2-Arylethenyl-2'-arylethynyl Sulfones: A Potential Source for some Spiroheterocycles

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The double Michael addition of dimethyl malonate to 2-arylethenyl-2'-arylethynyl sulfones (**3**) resulted in 3,5-diaryl-5,6-dihydro-4,4-dimethoxycarbonyl-1-thiin-1,1-dioxides (**4**). The latter on cyclocondensation with urea / thiourea / hydrazine hydrate / hydroxylamine hydrochloride gave spiroheterocycles.

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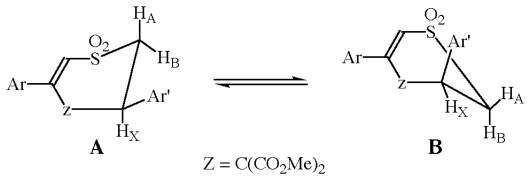
Our continued interest in activated olefins [1] led us earlier to report the preparation of 2-arylethenyl-2'-arylethynyl sulfones by utilizing the labile nature of the carbon-hetero atom bond in 1,2,3-selenadiazoles [2]. This method involved a series of steps, and as a result the overall yields were moderate. Reported here is a one pot synthesis of these eneyne sulfones with encouraging yields. In fact, some new spiro heterocycles have been developed through this method. Earlier, some bis (styryl) sulfones have been used as substrates in double Michael addition reactions with different active methylene compounds [3]. The *gem*-diester group in 1,1,-dimethoxy/-diethoxycarbonyl-2,6-diaryl-4-thian-4,4-dioxides has been subjected to double nucleophilic substitution reactions with urea, hydrazine hydrate and hydroxylamine hydrochloride to obtain various spiro-heterocycles [4].

The eneyne sulfones, 2-arylethenyl-2'-arylethynyl sulfones (**3**) have been prepared by the reaction of phenylacetylene (**1**) with styryl sulfonyl chlorides [5] (**2**) in the presence of sodium in dry ether at 25°C. The ^{1}H NMR spectra of these compounds showed two doublets for olefinic protons[2]. When **3** was subjected to double Michael addition with dimethyl malonate in the presence of Triton-B in benzene at reflux temperature, 3,5-diaryl-5,6-dihydro-4,4-dimethoxycarbonylthiin 1,1-dioxides (**4**) were formed. The ^{1}H NMR spectra of **4** generally should display ABX splitting pattern for methine proton at C-5 and methylene protons at C-6. This could be possible only if the atoms 1,2,3,4 and 5 are coplanar and consequently should exist in two conformations [6] (Structure A and Structure B).



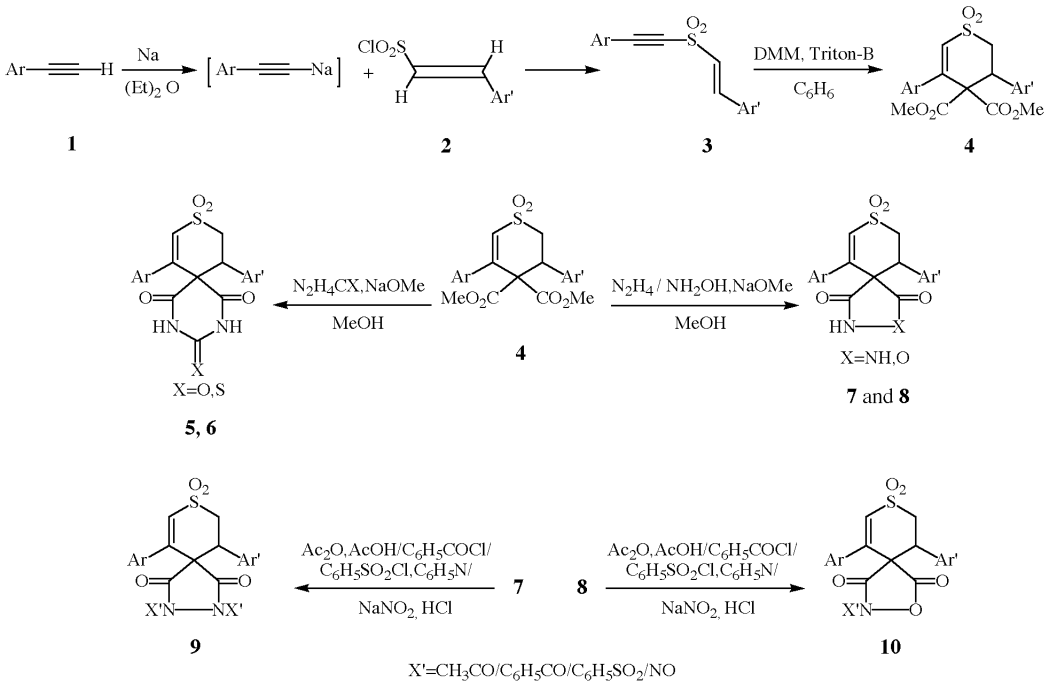
For the compound to exist in conformation **A**, coupling constants of J_{AX} = ~ 9.5 Hz, J_{BX} = ~ 3.5 Hz and J_{AB} = 12.8 Hz, should be observed. To exist as confomation **B**, coupling constants of J_{AB} ~ 13.0 Hz, $J_{AX} = J_{BX}$ = ~ 3.0 Hz should be observed. However, **4** displayed a triplet for the proton at C-5 and a doublet for the proton at C-6, following a simple splitting pattern. This may be due to rapid equilibrium between the two conformations, **A** and **B**. The methyl protons of the methoxycarbonyl groups were observed as a sharp singlet and the aromatic protons displayed multiplets.

