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TRIPLE EQUILIBRIUM IN N'-ARYL-N-TOSYLDIAZOMALONIMIDOLATES, 1-TOSYL-1,2,3-TRIAZOL-5-OLATES, AND 1-ARYL-1,2,3-TRIAZOL-5-OLATES

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A series of 1-tosyl-substituted 4-arylcarbamoyl-1,2,3-triazol-2-olates, which can undergo rearrangement to isomeric 1-aryl-4-tosylcarbamoyl-1,2,3-triazol-5-olates and N-tosyl-N'-aryldiazomalonimidolates, were synthesized. An equilibrium between these compounds is observed in solutions in DMSO. The introduction of an electron-withdrawing substituent into the aryl residue increases the stability of the 1-tosyl-1,2,3-triazoles but reduces the stability of the 1-aryl-1,2,3-triazoles. π-Donating substituents increase the stability of the open-chain structure.

Keywords: diazo compounds, sulfonamides, 1,2,3-triazoles, diazo transfer reaction, equilibrium.

The chemistry of sulfonamides has been the subject of much attention in the literature [1, 2]. The constant interest in compounds of this class can be explained by the fact that linear and cyclic compounds containing sulfonamide fragments have a broad spectrum of biological activity: antiulcerous [3], diuretic [4], fungicidal, insecticidal, herbicidal, antibacterial [5], inhibition of enzymes [6]. At the same time the reactivity of the N-sulfonyl derivatives of diazoacetamide [7], a knowledge of which is essential for the development of methods for the directed synthesis of azoles containing a sulfonamide group, has not so far been investigated.

Earlier [8] we showed that the reaction of the N-arylsulfonylamides of malonic acid with benzenesulfonyl azide in the presence of sodium ethoxide leads to the formation of 1-sulfonyl-1,2,3-triazol-5-olates. The aim of the present work was to synthesize the N-tosyl derivatives of diazomalonamides **1** and investigate their ring–chain isomerism.

Compounds **1** were synthesized by the method described in [8], starting from derivatives of the monotosylamide of malonic acid by the "diazo transfer" reaction. In the case of "diazo transfer" in unsymmetrically substituted malonodiamides **2a-g** a complex pattern of behavior is possible; here cyclization is probable both at the N atom of the sulfonamide group with the formation of 1-tosyl-1,2,3-triazoles **3** and at the N atom of the anilide function with the formation of 1-aryl-1,2,3-triazoles **4** [9]. However, during "diazo transfer" the individual 1-tosyltriazoles **3a-g** were isolated. In the ^{1}H NMR spectra of these compounds (Table 1) the signal of the methyl group was observed at 2.39 ppm, which is typical of the signals of the tosyl function at position 1 of the triazole ring [8]. For compounds **3a**,**b** the signal of the protons of the methoxy group in the ^{1}H NMR spectrum appears at 3.74-3.76 ppm, i.e., in an upfield region from the protons of the anisidine function at position 1 of the triazole ring.

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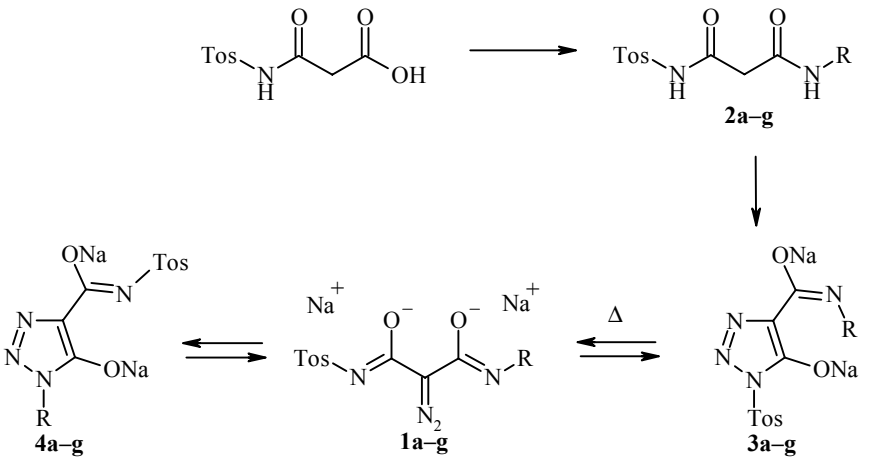


1–4 a R = 4-$MeOC_6H_4$, **b** R = 2-$MeOC_6H_4$, **c** R = Ph, **d** R = 3-$O_2NC_6H_4$, **e** R = 4-BrC_6H_4, **f** R = 2,4,6-$Cl_3C_6H_2$, **g** R = CH_2Ph

