Thiopyran 1,1-Dioxide Derivatives from Addition of Amines to Propargyl Sulfone

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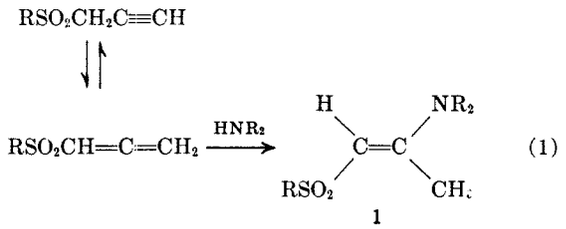
Received August 28, 1967

The addition of amines to bis(2-propynyl) sulfone (**3**) led to mixtures of 2H-thiopyran 1,1-dioxides, substituted at carbons 3 or 5 with the respective amino residue. Hydrolysis of these cyclic dienamine mixtures afforded a single ketone, *viz.*, 3-methyl-5-oxo-Δ^3-dihydrothiopyran 1,1-dioxide (**7**). Under appropriate conditions the addition of morpholine to **3** gave the monoadduct 2-N-morpholinyl-1-(2-propynylsulfonyl)propene (**9**), whereas the addition of dimethylamine yielded the diadduct bis(2-dimethylamino-1-propenyl) sulfone (**8b**). Both were readily converted into the respective mixtures of the cyclic dienamines above. A mechanism for the cyclization is discussed. Furthermore, a number of propargylic sulfides, sulfoxides, and sulfones are described. The products from reactions of the sulfones with nucleophilic reagents are recorded.

The ease with which activated acetylenes undergo Michael-type additions is well documented.[1] Similar reactions with α,β-allenic esters,[2a] ketones,[2b] and nitriles[2c] have also been demonstrated, and moreover, it has been shown[2a] qualitatively that they are more reactive than their acetylenic counterparts.

It was thought of interest to study the addition of nucleophilic reagents to allenic sulfones and sulfoxides which, with one exception,[3] were unknown at the time this work was initiated. Meanwhile, Stirling and coworkers[4] have, in a series of papers, reported an extensive study on the preparation and reactions of allenic and acetylenic sulfones. The addition of amines to propargylic and the corresponding allenic sulfones afforded the same sulfonyl enamine **1** (eq 1). Similar



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results have also been reported recently by Pourcelot and Cadiot.[5]

Part of our study is identical with work already described in these papers.[4,5] Some additional data, demonstrating the generality of the reaction, are given in the tables below. Tables I, II, and III contain a number of propargylic sulfides, sulfoxides, and sulfones, respectively, whereas the products from reactions of the sulfones with various nucleophiles are recorded in Table IV. The main purpose of this communication, however, is to describe the addition of secondary amines to bis(2-propynyl) sulfone (**3**), which resulted in the formation of some cyclic dienamines.

The oxidation of bis(2-propynyl) sulfide[6] with 1 or 2 equiv of *m*-chloroperbenzoic acid gave in good yields the corresponding sulfoxide (**2**) and sulfone (**3**), respectively. The addition of 2 molar equiv of piperidine to an ether suspension of the sulfone at room temperature resulted in a low-melting solid, which was not obtained pure. However, an intensive absorption band at 1550 cm^{-1} and the absence of ethynyl absorption in the infrared spectrum indicate that 2 moles of piperidine had reacted to give a bis-enamine (**8a**). When this product was heated under reflux in benzene or tetrahydrofuran, a high yield of a crystalline compound was obtained, whose analysis agreed with that of a monoaddition product. It was subsequently shown on the basis of the nmr spectrum that two isomers were present in a ratio of approximately 5:1. Since separation was unsuccessful, structural work was performed on the mixture. According to the spectral and chemical evidence described below, the structures 3-methyl-5-N-piperidyl-2H-thiopyran 1,1-dioxide (**4a**) and 5-methyl-3-N-piperidyl-2H-thiopyran 1,1-dioxide (**5a**) have been assigned to the major and minor components, respectively. The infrared spectrum shows an intensive band at 1540 cm^{-1}, characteristic of an enamine double bond. Ultraviolet absorption maxima at 246 mμ (ϵ 7600) and 319 mμ (ϵ 5400) prove that conjugated double bonds must be present, at least in the major component. Hydrogenation over a Raney nickel catalyst afforded in high yield the fully saturated compound **6**, while selective reduction of the enamine double bond with concentrated formic acid[7] failed. Acid hydrolysis also led to a single product, *viz.*, 3-methyl-5-oxo-Δ^3-dihydrothiopyran 1,1-dioxide (**7**), in agreement with the above assignments. The oxime and the 2,4-dinitrophenylhydrazone of this ketone were obtained in the usual way. The addition–ring closure reaction sequence, described above, is not limited to piperidine. An excess of dimethylamine was passed into an ether suspension of the sulfone **3** to yield a rather unstable compound, identified as the diadduct **8b**. The infrared spectrum of the latter was similar to that of the product from the piperidine addition. When a benzene solution of the compound was heated under reflux, dimethylamine evolved, and a mixture of the cyclic dienamines **4b** and **5b**, in a ratio of about 5:1, was obtained. In the case of morpholine, the addition of a small excess of 1 equiv to an ether suspension of **3** afforded the "normal" monoadduct **9** in 84% yield with no indication of any diadduct being present in the reaction mixture. However, by heating a tetrahydrofuran solution of **3** with the same amount of morpholine, a mixture of the cyclic dienamines **4c** and **5c**, in a ratio of approximately

