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REACTIONS OF α-KETOSULFENES WITH CYCLIC NITRONES[1]

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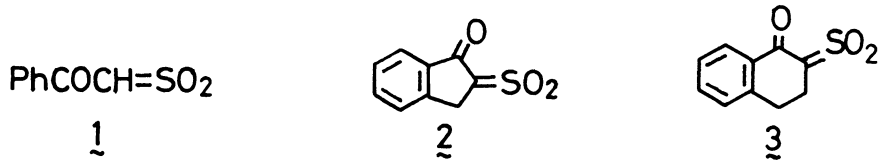
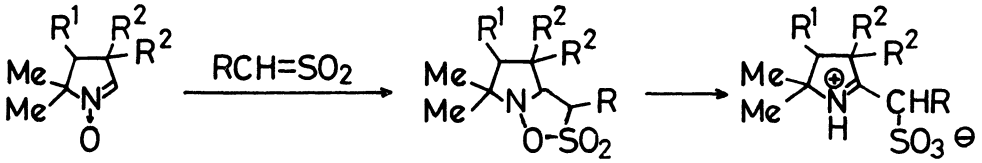
Benzoylsulfene 1 and two cyclic α-ketosulfenes 2 and 3, generated in situ from the corresponding sulfonyl chlorides and triethylamine, react with 1-pyrroline 1-oxides to produce the corresponding *cis-s-cis* β-aminoenones and/or β-imino sulfonic acids, whose relative yields greatly depended on the nature of solvents employed. The reaction pathways are also described.

Previously,[2] we reported that benzoylsulfene 1 and two cyclic α-ketosulfenes 2 and 3, generated in situ from the corresponding sulfonyl chlorides and triethylamine, react with C,N-diarylnitrones [ArCH=N(O)Ph] to yield the corresponding rearranged adducts, seven-membered cyclic azasultones, accompanied by the formation of by-products, which arise from the rearranged adducts with the elimination of the benzaldehyde (ArCHO), respectively. The above reactions, as well as that with simple sulfenes ($RCH{=}SO_2$),[3] proceed via 1,3-cycloaddition followed by rearrangement to yield cyclic azasultones.



1 2 3

If cyclic nitrones such as 1-pyrroline 1-oxides are used in place of acylic nitrones, the formation of stable 1,3-cycloadducts may be expected from the reaction with sulfenes, because rearrangement of the 1,3-cycloadducts to azasultones is impossible. In progress of our study on the reaction of α-ketosulfenes with 1-pyrroline 1-oxides,[4] we learned the study concerning the formation of β-imino sulfonic acids from the reaction of simple sulfenes with 1-pyrroline 1-oxides.[5] The 1,3-cycloadducts are suggested as unstable intermediates in the formation of β-imino sulfonic acids (Scheme 1).



Scheme 1

We now report on the reaction of α-ketosulfenes with 1-pyrroline 1-oxides leading to the formation of β-aminoenones and/or β-imino sulfonic acids, whose relative yields greatly depended on the nature of solvents employed.

