

## Reactions of Prop-2-yne-1-sulphonyl Chloride with $\alpha$ -Morpholinostyrene

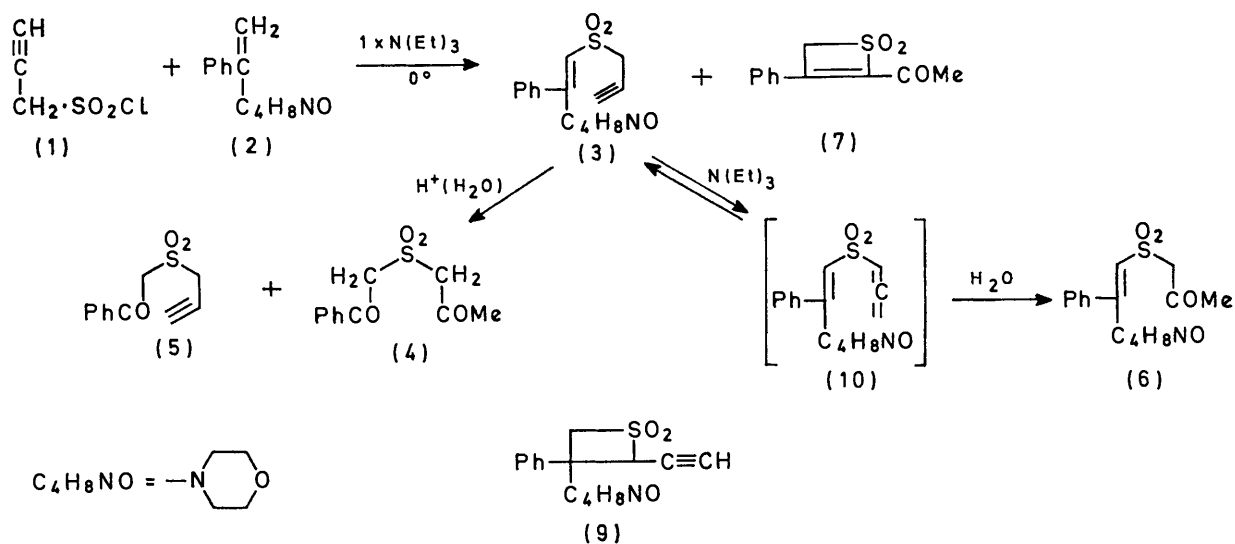
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The reaction between prop-2-yne-1-sulphonyl chloride and  $\alpha$ -morpholinostyrene was performed (a) in the presence of an equimolar amount of triethylamine at 0° to give 4-acetyl-3-phenyl-2*H*-thiet 1,1-dioxide (7) and 1-morpholino-1-phenyl-3-thiahex-1-en-5-yne 3,3-dioxide (3) or the corresponding 3-thiahex-1-en-5-one dioxide (6), depending on the work-up conditions; and (b) at -30° with triethylamine and sulphonyl chloride in a 3:1 ratio to give 3-morpholino-3-phenyl-2-vinylidenethietan 1,1-dioxide (11) and the open-chain sulphone (6). The origin of the products is discussed. Compound (11) and 1-morpholino-1-phenyl-3-thiahexa-1,4,5-triene 3,3-dioxide (10) are shown to be the possible precursors of the sulphones (7) and (6), respectively.

THE reaction between sulphens ( $R_2C=SO_2$ ) and enamines provides an easy route to thietan 1,1-dioxide derivatives. Our interest<sup>1</sup> both in sulphen chemistry and in the chemical behaviour of 2-functionalized thietan 1,1-dioxide derivatives has led us to synthesize a new

We now report reactions of compound (1) with  $\alpha$ -morpholinostyrene (2).

The reaction between 3-bromoprop-1-yne and sodium sulphite gave a mixture of the expected<sup>2</sup> sodium prop-2-yne-1-sulphonate and, probably, the corresponding



SCHEME 1

acetylenic sulphonyl chloride, prop-2-yne-1-sulphonyl chloride (1), whose reaction with enamines was expected to afford 2-acetylenic thietan 1,1-dioxide derivatives.

