Reactions of 2,4-diphenylbutadiene-1,4-sultone with some 1,2- and 1,3-nitrogen binucleophiles

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Abstract
Treatment of 2,4-diphenylbutadiene-1,4-sultone with hydrazine in boiling EtOH gives 1-amino-2,4-diphenyl-1*H*-pyrrole. On treatment of 2,4-diphenylbutadiene-1,4-sultone with phenyl hydrazine in glacial acetic acid, 4,5-dihydro-5-methyl-1,3,5-triphenyl-1*H*-pyrazole was isolated. On the other hand, 2,4-diphenylbutadiene-1,4-sultone reacts with 4*H*-1,2,4-triazol-3-amine and 5-amino-3-phenyl-1*H*-pyrazole to afford the novel heterocyclic compounds 2-(2,2-dioxo-4-phenyl-3,4-dihydro-8*H*-2λ^6-[1,2,4]triazolo[5,1-*c*][1,2,4]thiadiazin-4-yl)-1-phenylethan-1-one, the structure of which was established by X-ray crystallography, and 2-(2,2-dioxo-4,7-diphenyl-3,4-dihydro-6*H*-pyrazolo[5,1-*c*][1,2,4]thiadiazin-4-yl)-1-phenylethan-1-one.

Keywords: 1,4-Dienic sultone, nitrogen binucleophiles, 2-aminopyrazole, 2-amino-1,2,4-triazole

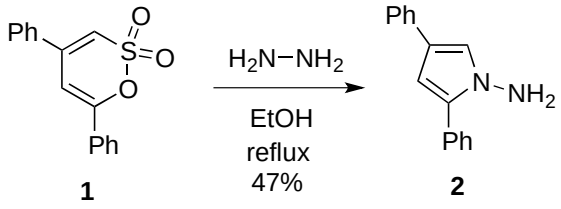
Introduction

Sultones are valuable compounds containing the -SO_2-O- group as part of a ring, i.e. an internal ester of a hydroxy-sulfonic acid. These heterocycles can react with a variety of nucleophilic compounds to introduce an alkyl sulfonic acid group.[1] Whereas sultones are sulfur analogues of lactones, they often behave differently when reacting with nucleophiles. Lactones are cleaved at the acyl-oxygen bond and behave as acylating agents, whereas sultones are cleaved at the carbon-oxygen bond and behave as sulfoalkylating agents.[2-4] There are few reports on reactions of 1,3-dienic δ-sultones.[5-7] To the best of our knowledge, the reactivity of sultones, especially of 2,4-disubstituted butadiene-1,4-sultones, towards 1,2- and 1,3-binucleophiles has not yet been reported. In view of this, and in continuation of our current interest in the chemistry of 1,2- and 1,3-binucleophiles towards various types of dienophile,[8-11] the goal of the present study was the

examination of the reactivity of 2,4-diphenylbutadiene-1,4-sultone towards selected 1,2- and 1,3-binucleophiles.

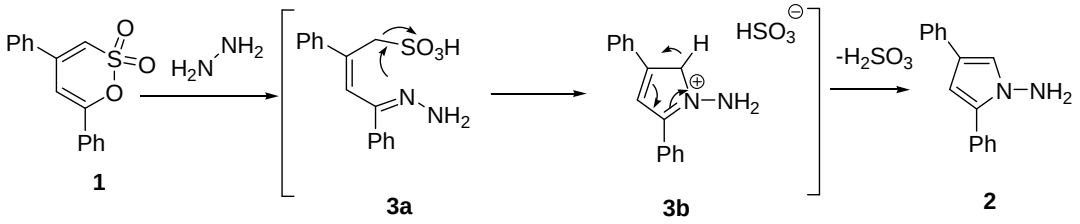
Results and Discussion

The reaction of 2,4-diphenylbutadiene-1,4-sultone (strictly, 4,6-diphenyl-1,2-oxathiin 2,2-dioxide) (**1**) with hydrazine hydrate was carried out in boiling EtOH. The progress of the reaction was monitored by TLC, which showed that conversion of the starting material was complete after 10 h. The structure of the product, separated using column chromatography (*n*-hexane/ethyl acetate-9/1), is proposed to be 1-amino-2,4-diphenyl-1*H*-pyrrole (**2**) (Scheme 1) on the basis of its spectroscopic data. The ^{1}H NMR spectrum of compound **2** revealed the presence of a signal at 5.45 ppm characteristic of an NH_2 group, and H-C(3) and H-C(5) of the pyrrole ring were observed as singlets at 6.55 and 7.46 ppm. Compound **2** has been reported previously, prepared from γ-bromodypnone.[12]



