(7) R. Jonas, H. Müller-Calgan, and H.-J. Schliep, U.S. Patent 3 980 797 (1976).
(8) G. W. Gribble, P. Lord, J. Skotnicki, S. Dietz, J. Eaton, and J. Johnson, *J. Am. Chem. Soc.*, **96**, 7812 (1974).
(9) A report on the reduction of indoles using borane–pyridine and aqueous or ethanolic mineral acids appeared during the course of our research, see: Y. Kikugawa, *J. Chem. Res.*, 212 (1977).
(10) For a survey of the reducing properties of **4** see: G. W. Kabalka, J. D. Baker, Jr., and G. W. Neal, *J. Org. Chem.*, **42**, 512 (1977).
(11) J. G. Berger, F. Davidson, and G. Langford, *J. Med. Chem.*, **20**, 600 (1977).
(12) For a report on $NaBH_3CN$ in acetic acid see: G. W. Gribble and J. H. Hoffman, *Synthesis*, 859 (1977).
(13) J. G. Berger, *Synthesis*, 508 (1974).
(14) Ethers, such as THF and anisole, can be cleaved by borane reagents; e.g., see M. Node, H. Hori, and E. Fujita, *J. Chem. Soc., Perkin Trans. 1*, 2237 (1976), and references cited therein.
(15) The isolated THF complex, **1**, was not stable to prolonged storage at room temperature under dry nitrogen. After a few days, no active hydride remained and the liquid became very viscous. Therefore, we suggest the use of freshly prepared material. In the preparation of **1**, too slow addition of BH_3–THF and unnecessary standing of the reaction mixture were avoided, since polymerization of THF was observed. Removal of excess THF to give **1** alleviated the polymerization problem.
(16) Catecholborane and **1** reduced **2** at about the same rate.

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Dimethylaluminum Methylselenolate: A Remarkable Reagent for the Preparation of Active Acyl-Transfer Agents

Summary: The preparation of a new aluminum reagent, dimethylaluminum methylselenolate (**1**), has been achieved. This reagent has been shown to react with a variety of *O*-alkyl esters to provide methylselenol esters, active acyl-transfer agents, in excellent yield.

Sir: We would like to report the preparation and use of a remarkably efficient and versatile reagent for the conversion of *O*-alkyl esters to their corresponding methylselenol esters. This reagent, dimethylaluminum methylselenolate (**1**), is conveniently prepared by heating a toluene solution of trimethylaluminum (Texas Alkyls) with powdered selenium (ROC/RIC) for 2 h at reflux.[1]

$$Me_3Al + Se \xrightarrow[\text{2 h}]{\text{toluene, reflux}} Me_2AlSeMe \quad \mathbf{1}$$

The yellow-colored solution so generated is then ready for use. Aliquots of the reagent are withdrawn by syringe and transferred to the reaction vessel containing the ester, or other organic substrate, dissolved in argon-degassed methylene chloride. All reactions are carried out under an argon atmosphere in a good fume hood.

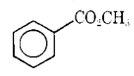
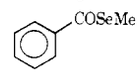
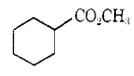
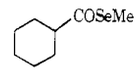
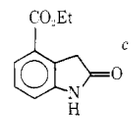
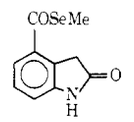
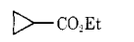
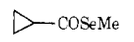
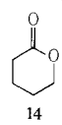
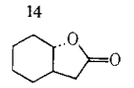
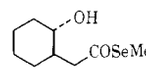
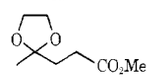
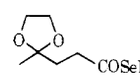
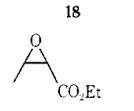
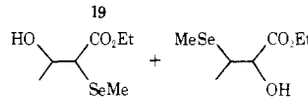
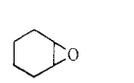
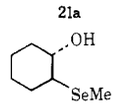
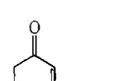
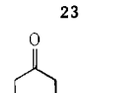
The transformation of a variety of exemplary methyl and ethyl esters to their corresponding selenol esters was found to be complete within 1 h (30 min at 0 °C, followed by an additional 30 min with warming to room temperature)!