† This product could form during chlorination from a direct hydrogen chloride addition (i) to the allenic and/or to the acetylenic bond of the isomeric sodium sulphonates; or (ii) to the allenic and/or the acetylenic bond of the two corresponding isomeric sulphonyl chlorides.

allenic isomer (see Experimental section). Chlorination of the crude material with phosphoryl chloride gave prop-2-yne-1-sulphonyl chloride (1) and 2-chloroprop-2-ene-1-sulphonyl chloride † in ca. 46 and 5–15% yields, respectively.

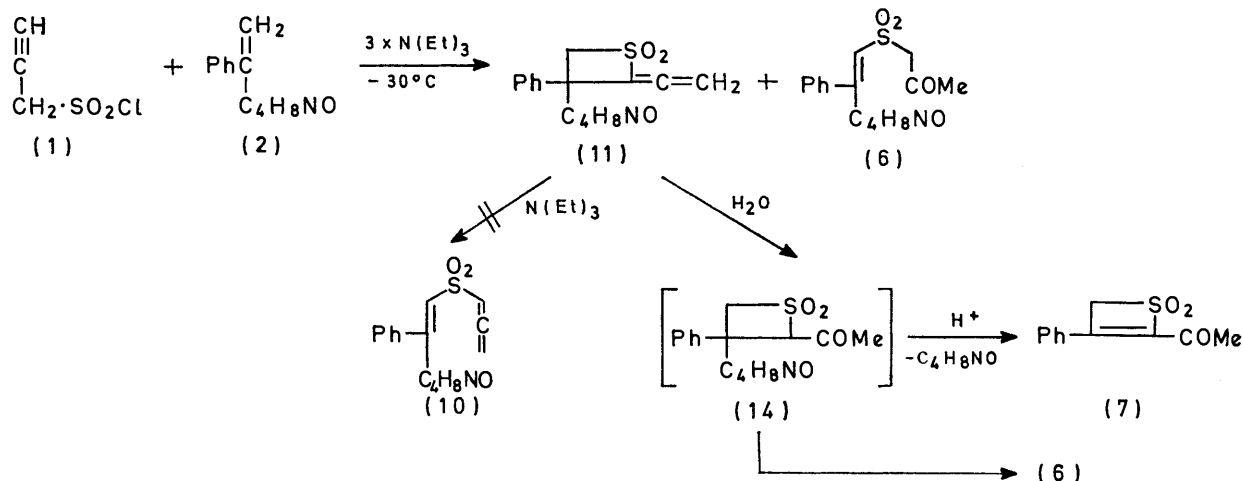
<sup>1</sup> S. Bradamante, S. Maiorana, and G. Pagani, *J.C.S. Perkin I*, 1972, 282.

<sup>2</sup> H. Pohlemann, Ger.P. 1,086,693 (*Chem. Abs.*, 1961, **55**, 15,347).

The reaction between prop-2-yne-1-sulphonyl chloride (1) and  $\alpha$ -morpholinostyrene (2) was carried out at first in the presence of an equimolar amount of triethylamine at 0°. The open-chain sulphone (3) and the four-membered ring sulphone (7) were isolated (Scheme 1), depending on the work-up conditions. The alternative structure (7a) for the cyclic sulphone (7) was ruled out on the basis of  $^1\text{H}$  n.m.r. data. The hypsochromic shift



of  $\nu_{\text{C=O}}$  observed in the i.r. spectrum of the thietan (8), produced by catalytic hydrogenation of (7), further supports structure (7). The expected 1,2-cycloaddition product (9) was not isolated.



SCHEME 2

On treatment of the open-chain sulphone (3) with base in aqueous solution, an easy hydration reaction took place leading to the enaminosulphone (6). The triene (10) is the probable intermediate in this process. Compound (3) was unaffected by water in neutral medium and in acidic aqueous solution it gave a mixture of phenacyl prop-2-ynyl sulphone (5) and acetyl phenacyl sulphone (4). Moreover in basic anhydrous medium compound (3) was present in equilibrium with the corresponding allenic derivative (10) (as shown by the i.r. spectrum; see Experimental section), which readily reacted with water to give compound (6). Thus, the formal hydration of the triple bond in structure (3) is easier than the hydrolysis of the enamine double bond because of the possibility of equilibration with an allenic derivative, whose electrophilic character is strongly enhanced by the sulphonyl group.<sup>3,4</sup>

The foregoing results suggested that the thiet dioxide (7) could originate, through hydration and elimination of morpholine, not only from structure (9), but also from the corresponding isomerization product (11); moreover the formation and stability of (11) would be favoured

\* It is known that the acetylenic sulphones can undergo nucleophilic attack under mild conditions<sup>4</sup> as a result of addition to the thermodynamically more stable allenic isomers.

by a more basic medium. In order to confirm this hypothesis the reaction between compounds (1) and (2) was carried out at  $-30^\circ$  with a triethylamine-sulphonyl chloride ratio of 3 : 1. The expected vinylidene derivative (11) was obtained, together with a small amount of the open-chain sulphone (6). Analytical, i.r., and  $^1\text{H}$  n.m.r. data support the assigned structures (see Experimental section).