Scheme 1

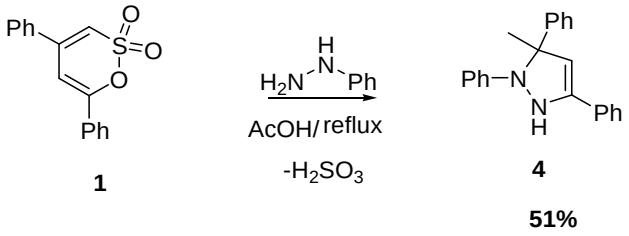
The formation of compound **2** is assumed to take place *via* nucleophilic attack by an amino group of the hydrazine at the carbon-oxygen bond in **1** to form the non-isolable intermediates **3a** and **3b** leading to **2** *via* loss of H_2SO_3 (Scheme 2).



Scheme 2

Filimonov and his group[13] have reported previously the reaction of 2,4-dinitrophenylhydrazine with 2,4-diphenylbutadiene-1,4-sultone (**1**) in aqueous acetic acid to obtain

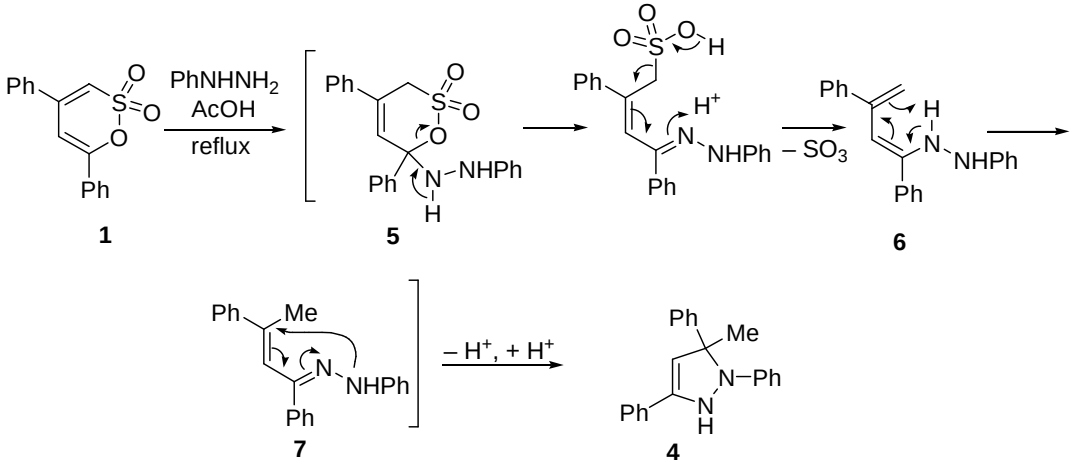
acetophenone 2,4-dinitrophenylhydrazone, formed by the reaction of acetophenone [from decomposition of the sultone in the water-acid mixture] with 2,4-dinitrophenylhydrazine.
In the present study, the reaction of **1** with phenylhydrazine was carried out in boiling glacial acetic acid for 18 h, and 2,5-dihydro-5-methyl-1,3,5-triphenyl-1*H*-pyrazole (**4**) was isolated after chromatographic separation (Scheme 3).



Scheme 3

The structure of compound **4** was established on the basis of its spectroscopic data. The ^{1}H-NMR spectrum of compound **4** revealed the presence of two characteristic signals at 2.42 and 7.34 ppm corresponding to CH_3 and CH-pyrazole protons, and in addition a signal at 13.12 ppm corresponding to the NH group.

