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Registry No.—*p*-Nitroacetanilide, 104-04-1.

References and Notes

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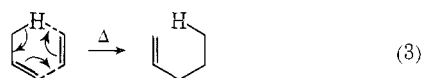
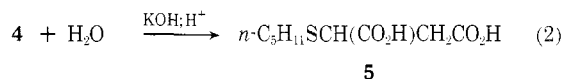
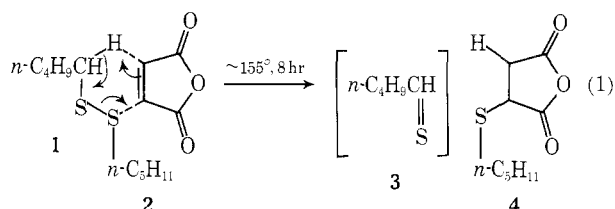
Organic Disulfides and Related Substances. 37. A Possible Counterpart of the Ene Reaction with Di-*n*-pentyl Disulfide and Maleic Anhydride¹

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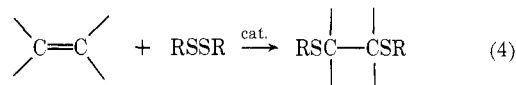
Interest in uncatalyzed reactions of disulfides with unsaturated systems prompted study of di-*n*-pentyl disulfide (1) with maleic anhydride (2) because the double-bond system of 2 seemed more likely than an isolated double bond to interact with unshared electrons of the sulfur atoms. The reaction that occurred is shown by eq 1 (with isolation of actual product, 5, after hydrolysis by eq 2).



Although the reaction is neither particularly clean nor perhaps synthetically attractive in its present form, it is noteworthy in that the structural outcome suggests a relationship to the broadly important ene reaction (eq 3).² According to both eq 1 and 3, a hydrogen atom and the third atom from it add to the anhydride, a widely used enophile.² However, development of the new double bond requires cleavage of the S-S bond for 1 in contrast merely to the shift of bond for an alkene. So far as we know, a sulfur counterpart of the ene reaction has not been specifically recognized as such before, although a formulation resembling that of eq 1 was suggested for the reaction of di-

n-butyl disulfide and acetylene,³ which also is an enophile.² The arrows in eq 1 and 3 are intended merely to point up the similarity of the reactions, not to make a point about the direction of electron shift.

Disulfides have long been known to react with a double bond as shown by eq 4, with suitable catalysis (iodine,⁴



hydrogen fluoride,⁵ cobalt sulfide,⁶ or ethanesulfonic acid⁷). Free-radical addition also has been observed but leads only to poor yields of 1:1 adducts.⁸

The only reaction apparently reported for a disulfide with 2 is that of eq 5,⁹ which also seems to be the only reaction where a disulfide has led to a mono- rather than a bithio ether. The sequence probably is that of the dotted arrows (eq 5), involving merely reduction of the disulfide to the thiolate ion, which then adds conventionally to 2.¹⁰

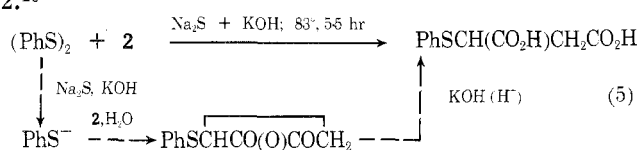


Table I, expt 1, shows conditions for the initial reaction when 1 was heated neat with 2 (eq 1). The fate of the presumed thio aldehyde 3 never became clear, not surprisingly, because 3 would be expected to be highly reactive. That the main product, after hydrolysis (eq 2), was 2-(*n*-pentylthio)succinic acid (5) was confirmed by independent synthesis.

Experiment 2 was done at lower temperature and with excess 1 (rather than the usual excess of 2) to improve the conversion to 5. The conversion was zero, but the result showed that the reactions of eq 1 and 5 must differ significantly (compare the conditions cited above the arrows). Indeed, when expt 1 was essentially repeated with diphenyl disulfide (15% excess) substituted for 1, 99% of this disulfide was recovered; cleavage alone of this S-S bond thus did not suffice for a reaction like that of eq 1, so that the α -CH₂ moiety of 1 clearly is essential. In expt 3, longer reaction at the lower temperature did lead to 5, indeed with better results than in expt 1 (*cf.* Table I, footnote *h*).