(1) R. A. Raphael, "Acetylenic Compounds in Organic Synthesis," Butterworth and Co., Ltd., London, 1955, p 45.

(2) (a) G. Eglinton, E. R. H. Jones, G. H. Mansfield, and M. C. Whiting, *J. Chem. Soc.*, 3197 (1954); (b) M. Bertrand and J. LeGras, *Compt. Rend.*, **260**, 6926 (1965); M. Bertrand, J. Elguero, R. Jacquier, and J. LeGras, *ibid.*, **262**, 782 (1966); (c) P. Kurtz, G. Heinrich, and H. Disselnkotter, *Ann.*, **624**, 1 (1959); S. R. Landor and P. M. Greaves, *Chem. Commun.*, 323 (1966).

(3) G. Pourcelot, P. Cadiot, and A. Willemart, *Compt. Rend.*, **252**, 1630 (1961).

(4) C. J. M. Stirling, *J. Chem. Soc.*, 5856, 5863, 5875 (1964); C. H. McMullen and C. J. M. Stirling, *ibid., Sect. B*, 1217 (1966); S. T. McDowell and C. J. M. Stirling, *ibid., Sect. B*, 351 (1967); see also W. E. Truce and D. G. Brady, *J. Org. Chem.*, **31**, 3543 (1966).

(5) G. Pourcelot and P. Cadiot, *Bull. Soc. Chim. France*, 3024 (1966).

(6) K. Sato, *Nippon Kagaku Zasshi*, **76**, 1404 (1955); *Chem. Abstr.*, **51**, 17760 (1957); see also U. S. Patent 2,707,714 (May 1955).

(7) N. J. Leonard and R. R. Sauers, *J. Am. Chem. Soc.*, **79**, 6210 (1957).