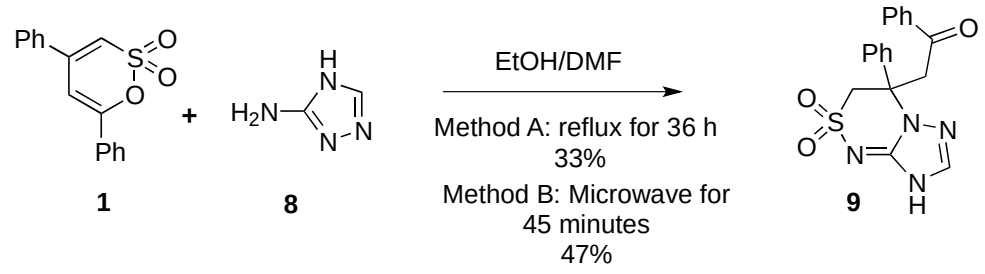
As presented in Scheme 4, the formation of compound **4** could occur via Michael addition of phenylhydrazine to the dienylsulfonate unit to give **5** followed by ring opening, loss of sulfur trioxide, proton transfer (arrows on **6**) and a final ring closure (arrows on **7**) to generate the dihydropyrazole system.



Scheme 4

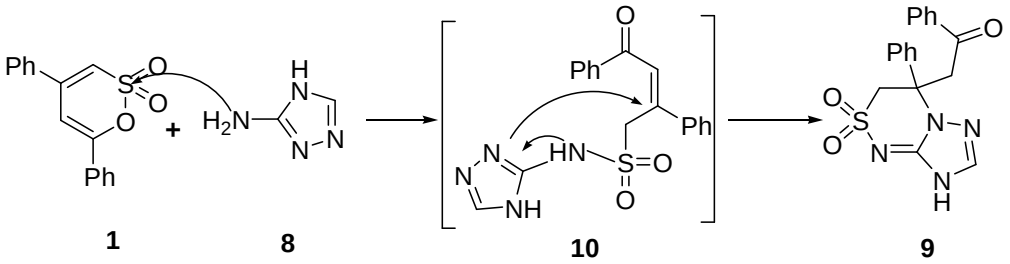
Aminoazoles as 1,3-binucleophiles are valuable building blocks for the synthesis of fused heterocycles.[8-11] They were used as Michael donors in reactions with electrophilic substrates, where the reaction was initiated by the attack of the NH_2 group onto an electron-deficient center

followed by cyclization via addition/elimination to give fused heterocycles.[10,11] The behavior of 2,4-diphenylbutadiene-1,4-sultone (**1**) towards some 1,3-binucleophilic aminoazoles was investigated. Thus, treatment of **1** with 4*H*-1,2,4-triazol-3-amine (**8**) in refluxing EtOH/DMF for 36 hours furnished a novel product identified as 2-(2,2-dioxo-4-phenyl-3,4-dihydro-8*H*-2λ^6-[1,2,4]triazolo[5,1-*c*][1,2,4]thiadiazin-4-yl)-1-phenylethan-1-one (**9**) (Scheme 5) in 33% yield. Using microwave irradiation improved the yield of **9** to 47% after 45 minutes.



Scheme 5

The formation of compound **9** can be explained on the basis of an initial sulfonamide formation *via* addition of the exocyclic NH_2 in 4*H*-1,2,4-triazol-3-amine (**8**) on the sulfonate function in **1** followed by protonation of the dienolate and then intramolecular aza-Michael addition as outlined in Scheme 6 to afford compound **9**.



Scheme 6

The structure of compound **9** was established on the basis of the spectroscopic data. The ^{1}H NMR spectrum revealed the presence of signals characteristics for two CH_2 groups (doublets at 3.82 and 4.22 ppm), CH-triazole (singlet at 7.56 ppm) and a D_2O-exchangeable NH (8.13 ppm). The mass spectrum of compound **9** had a peak at *m/z* 368 corresponding to its molecular ion. Moreover, the structure of compound **9** was unambiguously solved by X-ray diffraction analysis as shown in Figure 1.

