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CYCLIZATION OF β-KETOSULFOXIDE—III

SYNTHESIS OF NAPHTHALENE AND PHENANTHRENE DERIVATIVES

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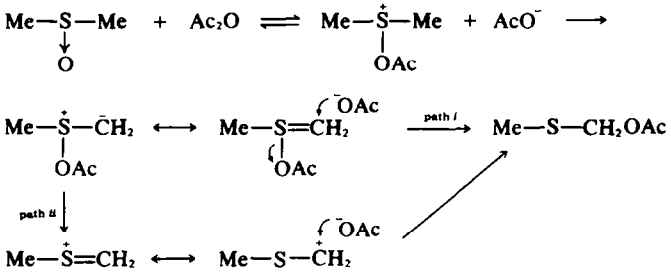
Abstract—On heating with trichloroacetic acid or trifluoroacetic acid, 2,4-dimethoxyphenethyl methylsulfinylmethyl ketone (1) cyclized to 2,3-dimethoxy-5-methylthio-6-oxo-5, 6, 7, 8-tetrahydronaphthalene (2) through an intramolecular nucleophilic substitution of a sulfonium ion intermediate (**20b**), while a β-ketosulfoxide having naphthalene nucleus (3) cyclized to a tetrahydrophenanthrene **4** *via* a Pummerer rearrangement product **23**. Treatment of 1 with *p*-toluenesulfonic acid gave a mixture of 2,3,6-trisubstituted naphthalenes (7–10), whose composition was dependent on the reaction conditions. The aromatization proceeded *via* 2.

Since the initial synthetic studies by Corey[1] and Russell[2], β-ketosulfoxides have been used as very important intermediates in various organic syntheses.

Oae *et al*[3] reported that a probable mechanism of the Pummerer rearrangement[4] of dimethylsulfoxide with acetic anhydride is as shown in path *i* in the following Scheme.



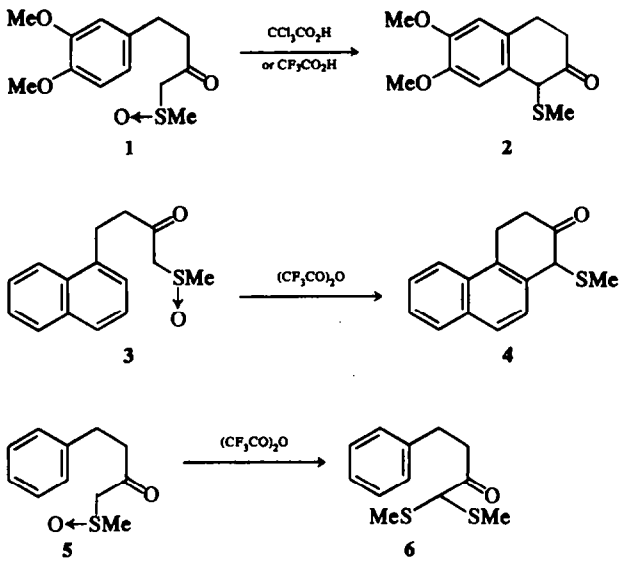
Since then, Johnson *et al*[5] have showed that the reaction proceeds *via* a sulfur-stabilized carbonium ion (path *ii*). If this is the correct mechanism, then, taking the place of the acetoxy anion, a nucleophilic moiety attached to the suitable position in a sulfoxide molecule may attack the carbonium ion intermediate intramolecularly. We report here the acid catalyzed cyclization reaction of β-ketosulfoxides having electron-rich aromatic nuclei as nucleophiles.

RESULTS

Acid-catalyzed cyclization of β-ketosulfoxides. On heating under reflux with 2 equivalents of trichloroacetic acid or trifluoroacetic acid in benzene for 1 hr, 3,4 - dimethoxyphenethyl methylsulfinylmethyl ketone (1) cyclized with the loss of water to 2,3-dimethoxy-5-methylthio-6-oxo-5,6,7,8 - tetrahydronaphthalene (2) in fairly good yield.[6] The structure assignment of **2** rests mainly on its spectral data. On the basis of the mass spectrum and the elemental analysis, **2** has the composition $C_{13}H_{16}O_3S$. Two aromatic protons in the NMR spectrum appear at δ 6·68 and 6·80 ppm as distinct singlets, indicating that **2** is a para cyclization product.

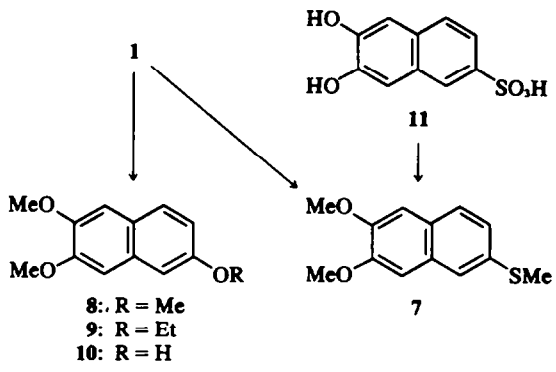
On the other hand, 2-(1-naphtyl)ethyl methylsulfinylmethyl ketone (3) and phenethyl methylsulfinylmethyl ketone (5) failed to cyclize under the same conditions, which may be explained by the lower nucleophilicity of the aromatic nuclei of 3 and 5. Compound 3 did give a cyclization product, 1 - methylthio - 2 - oxo - 1,2,3,4 - tetrahydrophenanthrene (4), in acetonitrile though in poor yield.

