7:3, 600 ml). Die mit $CHCl_3$/MeOH (4:1) ausfliessenden Fraktionen(A) enthielten I und II und die anschliessenden mit $CHCl_3$/MeOH(7:3) eluierten (B) Quercitrin. A und B wurden jeweils an Polyamidsäule (10 g, I.D.: 2.5 cm) mit MeOH chromatographiert. Die gelblichen Fraktionen bei A wurden durch DCCC aufgetrennt. Fraktionen 28—36 ergaben nach Kristallisation aus verdünntem MeOH 4 mg von I(Schmp. 167—175°) und Fraktionen 43—50 aus demselben Lösungsmittel 6 mg von II (Schmp. 170—177°). Die gelblichen Fraktionen bei B ergaben nach Kristallisation aus verdünntem MeOH 40 mg Nadeln vom Schmp. 175—179°. (Quercitrin).

PMR-Daten von trimethylsilyliertem I und II ($CDCl_3$, 60 MHz)——I und II wurden mit Hexamethyldisilazan und Trimethylchlorosilan in Pyridin bei Raumtemperatur silyliert.[6] TMS-Äther von I: 0.77 (3H, d, J=6 Hz, 6″-$C\underline{H}_3$), 2.00 (3H, s, 3″-OCO$C\underline{H}_3$), 3.17 (1H, qd, J=10 und 6 Hz, 5″-H), 3.56 (1H, t, J=10 Hz, 4″-H), 4.44 (1H,t, J=2 Hz, 2″-H), 4.84 (1H, dd, J=10 und 2 Hz, 3″-H), 5.11 (1H, d, J=2 Hz, 1″-H), 6.07 (1H, d, J=2 Hz, 6-H), 6.31 (1H, d, J=2 Hz, 8-H), 6.73 (1H, d, J=8 Hz, 3′-H), 7.12 (2H, m, 2′- und 6′-H). TMS-Äther von II: 0.72 (3H, d, J=6 Hz, 6″-$C\underline{H}_3$), 1.89 (3H, s, 4″-OCO$C\underline{H}_3$), 3.17 (1H, qd, J=10 und 6 Hz, 5″-H), 3.83 (1H, dd, J=10 und 2 Hz, 3″-H), 4.17 (1H, t, J=2 Hz, 2″-H), 4.80 (1H, t, J=10 Hz, 4″-H), 5.11 (1H, d, J=2 Hz, 1″-H), 6.07 (1H, d, J=2 Hz, 6-H), 6.31 (1H, d, J=2 Hz, 8-H), 6.73 (1H, d, J=8 Hz, 3′-H), 7.12 (2H, m, 2′- und 6′-H).

6) T.J. Marby, K.R. Markham und M.B. Thomas, "The Systematic Identification of Flavonoids," Springer-Verlag, Berlin, Heidelberg, New York, 1970, S. 255.

[Chem. Pharm. Bull. 26(11)3582—3584(1978)]

UDC 547.732'546.21.04 : 547.92.04

3-Sulfolene as an Alternative Reagent for Sulfur Dioxide[1]

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(Received May 20, 1978)

The successful use of 3-sulfolene as an alternative reagent for sulfur dioxide was demonstrated for the first time by two types of the reactions: i) deoxygenation of aromatic amine N-oxides and ii) isomerization of ergosterol and its derivatives.

