A New Route to 2,3,5-Trisubstituted 2,3-Dihydro-1,3,4-oxadiazoles via Stabilized Sulfuranes

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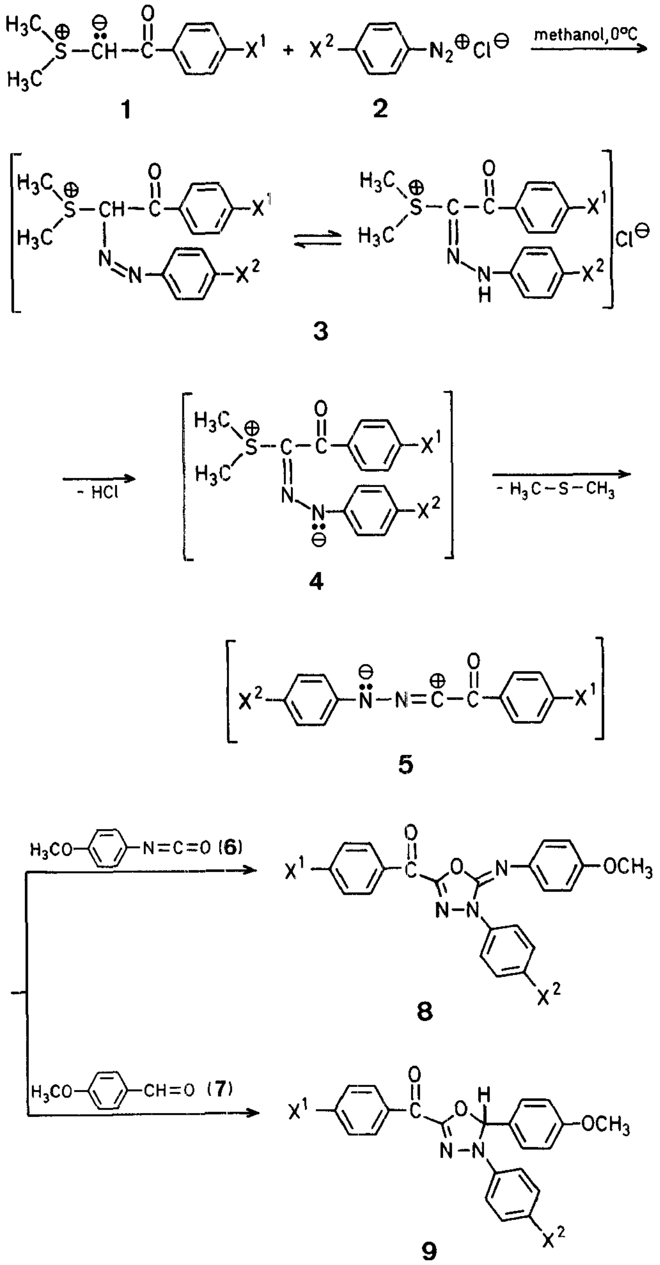
Sulfuranes of the type **1** have hitherto been used in a variety of syntheses, e.g., of epoxides[1], cyclopropanes[2], pyridines[3], and aziridines[4]. It has also been shown that phenacylidenedimethylsulfurane (**1**, $X^1 = H$) reacts with arenediazonium salts in methanol at 0 °C to give dihydrotetrazines[5]. This reaction proceeds via 1,3-dipolar dimerization of an intermediate nitrilimine which, in turn, is formed by attack of the carbanion of the ylide on the diazonium cation. The reaction is facilitated by the fact that the onium ion is a good leaving group. In view of the ability of dialkylsulfonio groups to act as excellent leaving groups, it was of interest to investigate a new synthesis of 2,3,5-trisubstituted 2,3-dihydro-1,3,4-oxadiazoles (**8**,**9**) using phenacylidenedimethylsulfurane (**1**, $X^1 = H$) or 4-methoxyphenacylidenedimethylsulfurane (**1**, $X^1 = OCH_3$) and 4-methoxyphenyl isocyanate (**6**) or 4-methoxybenzaldehyde (**7**), respectively.

Our synthesis of the dihydrooxadiazoles **8** and **9** consists of the reaction of compounds **1** with an equimolar amount of an arenediazonium salt (**2**) and 4-methoxyphenyl isocyanate (**6**) or 4-methoxybenzaldehyde (**7**), respectively, in methanol at 0 °C. The reaction presumably proceeds via the intermediacy of the species **3** which is transformed into the nitrilimine **5** which in turn adds exclusively to the C=O double bond of **6** and **7** to give the dihydrooxadiazoles **8** or **9**, respectively; the yields of products **8** and **9** are 62–88%. Conventional methods[6,7,8] are inappropriate for the synthesis of these oxadiazoles.



The structure of compounds **8** and **9** was established by microanalyses, physical, and spectral data.

Table. 2,3-Dihydro-1,3,4-oxadiazoles **8** and **9** prepared

Product	X^1	X^2	Yield [%]	m.p.[a] [°C]	Molecular formula[b]	M.S.[c] m/e(M^+)	I.R.[d] (Nujol) ν[cm^{-1}]		^{1}H-N.M.R. ($CDCl_3/TMS_{int}$)[e] δ[ppm]
							C=O	C=N	
8a	H	OCH_3	82	240–241°	$C_{23}H_{19}N_3O_4$ (400.4)	400	1640	1610, 1560	3.2 (s, 6H, $2OC\underline{H}_3$); 6.2–8.6 (m, 13H_{arom})
8b	OCH_3	OCH_3	80	249–250°	$C_{24}H_{21}N_3O_5$ (431.2)	431	1630	1600, 1550	2.8 (s, 6H, $2OC\underline{H}_3$); 3.2 (s, 3H, $OC\underline{H}_3$); 6.4–8.4 (m, 12H_{arom})
8c	H	F	62	237–238°	$C_{22}H_{16}FN_3O_3$ (389.5)	390	1640	1600, 1570	2.92 (s, 3H, $OC\underline{H}_3$); 6.8–8.4 (m, 13H_{arom})
9a	H	OCH_3	88	141–142°	$C_{23}H_{20}N_2O_4$ (390.2)	390	1650	1600	–
9c	H	F	71	150–151°	$C_{22}H_{17}FN_2O_3$ (376.2)	376	1640	1595	2.40 (s, 1H, 2-$\underline{H}$); 3.0 (s, 3H, $OC\underline{H}_3$); 6.6–8.2 (m, 13H_{arom})

[a] Melting points were determined using a Gallenkamp apparatus and are uncorrected.

[b] The microanalyses were in good accord with the calculated values: C, ±0.07; H, ±0.07; N, ±0.08.

[c] Recorded on a Varian Mat Spectrometer.

[d] Recorded on a Perkin Elmer Infracord instrument.

[e] Recorded on a Varian A-60 Spectrometer.

2,3,5-Trisubstituted 2,3-Dihydro-1,3,4-oxadiazoles (8); General Procedure:

A solution of phenacylidenedimethylsulfurane (**1**, X^1 = H; 1.8 g, 10 mmol) or 4-methoxyphenacylidenedimethylsulfurane (**1**, X^1 = OCH_3; 1.94 g, 10 mmol) in methanol (50 ml) is added dropwise to a freshly prepared, stirred aqueous solution of the diazonium salt (**2**; 10 mmol) at 0 °C during 5 min. Then, 4-methoxyphenyl isocyanate (**6**; 10 mmol) or 4-methoxybenzaldehyde (**7**; 10 mmol) is added dropwise at 0 °C during 15 min with stirring. The mixture is kept in an ice bath for a further 2 h. The solid which separates is recrystallized from methanol.

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