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Novel tandem reactions of 2,2′-sulfonylbis(1,3-diarylprop-2-en-1-ones) with hydrazine: formation of 3,6-diarylpyridazines and 3,5-diarylpyrazoles

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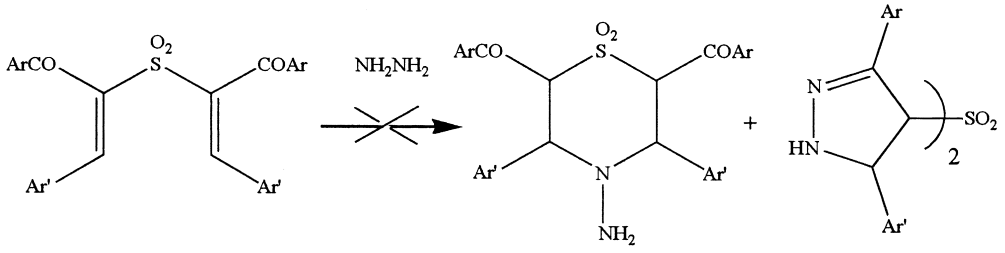
Abstract—The 2,2′-sulfonylbis(1,3-diarylprop-2-en-1-ones) undergo tandem reactions with hydrazine affording 3,6-diarylpyridazines and 3,5-diarylpyrazoles unexpectedly, the latter predominating.

We have been interested in the synthesis and/or reactions of bis(aroylmethyl) sulfides,[1] sulfoxides[2] and sulfones,[3] 2,2′-thiobis-[4] and 2,2′-sulfonylbis- (1,3-diarylprop-2-en-1-ones)[5] in view of their multi-functionalities and synthetic potential. Our recent studies have disclosed that 2,2′-sulfonylbis(1,3-diarylprop-2-en-1-ones) **1** react with ammonia[6] and methylamine[3] to give very good yields of 2,6-diaroyl-3,5-diaryltetrahydro-1,4-thiazine-1,1-dioxides by double aza-Michael addition. In contrast, the reaction of **1** with ethylamine furnished only moderate yields of tetrahydro-1,4-thiazine-1,1-dioxides along with bis(aroylmethyl) sulfones,[7] the latter formed by the cleavage of **1**, probably because of the enhanced steric interaction between the aryl groups at 3,5-positions and the *N*-ethyl group in the thiazine-1,1-dioxides. These results prompted us to investigate the reaction of **1** with the ambident nucleophile, hydrazine, which could lead to 4-amino-2,6-diaroyl-3,5-diaryltetrahydro-1,4-thiazine-1,1-dioxides **2** and/or bis(3,5-diaryl-4,5-dihydro-1*H*-pyrazol-4-yl) sulfones **3** (Scheme 1).

However, the reaction of **1** with hydrazine hydrate in acetic acid under reflux gave a mixture of 3,6-diarylpyridazines **4** and 3,5-diaryl-1*H*-pyrazoles **5** (Scheme 2), the latter predominating (Table 1). Neither 4-amino-2,6-diaroyl-3,5-diaryltetrahydro-1,4-thiazine-1,1-dioxides **2** nor bis(3,5-diaryl-4,5-dihydro-1*H*-pyrazol-4-yl) sulfones **3** arising respectively out of double aza-Michael addition or cyclocondensation of **1** was obtained.

A comparison of the mp and the NMR spectra of the products of the present study with those available in the literature clearly shows that the products formed are pyridazines and pyrazoles.[8–11] The unexpected formation of pyridazines **4** in one pot is tentatively explicable by Scheme 3 via a tandem sequence involving: (i) cleavage of **1** affording bis(aroylmethyl) sulfones **6**[3,12] triggered by the aza-Michael addition of hydrazine over both the C=C bonds sequentially, (ii) condensation of **6** with hydrazine to 3,6-diaryl-2,7-dihydro-1,4,5-thiadiazepine-1,1-dioxides **7**,



1 **2** **3**

Scheme 1.

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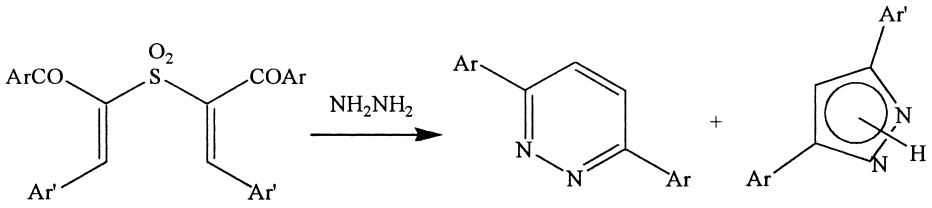

1 **4** **5**

1 & 5	Ar	Ar'	4	Ar
a	C_6H_5	C_6H_5	**a**	C_6H_5
b	C_6H_5	*p*-Cl-C_6H_4	**a**	C_6H_5
c	*p*-Cl-C_6H_4	*p*-Cl-C_6H_4	**b**	*p*-Cl-C_6H_4
d	*p*-Cl-C_6H_4	*p*-Me-C_6H_4	**b**	*p*-Cl-C_6H_4
e	*p*-Me-C_6H_4	C_6H_5	**c**	*p*-Me-C_6H_4

Scheme 2.