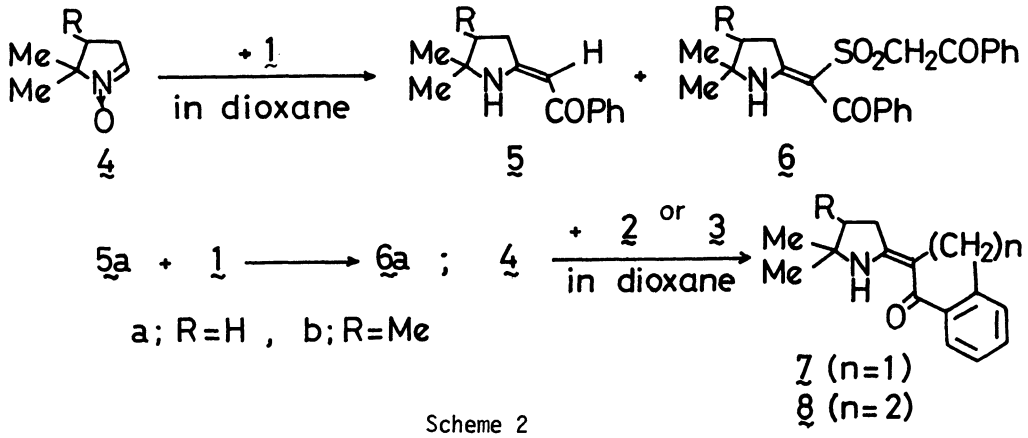
When a solution of benzoylmethanesulfonyl chloride in anhydrous dioxane was added dropwise to a stirred solution of equimolar quantities of 5,5-dimethyl-1-pyrroline 1-oxide (4a) and triethylamine in anhydrous dioxane at room temperature under nitrogen, there was an immediate precipitation of triethylammonium chloride. After the mixture was stirred at the same conditions for 3 hr, 2-benzoylmethylene-5,5-dimethylpyrrolidine (5a), mp 61-62°C, and 2-(benzoyl-benzoylmethanesulfonylmethylene)-5,5-dimethyl-

pyrrolidine (6a), mp 162-163°C, were obtained in 15 and 36% yields, respectively. The reaction of 5a with 1 afforded 6a in good yield. Structural elucidation of 5a and 6a was accomplished on the basis of spectral data.[6]

5a: IR(KBr) cm^{-1} 3250(NH), 1605(C=O), 1570, 1535(C=C); NMR(CCl_4) δ 1.35(6H, s, $C(CH_3)_2$), 1.78, 2.73 (each 2H, t, CH_2, J=7.5 Hz), 5.57(1H, s, =CH), 7.2-7.9(5H, m, ArH), 10.2(1H, br, NH); UV(EtOH) λ_{max} nm (log ε) 252(3.97), 345(4.33); mass spectrum m/e 215(M^+).

6a: IR(KBr) cm^{-1} 3320(NH), 1680, 1600(C=O), 1590, 1560(C=C), 1260, 1105(SO_2); NMR($CDCl_3$) δ 1.21(6H, s, $C(CH_3)_2$), 1.4-2.7(4H, m, CH_2), 5.0(2H, pseudo s, SO_2CH_2), 7.3-8.2(10H, m, ArH), 8.8(1H, br, NH); UV(EtOH) λ_{max} nm(log ε) 214(4.51), 257(4.38), 302(4.11); mass spectrum m/e 397(M^+).

Similarly, 1 reacted with 4,5,5-trimethyl-1-pyrroline 1-oxide (4b) to give the β-aminoenones 5b, mp 67-69°C, and 6b, mp 147-148°C, in 20 and 35% yields, respectively. The reactions of cyclic α-keto-sulfenes 2 and 3, generated in situ from the corresponding sulfonyl chlorides and triethylamine, with 4a and 4b under similar conditions afforded the corresponding β-aminoenones. 7a: mp 184-186°C, yield 69%. 7b: mp 142-143°C, yield 67%. 8a: mp 112-113°C, yield 56%. 8b: mp 73°C, yield 57%. Structural elucidation of all β-aminoenones was accomplished on the basis of their spectral data.