CHART I

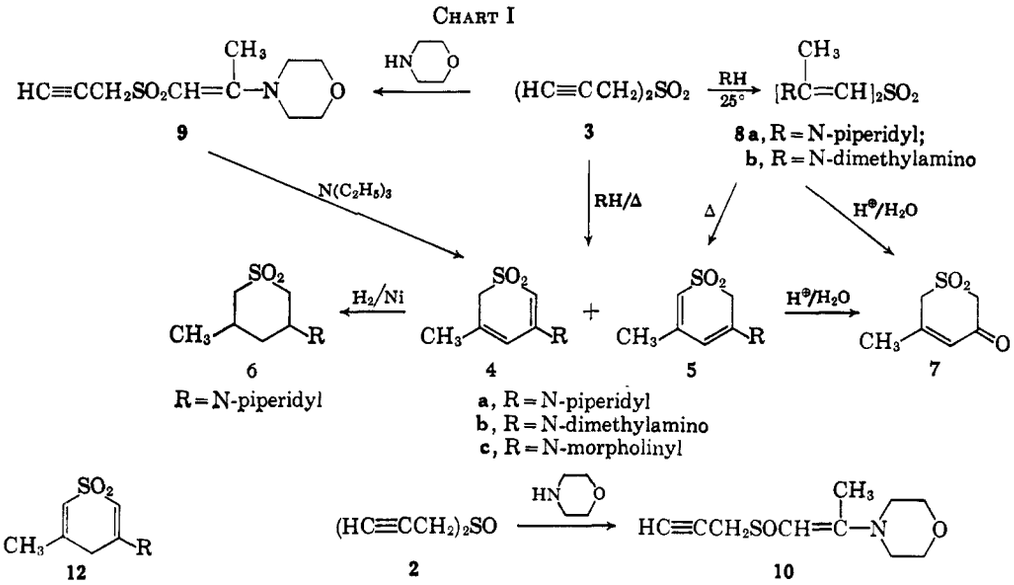


TABLE I

SULFIDES, $RSCH_2C{\equiv}CH$

R	Bp, °C (mm)	$n^{24}D$	Found, % C	Found, % H	Calcd, % C	Calcd, % H	Yield, %
p-$(CH_3)_2CHC_6H_4$—[b]	82 (0.15)	1.5517	76.34	7.88	76.44	7.89	73
 [c]	52 (0.3)	1.6022	54.55	3.75	54.50	3.92	66
$(C_6H_5)_2CH$—[d]	*a*		80.25	5.86	80.61	5.92	82
$HOCH_2CH_2$—[e]	60 (0.1)	1.5245	51.14	6.94	51.69	6.92	76
$ClCH_2CH_2$—[f]	70 (7)	1.5243	44.00	5.19	44.61	5.24	66

[a] Mp 71°, from ethanol. [b] Registry no.: 15285-82-2. [c] 15268-61-8. [d] 15268-62-9. [e] 5309-77-3. [f] 15268-64-1.

TABLE II

SULFOXIDES, $RSOCH_2C{\equiv}CH$

R	Mp, °C	Found, % C	Found, % H	Calcd, % C	Calcd, % H	Yield, %
$C_6H_5CH_2$—[c]	54	67.56	5.87	67.38	5.65	96
p-ClC_6H_4—[d]	55	54.31	3.48	54.41	3.55	72
$ClCH_2CH_2$—[e]	49	39.83	4.73	39.87	4.68	84
$HC{\equiv}CCH_2$—	49	56.76	4.75	57.11	4.79	75
n-C_4H_9—[f]	*a*	58.40	8.53	58.29	8.38	69
p-$(CH_3)_2CHC_6H_4$—[g]	64–66	70.75	7.23	70.86	7.32	27[b]

[a] Liquid, bp 80° (0.1 mm), $n^{24}D$ 1.4996. [b] Considerable losses during recrystallizations. [c] Registry no.: 14377-01-6. [d] 15268-66-3. [e] 15268-67-4. [f] 15268-68-5. [g] 15268-69-6.

TABLE III

SULFONES, $RSO_2CH_2C{\equiv}CH$

R	Mp, °C	Found, % C	Found, % H	Calcd, % C	Calcd, % H	Yield, %
p-$(CH_3)_2CHC_6H_4$—[b]	115	65.83	6.90	66.07	6.82	49
$(C_6H_5)_2CH$—[c]	129	70.68	5.25	71.08	5.22	88
	56	44.95	3.16	45.14	3.25	94
$HC{\equiv}CCH_2$— (3)	97–99	50.78	3.94	50.69	4.25	75
n-C_4H_9—[d]	36	52.65	7.62	52.47	7.55	93
$CH_2{=}CHCH_2$—[e]	*a*	49.73	5.58	49.98	5.59	67
$HC{\equiv}CCH_2SO_2(CH_2)_4$—[f]	150	45.78	5.38	45.78	5.58	77
$HC{\equiv}CCH_2SO_2(CH_2)_3$—[g]	136	43.42	4.88	43.53	4.87	73
p-$ClC_6H_4CH_2$—[h]	135	52.28	3.87	52.52	3.97	62

[a] Distilled at bath temperature 120–130° (0.07 mm), $n^{24}D$ 1.4995. [b] Registry no.: 15268-70-9. [c] 15268-71-0. [d] 15259-73-1. [e] 15259-74-2. [f] 15259-75-3. [g] 15259-76-4. [h] 15259-77-5.

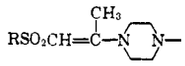
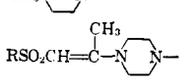
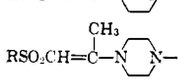
5:1, was obtained. The same mixture was also obtained by heating a dioxane solution of the enamine **9** containing some triethylamine for 24 hr. The yield from either reaction was 69%. Acid hydrolysis of these dienamines and of the diadducts **8** yielded as expected the ketone **7**. The mixture of dienamines **4c** and **5c** reacted with maleic anhydride to give a material which analyzed as a 1:1 adduct; the structure (or structures) was not ascertained because of extreme insolubility of the product. Finally, the reaction of morpholine and bis(2-propynyl) sulfoxide (2) under similar conditions provided the monoaddition product **10** in 78% yield, but attempts to cyclize this compound were not successful. The results are summarized in Chart I.

