5 mL of dry DME at room temperature. Upon cooling to 0 °C, 90.0 mg (0.647 mmol) of NCS was added all at once and stirring was continued for 1 h at 0 °C. The reaction mixture was poured into water and extracted with ether. The ether layers were washed with water and then with 10% aqueous sodium sulfite and dried. After evaporation in vacuo, the residue was passed through a 2 × 5 cm column of silica gel utilizing 5% ether in hexane to give 115 mg (85%) of the vinyl sulfide: IR (CCl_4) 1595, 1485, 940, 840 cm^{-1}; NMR (CCl_4) δ 1.80 (2 H, m), 2.16 (5 H, s + m), 2.49 (2 H, t, J = 7 Hz), 4.49 (1 H, s), 4.92 (1 H, s), 5.82 (2 H, s), 6.56 (3 H, m); MS m/e (relative %) 236 (10), 149 (9), 148 (100), 147 (7), 135 (33), 101 (28), 77 (9), 51 (6). Anal. Calcd for $C_{13}H_{16}O_2S$: 236.0871. Found: 236.0867.

The remaining examples are summarized in Table III. The spectral data for these cases appear as supplementary material.

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Registry No.—2-Methylthiopropionic acid, 58809-73-7.

Supplementary Material Available: Spectral data for additional examples of alkylation of 2-methylthiopropionic acid and oxidative decarboxylation (3 pages). Ordering information is given on any current masthead page.

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Evidence for Ipso Attack in the Peroxodisulfate Oxidation of Tertiary Aromatic Amines

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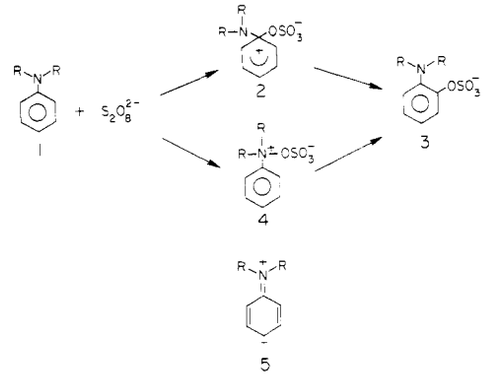
Studies from two laboratories have shown that the reaction between peroxodisulfate ions and aromatic amines (the Boyland–Sims oxidation) proceeds via electrophilic attack of the peroxodisulfate ion on the neutral amine.[1-5] Since the product is the *o*-aminoaryl sulfate (**3**) (the para isomer is only formed in significant quantity when both ortho positions are blocked),[6] the arylhydroxylamine-*O*-sulfonate (**4**) was proposed as an intermediate.[2] This proposal was supported by kinetic substituent effects which excluded rate-limiting attack at the ortho-carbon atom.[2,3] This proposal was also consistent with Boyland and Nery's observations on the stability of phenylhydroxylamine-*O*-sulfonate (**4**, R = H).[7] This compound, although stable enough to be isolated, rearranges to the ortho sulfate in acid and also during workup under neutral conditions. The related substance, *N*-acetyl-2-naphthylhydroxylamine-*O*-sulfonate also rearranges to the ortho sulfate at neutrality.[8] Other related rearrangements have been reported.[9]

Edward and Whiting,[10] however, synthesized **4**, R = Me, by reaction of *N,N*-dimethylaniline *N*-oxide with sulfur trioxide and showed that it did not rearrange to the ortho sulfate under Boyland–Sims conditions. Rather, it underwent hydrolysis to the parent *N*-oxide and sulfate ions. This finding excluded **4**, R = Me, as intermediate although previous work



had shown that the tertiary amines gave the expected ortho sulfate upon reaction with peroxodisulfate ions.[4,6]

Since the substituent effects which excluded rate-limiting attack at the ortho-carbon atom had been conducted only on primary amines, we carried out similar kinetic studies on two sets of ring-substituted *N,N*-dimethylanilines. These data are shown in Table I. They exclude rate-limiting attack at the ortho-carbon position for the tertiary amines as well since both the 2,4-dimethyl- and the 2-methyl-4-chloro-*N,N*-dimethylanilines react more rapidly than the corresponding 2,3 isomers. The opposite relative reactivity would be observed were rate-limiting attack at the ortho carbon.[2] The apparent discrepancy between Edward and Whiting's result and our present data may be rationalized by postulating ipso attack[11] with rearrangement via **2** to account for the formation of the ortho sulfate in the case of the tertiary amines. Ipso attack may also be involved for the primary and secondary amines,

Table I. Comparison of the Rates of Oxidation of 2,3- and 2,4-Disubstituted *N,N*-Dimethylanilines by Peroxodisulfate Ions[a]

compd	registry no.	no. of runs	concn range, 10^2 M	$10^3 k'$, min^{-1}	k, M^{-1} min^{-1}
2-methyl-4-chloro-*N,N*-dimethylaniline	67761-87-9	4	2.1–4.4	2.17–4.95	0.107 ± 0.008
2-methyl-3-chloro-*N,N*-dimethylaniline	67761-88-0	6	2.2–3.4	1.17–2.2	0.0575 ± 0.006
2,4-dimethyl-*N,N*-dimethylaniline	769-53-9	3	2–8	3.2–12.8	0.153 ± 0.002
2,3-dimethyl-*N,N*-dimethylaniline	24226-35-5	4	2–7.5	2.7–8.7	0.129 ± 0.01

[a] Reaction conditions: 30 °C, 0.1 M KOH in 50% ethanol–water (v/v), the initial amine–peroxodisulfate ratio was 10. Second-order rate constants were calculated by division of the pseudo-first-order constants by the initial concentration of the amine. Ethanol is not oxidized by peroxodisulfate at a significant rate at 30 °C.