Instead of just protonation, the acylation of the sulfinyl group may assist this cyclization, because an acetoxy group will act much more effectively as a leaving group than an OH group. In fact, when 3 was heated with 2 equivalents of trifluoroacetic anhydride, the yield of 4 was significantly improved. However, even under such conditions, 5 did not give a cyclization product, but was converted to a methylmercaptal 5 in 43% yield (based on 2 mol of 5), whose structure was easily confirmed by its mass and NMR spectra.



Naphthalene and phenanthrene derivatives. The treatment of **1** with *p*-toluenesulfonic acid or with trichloroacetic acid in the presence of an alcohol gave a mixture of aromatized products, 2,3,6-trisubstituted naphthalenes (**7–10**).[7] The results under a variety of conditions are summarized in Table 1, and the reaction conditions can be classified into three categories according to the major product formed as follows: (i) *p*-Toluenesulfonic acid in acetonitrile favors formation of the 6-OH compound **10**. (ii) Trichloroacetic acid in the same solvent containing a small amount of methanol or ethanol gives mainly the 6-methoxy **8** or 6-ethoxy compound **9**. (iii) *p*-Toluenesulfonic acid with acetic anhydride favors formation of the 6-methylthio compound **7**. Although toluenesulfonic acid in acetonitrile containing methanol gave a mixture of naphthalenes more efficiently, these conditions are inadequate for synthesis of the 6-methoxy compound **8** because of the concomitant formation of **10** and a small amount of **7**. Acetonitrile is the best solvent for this naphthalene synthesis.

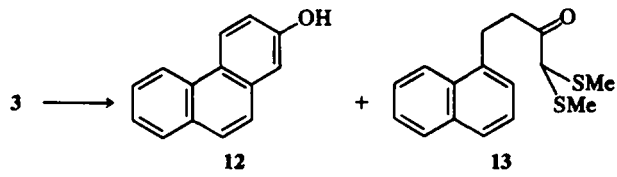
The naphthalenes have UV absorption characteristic for naphthalenes substituted at 2,3 and 6 positions, and they have characteristic IR absorption peaks at 855–860 cm^{-1} attributable to the out-of-plane deformation bands of two adjacent aromatic hydrogens. Compound **7** was shown by spectral data and the mixed m.p. to be identical with an authentic sample synthesized from 2,3 - dihydroxy-naphthalene - 6 - sulfonic acid (**11**). When **2** was heated with *p*-toluenesulfonic acid in acetonitrile, **10** was isolated in 69% yield. The reaction of **3** under similar conditions gave **12** and **13** in 30% and 62% (based on 2 mol of **3**) yield, respectively.



1-Substituted naphthalenes. The methylene group between the carbonyl and sulfoxide groups in a β-ketosulfoxide molecule is so reactive to an electrophile that a substituent can be easily intro-

Table 1. Yields of naphthalenes from 1 under various conditions

Run	Acid	Solvent	Temp	Time hr	Product(%) 7	8	9	10
1	TsOH	MeCN	reflux	1	3			50
2	CCl_3CO_2O	MeCN–MeOH	reflux	4		55		6
3	CCl_3CO_2H	MeCN–EtOH	reflux	4			51	6
4	TsOH–Ac_2O	MeCN	room temp	17	30			37
5	TsOH	MeCN–MeOH	reflux	1	4	40		29

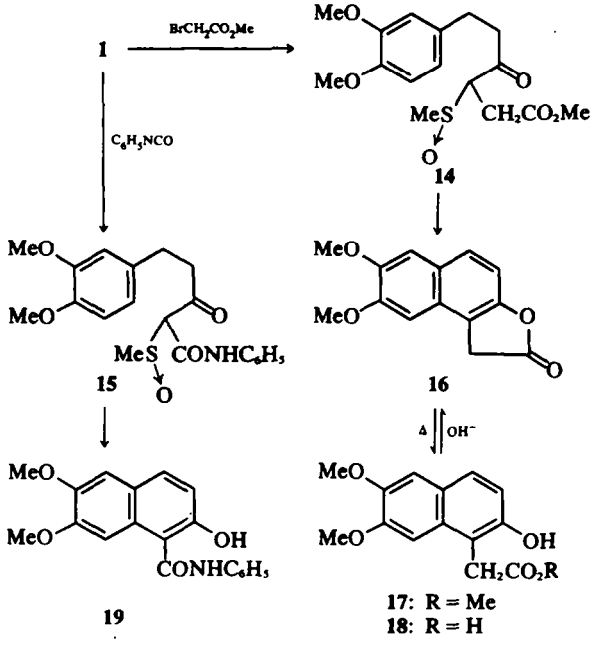


12 13

duced to the position prior[8] to naphthalene formation. A tetrahydrofuran solution of a sodium salt of 1 was treated with methyl bromoacetate and with phenylisocyanate to give 14 and 15, respectively, in good yield. On being heated with *p*-toluenesulfonic acid in benzene, 14 was converted to a lactone 16 in 60% yield. It is apparent that an initially formed naphthol 17 cyclized under these acidic conditions to 16. The lactone 16 was cleaved with sodium hydroxide in methanol to form 18 in quantitative yield. Compound 18 recyclized to 16 upon being heated at its m.p. Similarly, the acid-treatment of 15 gave 19 quantitatively.

nuclei of 1, 3 and 5 may indicate that the rate determining step lies in the final stage. If this is true and if the reaction proceeds via path B, a Pummerer rearrangement product 21 is expected to be detected in the course of the cyclization. However not a trace of 21a was either isolated from the reaction of 1 with trichloroacetic acid or detected during the course of the cyclization by careful NMR measurements. Therefore the cyclization seems to proceed through path A.