Individual products **4a-g**, which did not coincide chromatographically with the initial compounds, were also isolated when the tosyltriazoles **3a-g** were boiled for a long time in aqueous solutions. The ^{1}H NMR spectra of these compounds contained signals for the methyl group of the tosyl function at 2.32 ppm, which is typical of the position of the tosyl fragment in the carboxamide fragment [8]. For compounds **4a**,**b** a downfield shift of 0.12 ppm (3.86-3.90 ppm) is also observed for the signals of the protons of the methoxy groups in the aromatic fragment, indicating that the aryl residue is at position 1 of the triazole ring [8]. The absorption band characteristic of the diazo group does not appear in the IR spectrum. On the basis of these data the structure of isomeric 1-aryltriazoles **4a**,**b**, containing a sulfonyl group in the carboxamide function at position 4 of the heterocycle, was assigned to these compounds.

During the recrystallization of compounds **3a-g** from ethanol or carbon tetrachloride the diazo compounds **1a-g** were isolated. The signals for the protons of the methyl group in the tosyl function at 2.32 ppm and of the methoxy group (in the anilide residue for compounds **1a**,**b**) at 3.76-3.75 ppm were observed in the ^{1}H NMR spectra, and this is typical of aryl and tosyl fragments located in the carboxamide groups and not at position 1 of the triazole ring [8]. A band for the vibrations of the diazo group was observed in the IR spectrum at 2130 cm^{-1}.

The appearance, according to TLC, of 1-aryltriazoles **4a-g** and diazomalonodiimidolates **1a-g** in addition to the initial triazole **3a-g** was observed when the 1-sulfonyltriazoles **3a-g** were kept in DMSO solution for a long time at room temperature. It was not possible to separate the mixture. Similar results were obtained with solutions of compounds **4a-g** and **1a-g**. Table 2 gives data on the composition of the equilibrium mixtures of compounds **1**, **3**, and **4**, which were determined from the integral intensities of the signals for the protons of the methyl group and aromatic ring of the given compounds in solution in DMSO-d_6. The composition of the mixtures obtained from compounds **1** agreed within the experimental error limits (2-5%) with the composition of the mixtures obtained from compounds **3** and **4**. During analysis of Table 2 it is possible to arrange the substituents in the aryl group in the following order according to the effect on the stability of the compounds:

1-tosyl-1,2,3-triazole

3-$O_2NC_6H_4$ >> 2-$MeOC_6H_4$ > 4-BrC_6H_4 > Ph > 4-$MeOC_6H_4$ > $C_6H_2Cl_3$ >> Bn

1-aryl-1,2,3-triazole

Bn >> 4-$MeOC_6H_4$ > Ph > 4-BrC_6H_4 >> 3-$O_2NC_6H_4$~ 2-$MeOC_6H_4$ ~ $C_6H_2Cl_3$

diazomalonamide

$C_6H_3Cl_3$ > 2-$MeOC_6H_4$ > 4-$MeOC_6H_4$ > 4-BrC_6H_4 > Ph >> 3-$O_2NC_6H_4$ ~ Bn