The reaction mixtures were quenched with moist sodium sulfate and the products extracted with ether. Concentration of the organic extracts under reduced pressure and bulb-to-bulb distillation of the yellow oils gave the desired products in high yield and high purity as ascertained by NMR, IR, and mass spectral analysis (Table I).

The use of related aluminum reagents and their reactions with esters have previously been explored by Y. Ishii[2] (Et_2AlSEt) and E. J. Corey ($Me_2AlS(CH_2)_3SAlMe_2$, Me_2AlSPh, Me_2AlSCH_2Ph).[3] In addition, S. Weinreb and R. Hatch have recently reported the preparation of *tert*-butyl thioesters by reaction of dimethylaluminum 2-methyl-2-propanethiolate with *O*-alkyl esters.[4] Two equivalents of this aluminum reagent and a reaction time of 4–24 h were required for complete conversion of ester to *tert*-butyl thioester. In contrast, only 1.1 equiv of the selenium reagent **1** are required in most cases for the preparation of the selenol esters.

As is evidenced from Table I, methyl and ethyl esters react with equal facility. The ethyl ester of cyclopropanecarboxylate undergoes reaction without concomitant opening of the strained carbocycle. Only for 4-carboethoxyoxindole (**8**), which possesses a very acidic proton at C-3, is it essential to employ 2 equiv of **1** for complete conversion to the selenol ester

Table I. Reactions of Dimethylaluminum Methylselenolate (1)

starting material[a]	product[b]	isolated yield, %
$CH_3(CH_2)_5CO_2CH_3$ (**2**)	$CH_3(CH_2)_5COSeMe$ (**3**)	95
 (**4**)	 (**5**)	99
 (**6**)	 (**7**)	93
 (**8**)	 (**9**)	80
 (**10**)	 (**11**)	96
$EtO_2C(CH_2)_5CO_2Et$ (**12**)	$MeSeCO(CH_2)_5COSeMe$ (**13**)	95
 (**14**)	$HO(CH_2)_4COSeMe$ (**15**)	78
 (**16**)	 (**17**)	80
 (**18**)	 (**19**)	93
 (**20**)	 (**21a**, ~3:1; **21b**)	92
 (**22**)	 (**23**)	96
 (**24**)	 (**25**)	87

[a] All starting materials were distilled prior to reaction. [b] All products with the exception of **9** were purified by bulb-to-bulb distillation under reduced pressure. Compound **9**, which was obtained in near quantitative yield as the crude product, was recrystallized from methanol. [c] Prepared by the method of A. P. Kozikowski and M. Kuniak, *J. Org. Chem.*, **43**, 2083 (1978).

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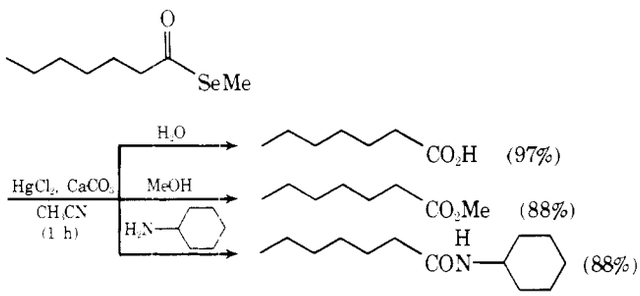
9. In contrast to the high reactivity of *O*-methyl and *O*-ethyl esters, the *tert*-butyl ester of octanoic acid fails to react under the standard conditions and is converted only in low yield to its selenol ester after prolonged heating with 2 equiv of **1**. While δ-valerolactone (**14**) is smoothly transformed to the δ-hydroxyselenol ester **15**, γ-butyrolactone is recovered unchanged on exposure to **1**, even after heating at the reflux temperature of methylene chloride for 24 h.[5] The fused γ-lactone **16**, on the other hand, is transformed to the hydroxyselenol ester **17** in 80% yield. At the temperature required to effect Kugelrohr distillation of this compound [118 °C (23 mm)], it was noted that substantial reversion of this selenol ester to starting lactone occurred.