It thus remained to establish the positions of the double bonds in the cyclic isomers. This was achieved by nmr studies including double-resonance experiments.[8] For reasons of simplicity the dimethylamino-substituted compounds **4b** and **5b** were used in this study. The nmr spectrum in deuteriochloroform shows two sets of peaks corresponding to the isomers; each contains two vinyl protons, two methylene protons, and three methyl protons besides a resonance due to the N-methyl groups, quite consistent with the structures **4b** and **5b**. In trifluoroacetic acid the compounds undergo C-protonation to yield a single immonium salt (**11**) whose nmr spectrum shows one vinyl proton (δ 7.05), two methylene groups (4.72, 4.33), two non-equivalent N-methyl groups (3.82, 3.80), and a C-methyl group (2.45); hence, the equilibria in eq 2 are established. Accordingly, acid-catalyzed D_2O exchange resulted in disappearance of the resonances due to the

(8) Kindly carried out by E. B. Whipple. We thank Dr. Whipple for valuable discussions of the nmr spectra.

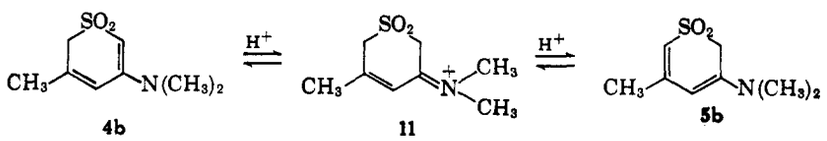
TABLE IV

VINYL SULFONES, $RSO_2CH{=}C(CH_3)X$

R	X	Registry no.	Mp, °C	Found, % C	Found, % H	Calcd, % C	Calcd, % H	Yield, %
$C_6H_5{-}CH_2{-}$		15268-72-1	137	59.49	6.93	59.76	6.81	91
$C_6H_5{-}CH_2{-}$		15268-73-2	198	60.83	7.00	60.73	6.37	93
$C_6H_5{-}CH_2{-}$	$HO_2CCH_2{-}$[a]	15268-74-3	182	56.36	5.57	56.68	5.55	76
$C_6H_5{-}CH_2$	$CH_3O{-}$[b]	15268-75-4	102–104	44.08	4.82	44.00	4.62	87
	$(CH_3)_2N{-}$	15268-76-5	110	46.70	5.53	46.73	5.66	99
		15268-77-6	127	48.37	5.50	48.33	5.53	86
		15268-78-7	70	52.66	6.38	53.11	6.31	86
		15268-79-8	128	50.24	6.34	50.32	6.33	98
		15268-80-1	207–211	47.54	4.85	47.14	4.84	83
$n\text{-}C_4H_9$		15268-81-2	112	52.97	8.68	53.17	8.43	93

[a] Prepared by addition of sodium malonate in tetrahydrofuran with subsequent hydrolysis and decarboxylation; the yield is over-all. [b] Obtained by addition of sodium methoxide in methanol.

higher field vinyl proton of the major component (δ 5.04) and the lower field vinyl proton (δ 5.74) of the minor component, which must be that adjacent to the sulfonyl group in structure **5b**. The higher field vinyl proton of the major component is strongly shielded and it is at the expected field for that adjacent to the sulfonyl group of structure **4b**; the vinyl protons of the related



4b **11** **5b**

open-chain compounds **8** and **9** as well as those of Table IV appear in the δ 4.8–5.3 region. Furthermore, double-resonance experiments demonstrated that the C-methyl protons of the major component are coupled[9] (J = 1.5 Hz) to the nonexchangeable vinyl proton, whereas the same group in the minor component is coupled only to the exchangeable vinyl proton. This is clear proof for the structures **4b** and **5b**, as major and minor components, respectively, and the other cyclic sulfones have been assigned their structures by analogy. The results, both chemical and spectroscopic, are not compatible with the 4H-thiopyran of the general structure **12**, and, as far as we could detect, this isomer is not a product from any of the reactions.

