones, benzyl bromide, 3-benzylsulfanil-5-aryl-4H-1,2,4-triazoles, 2,5-diaryl[1,3]thiazolo[3,2-*b*][1,2,4]triazoles, 3-phenyl-2-propenoic acid, recyclization.

We have recently proposed a new method for the synthesis of 2,5-diaryl-5,6-dihydro-7H-[1,2,4]triazolo[5,1-*b*][1,3]thiazin-7-ones involving the condensation of 3-aryl-4,5-dihydro-1H-1,2,4-triazole-5-thiones with 3-aryl-2-propenoyl chlorides [1,2]. Ali and Soliman [3] have reported the preparation of 2-aryl-5,6-dihydro-7H-[1,2,4]triazolo[5,1-*b*][1,3]thiazin-7-ones by heating 3-(5-aryl-4H-1,2,4-triazol-3-ylsulfanil)-propanoic acids with acetic anhydride and the reactions of these [1,2,4]triazolo[5,1-*b*][1,3]thiazin-7-ones with nucleophilic reagents such as amines and hydrazine. In the present work, we have investigated the reactions of 2,5-diaryl-5,6-dihydro-7H-[1,2,4]triazolo[5,1-*b*][1,3]thiazin-7-ones synthesized in our laboratory and 2-aryl-5,6-dihydro-7H-[1,2,4]triazolo[5,1-*b*][1,3]thiazin-7-ones described by Ali and Soliman [3] with aryl bromomethyl ketones and benzyl bromide, which were used in light of their high reactivity and thermal stability.

We have found that 5,6-dihydro-7H-[1,2,4]triazolo[5,1-*b*][1,3]thiazin-7-ones **1a-g** react with aryl bromomethyl ketones **2a**,**b** under vigorous conditions (fusion at 150-200°C). The direction of this reaction depends on the structure of substituent R in **1a-g**. When R = H, dehydrogenation of [1,2,4]triazolo[5,1-*b*]-[1,3]thiazin-7-ones **1a-c** occurs leading to 2-aryl-7H-[1,2,4]-triazolo[5,1-*b*][1,3]thiazin-7-ones **3a-c** and aryl methyl ketones **4a**,**b**. On the other hand, when R = Ph, thiazinones **1d-g** recyclize at 150°C to give 2-Ar^1-5-Ar^2-[1,3]thiazolo[3,2-*b*][1,2,4]triazoles **5a-e** as well cinnamic acid (**6**) (Scheme 1).

Benzyl bromide **7** does not react with [1,2,4]triazolo[5,1-*b*][1,3]thiazin-7-ones **1a-c** even at 200°C, while this bromide reacts with [1,2,4]triazolo[5,1-*b*][1,3]thiazin-7-ones **1d-f** already at 150°C. The products of this reaction are 3-benzylthio-5-aryl-4H-1,2,4-triazoles **8a-c** and 3-phenyl-2-propenoyl bromide (**9**) (Scheme 2).

The yields, melting points, and elemental analysis data of the reaction products are given in Table 1. 2-Phenyl-7H-[1,2,4]triazolo[5,1-*b*][1,3]thiazin-7-one (**3a**) was previously obtained by the cyclization of 3-(5-phenyl-4H-1,2,4-triazol-3-ylsulfanil)-2-propenoic acid in the presence of thionyl chloride [4], while

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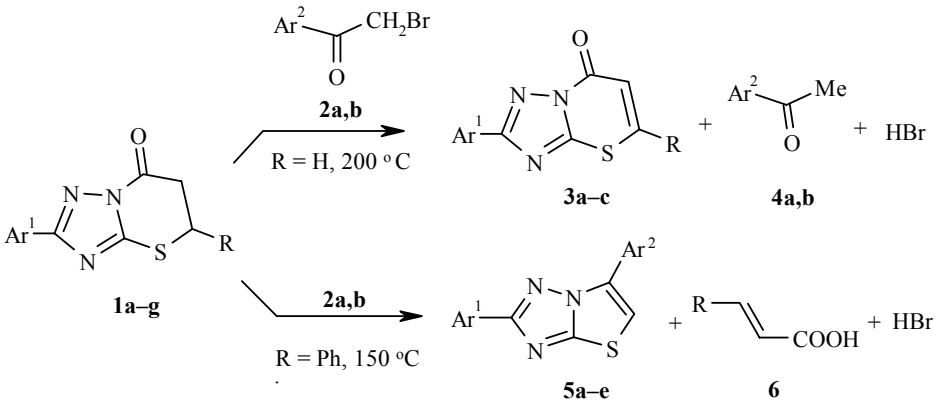
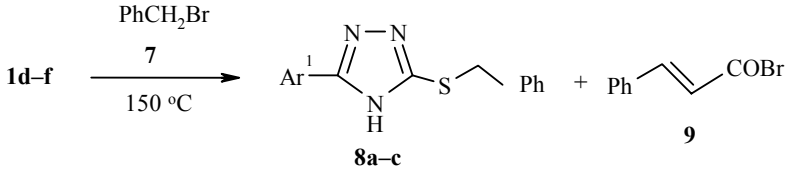
Scheme 1