TABLE 1. The ^{1}H NMR Spectra of Compounds **1**, **3**, and **4**

Compound	Chemical shift, δ, ppm, and multiplicity of the signals in DMSO-d_6
1a	7.82 (2H, d, ArH); 7.65 (2H, d, ArH); 7.40 (2H, d, ArH); 6.91 (2H, d, ArH); 3.74 (3H, s, $ArOCH_3$); 2.32 (3H, s, $ArCH_3$)
1b	8.30 (1H, ddd, ArH); 7.83 (2H, d, ArH); 7.38 (2H, d, ArH); 7.18 (1H, ddd, ArH); 7.13 (1H, ddd, ArH); 7.02 (1H, ddd, ArH); 3.76 (3H, s, OCH_3); 2.32 (3H, s, $ArCH_3$)
1c	7.55-7.66 (2H, m, Ph); 7.30-7.40 (3H, m, Ph); 7.34 (2H, d, ArH); 7.17 (2H, d, ArH); 2.32 (3H, s, $ArCH_3$)
1d	9.14 (1H, dd, ArH); 8.48 (1H, ddd, ArH); 8.00 (1H, ddd, ArH); 7.77 (2H, d, ArH); 7.70 (1H, dd, ArH); 7.19 (2H, d, ArH); 2.32 (3H, s, $ArCH_3$)
1e	8.05 (2H, d, ArH); 7.60 (2H, d, ArH); 7.80 (2H, d, ArH); 7.20 (2H, d, ArH); 2.32 (3H, s, $ArCH_3$)
1f	7.68 (2H, d, ArH); 7.58 (2H, s, ArH); 7.21 (2H, d, ArH); 2.32 (3H, s, $ArCH_3$)
1g	7.80 (2H, d, ArH); 7.38 (5H, s, Ph); 7.20 (2H, d, ArH); 5.35 (2H, s, $PhCH_2$); 2.32 (3H, s, $ArCH_3$)
3a	7.82 (2H, d, ArH); 7.68 (2H, d, ArH); 7.32 (2H, d, ArH); 6.85 (2H, d, ArH); 3.73 (3H, s, $ArOCH_3$); 2.36 (3H, s, $ArCH_3$)
3b	8.27 (1H, ddd, ArH); 7.87 (2H, d, ArH); 7.30 (2H, d, ArH); 7.18 (1H, ddd, ArH); 7.13 (1H, ddd, ArH); 7.02 (1H, ddd, ArH); 3.72 (3H, s, OCH_3); 2.36 (3H, s, $ArCH_3$)
3c	7.60-7.70 (2H, m, Ph); 7.20-7.30 (3H, m, Ph); 7.38 (2H, d, ArH); 7.13 (2H, d, ArH); 2.35 (3H, s, $ArCH_3$)
3d	9.15 (1H, dd, ArH); 8.39 (1H, ddd, ArH); 8.01 (1H, ddd, ArH); 7.78 (2H, d, ArH); 7.70 (1H, dd, ArH); 7.20 (2H, d, ArH); 2.39 (3H, s, $ArCH_3$)
3e	8.06 (2H, d, ArH); 7.58 (2H, d, ArH); 7.79 (2H, d, ArH); 7.16 (2H, d, ArH); 2.36 (3H, s, $ArCH_3$)
3f	7.83 (2H, d, ArH); 7.70 (2H, s, ArH); 7.28 (2H, d, ArH); 2.35 (3H, s, $ArCH_3$)
3g	7.85 (2H, d, ArH); 7.30 (5H, s, Ph); 7.29 (2H, d, ArH); 5.36 (2H, s, $PhCH_2$); 2.36 (3H, s, $ArCH_3$)
4a	7.84 (2H, d, ArH); 7.63 (2H, d, ArH); 7.36 (2H, d, ArH); 6.98 (2H, d, ArH); 3.84 (3H, s, $ArOCH_3$); 2.32 (3H, s, $ArCH_3$)
4b	8.28 (1H, ddd, ArH); 7.84 (2H, d, ArH); 7.38 (2H, d, ArH); 7.18 (1H, ddd, ArH); 7.14 (1H, ddd, ArH); 7.02 (1H, ddd, ArH); 3.90 (3H, s, OCH_3); 2.32 (3H, s, $ArCH_3$)
4c	7.58-7.65 (2H, m, Ph); 7.30-7.40 (3H, m, Ph); 7.34 (2H, d, ArH); 7.15 (2H, d, ArH); 2.32 (3H, s, $ArCH_3$)
4d	9.15 (1H, dd, ArH); 8.48 (1H, ddd, ArH); 8.02 (1H, ddd, ArH); 7.79 (2H, d, ArH); 7.70 (1H, dd, ArH); 7.20 (2H, d, ArH); 2.32 (3H, s, $ArCH_3$)
4e	8.07 (2H, d, ArH); 7.57 (2H, d, ArH); 7.78 (2H, d, ArH); 7.18 (2H, d, ArH); 2.32 (3H, s, $ArCH_3$)
4f	7.67 (2H, s, ArH); 7.64 (2H, d, ArH); 7.16 (2H, d, ArH); 2.32 (3H, s, $ArCH_3$)
4g	7.70 (2H, d, ArH); 7.55 (5H, s, Ph); 7.21 (2H, d, ArH); 5.60 (2H, s, $PhCH_2$); 2.32 (3H, s, $ArCH_3$)

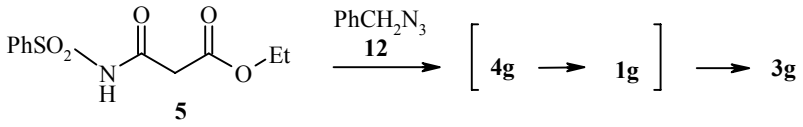
TABLE 2. The Composition of the Mixture of Triazoles **3** and **4** and the Diazo Compound **1** in DMSO-d_6