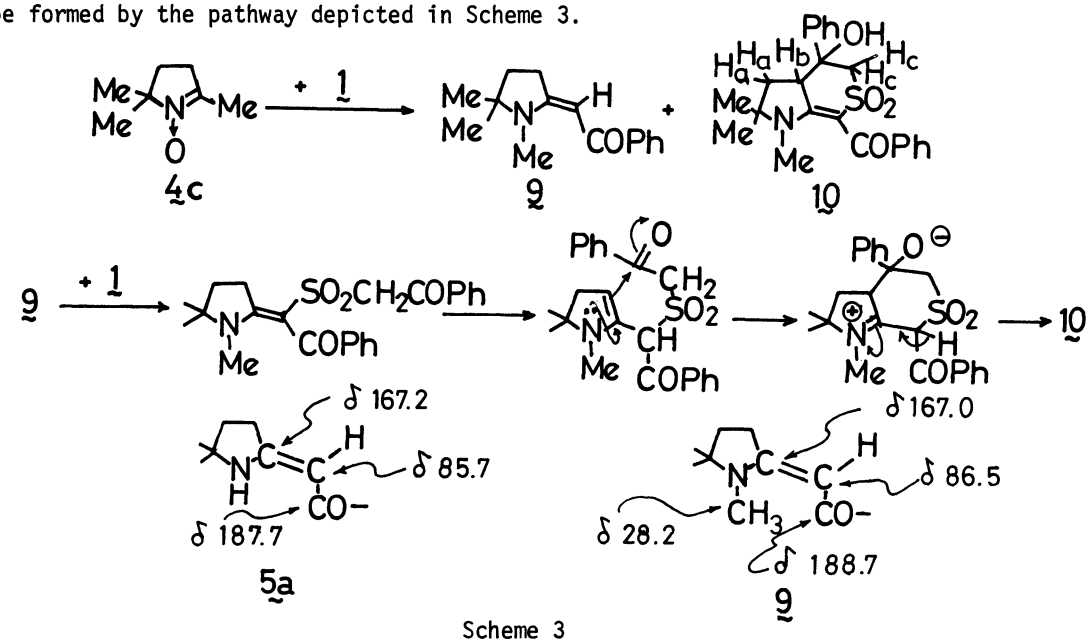
Scheme 2

In β-aminoenones 5 and 6 four geometrical isomers, *trans-s-trans*, *trans-s-cis*, *cis-s-trans* and *cis-s-cis*, are possible, whereas two isomers, *cis-s-trans* and *cis-s-cis*, are possible for β-aminoenones 7 and 8.[7] On the basis of NH proton NMR signals[8] and of UV absorption maxima of π→π* transition,[9] it was concluded that all β-aminoenones 5-8 possess the *cis-s-cis* structure.

In order to obtain an information concerning exclusion of sulfur trioxide and also in the hope of isolating the initial 1,3-cycloadduct, we explored the reaction of 1 with 2,5,5-trimethyl-1-pyrroline 1-oxide (4c) in dioxane.[10] In this case two crystalline compounds 9, mp 83-84°C, and 10, mp 197-201°C (decomp.), were isolated in 7 and 5% yields, respectively. On the basis of the following evidence, 9 was assigned to be 2-benzoylmethylene-1,5,5-trimethylpyrrolidine. IR(KBr) cm^{-1} 1620, 1600(C=O), 1585, 1550(C=C); NMR(CCl_4) δ 1.14(6H, s, $C(CH_3)_2$), 1.77, 3.22(each 2H, t, CH_2, J=7.5 Hz), 2.68(3H, s, NCH_3), 5.46(1H, s, =CH), 7.1-7.9(5H, m, ArH); UV(EtOH) λ_{max} nm(log ε) 252(3.67), 345(4.03). The ^{13}C-NMR signals shown in Scheme 3 support the assigned structures for 5a and 9.