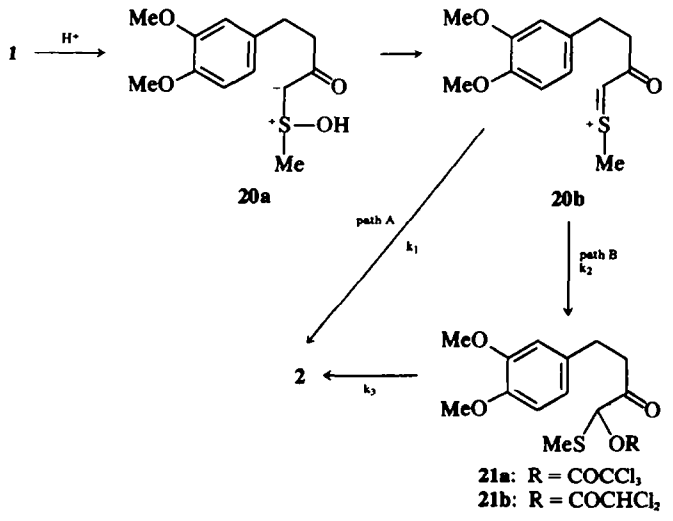
However there is still considerable doubt, since there is no proof that both 1 and 3 cyclize by the



DISCUSSION

Acid-catalyzed cyclization. The process of the formation of 2 from 1 may be summarized as shown in Scheme I. Two routes from 1 to 2 are possible. Protonation of the sulfinyl oxygen of 1 forms the ylide 20a, which can readily form the sulfonium ion intermediate 20b and then cyclize to 2 through intramolecular nucleophilic substitution (path A). Another pathway (B) involves a Pummerer rearrangement, followed by ring closure.

The clear difference in the cyclization reactions depending on the nucleophilicity of the aromatic same mechanism. The rate constants for cyclization (first order) and rearrangements (second order) are shown in Table 2. Taking account of the relatively large value of the rate constant of the Pummerer rearrangement, it is possible to assume that 1 cyclizes to 2 *via* path B with k_3 much larger than k_2. Nevertheless we can conclude that the cyclization of 1 proceeds *via* path A for the following reasons. (i) The treatment of 1 with a weaker acid, dichloroacetic acid, at 70° also gave 2. At 60° in carbon tetrachloride an intermediate 21b was isolated from the reaction, and 21b was not converted to 2 by the



SCHEME 1.

further treatment with the acid at 70° in benzene. This data indicates that the cyclization of **1** with dichloroacetic acid clearly proceeds *via* path A and that the order of the rate constants can be taken as $k_1 > k_2 > k_3$. (ii) Attempts to detect an intermediate **21a** in the treatment with trichloroacetic acid were unsuccessful. This means that the reaction proceeds either *via* path A with $k_1 > k_2$ *or via* path B with $k_3 > k_2 > k_1$. As the value of k_2 depends only on the acid used, and not on the aromatic nucleus, the acid dependence of the reaction of **3** was examined. When **3** was treated with a mixture of trichloroacetic acid and dichloroacetic acid (1:1), **21a** and **21b** were detected in the ratio 1:2·5. This means that the acetoxylation (k_2) with the stronger nucleophile, dichloroacetic acid, predominated, though the preceding protonation might occur mainly by the stronger acid, trichloroacetic acid, i.e., k_2 for $CHCl_2CO_2H > k_2$ for CCl_3CO_2H. Since the order of rate constants in the cyclization of **1** with dichloroacetic acid was $k_1 \geq k_2$, the order in the case of trichloroacetic acid can clearly be concluded to be $k_1 > k_2$.

The formation of **4** from **3** proceeds *via* path B. In this case, since k_3 is much smaller than k_2, an intermediate **23a** was easily isolated from the reaction mixture, and **23a** cyclized to **4** on further treatment with the acid. Trifluoroacetic anhydride, instead of trichloroacetic acid or trifluoroacetic acid, clearly accelerated the reaction. This indicates that the route of the cyclization with the anhydride was changed from path B to path A, because it is unlikely that k_3 is larger with the anhydride than with the acid.

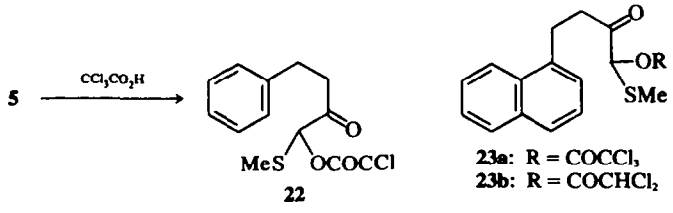


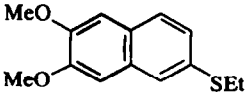
Table 2. Rate constants determined by NMR spectroscopy in benzene

Reaction	Acid	Temp °C	k
1→2	CCl_3CO_2H	80	$3{\cdot}33 \times 10^{-4}$ sec^{-1}
	CCl_3CO_2H	70	$1{\cdot}31 \times 10^{-4}$ sec^{-1}
	$CHCl_2CO_2H$	70	$4{\cdot}50 \times 10^{-5}$ sec^{-1}
5→22	CCl_3CO_2H	80	$2{\cdot}80 \times 10^{-3}$ l.mol^{-1} sec^{-1}
3→23a	CCl_3CO_2H	70	$1{\cdot}11 \times 10^{-3}$ l.mol^{-1} sec^{-1}
23a→4	CCl_3CO_2H	70	$2{\cdot}20 \times 10^{-3}$ sec^{-1}