There was a possibility that the hydrolysis and treatment with alkali used in isolating 5 (eq 2) actually might have led to conversion of 1, only at this late point, to give *n*-pentanethiolate ion, which then could have added to 2 to produce 4. Experiment 4 duplicated the isolation alone and, by giving no 5, ruled out the possibility that 5 merely was an artifact of isolation. That 5 also did not originate during the reaction itself simply through thermally induced cleavage of 1 to 1-pentanethiol was shown by demonstrating high thermal stability of 1 at *ca.* 155° (*cf.* Experimental Section).

Experiments 5-7 were done to improve the conversion further. A plot of conversion against time for expt 1 and 4-7 indicated that the product 4 undergoes further reactions that destroy it when heating is prolonged and that the optimum time of reaction would be *ca.* 7 hr. Experiment 8, based on this inference, gave the best conversion encountered, 44%.

In expt 5, 1 and 2 were carefully purified to obviate possible misinterpretations. An effort then was made to isolate all products. No pure sulfur compound other than 5 could be isolated, despite reworking of mother liquors, capitalization upon differing solubilities, distillation, and chromatography. The material balance was 98%, but the

Table I
Reaction of Di-*n*-pentyl Disulfide (1) with Maleic Anhydride (2)^a

Expt	Molar proportions		Reaction		Conversion, % ^c	Product (5)	
	Disulfide (1)	Anhydride (2)	Temp, °C ^b	Time, hr		Approx yield, % ^d	Mp, °C ^e
1	1	2	165 ^f	17	22		100–103
2	3	1	115	23	0 ^g	0 ^g	
3 ^h	3	1	115	43	34		103.5–107
4 ⁱ	1	2	25 ⁱ	0	0	0	
5	1	2	155	8.5	31	~79	106.5–107.5
6	1	2	155	6	31		101–103.5
7	1	2	155	2.3	9		103–105
8	1	8	155	7.6	44	~71	102.5–105
9	1	2	To 190 ^j	17	2 ^k		95–102.5
10 ^{h,l}	3	1	126	43	31	~81	103.5–105
11 ^m	1	2	155	6	32		104.5–106
12 ^m	1	2	155	25	18		95.5–100

^a Heated neat unless otherwise stated. ^b Approximate average; usual range *ca.* ±5° unless otherwise stated. ^c On the assumption of 1 as the limiting reagent in eq 1, except for expt 2, 3, and 10, where 2 is assumed to be limiting. ^d On the assumption that all solvent-extractable neutral material is recovered 1 [ir showed that a little was unhydrolyzed anhydride(s)] and that 1 actually consumed is starting material less this neutral material. For example, in expt 5 neutral material extracted after hydrolysis amounted to *ca.* 61% of 1 used (yield of 5, 79%); distillation reduced the 61% to 38% (yield of 5, 50%). ^e Melting point of pure 5, 108.5–109°. Identity of 5 checked by mixture melting point. ^f Range *ca.* ±15°. ^g Recovery of 1, 88%. ^h A little sulfur was added in the hope of catalyzing eq 1 or of inhibiting polymerizations. However, it may have changed the mechanism of reaction. ⁱ Control experiment at 25° to assure that 5 was not an artifact of the usual procedure of isolation. ^j Range *ca.* 150–190°; for several hours the temperature was *ca.* 190°. ^k The pH of the aqueous solution after neutralization and extraction was *ca.* 10 (usually *ca.* 7), suggesting loss of part of the carboxyl function during reaction. The benzene-soluble material (13.9 g) atypically was mostly insoluble in H₂O, suggesting that the water-insoluble "black oil," which usually was a by-product, had become the major product. ^l In AcOH as solvent. ^m In cumene as solvent.

crude hydrolysis product (eq 2) seemed to contain at least a dozen components. The usual black reaction product contrasts markedly with the negligible color 1 alone develops at *ca.* 155°. Early crops of 5 typically were contaminated by an intractable, water-insoluble "black oil" that could be removed reasonably well mechanically by washing and pressing and that seemed to contain at least four substances. Five recrystallizations were required to give the 5 reported in Table I.