The facile reactivity of the methoxycarbonyl groups of **4** allowed for the synthesis of spiropyrimidinetriones, thioxopyrimidinediones, pyrazolidinediones and isoxazolidinediones (see Scheme).

To accomplish these, **4** was subjected to cyclocondensation with urea, thiourea, hydrazine hydrate and hydroxylamine in the presence of sodium methoxide and methanol to give 7,11-diaryl-9-thia-2,4-diazaspiro[5,5]undec-7-ene-1,3,5-trione 9,9-dioxides (**5**) / 7,11-diaryl-3-thioxo-9-thia-2,4-diazaspiro[5,5]undec-7-ene-1,5-dione 9,9-dioxides (**6**), 6,10-diaryl-8-thia-2,3-diazaspiro[4,5]dec-6-ene-1,4-dione 8,8-dioxides (**7**) / 6,10-diaryl-2-oxa-8-thia-3-azaspiro[4,5]dec-6-ene-1,4-dione 8,8-dioxides (**8**). The *N*-substituted derivatives of **7** and **8** have been obtained by acylation, benzoylation, benzenesulfonylation and nitrosation. However **5** and **6** did not respond to either *N*-acylation nor *N*-nitrosation. This might be due to the enolization of -NHCO- moiety present in these systems. Although this moiety is also present in **7** and **8**, enolization could be effectively operative in **5** and **6** and may be the reason for their non-reactivity. The ^{1}H NMR spectra of **5**, **6**, **7** and **8** were similar to that of **4**. However, the NH signal was observed around 7.9 - 10.5 ppm in all the compounds. The spectra of **9** and **10** were replicas of **7a** and **8a** except for the signals due to NH protons.

In conclusion, we report a simple and more facile one pot reaction for eneyne sulfones (**3**). Furthermore, the efficient synthesis of spiropyrimidinetriones, thioxopyrimidinediones, pyrazolidinediones and isoxazolidinediones established the reactivity of **4**. The physical and spectral data of all the compounds are compiled in Tables 1 and 2.

Scheme



EXPERIMENTAL

Melting points were determined on a Mel-Temp apparatus and are uncorrected. The IR spectra (KBr-disc) were recorded on a Beckmann IR-18 spectrophotometer. All NMR spectra were recorded in $CDCl_3$ at 120 MHz on a varian EM-360 spectrophotometer, all chemical shifts were reported in ppm relative to TMS which was used as an internal standard. Elemental analyses were obtained from the University of Pune, Pune, India.

2-Arylethenyl-2'-arylethynyl sulfones **3a-c**.

General Procedure.