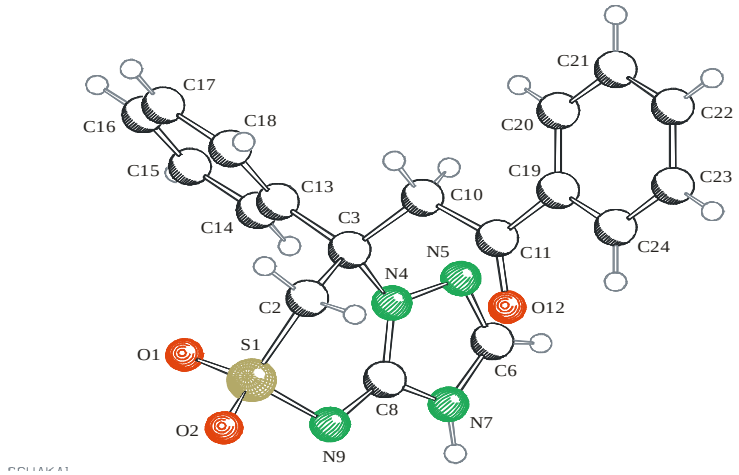
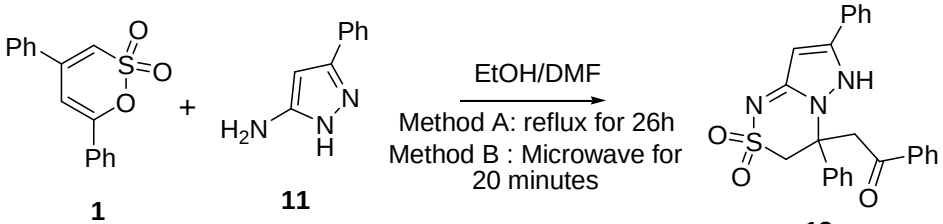


Figure 1. X-Ray crystal structure of compound **9**.

The reaction of 2,4-diphenylbutadiene-1,4-sultone (**1**) with 5-amino-3-phenyl-1*H*-pyrazole (**11**), was carried out in boiling EtOH/DMF. The progress of the reaction was monitored by TLC, which showed that conversion of the starting materials was complete after 26 hours improved to 49% yield after 20 minutes using microwave heating (Scheme 7).

The structure of the product is proposed to be 2-(2,2-dioxo-4,7-diphenyl-3,4-dihydro-6*H*-2λ^6-pyrazolo[5,1-*c*][1,2,4]thiadiazin-4-yl)-1-phenylethan-1-one (**12**) on the basis of the spectroscopic data. The IR spectrum of the later product revealed absorption bands at 3116 and 1662 cm^{-1} corresponding to NH and C=O groups, respectively. The ^{1}H NMR spectrum revealed the presence of signals characteristic for two CH_2 groups (doublets at 3.61, 4.01 ppm), CH-pyrazole (singlet at 6.80 ppm) and a D_2O-exchangeable NH (8.19 ppm). Its mass spectrum had a peak at *m/z* 443 corresponding to the molecular ion.



Scheme 7

Experimental Section

General. All melting points were measured on a Gallenkamp melting point apparatus (Weiss Gallenkamp, London, UK). The infrared spectra were recorded in potassium bromide discs on PyeUnicam SP 3300 or Shimadzu FT IR 8101 PC infrared spectrophotometers (PyeUnicam Ltd. Cambridge, England and Shimadzu, Tokyo, Japan, respectively). The NMR spectra were recorded on a Varian Mercury VX-300 NMR spectrometer (Varian, Palo Alto, CA, USA). ^{1}H NMR spectra were run at 300 MHz and ^{13}C NMR spectra were run at 75.46 MHz in deuterated chloroform ($CDCl_3$) or dimethyl sulfoxide (DMSO-d_6). Chemical shifts are given in parts per million and were related to that of the solvent. Mass spectra were recorded on a Shimadzu GCMS-QP 1000 EX mass spectrometer (Shimadzu) at 70 eV. Elemental analyses were recorded on Elementar-Vario EL (Germany) automatic analyzer. We prepared 2,4-diphenylbutadiene-1,4-sultone (**1**)[13] and 3-phenyl-1*H*-pyrazol-5-amine (**11**)[14,15] following the procedures reported in the literature. Microwave experiments were carried out using a CEM Discover LabmateTM microwave apparatus (300 W with ChemDriverTM Software).