Some other conclusions are possible. Experiment 9 (like expt 1 but at a temperature up to 25° higher) pointed to the bad effect on the conversion of too high a temperature; the amount of "black oil" was unusually large, confirming the probability that it arose from decomposition of 4. Although 38–61% of 1 was recovered in expt 5 (*cf.* Table I, footnote *d*), use of the still larger excess of 2 in expt 8 did not influence the conversion or yield significantly, perhaps because the excess 2 was consumed in side reactions (comparison of expt 3 with expt 1 suggests that use of excess 1 also may have little effect). Experiment 10, with acetic acid as a solvent, gave much the same result as expt 3 done neat, showing that a proton source has little effect. Experiments 11 and 12 explored use of cumene as a solvent. The thought was that if eq 1 involved thiyl radicals in a homolytic process, abstraction of H· from cumene (instead of by destruction of other thiyl radicals to form 3) could both improve the yield and indicate a homolytic nature for eq 1. "Cumene is normally particularly susceptible to side-chain hydrogen abstraction by free radicals . . ." ¹² However, the results of expt 11 were much like those of expt 6 done neat. It is worth adding that "the ene synthesis is little affected by solvent changes."² The implication from the negligible effect of cumene that homolysis may not play a major role in eq 1 was supported by the fact that no more than 2% of 5 could be isolated when 1 and 2 were strongly irradiated for 8 hr; in the perhaps analogous reaction mentioned of alkyl disulfides with acetylene, free-radical initiators had no effect.³ Experiment 12 confirmed that too long a period of heating has the same bad effect as that mentioned of too high a temperature (*cf.* expt 11 and 12).

Experimental Section¹³

Reaction of Di-*n*-pentyl Disulfide (1) with Maleic Anhydride (2).¹⁴ A. Typical Procedure with Excess 2 (Expt 8). A clear solution in 1 (20.10 g, 97.4 mmol) of 2 (76.4 g, 780 mmol, 8 molar proportions) was heated (Glascol mantle) at 151–163° for 7.6 hr in a 500-ml flask protected from moisture (CaCl₂) and provided with a thermometer, stirrer, and air condenser. Cooling to *ca.* 25° then gave a mobile, dark liquid. Water (300 ml) was added, and the mixture was stirred vigorously for 1 hr. "Black oil" (1?), which separated in many experiments at this point, did not appear. An iced solution of KOH (88.5 g, 1580 mmol) and H₂O (160 ml) then was added below 15° (to obviate attack on any 1 that remained). The mixture was stirred for 5 min (pH *ca.* 7) and extracted with Et₂O. The Et₂O extract, washed with H₂O, dried, and evaporated, gave 7.6 g of dark liquid, which an ir spectrum showed to be largely 1 (38% recovery) containing some form of anhydride(s) (ir 1725, 1788 cm⁻¹). The combined aqueous layers were acidified with concentrated HCl (132 ml) and extracted with 100 ml of benzene, then thrice more with 50 ml.¹⁷ The combined benzene extracts were washed twice with 10-ml portions of H₂O. Removal of the benzene (without drying, in expt 8, to obviate crystallization of the sparingly soluble 5) left dark oil, which crystallized to a greasy solid (23.6 g). Three recrystallizations from H₂O gave 9.42 g of 2-(*n*-pentylthio)succinic acid (5, 44% conversion, 71% yield assuming that the 7.6 g of liquid extracted was pure 1),¹⁸ mp 102.5–105°, undepressed by authentic 5.

B. Modifications. In expt 3, a typical one with excess 1 (except that 0.5 g of sulfur also was used; *cf.* Table I, footnote *h*), 1 (27.62 g, 133.9 mmol) and 2 (4.37 g, 44.6 mmol) were heated at *ca.* 110–120° for 44 hr. 5 was isolated as in A, except that recrystallization of 5 was from Cl(CH₂)₂Cl to the melting point in Table I, then from H₂O and *n*-BuCl to a constant melting point (and mixture melting point) of 108–108.5°. *Anal.* Calcd for C₉H₁₆O₄S: C, 49.07; H, 7.32; S, 14.56; neut equiv, 110. Found: C, 48.92; H, 7.13; S, 14.64; neut equiv, 111.