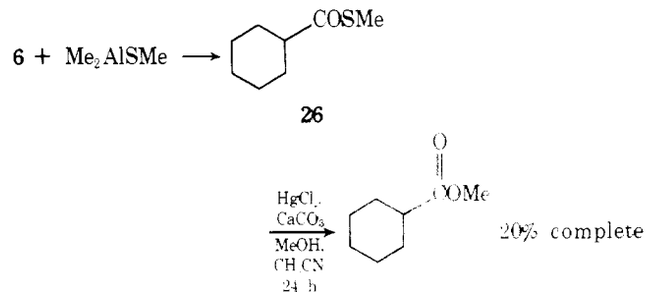
N-Methyl-3-cyclohexenylcarboxamide exhibits no evidence of conversion to selenol ester on reaction with either 1 or 2 equiv of **1** at room temperature. With the ethylene ketal of methyl levulinate (**18**) as reactant, conversion to selenol ester **19** proceeds without competing cleavage of the dioxolane group. Cyclohexene epoxide (**22**) undergoes facile ring opening with dimethylaluminum methylselenolate to furnish 2-methylseleno-1-cyclohexanol (**23**). With ethyl epoxybutyrate (**20**), opening of the epoxide ring takes place in preference to selenol ester formation. Reaction of **1** with 2-cyclohexenone furnishes **25**, the product of 1,4-conjugate addition. These latter observations thus serve to set some limits on the use of **1** for the preparation of selenol esters of polyfunctional molecules.

Finally, the ability of the selenol esters to serve as active acyl-transfer agents was readily demonstrated by the conversion of **3** to its corresponding acid, ester, or amide. This was accomplished by simply stirring the selenol ester with H_2O/CH_3CN, $MeOH/CH_3CN$, or cyclohexylamine/CH_3CN, respectively, at room temperature for 1 h in the presence of mercuric chloride and calcium carbonate.



The reactivity of the selenol esters was anticipated to be higher than that of the thiol esters as a consequence of the weak carbon–selenium bond.[6] In accord with this expectation, methanolysis of the 2-methylpropane-2-thiol ester of cyclohexanecarboxylic acid has been reported by Masamune to require 3 h of reflux in acetonitrile with $HgCl_2/CdCO_3$ present.[7] In contrast, the methylselenol ester **7** of this acid was transformed to *O*-methyl ester in 15 min at room temperature on treatment with $HgCl_2/CaCO_3$ in $MeOH/CH_3CN$.[8]

Since these rate differences may to some extent reflect the different steric demands of the substituents bound to the group 6A element (*tert*-butyl vs. methyl), the methylthiol ester of cyclohexanecarboxylic acid was also prepared. Methyl cyclohexanecarboxylate was treated with Me_2AlSMe (prepared from Me_3Al and S in refluxing toluene)[1] to give **26**, which was then reacted with methanol in the presence of $HgCl_2/CaCO_3/CH_3CN$. After 24 h at room temperature, the reaction mixture was found to consist of 80% starting thiol ester plus only 20% *O*-methyl ester by ^1H NMR analysis. This result clearly affirms the enhanced reactivity of selenol esters as acyl-transfer agents.