The base-catalyzed propargyl–allenyl rearrangement,[10] a prerequisite for enamine formation, is a rapidly established equilibrium. The rate of amine addition to the allenyl isomer, $RSO_2CH{=}C{=}CH_2$, most probably is affected by the nature of both the amine and the substituent R. McDowell and Stirling[11] have studied both factors on the reactivity of aryl vinyl sulfones toward amines. They observed the reactivity order of piperidine ≧ dimethylamine > morpholine, piperidine being about fifteen times faster than morpholine; moreover, *p*-nitrophenyl vinyl sulfone reacted about 40 times faster with *t*-butylamine than the *p*-methoxy analog. This is in accordance with previous reports[12] that an electron-attracting substituent (R) will stabilize a negative charge at the carbon adjacent to the sulfonyl group. In view of this and other data reported in the literature our results seem quite reasonable. The first mole of amine adds to dipropargyl sulfone forming a propargylsulfonyl enamine, having a *trans* configuration.[4] The second mole would then add at a considerably slower rate because of the electron-releasing properties of the enamine entity; hence, it is not surprising that compound **9** is isolated since morpholine is by far the least reactive of the amines used. It remains to explain why cyclization of these intermediates takes place so readily. The strong electron-withdrawing effect of the sulfonyl group renders compounds of the general structure **1** relatively unreactive as far as typical enamine reactions[13] are concerned; on the other hand, the same effect makes the methyl hydrogens sufficiently acidic to be abstracted by the enamine itself or by an added base. Cyclization will then take place on the protonated enamine in the case of **8** and on the allene in the case of **9**. From the former, dimethylamine should be formed, which indeed was observed. The three products with endocyclic double bonds, expected from both routes, would only differ in the positions of these bonds. The approximately constant ratios of the isomers obtained indicated that an equilibrium was established in each case. This was strongly supported by the fact that the ratios were not

(9) They are also equally coupled to the methylene protons and the other vinyl proton.

(10) For references see the recent review on allenes: R. D. Taylor, *Chem. Rev.*, **67**, 317 (1967). Propargyl sulfones undergo this rearrangement even in the presence of alumina or sodium bicarbonate.

(11) S. T. McDowell and C. J. M. Stirling, *J. Chem. Soc., Sect. B*, 343, 348 (1967).

(12) H. Hogeveen, G. Maccagnani, F. Montanari, and F. Taddel, *ibid.*, 4101 (1964), and references therein.

(13) For a review on enamine chemistry, see J. Szmuszkoviz, *Advan. Org. Chem.*, **4**, 1 (1963).

changed even after heating the mixtures with potassium *t*-butoxide in dimethyl sulfoxide. The absence of the 4H-thiopyran isomers, the expected initial product of the ring closure, is not surprising in view of the fact that Δ^2-dihydrothiopyran 1,1-dioxide is readily and irreversibly converted to the Δ^3 isomer with weak bases.[14] Some recent work[15] has shown that the compound previously reported as 4H-thiopyran 1,1-dioxide actually is the 2H isomer formed by rearrangement. The failure of the sulfoxide **10** to undergo ring closure under similar conditions is probably due to the weaker electron-attracting properties of the sulfoxide group as compared with the sulfonyl group.

The formation of the ketone **7** by acid hydrolysis of the bis-enamine **8** was quite expected and thereby confirmed the structures of both starting material and product. In this connection it should be mentioned that the 3-ethoxy[16] and 3-phenyl[17] analogs of **7** have been prepared recently, the latter from the corresponding diketone.

Experimental Section[18]

The propargyl sulfides (Table I) were prepared by treating the sodium salt of the respective thiol with propargyl bromide in methanol at room temperature. **Propargyl sulfoxides** (Table II) were obtained from the above sulfides by oxidation with 1 equiv of *m*-chloroperbenzoic acid in methylene chloride at 0°. **Propargyl sulfones** (Table III) were produced when 2 equiv of the peracid were used.

Addition Reactions.—The amines were added to ether solutions of the propargyl sulfones at 0° (Table IV).

3-Methyl-5-N-piperidyl-2H-thiopyran 1,1-Dioxide (4a) and 5-Methyl-3-N-piperidyl-2H-thiopyran 1,1-Dioxide (5a).—Piperidine (29.8 g, 0.35 mole) was added to a stirred solution of 46.1 g (0.32 mole) of bis(2-propynyl) sulfone (**3**) in 220 ml of benzene. The reaction mixture was heated under reflux for 2 hr. Evaporation of the solvent and recrystallization of the residue gave 66.0 g (94%) of product, mp 98–100°, which according to the nmr spectrum consisted of 86% of **4a** and 14% of **5a**. An analytical sample was obtained by recrystallization from ethyl acetate: mp 105°; ν_{max} (KBr) 1650, 1550 (C=C), 1285, 1110 cm^{-1} (SO_2); the uv spectrum is discussed in the theoretical part. The nmr spectrum of the major component shows broad singlets at δ 2.07 (CH_3) and 3.65 (CH_2), a broad singlet at 5.28 (CH=C—N), and a weakly split multiplet at 6.08 (C=CH). Corresponding peaks due to the minor component appear at 1.98, 3.78, 4.97, and 5.82. In addition there is absorption due to the piperidyl protons.