In conclusion, the cyclization of **1** proceeds *via* path A, while path B competes with or predominates over path A in the case of a β-ketosulfoxide having a less nucleophilic nucleus, such as **3** and **5**, unless a better leaving group is present on the sulfur atom.*

Aromatization. Since a naphthalene is formed from **2** as well as from **1** by treatment with *p*-toluenesulfonic acid, it is clear that the naphthalene fromation from **1** proceeds *via* **2**. In acetonitrile, elimination of methyl mercaptan mainly occurred to form a naphthol **10**. In the presence of an alcohol, the main product changed to an ether **8** or **7**. The treatment of **1** or **2** with trichloroacetic acid in the absence of alcohol did not give naphthalenes, but their formation was markedly accelerated in the presence of alcohol. This seems to be due to the formation of a hemiketal intermediate **24** (Scheme II) which is more favorable than **2** is for elimination of methyl mercaptan.

The formation of **7** is also of interest. A transient intermediate may be considered as **25**, which must form through the attack of the liberated methyl mercaptan and/or through 1,2-shift of the methylthio group in **2**. The treatment of **1** with *p*-toluenesulfonic acid in benzene in the presence of 16 equivalents of ethyl mercaptan gave a mixture of **7** and **26** in a ratio of about 1:2. Compound **2** gave also a similar result. The formation of a considerable amount of **7** may be due to mainly to the 1,2-shift and indicates the participation of sulfur such as in **27**. A similar mechanism has been proposed in the study of the oxime formation from α(phenylthio) cyclohexanone.[10]



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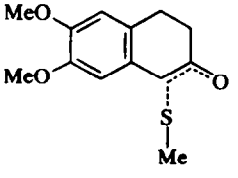
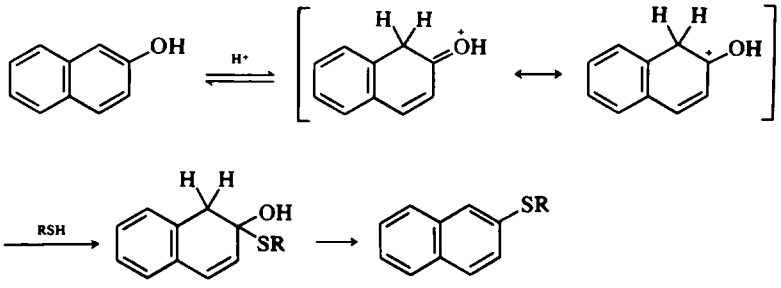


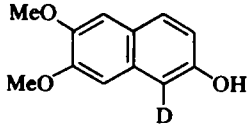
27

*The cyclization reaction of alkyl *o*-carboxyphenyl sulfoxide with acetic anhydride was recently reported. A mechanism *via* an initial Pummerer rearrangement has been proposed.[9]

It is still necessary to take into account an alternative mechanism, which proceeds *via* the initial formation of a naphthol **10**, because when β-naphthol is heated with methylmercaptan at 120° in the presence of *p*-toluenesulfonic acid, 2-methyl - thionaphthalene is obtained in almost quantitative yield.[11] The mechanism has been described as follows:



However, this mechanism does not play a major role in the formation of **7**, because a deuterated naphthol **10a** (D-content 9·0%) was recovered without loss of deuterium (D-content 9·2%) under the conditions most favorable for the formation of **7** (in Table 1, run 4). This indicates that protonation of **10a** leading to its ketoform did not occur. In addition, heating with *p*-toluenesulfonic acid in benzene in the presence of ethyl mercaptan did not convert **10** to **7**.



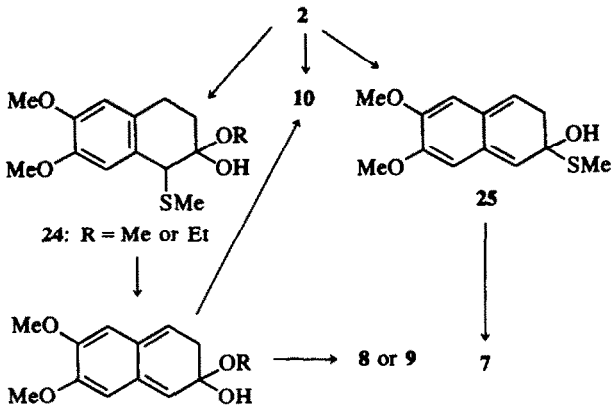
10a

Finally, on the basis of the above evidence, the mechanism of the naphthalene formation from **2** is best described as shown Scheme II.

EXPERIMENTAL

3,4-Dimethoxyphenethyl methylsulfinylmethyl ketone (**1**). The anion of dimethylsulfoxide was prepared according to the procedure by Corey[1] from 0·96 g of sodium hydride and 25 ml of DMSO. To this soln 4·48 g of ethyl 3,4 - di - methoxyphenylpropionate dissolved in 25 ml of dry THF was added dropwise at a temp below 10°. After being stirred for an additional 2 hr at room temp, the mixture was poured into ice-water (150 ml), acidified with HCl to pH 3–4 and then extracted with chloroform (40 ml × 4). The combined extracts were washed with water (40 ml × 4) then dried over $NaSO_4$. Evaporation of the solvent afforded 4·0 g of crude **1**, which was recrystallized from EtOAc to give colorless needles, mp 85–87°. (Found: C, 57·90; H, 6·55; S, 11·67. $C_{13}H_{18}O_4S$ requires: C, 57·77; H, 6·71; S, 11·84%).