Compound	Content in mixture, %		
	3	**4**	**1**
a	16	42	42
b	42	<0.1	58
c	30	35	35
d	99	0.8	0.2
e	35	25	40
f	10	<0.1	90
g	0.2	99.6	0.2

As seen from these series, the effect on the stability of the isomers differs: accepting substituents increase the stability of 1-tosyl-1,2,3-triazole **3** but reduce the stability of 1-aryl-1,2,3-triazoles **4**, while π-donating substituents increase the stability of the open-chain structure **1**. *ortho*-Substituted aryls destabilize the 1-aryl-1,2,3-triazoles **4**.

TABLE 3. The Characteristics of Compounds **1**-**4**

Compound	Empirical formula	Found, % / Calculated, %		mp, °C	Yield, %
		N	S		
1a	$C_{17}H_{14}N_4Na_2O_5S\cdot 2H_2O$	11.78 / 11.96	6.85 / 6.85	>200 dec.	91
1b	$C_{17}H_{14}N_4Na_2O_5S\cdot 2H_2O$	12.03 / 11.96	6.35 / 6.85	>200 dec.	78
1c	$C_{16}H_{12}N_4Na_2O_4S\cdot 2H_2O$	12.98 / 12.78	7.12 / 7.31	>200 dec.	85
1d	$C_{16}H_{11}N_5Na_2O_6S\cdot 2H_2O$	14.55 / 14.49	6.35 / 6.63	>200 dec.	82
1e	$C_{16}H_{11}BrN_4Na_2O_4S\cdot 2H_2O$	10.82 / 10.83	6.13 / 6.20	>200 dec.	68
1f	$C_{16}H_9Cl_3N_4Na_2O_4S\cdot 2H_2O$	10.08 / 10.33	5.55 / 5.92	>200 dec.	88
1g	$C_{17}H_{14}N_4Na_2O_4S\cdot 2H_2O$	12.36 / 12.38	6.87 / 7.09	>200 dec.	78
2a	$C_{17}H_{18}N_2O_5S$	7.68 / 7.73	8.97 / 8.85	179-181	68
2b	$C_{17}H_{18}N_2O_5S$	8.30 / 7.73	9.17 / 8.85	183-187	72
2c	$C_{16}H_{16}N_2O_4S$	8.31 / 8.43	9.57 / 9.65	186	65
2d	$C_{16}H_{15}N_3O_6S$	11.35 / 11.13	8.22 / 8.50	208-212	53
2e	$C_{16}H_{15}BrN_2O_4S$	7.10 / 6.81	7.59 / 7.80	210-212	58
2f	$C_{16}H_{13}Cl_3N_2O_4S$	6.93 / 6.43	7.18 / 7.36	210-213	72
2g	$C_{17}H_{18}N_2O_4S$	8.00 / 8.09	9.33 / 9.26	159-162	82
3a	$C_{17}H_{14}N_4Na_2O_5S\cdot 2H_2O$	11.65 / 11.96	6.75 / 6.85	>250 dec.	88
3b	$C_{17}H_{14}N_4Na_2O_5S\cdot 2H_2O$	11.78 / 11.96	6.33 / 6.85	>250 dec.	92
3c	$C_{16}H_{12}N_4Na_2O_4S\cdot 2H_2O$	12.50 / 12.78	7.03 / 7.31	>250 dec.	91
3d	$C_{16}H_{11}N_5Na_2O_6S\cdot 2H_2O$	14.23 / 14.49	6.33 / 6.63	>250 dec.	96
3e	$C_{16}H_{11}BrN_4Na_2O_4S\cdot 2H_2O$	10.38 / 10.83	6.05 / 6.20	>250 dec.	84
3f	$C_{16}H_9Cl_3N_4Na_2O_4S\cdot 2H_2O$	10.21 / 10.33	5.33 / 5.92	>250 dec.	83
3g	$C_{17}H_{14}N_4Na_2O_4S\cdot 2H_2O$	12.30 / 12.38	7.11 / 7.09	>250 dec.	77
4a	$C_{17}H_{14}N_4Na_2O_5S\cdot 2H_2O$	12.01 / 11.96	6.33 / 6.85	>250 dec.	82
4b	$C_{17}H_{14}N_4Na_2O_5S\cdot 2H_2O$	11.66 / 11.96	6.99 / 6.85	>250 dec.	88
4c	$C_{16}H_{12}N_4Na_2O_4S\cdot 2H_2O$	13.09 / 12.78	7.00 / 7.31	>250 dec.	87
4d	$C_{16}H_{11}N_5Na_2O_6S\cdot 2H_2O$	14.12 / 14.49	6.75 / 6.63	>250 dec.	86
4e	$C_{16}H_{11}BrN_4Na_2O_4S\cdot 2H_2O$	10.53 / 10.83	6.10 / 6.20	>250 dec.	89
4f	$C_{16}H_9Cl_3N_4Na_2O_4S\cdot 2H_2O$	10.00 / 10.33	5.62 / 5.92	>250 dec.	90
4g	$C_{17}H_{14}N_4Na_2O_4S\cdot 2H_2O$	12.18 / 12.38	6.85 / 7.09	>250 dec.	92