Anal. Calcd for $C_{11}H_{17}NO_2S$: C, 58.12; H, 7.54. Found: C, 58.06; H, 7.73.

The dropwise addition at room temperature of piperidine (60 mmoles) to a stirred ether suspension of **3** (30 mmoles) resulted in a homogeneous solution. Evaporation of the solvent under vacuum gave a viscous liquid which slowly crystallized. Attempted recrystallizations were unsuccessful. An infrared spectrum of the crude material shows ν_{max} 1550 (C=C), 1275, 1100 cm^{-1} (SO_2) in agreement with structure **8b**. A benzene solution was heated under reflux for 3 hr, yielding the mixture of **4a** and **5a** together with piperidine.

5-Methyl-3-N-piperidyltetrahydrothiopyran 1,1-Dioxide (6).—A solution of 5.0 g (22 mmoles) of a mixture of **4a** and **5b** in 50 ml of ethanol was hydrogenated over 8 g of Raney nickel catalyst for 16 hr at room temperature. Filtration and evaporation gave 4.2 g (84%) of **6**, mp 136°; the nmr and ir spectra show the absence of unsaturation. The compound was converted to the hydrochloride in 91% yield: mp 273°; ν_{max} (KBr) 2500 (≡NH⁺), 1305, 1120 cm^{-1} (SO_2).

Anal. Calcd for $C_{11}H_{22}ClNO_2S$: C, 49.33; H, 4.28. Found: C, 49.01; H, 4.36.

3-Methyl-5-oxo-Δ^3-dihydrothiopyran 1,1-Dioxide (7).—A mixture of 2.25 g (9.8 mmoles) of the dienamines **4c** and **5c** and 10 ml of 2 *N* sulfuric acid was warmed until a homogeneous solution was obtained. Upon standing 1.55 g (98%) of the ketone crystallized: mp 113–117° (recrystallization from ethanol raised the melting point to 119°); ν_{max} 3050, 1625 (C=C), 1675 (C=O), 1310 and 1115 cm^{-1} (SO_2); λ_{max} 232.5 mμ (ε, 11,400); nmr, singlet at δ 2.22 (CH_3), weakly split multiplet at 3.91 (CH_2), singlet at 4.05 (CH_2CO), and multiplet at 6.32 (C=CH) with a peak area ratio 3:2:2:1.

Anal. Calcd for $C_6H_8O_3S$: C, 44.99; H, 5.03. Found: C, 44.91; H, 5.03.

The compound formed a **2,4-dinitrophenylhydrazone**, mp 230°.

Anal. Calcd for $C_{12}H_{12}N_4O_6S$: C, 42.35; H, 3.55. Found: C, 42.52; H, 3.76.

An **oxime** was prepared in the usual way, mp 189–191°.

Anal. Calcd for $C_6H_9NO_3S$: C, 41.13; H, 5.18. Found: C, 40.93; H, 5.22.

The same ketone (**7**) was obtained from the mixtures **4a**, **5a** and **4b**, **5b**.

Bis(2-dimethylamino-1-propenyl) Sulfone (8b).—Dimethylamine was passed into an ice-cooled and stirred suspension of 4.3 g (30 mmoles) of the sulfone **3** in 40 ml of dry ether. After 1 hr the precipitate was filtered and dried at room temperature, yielding 5.3 g (86%) of the dienamine **8b**: mp 113–116° dec; ν_{max} 1560, 855 (C=C), 1250, 1020 cm^{-1} (SO_2); λ_{max} 256 mμ (ε 19,700); nmr, singlets at δ 2.25 (C–CH_3), 2.87 (N–CH_3), and 5.11 (C=CH), with peak area ratio of approximately 3:6:1. No satisfactory elemental analysis was obtained.

Anal. Calcd for $C_{10}H_{20}N_2O_2S$: C, 51.69; H, 8.68. Found: C, 50.80; H, 8.63.

When compound **8b** (40 mmoles) was added to 100 ml of 2 *N* sulfuric acid and heated, the ketone **7**, mp 117–118°, was obtained in 60% yield.

5-Dimethylamino-3-methyl-2H-thiopyran 1,1-Dioxide (4b) and 3-Dimethylamino-5-methyl-2H-thiopyran 1,1-Dioxide (5b).—A solution of the enamine **8b** in benzene was heated under reflux for 3.5 hr. Dimethylamine was evolved. Evaporation of the solvent and recrystallization from ethanol afforded in 94% yield a mixture of **4b** and **5b**: mp 136–138°; ν_{max} (KBr) 3050, 1650, 1550 (C=C), 1280, 1100 cm^{-1} (SO_2); λ_{max} 239 (ε 6900) and 325 mμ (ε 4800); the nmr spectrum of the major component shows a weakly split triplet at 2.10 (C=CCH_3), singlet at δ 2.93 (NCH_3), broad singlets at 3.67 (CH_2) and 5.08 (C=CH), and a multiplet centered at 6.20 (C=CH). Corresponding peaks due to the minor component appear at δ 2.00, 2.93, 3.88, 4.80, and 5.77.