To a mixture of 10 ml of dry diethyl ether and 1.0 mmol of sodium metal, 1.0 mmol of phenylacetylene was added while stirring. A slurry of sodium acetylide was formed after 45 min. To this, 1.0 mmol of styrylsulfonyl chloride was added slowly and stirred at room temperature for 16 hours. After completion of the reaction, methanol was added to decompose any traces of sodium metal remaining. The contents were poured on ice containing HCl. The resulting aqueous mixture was extracted with ether, washed with $NaHCO_3$ solution, water and dried. The solvent was removed under reduced pressure and the product obtained was purified by column chromatography to give **3**.

3,5-Diaryl-5,6-dihydro-4,4-dimethoxycarbonyl-1-thiin 1,1-dioxides **4a-c**.

General procedure.

To a solution of 1.0 mmol of **3** and 1.2 mmol of dimethyl malonate in 10 ml of benzene, a catalytic amount of Triton-B was added and refluxed for 2-3 hrs. The solvent was distilled off and the solid obtained was recrystallized from ethanol to give **4**.

7,11–diaryl-9-thia-2,4-diazaspiro[5,5]undec-7-ene-1,3,5-trione 9,9-dioxides **5a-c** / 7,11-diaryl-3-thioxo-9-thia-2,4-diazaspiro[5,5]undec-7-ene-1,5-dione 9,9-dioxides **6a-c** / 6,10-diaryl-8-thia-2,3-diazaspiro[4,5]dec-6-ene-1,4-dione 8,8-dioxides **7a-c** / 6-10-diaryl-2-oxa-8-thia-3-azaspiro[4,5]dec-6-ene-1,4-dione 8,8-dioxides **8a-c**.

General Procedure.

A solution of **4** (1.0 mmol), urea (1.0 mmol) / thiourea (1.0 mmol) / 50% hydrazine hydrate (1.5 mmol) / hydroxylamine hydrochloride (1.0 mmol) in 12 ml of methanol was taken and 5 ml of 10% sodium methoxide was added in case of **5, 6** and **8** and refluxed for 6-8 hours. The contents were cooled and poured into crushed ice containing HCl. The product obtained was recrystallized from methanol to give compounds **5-8**.

Acylation of **7** and **8**.

A solution of **7** or **8** (1.0 mmol) in pyridine (5 ml) was treated with benzoyl or benzenesulfonyl chloride (for acylation of **7** or **8** (1.0 mmol) was taken in a mixture containing glacial acetic acid (5 ml) and acetic anhydride (2 ml). The reaction mixture was heated for 3-4 hours and cooled. The contents were poured onto crushed ice containing conc. HCl. The product collected was washed with water, dried and recrystallized from methanol.

Nitrosation of **7** and **8**.

A well cooled solution of **7** or **8** (10 mmol) in 2 N HCl (8 ml) was treated with a cold saturated solution of sodium nitrite. The reaction mixture was cooled in an ice-bath for 2 hrs. The solid that separated was collected, washed with water, dried and recrystallized from ethanol.