Keywords——deoxygenation; aromatic amine oxides; isomerization; ergosterol and its derivatives; thermolysis of 3-sulfolene

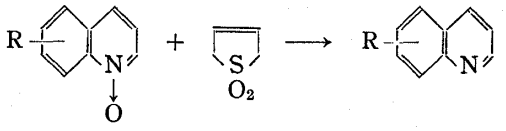
3-Sulfolene was synthesized from butadiene and sulfur dioxide in a high yield by heating them together at around 100° in a pressure bottle.[3] Backer and Blaas[4] noted that this substance can be used in place of 1,3-butadiene in the Diels-Alder reaction at 100—130°. Sample and Hatch[5] demonstrated that the Diels-Alder adduct can be obtained smoothly by heating 3-sulfolene with maleic anhydride in refluxing xylene in an open vessel. This fact indicates that there exists an equilibrium between 3-sulfolene and its degradation products (the diene and sulfur dioxide) at that temperature.[6]

1) Presented at the 45th Meeting of Hokuriku Branch, Pharmaceutical Society of Japan, Kanazawa, November, 1977.
2) Location: *Takara-machi, Kanazawa, 920, Japan.*
3) O. Grummitt, A.E. Ardia, and J. Fick, *J. Am. Chem. Soc.*, **72**, 5167 (1950).
4) H.J. Backer and T.A.H. Blaas, *Rec. Trav. Chim.*, **61**, 785 (1942).
5) T.E. Sample, Jr. and L.F. Hatch, *J. Chem. Educ.*, **45**, 55 (1968).
6) While benzyne does not act as a dienophile with butadiene, the latter genarated from 3-sulfolene (100°) reacts with the former to give 1,4-dihydronaphthalene. The reaction presumably occurs because the butadiene exists in the cisoid conformation in the above equilibrium: L.F. Hatch and D. Peter, *J. Chem. Soc., Chem. Commun.*, **1968**, 1499.

While there is no experiment using sulfur dioxide generated from 3-sulfolene, we now demonstrate that 3-sulfolene can be used efficiently as an alternative reagent for sulfur dioxide. The procedure is to heat the reactants (1.1—2 mol equivalents of sulfolene to the respective substrates) in benzene (10 ml for 1 mmol of the substrate) in a sealed tube at 100°.

Daniher and Hackley[7] found that introduction of a slow stream of sulfur dioxide into a refluxing dioxane solution of pyridine 1-oxide or its derivatives for 3 hr afforded the free base in a moderate yield. We have found that the use of sulfolene (2 mol equivalent) afforded the deoxygenated products in very high yields, if the reaction was continued for longer than 30 hr. The results are summarized in Table I. As expected from inertness of pyridine 1-oxides having an electron withdrawing group towards sulfur dioxide,[7] the N-oxides of 2-cyanoquinoline and 6-cyanophenanthridine could not be reduced at all.

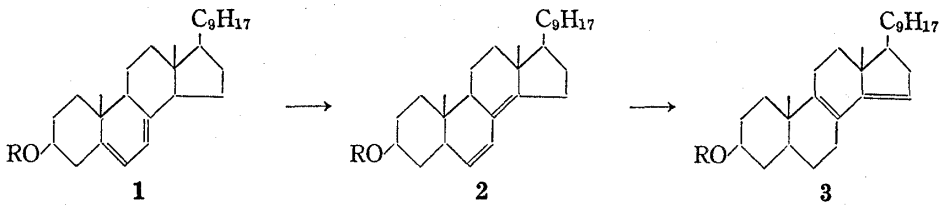
Table I. Deoxygenation of Aromatic Amine Oxides with 3-Sulfolene[a]



N-Oxide	Free base (% yield) Reaction time (hr)			mp
	5	20	30	
Quinoline	—	—	85	201—202°[b]
2-Phenylquinoline	18	63	81	84—85°
Benzo[*f*]quinoline	30	72	87	92—93°

a) Unreacted N-oxides were also recovered. *b*) Picrate.