Experiment 10 was essentially a repetition of expt 3 but with 25 ml of glacial AcOH as solvent. After the 43-hr reaction period (at the reflux temperature), AcOH was removed from the deep red solution, and isolation then was done as in A; Et₂O extraction recovered 24.13 g of 1. Experiment 11 was like expt 8 except for use of 19.00 g (194 mmol) of 2, 100 ml of cumene as a solvent (at the reflux temperature), the different conditions noted in Table I, and longer periods of stirring with H₂O (3 hr) and alkali (10 min) to achieve a neutral pH (~8) in the presence of the cumene; this cumene procedure seemed a clean one, promising for other studies. Experiment 12 was like expt 11 except for the longer reaction

period (Table I); the acidification led to ca. 35 g of a syrup that was insoluble in both H₂O and benzene and presumably represented secondary reaction products.

C. Effect of Light. A mixture of 1 (8.33 g, 40.4 mmol) and 2 (1.98 g, 20.2 mmol) was irradiated with occasional swirling in a quartz flask at ca. 50–75° using a 6-in. distant 250-W Hg lamp [General Electric Co. UA-2 Uviarc; rated per cents of wattage (Å range) were 4.6 (<2800), 4.3 (2800–3200), and 3.4 (3200–3800)]. A brown oil began to separate after ca. 1 hr. Considerable carbonization seemed to occur. After 8 hr, a brown solid and pale yellow supernatant layer resulted. Addition of H₂O (5 ml) and warming effected dissolution of the solid. An iced solution of KOH (2.29 g, 40.9 mmol) in H₂O (25 ml) was added, and the mixture was extracted well with Et₂O. Acidification (pH 7) and benzene extraction gave 0.07 g of material, a maximum yield of only 2% of 5.

Authentic 2-(*n*-Pentylthio)succinic Acid (5). Sodium hydroxide (5.3 g, 133 mmol) and purified *n*-pentyl iodide (27.8 g, 140 mmol) were added to a solution of mercaptosuccinic acid (19.4 g, 129 mmol)¹⁹ and Na₂CO₃ (13.7 g, 129 mmol) in H₂O (58 ml). The mixture was stirred at high speed under N₂ for 6 hr.²⁰ Heat was applied briefly at the outset to raise the temperature to 70°, after which the temperature remained at ca. 70–83°, mainly apparently because of the heat of stirring. The homogeneous mixture was washed with Et₂O, acidified, and extracted with benzene (300 ml) and Et₂O (200 ml) in several portions (5 is sparingly soluble). The combined extracts were washed (H₂O), dried (MgSO₄), and evaporated, yield, 20.0 g (70%), mp 105.5–107°. Recrystallization [H₂O, Cl(CH₂)₂Cl] gave 5 of constant mp 108.5–109°, undepressed by the analytically pure 5 described in B (lit. mp 99.5°,¹¹ 107°,²¹ 107.7–108°²²). *Anal.* Calcd for C₉H₁₆O₄S: C, 49.07; H, 7.32. Found: C, 49.26; H, 7.21.

When essentially the same mixture merely was shaken vigorously at ~25° for 28 hr, the yield of greasy 5 (mp 93–102°) was quite small.

Thermal Stability of 1. In a simulation of expt 1, 1 (7.45 g) was heated alone at 153–158° for 19 hr. In contrast to the dark color typically seen in less than 1 hr with 1 and 2 (e.g., in expt 1 and 8), 1 became only very pale yellow; no odor of a thiol or of H₂S was perceptible. Even the first fraction on distillation was pure 1 [0.46 g (6%), *n*_D²⁵ 1.4872 (lit.¹⁵ *n*_D²⁵ 1.4868, 1.4875)], and remaining fractions were quite pure as well [6.42 g (86%), bp 140–145° (19 mm), *n*_D²⁵ 1.4873, *n*_D²⁵ for 1-pentanethiol, 1.4439²³].

Substitution of Diphenyl Disulfide for 1. In a simulation of expt 1, recrystallized (PhS)₂ (7.68 g, 35.2 mmol) and 2 (3.00 g, 30.6 mmol) were heated at 160–170° for 23 hr. The (PhS)₂, isolated as in A, amounted to 7.62 g (99% recovery), mp and mmp 57–59°. Acidification of the aqueous layers and continuous Et₂O extraction gave 2.92 g (82%) of maleic acid, mp and mmp 126.5–129°.