Reaction of 2,4-diphenylbutadiene-1,4-sultone (**1**) **with hydrazine hydrate.** A mixture of hydrazine hydrate (60%, 1.5 mL) and 2,4-diphenylbutadiene-1,4-sultone (**1**) (0.284 g, 1 mmol) in EtOH (5 mL), was stirred at rt for 0.5 h then refluxed for 10 h. The reaction mixture was evaporated under reduced pressure and then purified using column chromatography (*n*-hexane/ethyl acetate-9/1-silica) to afford 1-amino-2,4-diphenyl-1*H*-pyrrole (**2**).

1-Amino-2,4-diphenyl-1*H*-pyrrole (**2**): yield 0.10 g (47%); mp:147-148 °C [reported[12] 143-145 °C]. white powder (EtOH); IR (KBr, cm^{-1}): ν_{max} 3272 (NH_2), ^{1}H NMR ($CDCl_3$): δ 5.45 (br, s, 2H, NH_2), 6.55 (s, 1H, CH-pyrrole-H-3), 6.81-7.40 (m, 10H, Ar-H), 7.46 (s, 1H, CH-pyrrole-H-5). ^{13}C NMR ($CDCl_3$): δ 98.1, 105.3, 115.3, 127.8, 128.4, 128.6, 128.7, 129.2, 130.0, 130.1, 133.1, 136.1. MS *m/z* (%): 234 [M^+] (10), 233 (100), 222 (45), 206 (10), 77 (45). Anal. Calcd. for $C_{16}H_{14}N_2$ (234.3): C, 82.02; H, 6.02; N, 11.96. Found: C, 82.22; H, 6.17; N, 11.89 %.

Reaction of 2,4-diphenylbutadiene-1,4-sultone (**1**) **with phenylhydrazine.** To a solution of the sultone **1** (0.284 g, 1 mmol) in glacial acetic acid (10 mL) was added phenylhydrazine (0.18 g, 1.5 mmol). The reaction mixture was refluxed for 18 h then left to cool, and 10 mL of $_{H2O}$ was added. The resulting yellowish solid precipitate was collected by filtration, washed with EtOH, dried, and then purified using column chromatography (*n*-hexane/ethyl acetate-8/2-silica) to afford 2,5-dihydro-5-methyl-1,3,5-triphenyl-1*H*-pyrazole (**4**).

2,5-Dihydro-5-methyl-1,3,5-triphenyl-1*H*-pyrazole (4): Yield (0.16 g, 51%); mp: 230-232 °C; yellowish-white powder (EtOH/DMF); IR (KBr, cm^{-1}): ν_{max} 3221 (NH). ^{1}H NMR ($CDCl_3$): δ 2.42 (s, 3H, CH_3), 7.34 (s, 1H, CH-pyrazole), 7.01-7.55 (m, 15H, Ar-H), 13.12 (s, 1H, NH). ^{13}C NMR ($CDCl_3$): δ 23.3, 65.8, 95.1, 111.4, 120.4, 125.3, 125.6, 126.2, 128.4, 128.3, 128.6, 128.8, 134.1, 142.6, 145.2, 152.1. MS *m/z* (%): 313 (10), 312 [M^+] (75), 297 (100), 235 (45), 223 (24), 91 (40), 77 (33), Anal. Calcd. for $C_{22}H_{20}N_2$ (312.41): C, 84.58; H, 6.45; N, 8.97. Found: C, 84.65; H, 6.52; N, 8.91%.

Reactions of 2,4-diphenylbutadiene-1,4-sultone (1) with heterocyclic 1,3-binucleophiles

Method A. To a mixture of 2,4-diphenylbutadiene-1,4-sultone (**1**) (0.284 g, 1 mmol) and the appropriate heterocyclic amine (1 mmol) (2-amino-1,3,4-triazole (**8**), 5-amino-3-phenyl-1*H*-pyrazole (**11**)) in EtOH/DMF (20/5 mL), were added a few drops of Et_3N. The resulting mixture was refluxed for 26-36 h then allowed to cool to rt. The solid that formed was collected by filtration, washed with EtOH, dried and the components separated using column chromatography (*n*-hexane/EtOAc-silica).