Table 1

Physical Properties of Compounds **3-10**

	Ar	Ar'	X'	Yield %	M.P. °C	Molecular Formula (Molecular weight)	Found (Calcd.) C%	H%	N%
3a	C_6H_5	C_6H_5	___	85	66-67	(lit. [1] mp 68-69°C)	___	___	___
3b	C_6H_5	4-$CH_3C_6H_4$	___	87	75-76	(lit. [1] mp 74-75°C)	___	___	___
3c	C_6H_5	4-ClC_6H_4	___	82	80-81	(lit. [1] mp 82-83°C)	___	___	___
4a	C_6H_5	C_6H_5	___	68	120-122	$C_{21}H_{20}O_6S$ (400.45)	62.78 (62.99	5.05 5.03)	___
4b	C_6H_5	4-$CH_3C_6H_4$	___	70	128-130	$C_{22}H_{22}O_6S$ (414.48)	63.50 (63.75	5.42 5.35)	___
4c	C_6H_5	4-ClC_6H_4	___	69	138-139	$C_{21}H_{19}ClO_6S$ (434.90)	59.40 (59.61	4.45 4.40)	___
5a	C_6H_5	C_6H_5	___	62	210-211	$C_{20}H_{16}N_2O_5S$ (396.42)	60.42 (60.60	4.12 4.07	7.14 7.07)
5b	C_6H_5	4-$CH_3C_6H_4$	___	60	215-216	$C_{21}H_{18}N_2O_5S$ (410.45)	61.25 (61.45	4.47 4.42	6.88 6.82)
5c	C_6H_5	4-ClC_6H_4	___	66	227-229	$C_{20}H_{15}ClN_2O_5S$ (430.87)	55.60 (55.75	3.56 3.51	6.58 6.50)
6a	C_6H_5	C_6H_5	___	71	202-203	$C_{20}H_{16}N_2O_4S_2$ (412.49)	58.00 (58.24	3.97 3.91	6.88 6.79)
6b	C_6H_5	4-$CH_3C_6H_4$	___	63	207-209	$C_{21}H_{18}N_2O_4S_2$ (426.52)	58.94 (59.14	4.30 4.25	6.63 6.57)
6c	C_6H_5	4-ClC_6H_4	___	65	206-207	$C_{20}H_{15}ClN_2O_4S_2$ (446.93)	53.55 (53.75	3.42 3.38	6.37 6.27)
7a	C_6H_5	C_6H_5	___	60	233-235	$C_{19}H_{16}N_2O_4S$ (368.41)	61.84 (61.94	4.48 4.38	7.50 7.60)
7b	C_6H_5	4-$CH_3C_6H_4$	___	63	237-239	$C_{20}H_{18}N_2O_4S$ (382.49)	62.61 (62.81	4.79 4.74	7.40 7.32)
7c	C_6H_5	4-ClC_6H_4	___	66	240-241	$C_{19}H_{15}ClN_2O_4S$ (402.86)	56.45 (56.65	3.70 3.75	6.99 6.95)
8a	C_6H_5	C_6H_5	___	67	170-172	$C_{19}H_{15}NO_5S$ (369.39)	61.88 (61.78	4.00 4.09	3.89 3.79)
8b	C_6H_5	4-$CH_3C_6H_4$	___	64	177-178	$C_{20}H_{17}NO_5S$ (383.42)	62.45 (62.65	4.57 4.47	3.45 3.65)
8c	C_6H_5	4-ClC_6H_4	___	68	180-181	$C_{19}H_{14}ClNO_5S$ (403.84)	56.73 (56.51	3.40 3.49	3.54 3.47)
9a	C_6H_5	C_6H_5	$COCH_3$	61	162-163	$C_{23}H_{20}N_2O_6S$ (452.48)	61.25 (61.05	4.50 4.46	6.25 6.19)
9b	C_6H_5	C_6H_5	COC_6H_5	63	166-167	$C_{33}H_{24}N_2O_6S$ (576.63)	65.60 (65.77	4.65 4.59	5.25 5.32)
9c	C_6H_5	C_6H_5	$SO_2C_6H_5$	60	170-171	$C_{31}H_{24}N_2O_8S_3$ (648.74)	57.59 (57.39	3.80 3.72	4.35 4.32)
9d	C_6H_5	C_6H_5	NO	60	140-141	$C_{19}H_{14}N_4O_6S$ (426.41)	53.00 (53.12	3.51 3.31	13.25 13.14)
10a	C_6H_5	C_6H_5	$COCH_3$	67	132-134	$C_{21}H_{17}NO_6S$ (423.45)	62.50 (62.40	4.15 4.05	3.30 3.31)
10b	C_6H_5	C_6H_5	COC_6H_5	68	140-141	$C_{26}H_{19}NO_6S$ (473.51)	65.90 (65.95	4.14 4.04	2.82 2.96)
10c	C_6H_5	C_6H_5	$SO_2C_6H_5$	65	133-135	$C_{25}H_{19}NO_7S_2$ (509.56)	58.80 (58.93	3.71 3.76	2.85 2.75)
10d	C_6H_5	C_6H_5	NO	62	111-113	$C_{19}H_{14}N_2O_6S$ (398.39)	57.18 (57.28	3.34 3.54	7.13 7.03)