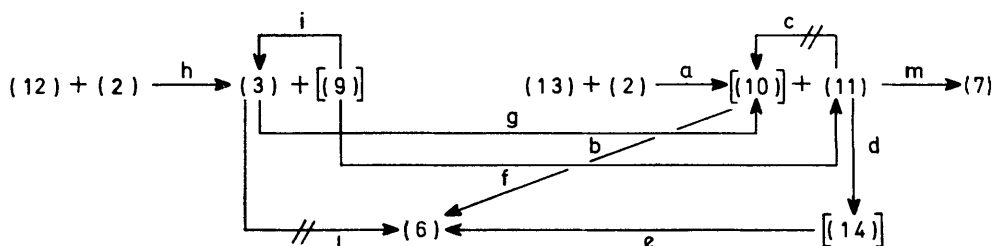
Compound (11) was stable towards triethylamine in anhydrous ether or benzene solution, and was also recovered unchanged after being heated for several hours at  $35^\circ$ . However, in the presence of water (*e.g.* 90% ethanol-water solution) it readily gave the open-chain sulphone (6), even in the absence of added base. Probably hydration of the vinylidene group in the four-membered ring derivative (11) [to give (14)] is followed

by a ring-opening reaction, which could be catalysed by the basicity of compound (14) itself (Scheme 2). Finally, compound (11) underwent an addition reaction with water also in acidic solution, but under these conditions a morpholine elimination reaction followed to give the expected thiet (7), showing the possibility of achieving this transformation directly.

In conclusion: (i) the expected intermediate sulphene derivative (12) can react with the enamine (2) to give the acetylenic sulphones (3) and (9) (path h, Scheme 3), which in the presence of excess of base can isomerize to the allenic isomers (10) and (11), respectively (paths g and f); (ii) the allenic sulphones (11) and (10) have been shown to be able to act as intermediates in the formation of compound (7) and (6) (paths m and b, respectively), through addition of water to the  $\alpha$ -sulphonylallenic system; \* (iii) in the presence of an excess of base the

<sup>3</sup> For leading references concerning the chemistry of acetylenes and allenes, see R. J. Bushby, *Quart. Rev.*, 1970, **24**, 585; D. R. Taylor, *Chem. Rev.*, 1967, **67**, 317; M. V. Mavrov and V. F. Kucherov, *Russ. Chem. Rev.*, 1967, **36**, 233; S. Patai, 'The Chemistry of Alkenes,' Interscience, New York, 1964, ch. 13; H. G. Viehe, 'The Chemistry of Acetylenic Compounds,' Dekker, New York, 1969.

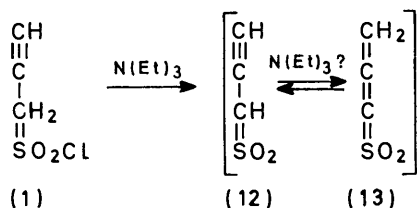
<sup>4</sup> C. J. M. Stirling, *J. Chem. Soc.*, 1964, 5856, and subsequent papers by this author.



SCHEME 3

isomeric sulphen derivative (13) can also react with the enamine (2) to give the vinylidene derivatives (11) and (10), *i.e.* the 1,2-cyclo-addition and acylation\* products of the enamine (path a).

Either the paths (g + b) and (f + m) or alternatively (a + b) and (a + m) would rationalize the formation of compounds (6) and (7), particularly in the presence of an excess of base. However, it is impossible at this stage to make a choice between the two cases.†



## EXPERIMENTAL

I.r. spectra were obtained with a Perkin-Elmer 137 instrument (solids as Nujol mulls, liquids as films).  $^1\text{H}$  N.m.r. spectra were determined with a Varian A60-A spectrometer for solutions in  $[\text{2H}]$ chloroform (tetramethylsilane, as internal standard).