A typical experimental procedure is illustrated by the preparation of the methylselenol ester of heptanoic acid. To a 50-mL side-arm flask containing 4.1 g (0.052 mol) of selenium powder was added 25.2 mL (0.05 mol) of a 17.0% solution of trimethylaluminum in toluene. The reaction mixture was heated at reflux for 2 h, then cooled to room temperature, allowing the unreacted selenium to settle from solution. A 1.1-mL (2.2 mmol) aliquot of **1** was transferred by syringe to a solution of methyl heptanoate (288 mg, 2.0 mmol) in 5 mL of argon-degassed dichloromethane at 0 °C. After 30 min at this temperature, the yellow solution was warmed to room temperature over 30 min and then treated with moist sodium sulfate. The resulting mixture was extracted with ether and the isolated crude product purified by bulb-to-bulb distillation (95 °C oven temperature, 30 mm) to yield 393 mg (95%) of **3** as a yellow oil: IR (film) 1729 cm^{-1}; NMR (CCl_4) δ 2.54 (t, 2 H), 2.16 (s, 3 H), 0.63–2.00 (br m, 11 H); mass spectrum (70 eV) m/e 204, 205, 206, 208, 210 (M^+), 113 (base peak).

The methanolysis of **3** was carried out as follows. A mixture of 109 mg (0.525 mmol) of *Se*-methyl selenoheptanoate, 293 mg (1.07 mmol) of freshly sublimed mercuric chloride, and 214 mg (2.14 mmol) of calcium carbonate in 2.75 mL of dry acetonitrile and 0.04 mL of dry methanol was stirred for 1 h at room temperature under an argon atmosphere. The reaction mixture was then extracted with pentane, the organic extracts were filtered through Celite, and the isolated crude product was purified by bulb-to-bulb distillation to yield 67 mg (88%) of methyl heptanoate.

Reagent **1** thus offers a convenient method for the single-step generation of active acyl-transfer agents from *O*-alkyl esters. The use of powdered sulfur and selenium for the preparation of aluminum thiolates and selenolates also extends the utility of these reagents in organic synthesis, for this method avoids the use of toxic and disagreeable thiols and selenols. The utility of dimethylaluminum methylselenolate in macrolactam and macrolactone construction and peptide synthesis must await further investigations. Studies to assess the reactivity of the aluminum enolates generated by conjugate addition of **1** to α,β-unsaturated carbonyl systems are also underway.

Acknowledgment. We are grateful to the National Institutes of Health (Grant No. R01-HL2059-01) and the donors of the Petroleum Research Foundation, administered by the American Chemical Society, for support of these investigations. We also thank Dr. Steven Weinreb for preprints of his publications.

References and Notes

(1) Two previous accounts of the preparation of aluminum selenolates ($Et_2AlSeEt$ and $i\text{-}Bu_2AlSe\text{-}i\text{-}Bu$) and thiolates by this method are present in the literature: L. I. Zakharkin and V. V. Gavrilenko, *Bull. Acad. Sci. USSR (Engl. Transl.)* 1294 (1960); Kali-Chemie, German Patent 1 031 306; *Chem. Abstr.*, **54**, 17269g (1960); see also T. Mole and E. A. Jeffery, "Organoaluminum Compounds", Elsevier, Amsterdam, 1972.
(2) T. Hirabayashi, K. Itoh, S. Sakai, and Y. Ishii, *J. Organomet. Chem.*, **25**, 33 (1970); T. Hirabayashi, H. Imaeda, K. Itoh, S. Sakai, and Y. Ishii, *ibid.*, **19**, 299 (1969).
(3) E. J. Corey and D. J. Beames, *J. Am. Chem. Soc.*, **95**, 5829 (1973); E. J. Corey and A. P. Kozikowski, *Tetrahedron Lett.*, 925 (1975).

(4) R. P. Hatch and S. M. Weinreb, *J. Org. Chem.*, **42**, 3960 (1977); A. Basha, M. Lipton and S. M. Weinreb, *Tetrahedron Lett.*, 4171 (1977).
(5) Failure to observe reaction in this case may be attributable either to competing enolate formation or to a facile back reaction converting hydroxyselenol ester to lactone. This question will be resolved in future studies.
(6) For a review of selenol acids and esters, see K. A. Jensen in "Organic Selenium Compounds: Their Chemistry and Biology", D. L. Klayman and W. H. Günther, Ed., Wiley, New York, N.Y., 1973, pp 263–272.
(7) S. Masamune, S. Kamata, and W. Schilling, *J. Am. Chem. Soc.*, **97**, 3515 (1975); S. Masamune, Y. Hayase, W. Schilling, W. K. Chan, and G. S. Bates, *ibid.*, **99**, 6756 (1977). The authors indicate in footnote 3 of this communication that selenol esters appear to offer no advantage over thiol esters as acyl-transfer agents.
(8) Preliminary experiments indicate the Cu(II) salts are equally effective in promoting the methanolysis of the selenol esters.