The new procedure has then been extended to the isomerization of ergosterol (**1a**) and its acetate (**1b**). Laubach *et al.*[8] showed that when **1b** was heated at 100° with a large excess of sulfur dioxide in the presence of its 2/3 volume of pyridine in a sealed tube, ergosta-6,8(14), 22-triene acetate (**2b**) was formed in 65% yield. Hudgell *et al.*[9] described the isomerization of **1a** under similar conditions but in the absence of pyridine to ergosta-8,14,22-triene (**3a**) in 65% yield. They explained the formation of **3a** by assuming the intermediacy of the triene (**2a**) and its subsequent isomerization to **3a** and speculated that the isomerization of **2a** to **3a** might be caused by moisture during the collection of liquid sulfur dioxide into the reaction vessel. In the present procedure, these transformations proceeded using 1.1 mol equivalent of sulfolene. Thus, when **1a** (2 mmol) and sulfolene (2.2 mmol) were heated in the presence of 6 mmol of pyridine for 20 hr, the triene (**2a**) was obtained in 80% yield. The same treatment of **1a** in the absence of pyridine resulted in the formation of **3a** in 65% yield. This and the fact that **2a** isomerized to **3a** in 85% yield under the same condition as above indicated that the isomerization of **2a** to **3a** occurred even in the complete absence of moisture. However,



1 **2** **3**

a: R=H
b: R=$COCH_3$

7) F.A. Daniher and B.E. Hackley, Jr., *J. Org. Chem.*, **31**, 4267 (1966).
8) G.D. Laubach, E.C. Schreiber, E.J. Agnello, and K.J. Brunings, *J. Am. Chem. Soc.*, **78**, 4743 (1956).
9) A.W.D. Hudgell, J.H. Turnbull, and W. Wilson, *J. Chem. Soc.*, **1954**, 814.

since the acetate (**1b**) by the present procedure (without pyridine: 20 hr) resulted in the formation of **2b** and **3b** in *ca.* 1: 1 ratio, it seems reasonable to assume that the free hydroxyl group in the steroids accelerated the isomerization of **2a** to **3a**.

The successful use of sulfolene for sulfur dioxide in the above reactions may indicates that 3-sulfolene[10] offers a useful alternative for sulfur dioxide, whose handling is troublesome by its suffocating odor, highly hygroscopic nature and a low boiling point (−10°). Furthermore, since an autogenous pressure during its use is relatively low at around 100° and thus a glass cylinder with a clamped-in stopper can be used, the present procedure is far more superior in its easy use than that using liquid sulfur dioxide. The experimental condition was also easily secured in the present procedure, such as a stoichiometric use of the reagent and an expulsion of moisture.

Experimental[11]

General Procedure for the Deoxygenation of Quinoline 1-Oxides——An N-oxide (1 mmol) and 3-sulfolene (2 mmol) in 10 ml of benzene was heated at 100° for 5—30 hr in a sealed tube. After the reaction, the solvent was removed under an aspirator pressure. The residue was made alkaline by addition of 20% potassium carbonate solution and the product was extracted with ether. The extract was dried over potassium carbonate, filtered, and evaporated to yield the product. The product was purified either by recrystallization or column chromatography and the structure was determined by mixed melting point determination with the authentic sample. The results are described in Table I. The other products identified were the recovered N-oxides and 3-sulfolene.

Isomerization of Ergosterol (1a) to Ergosta-6,8(14),22-triene (2a)——Ergosterol (**1a**; 792 mg, 2.0 mmol) and 3-sulfolene (260 mg, 2.2 mmol) in 20 ml of benzene in the presence of pyridine (240 mg, 6 mmol) were heated at 100° for 20 hr in a sealed tube. After the reaction, the solvent was removed under an aspirator pressure and the residue was recrystallized from methanol to afford **2a**. An additional amount of **2a** was furnished by silica gel column chromatography (hexane–ether 2: 1 v/v) of the mother liquor. The combined yield of **2a** was 634 mg (80%); mp 111—114°. Mass spectrum *m/e* 396 (M^+), 271, 253. UV λ_{max}^{MeOH} nm (log ε): 252 (4.37). ^{1}H-NMR ($CDCl_3$) δ: 3.70 (m, 1H, $W_{1/2}$=25 Hz, H-3); 5.15—5.35 (m, 3H, H-7, 22, and 23), 6.16 (dd, 1H, J=10 and 3 Hz, H-6). ^{13}C-NMR ($CDCl_3$) δ: 125.3 (s), 125.7 (d), 129.4 (d), 132.1 (d), 135.4 (d), 147.3 (s) [olefinic carbons]; 71.4 (d, C-3 carbon). *Anal.* Calcd. for $C_{28}H_{44}O$: C, 84.78; H, 11.18. Found: C, 84.63; H, 11.24.