*Prop-2-yne-1-sulphonyl Chloride* (1).—To a stirred solution of sodium sulphite (31.8 g, 0.252 mol) in water (126 g), 3-bromoprop-1-yne (30 g, 0.252 mol) was added during 35 min at 20°. The temperature of the mixture had risen in 19 min to 60°. After 1 h the mixture was heated at 70–80° for 2 min and evaporated to dryness under reduced pressure at 40–50° to give a solid, m.p. 220° (from methanol) (lit.,<sup>2</sup> 220°). The i.r. spectrum of the material showed the presence of an allenic derivative, probably sodium allenesulphonate,  $\nu_{\text{max}}$  1956 and 1980  $\text{cm}^{-1}$  ( $\text{CH}_2=\text{C}=\text{C}$  attached to an electron-withdrawing group<sup>7</sup>). The well dried salts were refluxed for 5 h with three times the stoichiometric amount of phosphoryl chloride. The excess of phosphoryl chloride was evaporated off under reduced pressure, the residue was taken up in chloroform (120 ml), and the solution was added to ice (150 g). The

\* In some cases<sup>1,5</sup> the enamine acylation products formed in the reactions between sulphen derivatives and enamines arise from an independent reaction path, although in other cases they originate from a base-catalysed ring opening of 1,2-cycloaddition products.<sup>6</sup> Compound (9) has not been isolated so it is impossible to say if path i actually takes place. In contrast compound (11) showed a great stability towards basic agents in anhydrous medium (path c does not occur). However, the presence of a very small amount of water in the reaction medium would have been enough to cause the formation of (6) (7% yield) through (14) as shown before (paths d and e).

† Attempts to identify the nature of the intermediate sulphen derivatives by  $^1\text{H}$  n.m.r. analysis at –40° of the reaction between compound (1) and trimethylamine in acetonitrile failed, a fast polymerization reaction taking place.

chloroform layer was washed with water, dried, and distilled (yield 21 g; b.p. 42–60° at 0.6 mmHg). Fractional distillation on a Todd column gave pure *propynesulphonyl chloride* (1) (16.4 g, 46.5%), b.p. 49° at 0.6 mmHg (Found: C, 25.6; H, 2.2.  $\text{C}_3\text{H}_3\text{ClO}_2\text{S}$  requires C, 26.0; H, 2.2%).  $\nu_{\text{max}}$  3180 and 2100  $\text{cm}^{-1}$  ( $\text{CH}\equiv\text{C}$ ), and 1170 and 1370  $\text{cm}^{-1}$  ( $\text{SO}_2$ ),  $\tau$  5.52 (2H, d,  $J$  2.57 Hz,  $\text{CH}_2\cdot\text{SO}_2$ ), 7.22 (1H, t,  $J$  2.57 Hz,  $\text{CH}\equiv\text{C}$ ), and 2-chloroprop-2-ene-1-sulphonyl chloride (4 g, 9.2%), b.p. 60° at 0.6 mmHg (Found: C, 20.2; H, 2.2.  $\text{C}_3\text{H}_4\text{Cl}_2\text{O}_2\text{S}$  requires C, 20.6; H, 2.3%),  $\tau$  4.18 (2H, s,  $\text{CH}_2=\text{C}$ ) and 5.42 (2H, s,  $=\text{CCl}-\text{CH}_2-\text{SO}_2$ ).