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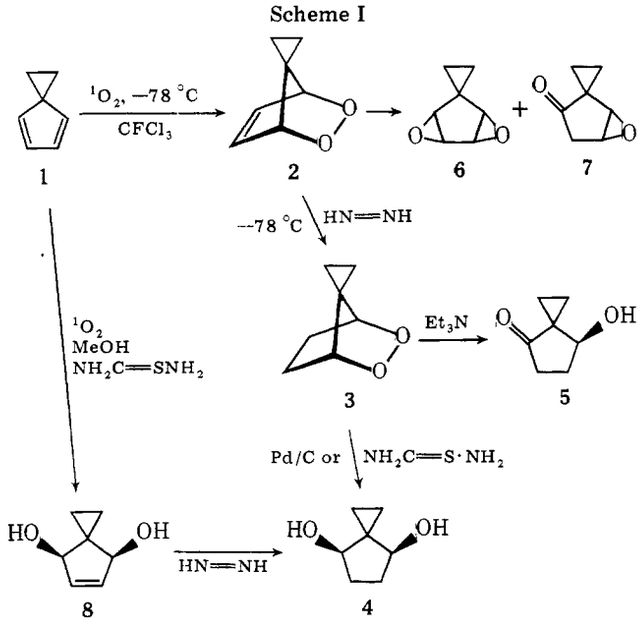
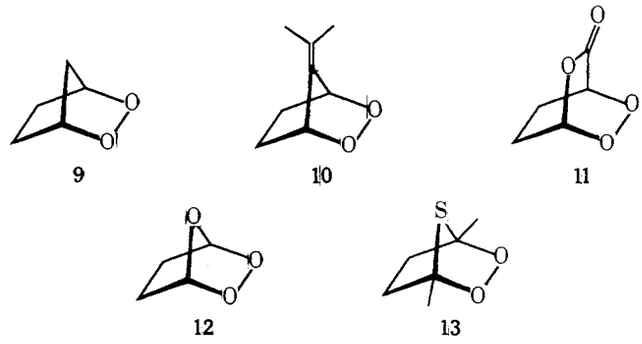
Synthesis and Characterization of 7-Spirocyclopropyl-2,3-dioxabicyclo[2.2.1]hept-5-ene[1]

Summary: The title compound, **3**, was prepared by diimide reduction of the unstable endoperoxide **2** which was obtained by photooxygenation of spiro[2.4]hepta-4,6-diene (**1**) and characterized by catalytic reduction to its diol **4** and base-catalyzed rearrangement to its ketol **5**.

Sir: Although the singlet oxygenation of spiro[2.4]hepta-4,6-diene (**1**) has been reported,[2] the intermediacy of the expected endoperoxide **2** could only be inferred from the formation of the diepoxide **6** and ketoepoxide **7** as the major rearrangement products (cf. Scheme I). Recently we have been successful in trapping the unstable singlet oxygen adducts derived from cyclopentadiene,[3] 6,6-dimethylfulvene, α-pyrone,[5] furan,[6] and 2,5-dimethylthiophene[7] by diimide reduction to their respective bicyclic peroxides **9–13.** In view of this convenient peroxide bond-preserving technique, we have reinvestigated the singlet oxygenation of the spirodiene **1** and established the intervention of its unstable endoperoxide **2** by direct NMR monitoring and reductive trapping in the form of the stable bicyclic peroxide **3.**