2-(1-Naphthyl)ethyl methylsulfinylmethyl ketone (**3**). Compound **3** was synthesized from ethyl 3-(1-



SCHEME 2.

naphthyl) propionate and DMSO in 80% yield, mp 94–96° (from EtOAc). (Found: C, 69·39; H, 6·31; S, 12·27. $C_{15}H_{16}O_2S$ requires: C, 69·21; H, 6·20; S, 12·30%).

Phenethyl methylsulfinylmethyl ketone (**5**). Compound **5** was synthesized from ethyl phenylpropionated in 75% yield. Recrystallization from EtOAc gave colorless needles, m.p. 62–64°. (Found: 62·63; H, 6·66; S, 15·08. $C_{11}H_{14}O_2S$ requires: C, 62·84; H, 6·71; S, 15·22%).

2,3 - *Dimethoxy* - 5 - *methylthio* - 6 - *oxo* - 5,6,7,8 - *tetrahydronaphthalene* (**2**). (i) Compound **1** (0·27 g, 1 mmol) was heated under reflux for 1 hr with trichloroacetic acid (2 mmol) in benzene (12 ml). The soln was washed with sat $NaHCO_3$ aq, dried and evaporated. The residue was purified on a silica-gel column(20 g) eluting with benzene-EtOAc (6:1) to give **2** in 60% yield. Recrystallization from EtOH gave colorless needles, m.p. 99–102°; *m/e* 252 (M^+); δ ($CDCl_3$) 2·16 (s, 3H), 2·4–3·4 (m, 4H), 3·94 (s, 6H), 4·04 (s, 1H), 6·68 (s, 1H), 6·80 (s, 1H). (Found: C, 61·91; H, 6·34; S, 12·49. $C_{13}H_{16}O_3S$ requires: C, 61·89; H, 6·39; S, 12·68%). (ii) Treatment of **1** with trifluoroacetic acid instead of trichloroacetic acid, gave **2** in 72% yield.

(iii) An acetonitrile soln (12 ml) of **1** (1 mmol) was treated with trichloroacetic acid (2 mmol). To the soln, $NaHCO_3$ aq was added, and the neutralized soln was concentrated *in vacuo* to remove the acetonitrile and then extracted with chloroform. The extract was dired and evaporated to leave crude **2**, which was purified as described above to give pure **2** in 70% yield.

(iv) For preparation of **2**, a soln of 1·35 g of **1** and 1·14 g of trifluoroacetic acid in 60 ml of benzene was heated under reflux for 1·5 hr. The soln was washed with sat $NaHCO_3$ aq and then dried. The solvent was evaporated to give a red syrup, which was crystallized by scratching. Recrystallization from EtOH afforded 0·81 g (64%) of colorless crystals.

1 - *Methylthio* - 2 - *oxo* - 1,2,3,4 - *tetrahydrophenanthrene* (**4**). (i) A soln of **3** (0·13 g, 0·5 mmol) and trifluoroacetic acid (0·114 g, 1 mmol) in acetonitrile (4 ml) was heated under reflux for 1 hr. After work-up as described above, 33 mg (27%) of **4** was isolated. Recrystallization from EtOH gave colorless needles, m.p. 109–112°; *m/e* 242 (M^+); ν_{max} 1700 cm^{-1}; δ ($CDCl_3$) 2·20 (s, 3H), 2·4–2·7 (m, 1H), 3·2–3·8 (m, 3H), 4·20 (s, 1H), 7·2–8·0 (m, 6H). (Found: C, 74·29; 5·79; S, 13·04. $C_{15}H_{14}OS$ requires: C, 74·36; H, 5·83; S, 13·21%).

(ii) Compound **3** (0·26 g, 1 mmol) and trifluoroacetic anhydride (0·42 g, 2 mmol) in acetonitrile (8 ml) was heated under reflux for 1 hr. After evaporation of the solvent, the residue was dissolved in chloroform and the soln was washed with $NaHCO_3$ aq and dried. Evaporation of the solvent gave an oil, which was chromatographed on a silica-gel column (13 g), eluting with chloroform to give 0·14 g (58%) of **4**.

Phenethyl (bismethylthio) methyl ketone (**6**). A soln of 0·21 g (1 mmol) of **5** and 0·42 g (2 mmol) trifluoroacetic anhydride in 10 ml acetonitrile was heated under reflux for 1 hr. After evaporation of the solvent, the residue was dissolved in chloroform, and the soln was washed with $NaHCO_3$ag and dried. Evaporation of the solvent gave an oil, which was chromatographed on a silica-gel column (20 g). Elution with benzene gave 50 mg (42%) of **6** as a colorless oil; *m/e* 240 (M^+); ν_{max} 1700 cm^{-1}; δ ($CDCl_3$) 1·95 (s, 6H), 2·95 (s, 4H), 4·25 (s, 1H), 7·20 (s, 5H).

Synthesis of naphthalenes from **1**

(i) *With* TsOH *in* MeCN. A soln of 0·27 g (1 mmol) of **1** and 0·38 g (2 mmol) *p*-toluenesulfonic acid monohydrate in 12 ml acetonitrile was heated under reflux for 1 hr. After evaporation of the solvent, the residue was dissolved in chloroform, and the soln was washed with $NaHCO_3$ aq and then extracted with 10% NaOH. From the chloroform layer 7 mg (3%) of **7** was isolated (see below).