1a,d, 3a, 5a Ar^1 = Ph, **1b,f, 3b, 5c** Ar^1 = *p*-ClC_6H_4, **1c,g, 3c, 5d** Ar^1 = *p*-FC_6H_4, **1e, 5b,e** Ar^1 = *p*-$MeOC_6H_4$; **2a, 4a, 5a-d** Ar^2 = Ph, **2b, 4b, 5e** Ar^2 = *p*-ClC_6H_4; **1a-c, 3a-c** R = H, **1d-g, 6** R = Ph

Scheme 2



8 a Ar^1 = Ph, **b** Ar^1 = *p*-ClC_6H_4 , **c** Ar^1 = *p*-$MeOC_6H_4$

[1,3]thiazolo[3,2-*b*][1,2,4]triazoles **5a-c,e** have been synthesized by heating 1-aryl-2-(5-aryl-4H-1,2,4-triazol-3-ylsulfanil)-1-ethanones in absolute ethanol at reflux [5] or in the thermal decomposition of 4-aryl-2-(5-aryl-1H-1,2,3,4-tetrazol-1-yl)-1,3-thiazoles [6]. Since the compounds described by Potts [5] and Ramachandraiah [6] were not characterized by spectral methods, we found it necessary to give the ^{1}H NMR and IR spectral data of the compounds synthesized in the present work (Table 2).

The reaction temperatures indicate the relative stability of the 1,3-thiazine ring in the starting [1,2,4]triazolo[5,1-*b*][1,3]thiazin-7-ones lacking a substituent at $C_{(5)}$ (**1a-c**, R = H) and with a phenyl substituent at this position (**1d-g**). Thiazinones **1d-f** react with aryl methyl ketones **2a**,**b** at 150°C, while thiazinones **1a-c** react with these ketones only at 200°C.

In all likelihood, the alkylation of [1,2,4]triazolo[5,1-*b*][1,3]thiazin-7-ones **1a-c** and **1d-g** initially occurs at $S_{(4)}$ with formation of unstable sulfonium salt **A**, which loses a proton and converts to intermediate **B**.

Then, the direction of the decomposition of **B** depends on the structure of substituent R at $C_{(5)}$. If R = H, intermediate **B** probably transforms into [1,2,4]triazolo[5,1-*b*][1,3]thiazin-7-one **3** and aryl methyl ketone **4**. On the other hand, if R = Ph, the S–$C_{(5)}$ is cleaved, and the amide of 3-aryl-2-propenoic acid **C** may possibly be formed, which then likely is converted into [1,3]thiazolo[3,2-*b*][1,2,4]triazole **5** and 3-phenyl-2-propenoic acid **6**.