Table 2
Spectral Data of Compounds **4 -10**

	IR cm^{-1} (KBr)					^{1}H - NMR δ ppm
4a	1730	1630	1325	1140		3.78 (s, 6H), 3.88 (d, 2H), 4.51 (t, 1H,), 6.88 (s, 1H), 6.97 – 7.35 (m, 10H) ($CDCl_3$)
4b	1740	1635	1330	1135		2.2 (s, 3H), 3.81 (s, 6H), 3.94 (d, 2H), 4.49 (t, 1H), 6.76 (s, 1H), 6.94 – 7.27 (m, 9H) ($CDCl_3$)
4c	1735	1640	1335	1135		3.84 (s, 6H), 3.92 (d, 2H), 4.55 (s, 1H), 6.79 (s, 1H), 7.01 – 7.37 (m, 9H) ($CDCl_3$)
5a	3350	1670	1630	1338	1125	3.82 (d, 2H), 4.40 (d, 1H), 6.80 (s, 1H), 7.02 – 7.45 (m, 10H), 8.24 (s, 2H) ($CDCl_3$)
5b	3355	1680	1628	1325	1140	2.21 (s, 3H), 3.74 (d, 2H), 4.42 (t, 1H) 6.75 (s, 1H), 7.0 – 7.46 (m, 9H), 8.41 (s, 2H) ($CDCl_3$)
5c	3400	1673	1642	1336	1124	3.76 (d, 2H), 4.46 (t, 1H), 6.82 (s, 1H), 6.98 – 7.45 (m, 9H), 8.45 (s, 2H) ($CDCl_3$)
6a	3385	1680	1638	1340	1127	3.79 (d, 2H), 4.43 (t, 1H), 6.75 (s, 1H), 6.94 – 7.28 (m, 10H), 8.28 (s, 2H). ($CDCl_3$)
6b	3470	1670	1626	1338	1130	2.24 (s, 3H), 3.81 (d, 2H), 4.40 (t, 1H), 6.81 (s, 1H), 6.96 – 7.30 (m, 9H), 8.26 (s, 2H). ($CDCl_3$)
6c	3430	1665	1632	1340	1120	3.78 (d, 2H), 4.46 (t, 1H), 6.80 (s, 1H), 7.02 – 7.30 (m, 9H), 8.26 (s, 2H) ($CDCl_3$)
7a	3410	1680	1640	1330	1125	3.80 (d, 2H), 4.42 (t, 1H), 6.68 (s, 1H) 7.01 – 7.45 (m, 10H), 8.78 (s, 2H) ($CDCl_3$)
7b	3430	1685	1636	1340	1124	2.21 (s, 3H), 3.82 (d, 2H), 4.39 (t, 1H) 6.72 (s, 1H), 6.94 – 7.29 (m, 9H), 8.79 (s, 2H) ($CDCl_3$)
7c	3450	1682	1630	1328	1125	3.79 (d, 2H), 4.48 (t, 1H) 6.80 (s, 1H) 6.95 – 7.27 (m, 9H), 8.85 (s, 2H) ($CDCl_3$)
8a	3440	1725	1630	1340	1145	3.78 (d, 2H), 4.45 (t, 1H), 6.82 (s, 1H) 6.98 – 7.42 (m, 10H), 9.01 (s, 1H) ($CDCl_3$)
8b	3450	1710	1632	1335	1125	2.18 (s, 3H), 3.75 (d, 2H), 4.52 (t, 1H) 6.84 (s, 1H), 7.05 – 7.46 (m, 9H), 9.02 (s, 1H) ($CDCl_3$)
8c	3430	1730	1625	1338	1124	3.81 (d, 2H), 4.48 (t, 1H), 6.85 (s, 1H) 7.01 – 7.45 (m, 9H), 9.05 (s, 1H) ($CDCl_3$)
9a	1685	1680	1634	1332	1124	
9b	1685	1680	1642	1340	1127	
9c	1678	1638	1340	1127		
9d	1680	1640	1344	1130		
10a	1725	1690	1643	1343	1130	
10b	1717	1683	1640	1340	1132	
10c	1720	1630	1337	1125		
10d	1730	1634	1345	1130		

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