Registry No.—1, 112-51-6; 2, 108-31-6; 5, 5413-66-1; diphenyl disulfide, 882-33-7.

References and Notes

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- (10) Chilcote has added thiols to 2 in the presence of enough aqueous KOH to engender thiolate ions (96°, 2 hr).¹¹
- (11) W. B. Chilcote, U. S. Patent 2,581,514 (1952); *Chem. Abstr.*, **47**, 4363 (1953).
- (12) R. L. Dannley, J. E. Gagen, and O. J. Stewart, *J. Org. Chem.*, **35**, 3076 (1970).
- (13) Melting points are corrected, and boiling points are uncorrected.
- (14) Good commercial grades of 1 and 2 usually were used; as a check, however, for expt 5 the disulfide 1 was fractionally distilled (also used in expt 8), *n*_D²⁵ 1.4869 (lit.¹⁵ *n*_D²⁵ 1.4868, 1.4875), and the anhydride 2 was recrystallized from Cl(CH₂)₂Cl, mp 52.5–54° (lit.¹⁶ mp 52.8°).
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- (16) "Handbook of Chemistry," 10th ed, N. A. Lange, Ed., McGraw-Hill, New York, N. Y., 1961, p 592.
- (17) Benzene proved best for extracting crude 5, while leaving maleic and fumaric acids mainly in the aqueous phase. However, it is a rather poor solvent and in some experiments (when the extract was dried) Et₂O had to be added to preclude crystallization of 5.
- (18) Typically, after the first recrystallization, products were washed with a little ice water and then pressed on a vacuum filter with a rubber dam. The water expressed carried more or less of the "black oil" that appeared in the filtrate in each such instance except in expt 11. Decolorizing carbon was used frequently in the recrystallizations.
- (19) Kindly provided by Evans Chemetics, Inc., New York, N. Y.
- (20) Apparatus of A. A. Morton, B. Darling, and J. Davidson, *Ind. Eng. Chem., Anal. Ed.*, **14**, 734 (1942).
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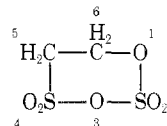
Hydrolytic Reactions of Carbyl Sulfate

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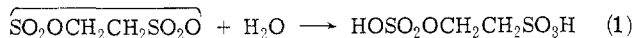
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Carbyl sulfate (2,2,4,4-tetraoxo-1,3,2,4-dioxadithiane, 1) is a colorless, crystalline solid, mp 107–108°, commonly prepared by the direct reaction of ethylene with SO₃.^{1b,2} Crude "carbyl sulfate" of mp 80°^{1b} has been shown to be complexed with excess SO₃.² The pure compound reacts vigorously with alcohols,³ amines,⁴ and other compounds possessing active hydrogens. The reaction of carbyl sulfate with water has been reported to produce ethionic acid (HOSO₂OCH₂CH₂SO₃H),^{2,5} isethionic acid (HOCH₂CH₂SO₃H),^{5,6} and/or vinylsulfonic acid or its sodium salt.^{2,3,5-7} We have sought to elucidate the reactions of carbyl sulfate with water.



1

When 0.01 mol of purified carbyl sulfate is added to 200–400 ml of water at 0–80° a fast exothermic reaction goes to completion within seconds. Titration shows formation of 2 equiv of strong acid. Similar results are obtained when carbyl sulfate is predissolved in 1,2-dichloroethane or dioxane, and when water is replaced by dilute mineral acid. The reaction product is ethionic acid.



Dilute acidic aqueous solutions of ethionic acid are stable for days at room temperature. At about 60° and above, the ratio (equivalents of acid formed):(moles of carbyl sulfate reacted) slowly increases from 2.0 to 3.0, following pseudo-first-order kinetics. At 70° *k* ≈ 1 × 10⁻⁶ sec⁻¹. The activation energy (70–90°) is approximately 33 kcal mol⁻¹. A solution of ethionic acid in water was held at 80° for 24 hr, then cooled and titrated with BaCl₂ to remove sulfate. The filtrate was neutralized with dilute NaOH and water was removed to yield sodium isethionate. The only reaction evident in hot acidic aqueous solutions is