The aqueous layer was acidified with 10% HCl and then extracted with chloroform. The extract was dired and concentrated to give 0·1 g (50%) of 2,3 - *dimethoxy* - 6 - *hydroxynaphthalene* (**10**), which was recrystallized from CCl_4-EtOH (35:1) to afford colorless needles, m.p. 162–164°; λ_{max} (EtOH) 232, 267 (sh), 275 (sh), 286 (sh), 320, 333 nm; λ_{max} (EtOH–NaOH) 243, 273 (sh), 284 (sh), 347 nm; ν_{max} 3440 cm^{-1}; *m/e* 204 (M^+); δ($CDCl_3$) 3·93 (s, 6H), 6·80–7·05 (m, 4H), 7·53 (d, 1H, J = 8 Hz). (Found: C, 70·50; H, 6·23. $C_{12}H_{12}O_3$ requires: C, 70·57; H, 5·92%).

(ii) *With* CCl_3CO_2H *in* MeCN–MeOH. A soln of 0·27 g of **1** and 0·98 g (6 mmol) trichloroacetic acid in 12 ml acetonitrile containing 0·4 ml MeOH was heated under reflux for 4 hr. The soln was cooled, neutralized by the addition of $NaHCO_3$ aq, concentrated *in vacuo* to remove the organic solvents, then extracted with chloroform. The chloroform soln was extracted with 10% NaOH. The aqueous layer was acidified with HCl to give 12 mg (6%) of **10**. The remaining chloroform layer was dired and concentrated to leave an oil, which was chromatographed on a column of silica-gel (10 g). Elution with benzene-EtOAc (20:1) gave 0·12 g (55%) of 2,3,6-*trimethoxy*-

naphthalene (**8**), which was recrystallized from MeOH to give colorless crystals, m.p. 139–140°; λ_{max} (EtOH) 233, 265 (sh), 273 (sh), 285 (sh), 318, 332 nm; *m/e* 232 (M^+); δ(CCl_4) 1·40 (t, 3H, J = 6 Hz), 3·93 (s, 6H), 4·05 (q, 2H, J = 6 Hz), 6·92 (4H), 7·50 (d, 1H, J = 9 Hz). (Found: C, 71·67; H, 6·60. $C_{13}H_{14}O_3$ requires: C, 71·54; H, 6·47%).

(iii) *With* CCl_3CO_2H *in* MeCN–EtOH. When EtOH was used in the place of MeOH in the foregoing experiment, 2,3-*dimetoxy*-6-*ethoxynaphthalene* (**9**) was isolated in 51% yield (0·118 g). Recrystallization from MeOH afforded colorless crystals, m.p. 144–146°; λ_{max} (EtOH) 233, 265 (sh), 273 (sh), 285 (sh), 318, 332 nm; *m/e* 232 (M^+); δ (CCl_4) 1·40 (t, 3H, J = 6 Hz), 3·93 (s, 6H), 4·05 (q, 2H, J = 6 Hz), 6·92 (4H), 7·45 (d, 1H, J = 9 Hz). (Found: C, 72·48; H, 7·13. $C_{14}H_{16}O_3$ requires: C, 72·39; H, 6·94%).

(iv) *With* TsOH–Ac_2O *in* MeCN. A soln of 0·27 g of **1** and 0·2 g *p*-toluenesulfonic acid monohydrate in 12 ml acetonitrile containing 0·4 ml Ac_2O was allowed to stand at room temp for 17 hr. The solvent was removed under reduced pressure and the residue was dissolved in chloroform. The soln was washed with $NaHCO_3$ aq and then extracted with 10% NaOH. After acidification of the NaOH-extract, the acidified soln was extracted with chloroform. The extract was dried and concentrated to give 76 mg (37%) of **10**. The initial chloroform layer was washed with water, dried and concentrated to give an oil, which was chromatographed on a column of silica-gel (10 g). Elution with benzene–EtOAc (20:1) gave 70 mg (30%) of 2,3 - *dimethoxy* - 6 - *methylthionaphthalene* (**7**), which was recrystallized from MeOH, m.p. 93–95°; λ_{max} (EtOH) 239, 245, 253, 273, 282, 329, 342 nm; *m/e* 234 (M^+); δ (CCl_4) 2·46 (s, 3H), 3·83 (s, 6H), 6·80–7·50 (m, 5H). (Found: C, 66·66; H, 5·98; S, 13·65. $C_{13}H_{14}O_2S$ requires: C, 66·65; H, 6·02; S, 13·66%).

An authentic sample of **7** was synthesized from **11** by an analogous procedure according to the literature for 2-methoxy - 6 - methylthionaphthalene.[12]

(v) *With* TsOH *in* MeCN–MeOH. A soln of acetonitrile (6 ml) containing 0·2 ml of MeOH 0·135 g (0·5 mmol) of **1** and 0·19 g (1 mmol) *p*-toluenesulfonic acid was heated under reflux for 1 hr. After being cooled, the soln was neutralized by the addition of a $NaHCO_3$ aq, concentrated *in vacuo* and extracted with chloroform. The chloroform layer was extracted with 10% NaOH. The remaining chloroform layer was chromatographed on a column of silica-gel, eluting with benzene-EtOAc (20:1) to give 5 mg (4%) of **7** and 44 mg (40%) of **8**. From the aqueous layer, 30 mg (29%) of **10** was obtained.