The spectral data of 10 are as follows. IR(KBr) cm^{-1} 3340(OH), 1620(C=O), 1565(C=C), 1225, 1105 (SO_2); NMR($CDCl_3$) at 100 MHz δ 1.24, 1.38 (each 3H, CH_3), 1.59(1H, dd, Ha, J=8.5, 13.0 Hz), 2.04(1H, dd, Ha, J=11.0, 13.0 Hz), 2.60(3H, s, NCH_3), 3.52, 3.90(each 1H, d, Hc, J=14.0 Hz), 3.91(1H, dd, Hb, J=8.5, 11.0 Hz), 4.65(1H, br, OH), 7.2-8.1(10H, m, ArH); mass spectrum m/e 411(M^+), 393($M^+ - H_2O$); UV (EtOH) λ_{max} nm(log ε) 212(4.40), 258(4.58), 328(3.90). The compound 10 was formed readily from the reaction of 9 with 1. On the basis of the above observations, 10 was deduced to be 7-benzoyl-4-hydroxy-4-phenyl-1,2,2-trimethyl-5H-2,3,3a,4-tetrahydropyrrolo[2,3-c]thiopyran 6,6-dioxide which would

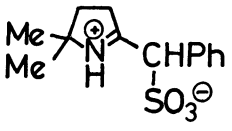
probably be formed by the pathway depicted in Scheme 3.



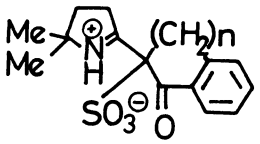
Scheme 3

The reaction of phenylsulfene with 4a in dioxane afforded the β-imino sulfonic acid 11, mp 239-242°C(decomp.), in 71% yield.[11] 11: IR(KBr) cm^{-1} 3000-2500(NH), 1675(C=N), 1260, 1220, 1040(SO_3); NMR (CD_3NO_2) δ 1.55, 1.58(each 3H, s, CH_3), 2.21(2H, pseudo t, CH_2, J=8 Hz), 3.42(2H, pseudo q, CH_2, J=8 Hz), 5.79(1H, s, CH), 7.3-7.9(5H, m, ArH), NH or OH proton signal was not observed; mass spectrum m/e 267(M^+), 252, 187(M^+ - SO_3), 172(187$^+$ - Me, base peak).

We found that the β-imino sulfonic acid 12 or 13 was formed from the reaction of cyclic α-ketosulfene 2 or 3 with 4a in such solvents as acetonitrile and methylene chloride.[12] The results in various solvents are given in Table 1.



11



12 (n= 1)
13 (n= 2)

Table 1

Solvent	Dielectric constant	pK_a	From 2 and 4a Yield, % 7a	12	From 3 and 4a Yield, % 8a	13
dioxane	2.21	- 2.92	69	0	56	0
tetrahydrofuran	7.58	- 2.08	63	0	21	48
tetrahydropyran	5.61	- 2.79	53	0	-	-
monoglyme	7.20	- 2.97	18	53	13	59
acetonitrile	37.5	- 10.12	8	70	13	72
methylene chloride	8.93		11	66	6	77
toluene	2.38		6	61	9	81

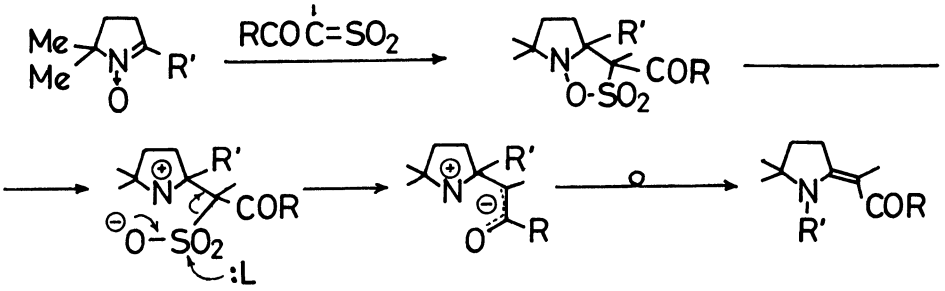
Structural elucidation of 12 and 13 was accomplished on the basis of spectral data.