Scheme I





The photooxygenation of **1** in $CFCl_3$ at −78 °C with tetraphenylporphyrin (TPP) as sensitizer using a General Electric 400-W sodium lamp gave after warm-up to room temperature the reported[2] rearrangement products **6** and **7.** However, when the singlet oxygenation was monitored by subambient (−50 °C) NMR analysis, after 5 h of irradiation the characteristic spirodiene **1** resonances at δ 1.50 (singlet, cyclopropyl, 4 H) and δ 5.85 and 6.30 (multiplets, olefinic, 4 H) had been completely replaced by new resonances at δ 0.90 (broad singlet, cyclopropyl, 4 H), 4.58 (triplet, J = 2.0 Hz, bridgehead, 2 H), and 6.53 (triplet, J = 2.0 Hz, olefinic, 2 H), ascribed to the unsaturated endoperoxide **2** as the expected singlet oxygenation adduct of **1.** Not even traces of the diepoxide **6** and ketoepoxide **7** rearrangement products of **2** could be detected by NMR at −50 °C in $CFCl_3$. Warming of the reaction mixture to 0 °C promoted rapid replacement of the above signals assigned to **2** by those reported[2] for **6** and **7.** Furthermore, photooxygenation of the spirodiene **1** in MeOH with Rose Bengal as sensitizer in the presence of thiourea afforded the unsaturated diol **8** in 60% yield, liquid, n^{20}_D 1.4930 (after VPC collection on a 5 ft × ¼ in. aluminum column packed with 5% SE 30 on Chromosorb P and operated at a column temperature of 125 °C). Its characterization rests on satisfactory elemental analysis, ^1H NMR ($CDCl_3$, Me_4Si) resonances at δ 0.85 (s, cyclopropyl, 4 H), 2.60 (broad s, OH, exchanged with D_2O, 2 H), 3.98 (s, OCH, 2 H), and 6.05 (s, olefinic, 2 H), and IR ($CHCl_3$) bands at 3710–3125 (OH), 3070–3020 (cyclopropyl CH and olefinic CH), 2990–2900 (aliphatic CH), and 1710 cm^{-1} (C═C).

Treatment of the photooxygenate with excess diimide, generated in situ from potassium azodicarboxylate as described previously,[3] at −78 °C in $CFCl_3$ afforded the stable saturated endoperoxide **3** in 68% yield, pale yellow needles, mp 32 °C [after sublimation at 30 °C (0.15 mmHg)]. The bicyclic peroxide **3** gave a satisfactory elemental analysis and exhibited ^1H NMR (CCl_4) resonances at δ 0.85 (m, cyclopropyl, 4 H), 1.87 (broad s, methylenic, 4 H), and 3.80 (broad s bridgehead, 2 H) and IR (CCl_4) bands at 3080 (cyclopropyl CH), 2980–2940 (aliphatic CH), 1460 (CH_2 bending), and 1018 cm^{-1} (peroxide). The following chemical transformations confirm this structure assignment. Thus, catalytic hydrogenation of **3** over 10% Pd/C as well as thiourea reduction in MeOH gave the *cis*-diol **4** in 92% yield, n^{20}_D 1.4935 (after VPC collection under the conditions described for diol **8**). Diol **4** gave a satisfactory elemental analysis and exhibited ^1H NMR ($CDCl_3$) resonances at δ 0.30–1.00 (m, cyclopropyl, 4 H), 1.95 (broad s, CH_2, 4 H), 2.39 (broad s, –OH, exchanged with D_2O, 2 H), and 3.48 (m, OCH, 2 H) and IR ($CHCl_3$) bands at 3710–3200 (OH), 3065 (cyclopropyl CH), 2995–2860 (aliphatic CH), 1420 (CH_2 bending), and 1040 cm^{-1} (CO). Diol **4** could also be obtained by diimide reduction of the unsaturated diol **8** in MeOH at 0 °C, showing identical spectral data. Finally, treatment of the saturated endoperoxide **3** with triethylamine in CH_2Cl_2 at 0 °C gave the ketol **5** in 87% yield, n^{20}_D 1.4856 (after VPC collection under the conditions described for diol

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