(iii) tautomerisation of **7** to **8**, (iv) isomerisation of **8** into the acyclic heterotriene **9**, (v) electrocyclic ring closure of **9** to dihydropyridazines **10** and (vi) elimination of sulfoxylic acid from **10** affording the heteroaromatics, 3,6-diaryl-pyridazines **4**.

It is pertinent to note that in previous studies,[8,13] **4** were obtained by the thermal decomposition of either **7** or its sulfide counterpart 2,7-dihydro-3,6-disubstituted-1,4,5-thiadiazepines **11** which in turn, were obtained by the reaction of corresponding bis(aroylmethyl) sulfones or sulfides with hydrazine. The formation of the 3,6-diaryl-pyridazines **4** from **11** was explained by reactions similar to those shown for the transformation of thiadiazepine-1,1-dioxides **7** into **4** in Scheme 3.[8] The formation of **7** via a mechanism involving cyclization by reaction of hydrazine at both carbonyl groups followed by a double reverse Knoevenagel reaction is also possible.

The formation of the major product, pyrazoles **5**, occurs presumably as shown in Scheme 4 via bis(3,5-diaryl-4,5-dihydro-1*H*-pyrazol-4-yl) sulfones **3** formed from double cyclocondensations of 2,2′-sulfonylbis(1,3-diarylprop-2-en-1-ones) **1** with hydrazine. These **3** presumably undergo eliminations affording two pyrazole molecules **5**, whose aromatic stability providing the required impetus.

Table 1. Yield and mp of pyridazines **4** and pyrazoles **5**

Reactant	Product	Yield (%)	Mp (°C)	Lit. mp (°C)
1a	**4a**	26	220–222	222–223[8]
	5a	48	198–200	199–200[9]
1b	**4a**	26	220–222	222–223[8]
	5b	51	215–217	214–215[9]
1c	**4b**	20	268–269	265–267[8]
	5c	52	238–240	237[10]
1d	**4b**	23	268–269	265–267[8]
	5d	61	223–224	228[11]
1e	**4c**	27	230–231	231–232[8]
	5e	53	182–183	183–184[9]

1. Experimental

1.1. Reaction of 2,2′-sulfonylbis(1,3-diarylprop-2-en-1-ones) 1 with hydrazine: a typical procedure

Hydrazine hydrate (8 mL, 99% w/w) was added to a solution of 2,2′-sulfonylbis(1,3-diphenylprop-2-en-1-one)[14] (4.78 g, 10 mmol) in acetic acid (500 mL). The mixture was refluxed for 2 h and kept aside at room temperature for 24 h. The mixture was then poured into ice water. The solid obtained was filtered and the products separated by column chromatography over silica gel using petroleum ether–chloroform (1:4 v/v) mixture as eluent. 3,6-Diarylpyridazines **4** eluted first followed by 3,5-diaryl-1*H*-pyrazoles **5**. Both pyridazines and pyrazoles were crystallized from chloroform–ethanol mixture. The ^{1}H NMR data of the compounds are in consonance with the structures. Representative NMR spectroscopic data are given as follows for **4b** and **5b**. ^{1}H NMR of **4b** (DMSO-d_6): 8.38 (s, 2H); 8.28 (d, 4H); 7.66 (d, 4H). ^{1}H NMR of **5b** (DMSO-d_6): 13.43 (s, 1H); 7.23 (s, 1H); 7.37–7.84 (m, 9H).