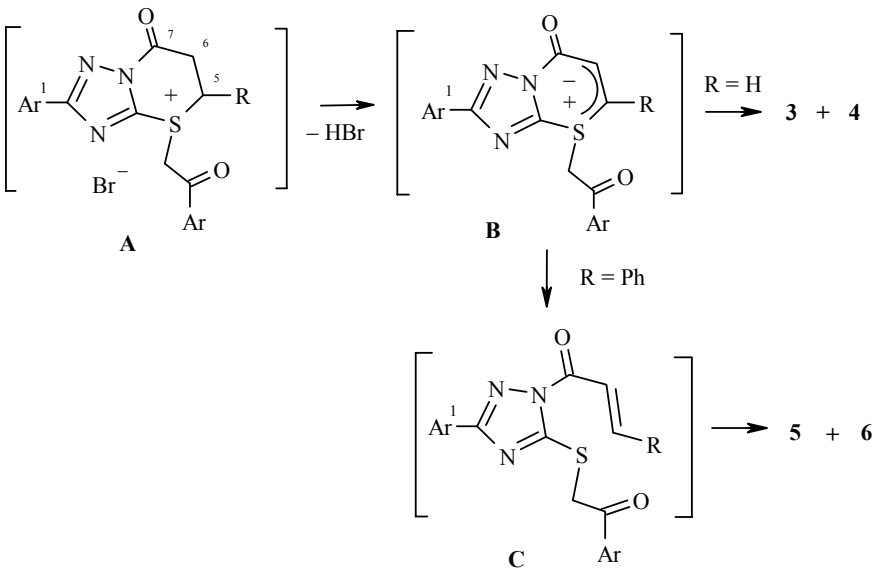


TABLE 1. Characteristics of Synthesized Compounds

Compound	Empirical formula	Found, % / Calculated, %			mp, °C	Yield, %
		C	H	N		
3a	$C_{11}H_7N_3OS$	57.47 / 57.63	3.31 / 3.08	18.10 / 18.33	260-262 264-266 [4]	35
3b	$C_{11}H_6ClN_3OS$	50.32 / 50.10	2.20 / 2.29	16.22 / 15.93	268-270	37
3c	$C_{11}H_6FN_3OS$	53.67 / 53.44	2.69 / 2.45	17.29 / 17.00	250-252	33
4a	C_8H_8O	79.70 / 79.97	6.49 / 6.71	—	17-18 20-20.5 [7]	45
4b	C_8H_7ClO	62.31 / 62.15	4.33 / 4.56	—	16-18 20 [8]	42
5a	$C_{16}H_{11}N_3S$	69.58 / 69.29	4.29 / 4.00	15.39 / 15.15	135-137 137-139 [5, 6]	43
5b	$C_{17}H_{13}N_3OS$	66.76 / 66.43	4.41 / 4.26	13.45 / 13.67	140-141 153 [6]	40
5c	$C_{16}H_{10}ClN_3S$	61.78 / 61.64	3.46 / 3.23	13.19 / 13.48	150-152 158 [6]	39
5d	$C_{16}H_{10}FN_3S$	65.29 / 65.07	3.70 / 3.41	13.94 / 14.23	138-140	45
5e	$C_{17}H_{12}ClN_3OS$	59.96 / 59.74	3.70 / 3.54	12.57 / 12.29	170-172 171 [6]	41
6	$C_9H_8O_2$	72.71 / 72.96	5.31 / 5.44	—	131-133 135 [9]	50
8a	$C_{15}H_{13}N_3S$	67.61 / 67.39	4.61 / 4.90	15.43 / 15.72	78-80	45
8b	$C_{15}H_{12}ClN_3S$	59.52 / 59.70	4.31 / 4.01	13.81 / 13.92	115-117	42
8c	$C_{16}H_{15}N_3OS$	64.33 / 64.62	4.81 / 5.08	13.85 / 14.13	87-89	40
9	C_9H_7BrO	51.51 / 51.22	3.07 / 3.34	—	39-40 43 [10]	38

TABLE 2. IR and ^{1}H NMR Spectral Data of Products

Compound*	IR spectrum, ν, cm^{-1}	^{1}H NMR spectrum, δ, ppm. (*J*, Hz)
3a	—	6.99 (1H, d, *J* = 9.5, H-6); 7.57 (3H, m, C_6H_5); 8.17 (2H, m, C_6H_5); 8.38 (1H, d, *J* = 9.5, H-5)
3b	3050, 1700 (C=O), 1605 C=N), 1560, 1520, 1480, 1410, 1370, 1310	6.99 (1H, d, *J* = 9.4, H-6); 7.61 (2H, d, *J* = 7.6, *m*-H_{Ar}); 8.16 (2H, d, *J* = 7.6, *o*-H_{Ar}); 8.42 (1H, d, *J* = 9.4, H-5)
3c	3050, 1700 (C=O), 1620 C=N), 1560, 1490, 1450, 1420, 1370	6.99 (1H, d, *J* = 9.6, H-6); 7.40 (2H, m, *m*-H_{Ar}); 8.19 (2H, m, *o*-H_{Ar}); 8.42 (1H, d, *J* = 9.6, H-5)
5a	3100, 1610, 1550, 1500, 1480, 1460, 1400, 1330, 1300, 1290	7.45-7.59 (6H, m, H_{Ar}); 7.96 (1H, s, H-6); 8.16 (2H, m, H_{Ar}); 8.32 (2H, m, H_{Ar})
5b	3100, 2830, 1620, 1590, 1530, 1500, 1470, 1430, 1320, 1310	3.82 (3H, s, CH_3O); 7.07 (2H, d, *J* = 8.9, *m*-H_{Ar}); 7.59 (3H, m, H_{Ar}); 7.90 (1H, s, H-6); 8.07 (2H, d, *J* = 8.9, *o*-H_{Ar}); 8.28 (2H, m, H_{Ar})
5c	3100, 3050, 1600, 1550, 1500, 1470, 1450, 1410, 1320	7.61 (5H, m, H_{Ar}); 7.96 (1H, s, H-6); 8.09 (2H, d, *J* = 9.0, *o*-H_{Ar}); 8.29 (2H, m, H_{Ar})
5d	3100, 1610, 1530, 1500, 1470, 1420, 1320, 1280, 1230	7.40 (2H, m, H_{Ar}); 7.64 (3H, m, H_{Ar}); 7.95 (1H, s, H-6); 8.16 (2H, m, H_{Ar}); 8.30 (2H, m, H_{Ar})
5e	3050, 1610, 1580, 1530, 1500, 1470, 1430, 1320, 1310, 1270	3.84 (3H, s, CH_3O); 7.11 (2H, d, *J* = 8.4, *m*-H_{Ar}); 7.70 (2H, d, *J* = 8.1, *m*-H_{Ar}); 7.99 (1H, s, H-6); 8.09 (2H, d, *J* = 8.4, *o*-H_{Ar}); 8.36 (2H, d, *J* = 8.1, *o*-H_{Ar})
8b	3000, 1620, 1500, 1460, 1410, 1340, 1280	4.44 (2H, s, SCH_2); 7.28-7.68 (7H, m, H_{Ar}); 7.99 (2H, d, *J* = 9.1, *o*-H_{Ar})
8c	3000, 1610, 1590, 1510, 1460, 1410, 1350, 1300, 1270	3.80 (3H, s, CH_3O); 4.40 (2H, s, SCH_2); 7.09 (2H, d, *J* = 8.9, *m*-H_{Ar}); 7.31 (3H, m, C_6H_5); 7.42 (2H, m, C_6H_5); 7.89 (2H, d, *J* = 8.9, *o*-H_{Ar})