Method B. A mixture of 2,4-diphenylbutadiene-1,4-sultone (**1**) (0.284 g, 1 mmol) and the appropriate heterocyclic amine (1 mmol) in EtOH/DMF (20/2 mL), were mixed in a quartz vial and the mixture was then heated under microwave irradiating conditions at 120 °C and 250 W for 20–45 min. The solid that formed was collected by filtration, washed with EtOH, dried and finally the components separated using column chromatography (*n*-hexane/EtOAc-silica) to afford first compound **9** and then compound **12**.

2-(2,2-dioxo-4-phenyl-3,4-dihydro-8*H*-2λ^6-[1,2,4]triazolo[5,1-*c*][1,2,4]thiadiazin-4-yl)-1-phenylethan-1-one (**9**). Yield by method A: 0.12 g, (33%); method B: 0.17 g. (47%); light brown crystals (EtOH/DMF), mp 167-169 °C. IR (KBr, cm^{-1}): ν_{max} 3115 (NH), 1680 (C=O). ^{1}H NMR (DMSO-d_6): δ 3.74 (1H, d, *J* = 16.5), 3.82 (1H, d, *J* = 16.5), 4.22 (1H, d, *J* = 17.1), 4.35 (1H, d, *J* = 17.1), 7.11-7.48 (m, 10H, Ar-H), 7.56 (d, 1H, triazole-H-5), 8.13 (br.s, 1H, NH), ^{13}C NMR (DMSO-d_6): δ 45.33, 46.29, 64.9, 95.12, 125.44, 127.60, 127.90, 128.23, 128.75, 133.67, 136.28, 139.13, 141.35, 196.24. MS *m/z* (%): 369 (12), 368 [M$^+$] (5), 314 (5), 105 (95), 77 (100). Anal. Calcd. for $C_{18}H_{16}N_4O_3S$ (368.41): C, 58.68; H, 4.38; N, 15.21. Found: C, 58.73; H, 4.31; N, 15.35 %.

Crystal data for compound 9. $C_{18}H_{16}N_4O_3S$, M = 368.41, Monoclinic, a [Å] = 11.907 (1), b [Å] = 11.243 (1), c [Å] =16.067 (1), α [°] = 90.00, β [°] = 127.57 (1), γ [°] = 90.00, V [Å^3] = 1704.8 (2), T [°C] = 75 (2). Figure 1 illustrates the structure as determined. Full data can be obtained on request from the CCDC.[16]

2-(2,2-Dioxo-4,7-diphenyl-3,4-dihydro-6*H*-pyrazolo[5,1-*c*][1,2,4]thiadizin-4-yl)-1-phenyl-ethan-1-one (**12**). Yield by method A: 0.17 g (39%; method B 0.21 g, (49%); pale yellow crystals (EtOH/DMF), mp: 155-157 °C. IR (KBr, cm^{-1}): ν_{max} 3116 (NH), 1662 (C=O). NMR (DMSO-d_6): δ 3.61, 3.72 (2d, 2H, CH_2, *J*=16.6), 4.01, 425 (2d, 2H, CH_2, *J*=17.3), 6.81 (s, 1H, pyrazole-H), 7.01-7.67 (m, 15H, Ar-H), 8.19 (s, 1H, NH), ^{13}C NMR (DMSO-d_6): δ 39.4, 58.3, 62.3, 125.6, 125.7, 126.0, 126.4, 127.3, 127.9, 128.3, 128.4, 128.8, 129.0, 133.7, 137.10, 146.5, 149.7, 164.3, 191.9. MS *m/z* (%): 444 (21), 443 [M$^+$] (100), 364 (70), 105 (23), 77 (30). Anal. Calcd. for $C_{25}H_{21}N_3O_3S$ (443.52): C, 67.70; H, 4.77; N, 9.47. Found: C, 67.85; H, 4.70; N, 9.53 %.

Acknowledgements

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References and Notes

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16. Crystal data for compound **7** (ref. CCDC 1061207) can be obtained on request from the director, Cambridge Crystallographic Data Center, 12 Union Road, Cambridge CB2 1EW, UK.