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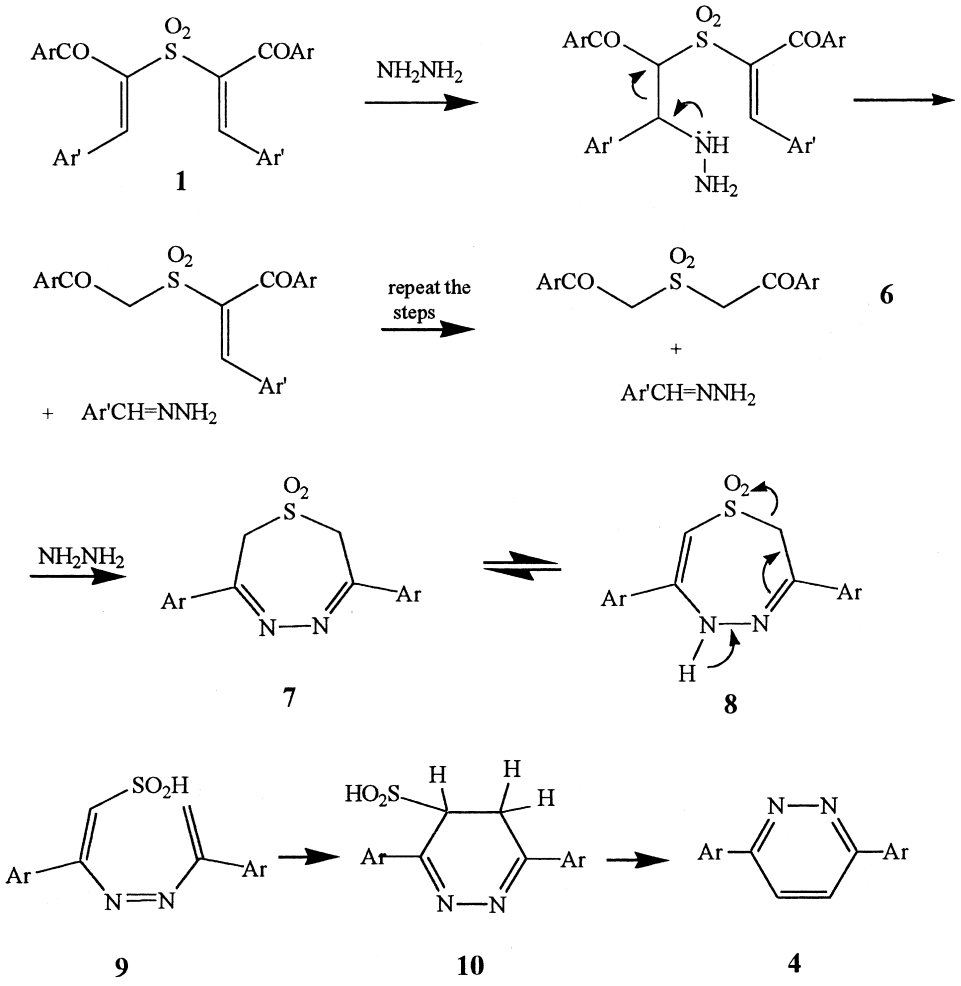
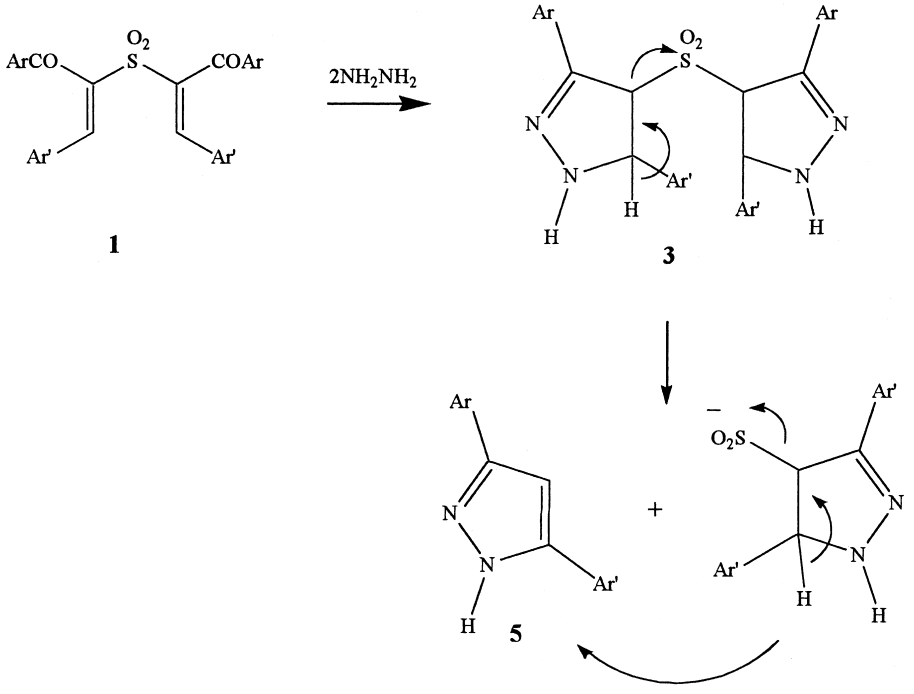


Scheme 3.



Scheme 4.

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