* The IR spectrum of **3a** corresponds to the spectrum reported by Heindel [4]. The IR and ^{1}H NMR spectra of **8a** correspond to the spectra given by Barbier et al. [11].

We note that, in both cases, reaction products **3a-c** and **5a-e** contain aromatic heterocyclic systems, while starting compounds **1a-g** have a single thiazole ring. This is evidence of the greater chemical and thermodynamic stability of heteroaromatic compounds in comparison with alicyclic heterocycles.

EXPERIMENTAL

The ^{1}H NMR spectra were taken on a Varian 300 spectrometer at 300 MHz for solutions in DMSO-d_6 with TMS as the internal standard. The IR spectra were taken for KBr pellets on a UR-20 spectrometer.

2-Aryl-7H-[1,2,4]triazolo[5,1-*b*][1,3]thiazin-7-ones 3a-c and Aryl Methyl Ketones 4a,b. A mixture of 2-aryl[1,2,4]triazolo[5,1-*b*][1,3]thiazin-7-one **1a-c** (10 mmol) and aryl bromomethyl ketones **2a** or **2b** (10 mmol) was heated for 4 min at 200°C and then cooled. The reaction mixture was extracted with three 7-ml ether portions. The precipitate of **3a-c** was filtered off, dried, and recrystallized from acetic acid. The ethereal extract containing ketone **4a** or **4b** was evaporated and the resultant oil was extracted with three 5-ml hot hexane portions. Hexane was evaporated and **4a** or **4b** was distilled in vacuum. The yields and physical constants of **3a-c**, **4a**,**b** are given in Table 1.

2,5-Diaryl[1,3]thiazolo[3,2-*b*][1,2,4]triazolo[5,1-*b*][1,3]-triazoles 5a-e and 3-Phenyl-2-propenoic Acid (6). A mixture of 2,5-diaryl[1,2,4]triazolo[5,1-*b*][1,3]thiazin-7-one **1d-g** and aryl bromomethyl ketone **2a** or **2b** (10 mmol) was heated for 7 min at 150°C and cooled. The reaction mixture was treated with three 10-ml

portions of 10% aq. sodium bicarbonate. Products **5a-e**, which are insoluble in the sodium bicarbonate solution, were filtered off and recrystallized from acetic acid. The aqueous sodium bicarbonate solution containing acid **6** was acidified by adding concentrated hydrochloric acid and maintained for 6 h in the cold. Cinnamic acid **6** was filtered off, dried, and recrystallized from 4:1 aqueous ethanol.

5-Aryl-3-benzylthio-4H-1,2,4-triazoles 8a-c and 3-Phenyl-2-propenoyl Bromide (9). A mixture of 2,5-diaryl[1,2,4]triazolo[5,1-*b*][1,3]thiazin-7-one **1d-f** (10 mmol) and benzyl bromide **7** (11 mmol) was heated for 10 min at 150°C and cooled. The reaction mixture was extracted with three 10-ml dry ether portions. The insoluble residue of **8a-c** was filtered off, dried, and recrystallized from ethanol. The ethereal extracts were combined and evaporated to yield bromide **9**.

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