*Reactions of Compound (1) with  $\alpha$ -Morpholinostyrene (2).*—(a) *Sulphonyl chloride and triethylamine in a 1:1 ratio.* Prop-2-yne-1-sulphonyl chloride (15 g, 0.108 mol) in carefully dried ether (50 ml) was added dropwise (20–30 min) to a stirred solution of  $\alpha$ -morpholinostyrene (20.4 g, 0.108 mol) and triethylamine (11 g, 0.11 mol) in anhydrous ether (300 ml), with the temperature kept at –5 to 0°. After 1 h at room temperature the solid (triethylamine hydrochloride) was collected and the ether was evaporated off under reduced pressure. The oily residue was taken up in anhydrous ethanol (20 ml) and the collected solid was crystallized from ethanol to give 1-morpholino-1-phenyl-3-thiahex-1-en-5-yne 3,3-dioxide (3) (9 g, 28.5%), m.p. 155° (Found: C, 61.3; H, 5.8; N, 4.8.  $\text{C}_{15}\text{H}_{17}\text{NO}_3\text{S}$  requires C, 61.8; H, 5.9; N, 4.8%),  $\nu_{\text{max}}$  3215 and 2130 ( $\text{CH}\equiv\text{C}$ ), 1610 ( $\text{C}=\text{C}$ ), and 1300 and 1140  $\text{cm}^{-1}$  ( $\text{SO}_2$ ),  $\tau$  2.65 (5H, m, Ph), 4.64 (1H, s,  $\text{C}=\text{CH}$ ), 6.53 (2H, d,  $J$  2.7 Hz,  $\text{CH}_2\cdot\text{SO}_2$ ), 7.6 (1H, t,  $J$  2.7 Hz,  $\text{C}=\text{CH}$ ), and 6.3–6.93 (8H, m, morpholine). The oily residue from the ethanolic mother liquors was chromatographed on alumina (activity III; chloroform) to give 1-morpholino-1-phenyl-3-thiahex-1-en-5-yne 3,3-dioxide (6) (9 g), m.p. 162° (from ethanol) (Found: C, 58.4; H, 6.2; N, 4.5.  $\text{C}_{15}\text{H}_{19}\text{NO}_3\text{S}$  requires C, 58.2; H, 6.2; N, 4.5%),  $\nu_{\text{max}}$  1710 ( $\text{C}=\text{O}$ ) and 1280 and 1120  $\text{cm}^{-1}$  ( $\text{SO}_2$ );  $\tau$  2.73 (5H, m, Ph), 4.87 (1H, s,  $\text{C}=\text{CH}$ ), 6.3 (2H, s,  $\text{CH}_2\cdot\text{SO}_2$ ), 6.4–6.95 (8H, m, morpholine), and 7.75 (3H, s, MeCO). Alternatively the same oily residue (1 g) was heated at 40–50° for 5 min with 10% sulphuric acid (7 ml). The crude material collected by filtration was treated with a small amount of hot ethanol, from which the 4-acetyl-3-phenyl-2H-thiet 1,1-dioxide (7) (0.15 g) was filtered; m.p. 192° (from ethanol) (Found: C, 59.4; H, 4.5.  $\text{C}_{11}\text{H}_{10}\text{O}_3\text{S}$  requires C, 59.5; H, 4.5%),  $\nu_{\text{max}}$  1665 ( $\text{C}=\text{O}$ ) and 1300 and 1130  $\text{cm}^{-1}$  ( $\text{SO}_2$ );  $\tau$  2.45 (5H, m, Ph), 4.7 (2H, s,  $\text{CH}_2\cdot\text{SO}_2$ ), and 7.42 (3H, s, MeCO). From the ethanolic mother liquors of this filtration, acetyl phenacyl sulphone (4) (0.45 g) slowly crystallized m.p. 114° (lit.,<sup>8</sup> 114°).

<sup>5</sup> K. Nagarajan and S. R. Mehta, *J. Org. Chem.*, 1970, **35**, 4248.

<sup>6</sup> J. J. Looker, *J. Org. Chem.*, 1966, **31**, 2973; J. M. Wells and F. S. Abbott, *J. Medicin. Chem.*, 1966, **3**, 489.

<sup>7</sup> See ref. 4, S. Patai, p. 1130.

<sup>8</sup> G. Pagani, *Gazzetta*, 1967, **97**, 1518.

(b) *Sulphonyl chloride and triethylamine in a 3:1 ratio* (with M. TRAUTLUFT). The reaction was carried out as described in (a) at  $-30^\circ$  and with a 3:1 molar ratio of triethylamine and sulphonyl chloride. A large amount of ether- and water-insoluble polymeric material was formed. The oily residue from the ethereal mother liquors was taken up in absolute ethanol and the solid *3-morpholino-3-phenyl-2-vinylidenethietan 1,1-dioxide* (11) was collected and crystallized (15% yield), m.p.  $139^\circ$  (from methanol) (Found: C, 61.6; H, 5.8; N, 4.7.  $C_{15}H_{17}NO_3S$  requires C, 61.8; H, 5.9; N, 4.8%),  $\nu_{\max}$  1960 ( $C=CH_2$ ) and 1300 and 1110  $cm^{-1}$  ( $SO_2$ );  $\tau$  2.75 (5H, m, Ph), 5.25 (2H, s,  $C=CH_2$ ), 5.93—6.36 (AB system,  $J$  14 Hz,  $CH_2\cdot SO_2$ ), and 6.5—7.6 (8H, m, morpholine). From the ethanolic mother liquors the keto-sulphone (6) slowly crystallized (2—3 days) (7% yield). Alternatively, direct acidic treatment (2 h; 10%  $H_2SO_4$ ; room temperature) of the residue obtained from the starting ethereal mother liquors, followed by chloroform extraction, gave compounds (7) (8%) and (4) (2%), which were separated by fractional crystallization from ethanol.

