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NOVEL ADDUCTS OF SULFIDES AND 4-SUBSTITUTED 1,2,4-TRIAZOLINE-3,5-DIONES(TAD)

—— A SIMILARITY OF TAD AND SINGLET OXYGEN($^1O_2$) ——

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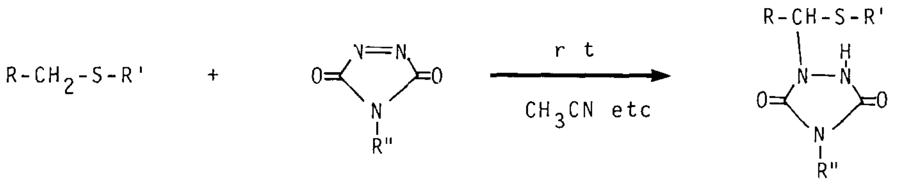
Abstract The 4-substituted 1,2,4-triazoline-3,5-diones(2) afford with sulfides(1) having acidic α-hydrogens the 1,4-disubstituted urazoles(3) Reactivity of the triazolinedione shows similarity in possible reaction modes with that of singlet oxygen

The 4-substituted 1,2,4-triazoline-3,5-dione(TAD) should be an interesting and useful substrate for exploring [2+4] cycloaddition, [2+2] cycloaddition, and ene reaction of olefins.[1,2] Although its reaction modes resemble those of singlet oxygen($^1O_2$), such data are little for sulfur compounds[3] which also react with $^1O_2$.[4] Consequently, the study on the reaction of TAD with sulfur compounds provides an excellent opportunity for detail investigation of the $^1O_2$ oxidation of sulfur compounds.

We have investigated reactivity of sulfides toward TAD in comparison with $^1O_2$ oxidation Diphenyl sulfide is unreactive toward TAD, while alkyl substituted sulfides lead to an interactable product mixture.[5] However, on treatment with TAD at 25°C in appropriate solvent, benzylic and β-ketosulfides gave the adducts, i.e. 1,4-disubstituted urazoles 3, in moderate yields(eq 1, Table 1).

To a solution of benzoylmethyl methyl sulfide(1b, 2 mmole) in dry acetonitrile(10 ml), 4-phenyl-1,2,4-triazoline-3,5-dione(2a, 1 mmole) in dry acetonitrile(8 ml) was added dropwise at room temperature(at ca 25°C) and the mixture was stirred for 14 h under N_2. After usual work-up and separation



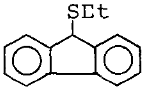
(1)

1

2a, R''= Ph
2b, R''= Me

3

Table 1. Adducts in the Reaction of TAD(2a) with Sulfides(1)a)

Substrate		Solvent(ml)	Time[h]	Isolated Yield of 3[%]b)	
$PhCH_2SCH_2Ph$	1a	$CHCl_3$(7)	2	23	
"	"	CH_3CN(20)	14	41	
$PhCOCH_2SCH_3$	1b	CH_3CN(18)	14	73	c)
	1c	CH_3CN(21)	20	16	
$PhCH_2SPh$	1d	CH_2Cl_2(17)	48	13	
$PhCH_2SCH_2Ph$	1a	CH_3CN(18)	40	18	d)

a) The reaction was carried out by such a procedure as described in the text b) Usually product 3 was accompanied with high molecular weight substance which mainly consists of TAD Yields of 3 were based on the amount of TAD c) As for the structure, see ref 6 d) TAD(2b, R"= Me) was used

of the products by column chromatography, 3(R= C(O)Ph, R'= Me, R"= Ph, 73%)[6] was obtained as a major product with being accompanied with polymeric white powder(27 mg), 4-phenyl urazole(trace), and recovered sulfide(127%, based on TAD) Other sulfides(1a, 1c and 1d) also gave the corresponding products (3) in yields ranging from 13 to 41% in various solvents, CH_2Cl_2 etc. The formation of 3 was hardly affected by light.[7]