2,3-*Dimethoxy* - 6 - *hydroxynaphthalene* (**10**) *from* **2**. A soln of 0·126 g (0·5 mmol) of **2** and 0·196 g (1 mmol) *p*-toluenesulfonic acid monohydrate in 5 ml acetonitrile was heated under reflux for 1 hr. Work-up as before gave 70 mg (69%) of **10**.

Treatment of **3** *with* TsOH. A soln of **3** (0·26 g, 1 mmol) and *p*-toluenesulfonic acid monohydrate (0·38 g, 2 mmol) in acetonitrile (8 ml) was heated under reflux for 1·5 hr. The soln was treated in a manner similar to the reaction of **1** with *p*-toluenesulfonic acid in acetonitrile. From the aqueous layer, 60 mg (30%) of **12** was isolated. This was recrystallized from benzene-n-hexane to give colorless needles, m.p. 168–170°; *m/e* 194 (M^+), (Found: C, 86·15; H, 5·35. $C_{14}H_{10}O$ requires: C, 86·57; H. 5·19%). From the chloroform layer, 90 mg (62% based on 2 mol of **3**) of **13** was isolated. This was recrystallized from EtOH to give colorless needles, m.p. 59–60°; *m/e* 290 (M^+); ν_{max} 1700 cm^{-1}. (Found: C, 66·23; H, 6·35; S, 21·89. $C_{16}H_{18}OS_2$ requires: C, 66·19; H, 6·25; S, 22·04%).

3,4 - *Dimethoxyphenethyl* 1 - *methylsulfinyl* - 2 - *methoxycarbonylethyl ketone* (**14**). To an ice-cooled soln of the sodium salt of **1**, prepared from 1·35 g of **1** and 0·12 g of sodium hydride in 30 ml THF, 0·75 g of methyl bromoacetate in 5 ml of THF was added with stirring. After stirring for 2 hr at room temp, the mixture was concentrated *in vacuo* and then diluted with 20 ml water. The soln was acidified with HCl at pH 5 and extracted with chloroform. The extract was dried and concentrated to leave 1·32 g (77%) of crude **14**, which was recrystallized from EtOAc, m.p. 83–90°; ν_{max} 1740, 1710, 1040 cm^{-1}. (Found: C, 56·30; H, 6·50; S, 9·31. $C_{16}H_{22}O_6S$ requires: C, 56·13; H, 6·48; S, 9·35%).

3,4-*Dimethoxyphenethyl methylsulfinyl* - *phenylcarbamoylmethyl ketone* (**15**). To an ice-cooled soln of the sodium salt of **1** prepared from 0·675 g of **1** and 60 mg sodium hydride in 15 ml THF, 0·3 g phenylisocyanate in 4 ml THF was added dropwise. After being stirred for 1 hr at room temp, the soln was diluted by the addition of 40 ml water, acidified with HCl at pH 4–5, and extracted with chloroform. The extract was washed with water and dried. Evaporation of the solvent gave 0·87 g (92%) of a syrup, which crystallized within several hr. Recrystallization from EtOH gave colorless needles, m.p. 135–136°; ν_{max} 1710, 1660, 1030 cm^{-1}. (Found: C, 61·49; H, 6·01; N, 3·37; S, 8·17. $C_{20}H_{23}NO_5S$ requires: C, 61·69; H, 5·95; N, 3·60; S, 8·22%).

1,2-*Dihydroxy* - 7,8 - *dimethoxy* - 2 - *oxo* - *naphtho* [2,1-b] *furan* (**16**). A soln of 0·342 g (1 mmol) of **14** and 0·38 g (2 mmol) *p*-toluenesulfonic acid monohydrate in 12 ml acetonitrile was heated under reflux for 1 hr. After evaporation of the solvent, the residue was dissolved in chloroform and the soln was washed with 5% $NaHCO_3$ aq. Evaporation of the solvent left 268 mg of an oil, which was purified by passing in benzene-EtOAc (6:1) through a silica-gel column to give 146 mg (60%) of **16**. Recrystallization from benzene gave colorless prisms, mp 201–203°; ν_{max} 1800 cm^{-1}; *m/e* 244 (M^+). (Found: C, 68·64; H, 4·81. $C_{14}H_{12}O_4$ requires: C, 68·84; H, 4·95%).

1 - *Carboxymethyl* -6,7 - *dimethoxy* - 2 - *hydroxynaphthalene* (**18**). A soln of 0·104 g of **16** in 2 ml MeOH and 2 ml 10% NaOH aq was allowed to stand at room temp for 3 hr, and then diluted by the addition of 2 ml water. The soln was acidified with HCl and cooled in an ice-bath. Precipitated colorless needles of **18** (0·1 g, 99%) were collected by filtration, mp 152–155°; ν_{max} 3300, 1710 cm^{-1}. (Found: C, 68·13; H, 5·60. $C_{14}H_{14}O_5$ requires: C, 68·28; H, 5·73%).

6,7 - *Dimethoxy* - 2 - *hydroxynaphthalene* - 1 - *carboxanilide* (**19**). A soln of 0·195 g (0·5 mmol) of **15** and 0·19 g (1 mmol) *p*-toluenesulfonic acid monohydrate in 6 ml acetonitrile was heated under reflux for 1 hr. After removal of the solvent, the residue was dissolved in chloroform, and the chloroform soln was washed with $NaHCO_3$ aq and dried. Evaporation of the solvent gave 0·165 g (100%) of **19**, which was recrystallized from EtOH, m.p. 205–215° (sublimed); *m/e* 323 (M^+); ν_{max} 3325, 3200, 1650 cm^{-1}. (Found: C, 70·52; H, 5·28; N, 4·46. $C_{19}H_{17}NO_4$ requires: C, 70·57; H, 5·30; N, 4·33%).