Anal. Calcd for $C_8H_{13}NO_2S$: C, 51.31; H, 7.00. Found: C, 51.23; H, 7.08.

***trans*-2-N-Morpholinyl-1-(2-propynylsulfonyl)propene (9).**—A solution of 3.1 g (37 mmoles) of morpholine in 25 ml of ether was added dropwise at room temperature to a stirred suspension of 5.2 g (37 mmoles) of **3** in 75 ml of ether. After 2 hr the resulting white solid was filtered to obtain 7.0 g (84%) of **9**: mp 107° after recrystallization from ethanol; ν_{max} (KBr) 3230, 2250 (C≡CH), 1550 (C=C), 1295, 1115 cm^{-1} (SO_2); nmr, singlet at δ 2.33 (CH_3), triplet at 2.47 (C≡CH), doublet at 3.87 (CH_2), singlet at 5.06 (C=CH), and characteristic absorption due to the morpholine hydrogens.

Anal. Calcd for $C_{10}H_{15}NO_3S$: C, 52.38; H, 6.59. Found: C, 52.54; H, 6.77.

3-Methyl-3-N-morpholinyl-2H-thiopyran 1,1-Dioxide (4c) and 5-Methyl-3-N-morpholinyl-2H-thiopyran 1,1-dioxide (5c). A.—A solution of 28.6 g (0.33 mole) of morpholine in 30 ml of tetrahydrofuran was added dropwise to a stirred solution of 28.1 g (0.20 mole) of the sulfone **3** in the same solvent. The reaction mixture was heated under reflux for 4 hr. The resulting precipitate was filtered to give 31.0 g (69%) of a mixture of **4c** and **5c**: mp 200° after recrystallization from ethanol; ν_{max} (KBr) 3090, 1605,

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(18) Boiling points and melting points are uncorrected. The infrared spectra were obtained on Beckman IR 5A and IR 10 spectrometers. The ultraviolet spectra were measured in methanol solution, when not otherwise stated, on a Cary Model 14 spectrometer. The nmr spectra were recorded on a Varian A 60A instrument with deuterated chloroform or carbon tetrachloride as solvents and tetramethylsilane as internal standard, when not otherwise stated. The chemical shifts are given in δ values. The double resonance experiments were performed on a Varian HR-60 spectrometer modified for a 2.00-KHz internal field frequency lock and frequency sweep capabilities.

1550 (C=C), 1315, 1125 cm^{-1} (SO_2); λ_{max} 246 mμ (ε 8800) and 311 mμ (ε 6500). The compound was only sparingly soluble in the usual nmr solvents; hence, the data for the minor component are not reliable. The major component shows broad singlets at δ 2.09 (CH_3) and 3.70 (CH_2). The olefinic protons appear as a broad singlet at δ 5.33 and a weakly split multiplet at 6.10. The spectrum indicates that the minor component is present in about 15%. Acid hydrolysis of the mixture afforded the ketone **7** in good yield.

Anal. Calcd for $C_{10}H_{15}NO_3S$: C, 52.38; H, 6.59. Found: C, 52.23; H, 6.44.

B. A solution of 1.6 g (7 mmoles) of the enamine **9** and five drops of triethylamine in 50 ml of dioxane was heated under reflux for 24 hr. From the reaction mixture 1.1 g (69%) of a mixture of compounds **4c** and **5c**, mp 194–196°, was isolated.

Maleic Anhydride Adduct.—The above mixture (800 mg, 3.5 mmoles) and 340 mg (3.5 mmoles) of maleic anhydride in 20 ml of xylene was heated under reflux for 2 hr. When cold, the precipitate was filtered and washed with ethanol yielding 800 mg of product: mp 254–255°; ν_{max} 1780, 1810 cm^{-1} (anhydride C=O). The substance was insoluble in all common solvents. It formed a homogeneous solution with aqueous sodium hydroxide.

Anal. Calcd for $C_{14}H_{17}NO_6S$: C, 51.37; H, 5.23; N, 4.28; O, 29.32. Found: C, 51.15; H, 5.20; N, 4.31; O, 29.22.