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but in these cases attack at nitrogen may also lead to the ortho sulfate as well as to the other oxidation products previously discussed.[2]

Sabesan and Venkatasubramanian[4] have measured the rate constant for the reaction between *N,N*-dimethylaniline and peroxodisulfate ion under substantially the same conditions as those given in Table I. We confirm their value (1.7 M^{-1} min^{-1}) and point out that the rates we observe for the *o*-methyl derivatives are all of the order of one-tenth of this value. Diminished reactivity for the reactions of ortho-substituted *N,N*-dialkylanilines with electrophiles to yield ortho- and para-substituted anilines is well-known[12] and has been shown to be due to steric inhibition of resonance forms such as **5**. This effect also reflects itself in the increased basicity of the ortho-substituted *N,N*-dialkylanilines.[13] Therefore, were peroxodisulfate to attack at nitrogen, we would expect that the ortho-substituted *N,N*-dimethylanilines would react more rapidly than the parent *N,N*-dimethylanilines. The opposite is the case. Since the substituent effect discussed above argues against rate-limiting attack at the available ortho carbon, the decreased rate of reaction for the ortho-substituted *N,N*-dimethylanilines is also consistent with reaction at the ipso position.

Experimental Section

The primary anilines, supplied by Aldrich, were converted to *N,N*-dimethylanilines according to the procedure of Billman et al.[14] The IR spectra showed no NH stretch. Other physical properties of the *N,N*-dimethylanilines follow.

2,3-Dimethyl: bp 105–105.5 °C (28 mm); n^{25}_D 1.5245 (lit.[13] 1.5241); NMR δ 2.18 (s, 6, Me, Me), 2.58 (s, 6, NMe_2), 6.86 (m, 3).

2,4-Dimethyl: bp 100–101.5 °C (27 mm); n^{25}_D 1.5165 (lit.[13] 1.5170); NMR δ 2.22 (s, 3, Me), 2.25 (s, 3, Me), 2.58 (s, 6, NMe_2), 6.85 (s, br, 3).

2-Methyl-3-chloro: bp 120.5–122 °C (28 mm); n^{25}_D 1.5440; NMR δ 2.34 (s, 3, Me), 2.60 (s, 6, NMe_2), 6.9 (m, 3).

2-Methyl-4-chloro: bp 121–122 °C (26 mm); n^{25}_D 1.5410; NMR δ 2.25 (s, 3, Me), 2.60 (s, 6, NMe_2), 6.9 (m, 3).

The NMR data were taken at 35 °C at 60 MHz in CCl_4 with Me_4Si as internal standard. Kinetics were carried out under pseudo-first-order conditions, peroxodisulfate limiting, as previously described.[2] Product from 2,3-dimethyl-*N,N*-dimethylaniline was detected in the ethanol-soluble fraction of reaction mixtures upon paper electrophoresis at pH 8 as a UV-absorbing, negatively charged species with a mobility slightly less than that of picrate ion. This material reduced the Folin phenol reagent but not the Folin–Denis uric acid reagent.[15] Following hydrolysis in acid, the product reduced the uric acid reagent as well. Quantitative estimation with the uric acid reagent[15] suggested a yield in the 30–40% range in accord with previous work.[2]

Registry No.—Peroxodisulfate, 15092-81-6.

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Structure, Absolute Configuration, and Synthesis of Stramonin-B, a New Cytotoxic Pseudoguaianolide

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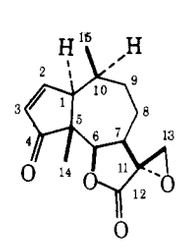
In our continuing investigation of naturally occurring and synthetic sesquiterpene lactones that exhibit antitumor and allergenic properties,[1] a new sesquiterpene lactone has been isolated from the chloroform extracts of the medicinal plant *Parthenium tomentosum* var. *stramonium* (Compositae).[2] We report the isolation, structural elucidation, absolute configuration, and synthesis of stramonin-B (1), the first naturally occurring epoxidized α-methylene lactone of a pseudoguaianolide. Stramonin-B exhibited significant activity



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(ED_{50} = 2.9 μg/mL) in vitro against KB cells in tissue culture.[3,4]

Chromatography on activated silica gel of a chloroform extract of ground leaves of *Parthenium tomentosum* var. *stramonium* (Greene) Rollins resulted in isolation (0.07%) of a new pseudoguaianolide. Stramonin-B (1), crystallized from isopropyl ether–chloroform: mp 175–176 °C; $[\alpha]^{27}_D$ −125° (*c* 1.14, chloroform).

The ^1H NMR spectrum (250 MHz, $CDCl_3$) of stramonin-B [$C_{15}H_{18}O_4$, M^+ *m/e* 262, UV (MeOH) 226 nm (ε 8947)] exhibited a one-proton doublet of doublets (*J* = 2 Hz, 6 Hz) located at δ 7.48 and a one-proton doublet of doublets (*J* = 3 Hz, 6 Hz) at δ 6.12 which, together with IR (KBr) bands at 1720 and 1595 cm^{-1}, indicated the presence of a cyclopentenone ring. The IR spectrum also showed a band at 1775 cm^{-1} (γ-lactone) and a series of bands at 1250, 980, and 835 cm^{-1} (terminal epoxide). The nature of the epoxide (terminal disubstituted) was elucidated from the ^1H NMR spectrum which revealed a two-proton AB quartet (*J* = 5.5 Hz) centered at δ 3.29 ($\Delta\nu_{AB}$ = 36.1 Hz). The ^1H NMR spectrum also indi-

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