Phenethyl methylthio - *trichloroacetoxymethyl ketone* (**22**). A soln of 0·21 g (1 mmol) of **5** and 0·326 g (2 mmol) trichloroacetic acid in 10 ml benzene was heated under reflux for 1·5 hr. Evaporation of the solvent, followed by purification on a silica-gel column (15 g) eluting with benzene afforded 0·23 g (65%) of **22** as a colorless oil; ν_{max} 1720, 1765 cm^{-1}; δ($CDCl_3$) 2·00 (s, 3H), 6·00 (s, 1H). The second fraction was 4 mg (3%) of **4**.

Reaction of **1** *with* $CHCl_2CO_2H$ *in* CCl_4. A soln of 0·135 g of **1** and 0·129 g dichloroacetic acid in 6 ml CCl_4 was heated at 60° for 2·5 hr. The soln was washed with 5% $NaHCO_3$ aq, dried and concentrated to give an oil, which was chromatographed on a column of silica-gel. Elution with benzene-EtOAc (20:1) gave two fractions. The first fraction was 42 mg (22%) of **21b** as an oil; ν_{max} 1760, 1720 cm^{-1}; $\delta(CDCl_3)$ 1·85(s, 3H), 6·00 (s, 1H), 6·10 (s, 1H). The second fraction was 38 mg (30%) of **2**.

Treatment of **21b** *with* $CHCl_2COOH$. A soln of **21b** (0·125 M) and dichloroacetic acid (0·25 M) in benzene was heated at 70° for 1 hr. Compound **2** was not detected by NMR spectrometry and **21b** was recovered unchanged.

Reaction of **3** *with a mixture of* CCl_3CO_2H *and* $CHCl_2H$. A soln of 0·13 g **3**, 65 mg (1 eq.) dichloroacetic acid and 82 mg (1 eq.) trichloroacetic acid in 5 ml benzene was heated at 70° for 2 hr. The soln was washed with 5% $NaHCO_3$ aq, dried and concentrated to give an oil, which was chromatographed on a silica-gel thin layer plate. Elution with benzene-n-hexane (3:1) gave two fractions. The first fraction was 30 mg (13%) of **23a** as an oil and the second fraction was 62 mg (33%) of **23b** as an oil; ν_{max} 1760, 1720; $\delta(CDCl_3)$ 1·95 (s, 3H), 5·90 (s, 1H), 6·00 (s, 1H).

2,3 - *Dimethoxy* - 6 - *hydroxynaphthalene* - 5 - D (**10a**). To a stirred soln of 48 mg of oil-free sodium hydride in 10 ml THF was added dropwise a soln of 0·54 g of **1** in 6 ml THF and stirring continued until the evolution of H_2 ceased. The soln was cooled in an ice-bath, followed by neutralization with monodeuteroaceic acid (D-content 99%). The soln was concentrated *in vacuo* and the residue was extracted with chloroform. The extract was washed with water, dried and the solvent was evaporated to give 0·51 g of monodeuterated **1**, m.p. 86–89° (from EtOAc), deuterium content estimated from the mass spectrum was 41%. Compound **10a** was synthesized from 0·135 g of the deuterated **1** by the same procedure described for the preparation of **10**. The deuterium content was 9·0%.

Treatment of **10a** *with* TsOH. A soln of 10 mg of **10a** and 40 mg *p*-toluenesulfonic acid monohydrate in 3 ml acetonitrile containing 0·1 ml Ac_2O was allowed to stand at room temp for 19 hr. The naphthol **10a** was recovered by usual manner and the deuterium content was 9·2% judging from its mass spectrum.

Treatment of **10** *with* TsOH *in the presence of* EtSH. Compound **10** (30 mg) was heated under reflux with *p*-toluenesulfonic acid monohydrate (60 mg) in 5 ml benzene containing 0·2 ml ethyl mercaptan for 1 hr. No trace of **26** was detected by TLC and **10** was recovered unchanged.

Reaction of **1** *with* TsOH *in the presence of* EtSH. A soln of **1** (0·135 g, 0·5 mmol), ethyl mercaptan (0·6 ml, 8 mmol) and *p*-toluenesulfonic acid monohydrate (0·19 g, 1 mmol) in benzene (6 ml) was heated under reflux for 1 hr. After evaporation of the solvent, the residue was dissolved in chloroform and chromatographed on a column of silica-gel (12 g). Elution with benzene-EtOAc (20:1) afforded 66 mg of a mixture of **7** and **26** in the ratio 1:1·83 as judged from the intensities of the NMR peaks at δ2·52 (singlet) for **7** and 1·30 (triplet) for **26**.

Kinetic methods. The reaction rates were followed NMR spectrophotometrically. A benzene soln of **1** (0·125 M) and either trichloroacetic acid or dichloroacetic acid (0·25 M) in a sealed NMR tube was heated at 70° or 80°. The intensities of S-methyl signals of **1** (δ2·15) and **2** (δ1·75) were measured and the rate determined by the usual method was found to correlate with first order kinetics.

Compounds **5**, **3** and **23a** were treated in the same way. Signals of S-Me groups measured for the rate determination are as follows: **5**, δ2·10; **22**, δ1·70; **3**, δ2·10; **23a**, δ 1·70; **4**, δ2·03. The results are summarized in Table 2.

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