Scheme 1

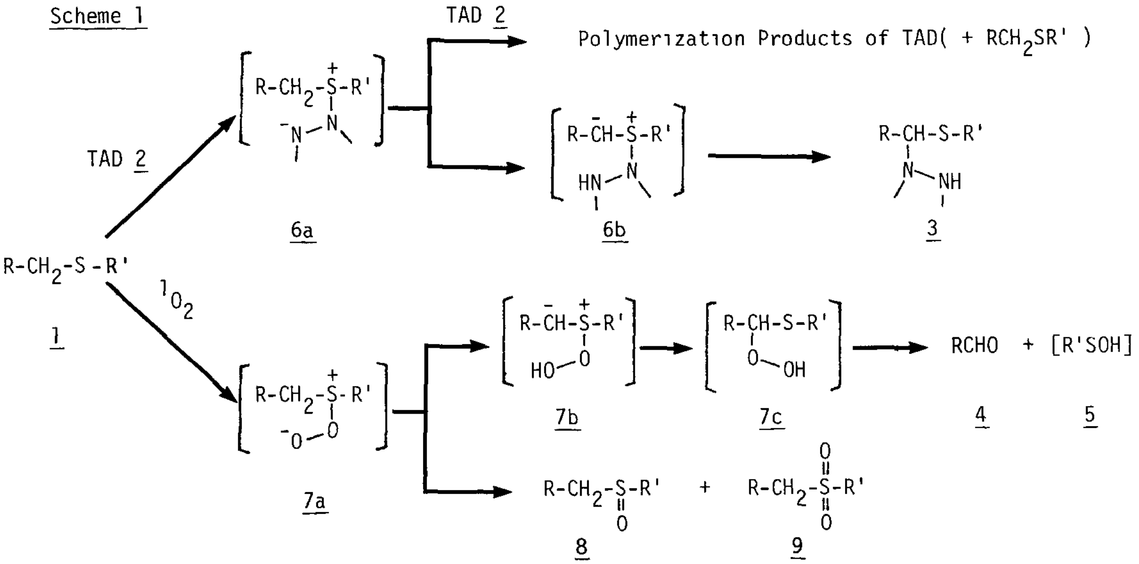


Table 2 The Reactions of p,p'-Disubstituted Dibenzyl Sulfides ($(p\text{-}X\text{-}C_6H_4CH_2)_2S$) with TAD(2a)[a] and $^1O_2$[b]

Substrate		With TAD[c,e]	With $^1O_2$[d,f]			
X=		3	4	8	9	1(recovery)
MeO	1e	0%	0%	-[g]	-[g]	0%
Me	1f	21	38	46%	11%	0
H	1a	41	51	39	8.5	trace
Cl	1g	27	28	49	8.9	7.5
NO_2	1h	0	0	0	0	90

a) The reaction was carried out as described in the text b) The oxidation was employed using zinc 5,10,15,20-tetraphenylporphyrin(3 mg) and substrate(0 1 mmole) in $CDCl_3$(0 4 ml) at 25°C with bubbling oxygen under irradiation by xenone lamp(2 kw) for 30 min. c) Isolated yields based on the amounts of the sulfides used d) NMR yields based on the amounts of the sulfides used e) Most sulfide other than that incorporated into the products(3) was recovered However, TAD was not recovered but gave polymeric product and urazole(except for 1h) (note h) and ref 5) f) Both sulfoxides and sulfones were completely unreactive toward $^1O_2$ under the conditions applied g) The products were sulfoxide and sulfone, but the yields could not be well determined h) No reaction(most of TAD and sulfides was recovered)

While usual organic sulfides react with $^1O_2$ to afford the corresponding sulfoxides and sulfones,[4] alkyl benzyl sulfides afford products(4 and 5) via C-S bond cleavage, besides the usual S-oxidation products(Scheme 1).[8] Meanwhile, inspection of data in Table 2 reveals the similar reactivity of TAD and $^1O_2$ in the formations of the adducts 3 and C-S bond cleavage products 4, by comparing the electronic effects on p,p'-disubstituted dibenzyl sulfides. Therefore, the adduct 3 and possible intermediates(6a and 6b) seem to resemble likely intermediates(7a, 7b and 7c, respectively) suggested in the reaction of benzylic sulfides with $^1O_2$, as shown in Scheme 1. For these electronic effects in the formations of 3 and/or 4, important is a mixed effect of two factors controling the reaction paths and products, i.e the electron density on sulfur and the acidity of α-hydrogen of sulfide. For example, increasing electron density on sulfur of the sulfide by substitution of electron-donating group, increases the rate of the reaction with TAD(or polimerization of TAD), but decreases the formation of 3 because of less acidic α-hydrogen. $^1O_2$ also shows the similar reactivity sequence for the reaction with sulfides. The reaction of sulfide with $^1O_2$ proceeds more readily in more electron-rich sulfide, while $^1O_2$ tends to promote the aldehyde(4) formation in increasing acidity of α-hydrogen of sulfide by substitution of electron-withdrawing group, though the reaction rate with the sulfide decreases.