12: mp 219-222°C(decomp.); IR(KBr) cm^{-1} 3140(NH), 1705(C=O), 1640(C=N), 1250, 1220, 1045, 1025(SO_3); NMR(DMSO-d_6) δ 1.40(6H, s, $C(CH_3)_2$), 1.98(2H, pseudo t, CH_2, J=7.5 Hz), 3.53, 3.94(1H, d, CH_2, J=18 Hz), 3.5(2H, pseudo dd, CH_2), 7.2-8.0(4H, m, ArH), 12.6(1H, br, NH or OH, exchanged with D_2O); NMR(CD_3NO_2) δ 1.60, 1.63(each 3H, s, CH_3), 2.26, 3.54(each 2H, t, CH_2, J=7.5 Hz), 3.59, 4.12(1H, d, CH_2, J=18 Hz), 7.3-8.0(4H, m, ArH), NH or OH proton signal was not observed; mass spectrum 227(M^+ - SO_3).

13: mp 189-191°C(decomp.); IR(KBr) cm^{-1} 3180(NH), 1690(C=O), 1650(C=N), 1245, 1235, 1050, 1040(SO_3);

NMR(DMSO-d_6) δ 1.36(6H, s, CH_3), 1.89(2H, t, CH_2, J=7.5 Hz), 2.3-3.3(6H, m, CH_2), 7.2-8.0(4H, m, ArH), 11.9(1H, br, NH or OH); mass spectrum m/e 241(M^+ - SO_3).

When treated with excess of triethylamine or pyridine, 12 and 13 were readily converted to 7a and 8a, respectively. On treatment with triethylammonium chloride in dioxane, however, 12 and 13 were unchanged; this suggests that 7a and 8a shown in Table 1 did not arise from 12 and 13. Although the correlation between the yields of products and polarities or basicities of solvents employed cannot be derived from the data in Table 1, it seems reasonable to conclude that β-aminoenones are predominantly formed in solvents which have a strong affinity for sulfur trioxide. The pathway for the formation of β-aminoenones is outlined in Scheme 4. The formation of β-aminoenones might be classified into a special reaction, because only a few examples involving exclusion of SO_x in the sulfene chemistry appeared in the literature.[13]



L: Solvent

Scheme 4

References and Notes

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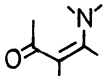
4. This work was partly presented at the 26th (April, 1972) and 32rd Annual Meeting of the Chemical Society of Japan (April, 1975).
5. D. St. C. Black and V. C. Davis, Tetrahedron Lett., 1993 (1975).
6. All new compounds gave satisfactory elementary analyses.
7. *trans-s-trans*  , *cis-s-trans*  , *trans-s-cis*  , *cis-s-cis* 
8. The NH proton NMR signals of β-aminoenones with the *cis-s-cis* structure appear at δ 9.0-15 ppm.[14] On the other hand, the NMR spectrum of $\Delta^{6,9}$-octahydro-7-quinolone having the *trans-s-trans* structure shows the NH proton signal at δ 5.9 ppm.[15]
9. On the basis of the observed λ_{max} (256 nm) of 1-phenyl-2-buten-1-one,[16] the λ_{max} values of 5 with *cis-s-cis*, *cis-s-trans* and *trans-s-cis* structures were calculated using the substituent constants reported by Ostercamp[17]; 346 nm for *cis-s-cis*, and 336 nm for *cis-s-trans* and *trans-s-cis*.
10. The reaction of 2 and 3 with 4c under similar conditions gave unidentified products.
11. Black and Davis[5] reported the formation of 11 in the reaction of phenylsulfene with 4a in benzene, but physical and spectral data of 11 were not described.
12. The reaction of 1 with 4a in methylene chloride afforded the corresponding β-imino sulfonic acid which could not be isolated in a pure form.
13. For example, H. Staudinger and F. Phenninger, Ber., 49, 1941 (1916); N. Tokura, T. Nagai, and S. Matsumura, J. Org. Chem., 31, 349 (1966); C. R. Hall and D. J. H. Smith, Tetrahedron Lett., 3633 (1974); T. Durst and J. F. King, Can. J. Chem., 44, 1869 (1966).
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