*Addition of Water to the Thietan Dioxide* (11).—Compound (11) (1 g, 3.34 mmol), stirred for 18 h at room temperature in ethanol–water (95:5; 30 ml) gave compound (6) (80%), isolated by dilution with water and extraction with chloroform.

Compound (11) (0.2 g, 0.686 mmol) was stirred for 2—3 h at room temperature in 10% sulphuric acid (3 ml). The mixture was then extracted with chloroform, the extract was dried and evaporated, and the residue was crystallized from ethanol to give compound (7) (60%) and a small amount of (4).

*2-Acetyl-3-phenylthietan 1,1-Dioxide* (8).—A solution of 4-acetyl-3-phenyl-2H-thiet 1,1-dioxide (7) (0.5 g, 2.25 mmol) in acetic acid (15 ml) was hydrogenated (10% Pd–C). After 1 mol. equiv. of hydrogen had been absorbed, the solvent was evaporated off to give the *thietan* (8) (95%),

m.p.  $88-89^\circ$  (from ethanol) (Found: C, 58.2; H, 5.2.  $C_{11}H_{12}O_3S$  requires C, 58.7; H, 5.4%),  $\nu_{\max}$  1725 (C=O) and 1320 and 1130  $cm^{-1}$  ( $SO_2$ ),  $\tau$  2.65 (5H, m, Ph), 4.85 (1H, m, CH-COMe), and 5.7 (3H, m,  $CH_2\cdot SO_2\cdot CHPh$ ).

*Acidic Treatment of Compound (3): Phenacyl Prop-2-ynyl Sulphone (5) and Acetonyl Phenacyl Sulphone (4)*.—Compound (3) (1.5 g, 5.16 mmol) in 10% sulphuric acid (30 ml) was stirred for 5 min at room temperature. The solution was extracted with chloroform; the extract was washed with water, dried, and evaporated and the residue was taken up in ethanol (10 ml). Compound (5) (0.5 g, 43.6%) was directly filtered off; m.p.  $96^\circ$  (from ethanol) (Found: C, 60.0; H, 4.8.  $C_{11}H_{10}O_3S$  requires C, 59.5; H, 4.5%),  $\nu_{\max}$  3220 and 2110 ( $C\equiv CH$ ), 1665 (C=O), and 1320 and 1130  $cm^{-1}$  ( $SO_2$ );  $\tau$  1.95—2.55 (5H, m, Ph), 5.17 (2H, s,  $CH_2\cdot SO_2$ ), 4.95 (2H, d,  $J$  2.7 Hz,  $CH_2\cdot C\equiv$ ), and 7.45 (1H, t,  $CH\equiv C$ ). From the ethanolic mother liquors, compound (4) was obtained (0.5 g, 40.4%); m.p.  $114^\circ$  (from ethanol) (lit.,<sup>8</sup>  $114^\circ$ ).

*Basic Treatment of Compound (3)*.—Compound (3) (0.5 g, 1.72 mmol) was stirred for 1 h in absolute ethanol or chloroform solution (20 ml) in the presence of triethylamine (0.6 g, 5.94 mmol). The i.r. spectrum showed that the crude material obtained after evaporation of the solvent was a mixture of starting material (3) and of an allenic derivative, probably (10),  $\nu_{\max}$  3215 ( $C\equiv CH$ ) and 1920 and 1960  $cm^{-1}$  ( $C=C=CH_2$ ). Treatment of the crude material with 95% ethanol–water (4 ml) at room temperature gave a slurry from which compound (6) was filtered after 2 h (65% yield). Compound (6) was also obtained by treating with a few drops of triethylamine a slurry of (3) (0.1 g, 0.344 mmol) in water (2 ml).

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