2-N-Morpholinyl-1-(2-propynylsulfinyl)propene (10).—To a solution of 2.5 g (20 mmoles) of the sulfoxide **2** in 20 ml of dry ether was added dropwise 3.5 g (40 mmoles) of morpholine. The reaction mixture was left at room temperature overnight. Filtration gave 3.3 g (78%) of the adduct **10**, mp 108–110°. An analytical sample was obtained by recrystallizations from ethanol: mp 118°; ν_{max} 3200 (C≡CH), 1560 (C=C–N) 1005 cm^{-1} (SO); nmr, singlet at δ 2.27 (CH_3), triplet at 2.42 (C≡CH), doublet at 3.56 (CH_2), singlet at 5.25 (CH), and characteristic absorption due to the morpholine protons (the peak area ratio is 3:1:2:2, respectively).

Anal. Calcd for $C_{10}H_{15}NO_2S$: C, 56.31; H, 7.09. Found: C, 56.36; H, 7.04.

Registry No.—**2**, 15292-69-0; **3**, 14039-88-4; **4a**, 15292-71-4; **4b**, 15292-72-5; **4c**, 15292-73-6; **6**, 15292-74-7; **7**, 15292-75-8; **7** 2,4-dinitrophenylhydrazone, 15268-82-3; **7** oxime, 15268-83-4; **8b**, 15268-58-3; **9**, 15268-59-4; **10**, 15268-60-7; **6**·HCl, 15268-54-9; **5a**, 15268-55-0; **5b**, 15268-56-1; **5c**, 15268-57-2.

The Preparation and Properties of Some Acylguanidines[1a]

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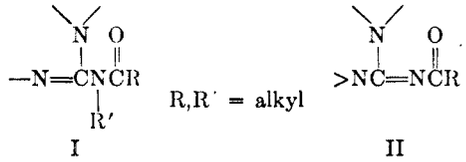
Received August 18, 1967

The preparation and properties of a number of monoacylguanidines are described. Ultraviolet spectral studies in aqueous and ethanolic solutions as a function of pH and observation of hydrolytic behavior have been found to be useful in distinguishing between acylguanidines of the acylamino and acylimino types. Examination of their pK_a's revealed significant differences with specific series. However, the wide range of values obtained made the pK_a's of little utility for structural correlations among the various acylguanidines.

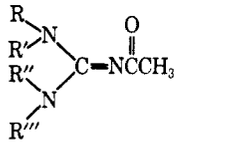
Our interest in acylguanidines was stimulated by the possible presence of such a moiety in a natural substance and its degradation products. There exist two possible substituted monacylguanidine types, but a literature search revealed that no clear distinction has been made between the acylamino (I) and acylimino (or potential acylimino) (II) forms. In particular, we were interested in the ultraviolet spectral behavior of the two types as a function of pH and in their pK's.



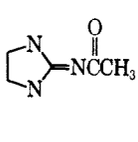
I II

A series of substituted guanidines has been monoacetylated, and the resulting derivatives are reported[2] to absorb in the ultraviolet between 230–235 mμ. Since neither guanidine nor primary or secondary amides absorb strongly above 210 mμ, this absorption was interpreted to indicate conjugation of the acetyl carbonyl with the guanidine moiety. Further, from this evidence it was concluded that monoacetylguanidines exist in the acetylimino form. Although our present work confirms these structural assignments, it also clearly demonstrates the difference in ultraviolet absorption of types I and II. Since there are only a few reported[3-9] compounds of the acylamino type and no spectral and limited pK data for them, we have synthesized a series of suitable compounds for comparison with some acyliminoguanidines of proven structure.

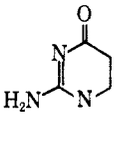
Synthesis of Acylimino Type.[10]—Compounds III, V, VII, and VIII were prepared as reported;[2,11,12] creatinine (IX) was a commercial sample. Acetyl-N,N,-



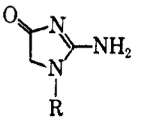
III, R = R' = R'' = R''' = H
IV, R = R''' = CH_3; R' = R'' = H
VI, R = R' = R'' = R''' = CH_3



V



VII



VIII, R = H
IX, R = CH_3

(1) (a) Supported in part by the U. S. Army Research Office, Durham, N. C.; (b) National Institutes of Health Predoctoral Fellow.

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(10) Where tautomeric structures are possible, we have adopted the following convention in drawing and naming compounds: (a) acylimino forms are used whenever possible, (b) the exocyclic double bond isomer is preferred for five-membered ring compounds, and (c) the endocyclic double bond isomer is preferred for six-membered ring compounds.

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