Thus, the studies using TAD are expected to provide the more detail investigation of $^{1}O_2$ oxidation of sulfur compounds

REFERENCES AND FOOTNOTES

1) For example, Adam, W., De Lucchi, O. Tetrahedron Lett.,(1981), 22, 929.
2) As for the similar deuterium isotope effect of TAD with $^{1}O_2$, a) Stephenson, L. M. Tetrahedron Lett.,(1980), 21, 1005, b) Drdina, B., Orfanopoulos, M., Stephenson, L. M. J. Am. Chem. Soc.,(1979), 101, 3111.
3) The reactions of azodicarboxylates with thiols(to disulfides),[3a,3b] sulfur-containing amino acids(sulfides to sulfoxides in the presence of water),[3c] sulfides(addition),[3d-3h] and vinyl sulfides(cycloaddition)[3i] have been reported so far. Although simple sulfides had been reported not to react with azodicarboxylate,[3i] several reports have shown that they can react to afford the adducts when the reactions are carried out under drastic conditions.[3d-3h] No reaction has been investigated in view point of similar reactivity between $^{1}O_2$ and azodicarbonyl compounds: a) Kato, K., Mitsunobu, O. J. Org. Chem.,(1970), 35, 4227; b) Yoneda, F.; Suzuki, K., Nitta, Y. J. Am. Chem. Soc., (1966), 88, 2328; c) Axen, R., Chaykovsky, M., Witkop, B. J. Org. Chem.,(1967), 32, 4117, d) Woodward, R. B. Science, 153, 487; e) Woodward, R. B., Heusler, K.; Gosteli, J , Naegeli, P.; Oppolzer, W.; Ramage, R.; Ranganathan, S.; Vorgruggen, H. J. Am. Chem. Soc.,(1966), 88, 852, f) Ahlgren, G. Tetrahedron Lett.,(1974), 2779, g) Wilson, Jr., G. E.; Martin, J. H. J. Org. Chem.,(1972), 37, 2510; h) Smissman, E. E., Makriyannis, A. J. Org. Chem.,(1973), 38, 1652, i) Firl, J., Sommer, S. Tetrahedron Lett.,(1972), 4713.
4) Ando, W. Sulfur Report,(1981), 1, 147.
5) TAD was consumed very fast in the reaction with dialkyl sulfides, and the product was only polymeric white powder mainly consisting of TAD(by NMR, IR, MS, etc.), along with a small amount of 4-substituted urazole.
6) The structure of the adduct was determined by the following spectroscopies: ^{1}H-NMR(δ, $CDCl_3$) 2.14(s, 3H), 6.86(s, 1H), 7.19 - 8.60(m, 10H), 8.26 - 9.33(bs, 1H), ^{13}C-NMR(δ, $CDCl_3$) 191.3(C=O), 153.7 & 153.5(amido C=O), 62.1(-CH$<$), 14.8(CH_3), IR(CCl_4, cm^{-1}) 3550 - 3700(NH), 1780(C=O), 1725(C=O), 1680(C=O); MS(m/e) 293(M^+ - 48), 119(M^+ - 222).
7) Under photo-irradiation conditions the formations of α-C-H insertion products derived from ethers and azodicarboxylates have been reported by Cookson, Stevens and Watts(Chem. Commun.,(1965), 295). However, even under the dark conditions the reaction of TAD with sulfides easily occured with no difference from that under room light.
8) a) Corey, E. T.; Ouannēs, C. Tetrahedron Lett.,(1976), 4263; b) Ando, W.; Nagashima, T.; Saito, K., Khomoto, S. J. Chem. Soc., Chem. Commun.,(1979), 154.

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