In order to confirm the structure of the compounds we tried to synthesize compound **4g** by an alternative method by the reaction of malonamide **5** with benzyl azide. However, the reaction (boiling in an alcohol solution of sodium ethoxide) resulted in the isolation of the rearrangement product **3g**, which according to spectral data and TLC and elemental analysis coincided with previously obtained compound.

Thus, it was demonstrated as a result of the work that 1-tosyl-1,2,3-triazol-5-olates **3** are labile compounds. With heat or during prolonged standing in solution they isomerize to diazomalonimidolates **1** and 4-tosylcarbamoyltriazol-5-olates **4**. Here the stability of the isomers is determined to a large degree by the electronic and steric characteristics of the substituents in the anilide residue.

EXPERIMENTAL

The ^{1}H NMR spectra were recorded on a Bruker 250 instrument at 250 MHz. The IR spectra were recorded on a UR-25 spectrometer for tablets with potassium bromide. The reactions and the purity of the products were monitored by TLC on Silufol UV-254 plates in chloroform, 3:1 ethyl acetate–hexane, 9:1 chloroform–ethanol, and 60:11:1 chloroform–ethanol–ammonia (25%). The melting points were not corrected.

N-Aryl-N'-arylsulfonylmalonamides (2a-g). General Procedure. To a solution of the monotosylamide (0.01 mol) of malonic acid and the respective anilide (0.01 mol) in dry dioxane (15 ml) we added in portions with stirring at room temperature dicyclohexylcarbodiimide (2.37 g, 11.5 mmol). The mixture was stirred for 10-15 h. The isolated dicyclohexylurea was filtered off and washed with dioxane (2 ml). The obtained solution was acidified to pH 2-3 with 1 N hydrochloric acid and diluted with water (60 ml). The oil that separated initially gradually began to crystallize. The compound was filtered off and reprecipitated from aqueous ammonia (10%) by the addition of 1 N hydrochloric acid to pH 2-3 and was then recrystallized from aqueous dioxane.

Disodium 4-N-Arylcarbimidoyl-1-tosyl-1,2,3-triazol-5-ate (3a-g). General Procedure. To a solution or suspension of the malonamide **2a-g** (5 mmol) in absolute ethanol (20 ml) with stirring at room temperature we added a solution of sodium (0.23 g, 10 mmol) in absolute ethanol (5 ml) and then benzenesulfonyl azide (1.0 g, 5.5 mmol). The mixture was left at room temperature for 24 h. The precipitate was filtered off and washed with ethanol (2 ml). The product was dried over phosphorus pentoxide under vacuum.

Disodium N-Aryl-N'-tosyldiazomalonimidolate (1a-g). General Procedure. The malonamide **3a-g** (5 mmol) was boiled in absolute ethanol (20 ml) or carbon tetrachloride for 4-8 h. The mixture was cooled, and the precipitate was filtered off. The product was dried over phosphorus pentoxide under vacuum.

Disodium 1-Aryl-4-N-tosylcarbimidoyl-1,2,3-triazol-5-ate (4a-g). General Procedure. To a solution or suspension of the malonamide **3a-g** (5 mmol) in absolute ethanol (20 ml) with stirring at room temperature we added a solution of sodium (0.23 g, 10 mmol) in absolute ethanol (5 ml) and then benzenesulfonyl azide (1.0 g, 5.5 mmol). The mixture was left for 24 h. The reaction mixture was evaporated at reduced pressure, and water (15 ml) was added. The benzenesulfonamide was filtered off, and the filtrate was boiled for 2-3 h with a reflux condenser. The reaction mixture was evaporated to dryness at reduced pressure. The product was dried over phosphorus pentoxide under vacuum.

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