Ergosta-8,14,22-triene (3a)——From Ergosta-6,8(14),22-triene (**2a**): The triene (**2a**) obtained as above (396 mg, 1.0 mmol) and 3-sulfolene (130 mg, 1.1 mmol) in 10 ml of benzene were heated at 100° for 20 hr in a sealed tube. The residue obtained after evaporation of solvent was recrystallized from ethanol to give **3a**. An additional amount of **3a** was obtained from the mother liquor by column chromatography on silica gel (hexane–ether 2: 1 v/v). The combined yield of **3a** was 336 mg (85%); mp 133—135°. Mass spectrum: *m/e* **396** (M^+), 381, 271, 270, 255. UV λ_{max}^{MeOH} nm (log ε): 252 (4.26). ^{1}H-NMR ($CDCl_3$) δ: 3.65 (m, 1H, $W_{1/2}$= 22 Hz, H-3); 5.26 (m, 2H, H-22 and 23); 5.36 (*t*, 1H, J=2 Hz, H-15). ^{13}C-NMR ($CDCl_3$) δ: 117.8 (d), 123.2 (s), 132.1 (d), 135.5 (d), 140.7 (s), 150.9 (s) [olefinic carbons]; 71.1 (d, C-3 carbon). *Anal.* Calcd. for $C_{28}H_{44}O$: C, 84.78; H, 11.18. Found: C, 84.67; H, 11.22.

From Ergosterol (**1a**): The compound (**3a**) was obtained in the same manner as above from **1a**; yield: 65%, mp 133—135°. The identity of this product with **3a** obtained as above was assured by the mixed melting point determination and the comparison of spectral data.

Isomerization of Ergosterol Acetate (1b) to Ergosta-8,14,22-triene Acetate (3b) and Ergosta-6,8(14),22-triene Acetate (2b)——The acetate (**1b**; 439 mg, 1.0 mmol) and 3-sulfolene (152 mg, 1.29 mmol) in 10 ml of benzene were heated at 100° for 20 hr in a sealed tube. After the reaction, the solvent was removed under an aspirator pressure and the residue was recrystallized from ethanol to give a mixture of **2b** and **3b** as colorless needles; yield: 357 mg (81%); mp 120—123°. The proportion of **2b** and **3b** in the product was determined to be approximately 1: 1 by the inspection of its ^{1}H-NMR. ^{1}H-NMR ($CDCl_3$) δ: 4.75 [m, 2H (relative intensity), H-3 of **2b** and **3b**], 5.1—5.4 (m, 6H, olefinic protons of **3b** and H-7, −22, and −23 of **2b**), 6.15 (dd, 1H, J=10 and 3 Hz, H-6 of **2b**).

Acknowledgement The authors are indebted to Mr. Y. Itatani and Misses, Y. Arano and K. Ohata at Kanazawa University for elemental analyses and Mass and ^{13}C-NMR spectral determinations.

10) 3-Sulfolene is a crystalline solid (mp 64—65°), nonflammable, nontoxic and nonhygroscopic: T.E. Sample, Jr. and L.F. Hatch, *Org. Syn.*, **50**, 43 (1970).

11) All melting points are uncorrected. Spectra reported herein were measured with a Hitachi Model 323 UV spectrophotometer, a JEOL-JMS-01SG mass spectrometer, and a JEOL-JNM-60H (for ^{1}H) or -JNM-PS-100 FT-NMR (for ^{13}C) spectrometer at 23° using tetramethylsilane as an internal standard.