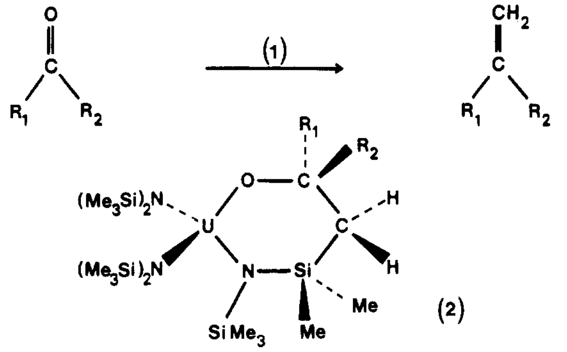
Scheme I



R_1, R_2 = acyclic (**2A,B**) or cyclic moieties (**2C–H**)

Table II. ^{1}H NMR Chemical Shifts (δ) of Significant Protons[a] for 2C-H Spiro Compounds

	CH_2	$SiMe_2$	$NSiMe_3$	$[N(SiMe_3)_2]_2$
$2C_\alpha$[b]	3.72	0.50	−12.62	−4.79[c]
$2C_\beta$	6.85	2.10	−13.41	−5.03[c]
2D	11.85	2.82	−11.24	−13.12
2E	16.75[c,d]	−0.30[c]	−22.37[c]	−4.80[c]
2F	16.03[c,d]	4.06[c]		−3.10[c]
	5.51[c]	−2.90[c]		−8.49[c]
$2G_\alpha$	28.66[c,d]	−2.01[c]	−12.35	−6.04[c]
	14.79	−2.91[c]		−7.30[c]
$2H_\alpha$	32.35[c]	−4.07[c]	−10.82	−8.37[c]
	18.76	−4.15[c]		−10.23[c]
$2H_\beta$	21.4[c,d]	−4.10[c]	−13.02	−2.85[c]
	16.1[c,d]	−3.25[c]		−1.03[c]

[a] Other protons were omitted for clarity. [b] α, major isomer; β, minor isomer. [c] Broadened signal at room temperature. [d] Recorded at 60 °C; all signals sharpened upon raising the temperature.

procedure.[11] Handling of this air- and moisture-sensitive complex was facilitated by employing standardized solutions in organic solvents (aromatic or aliphatics, 0.2–0.5 M); these solutions can be stored under argon at room temperature during several months without loss of reactivity. The reactions with carbonyl compounds were very clean and rapid (1–2 min) (Scheme I). After workup, the methylenation product is the only compound observed and can be isolated in high yields. The list of representative carbonyl compounds employed in this study is illustrated in Table I.

Inspection of Table I reveals that the reaction of the uranium metallacycle 1 with a variety of aliphatic, aromatic, and cyclic carbonyl compounds is a general high yield operation. Entries C, D, and F–H illustrate the important point that no olefin isomerization occurs in any of these reactions. Entries F and G show that the reaction can be extended to easily enolizable ketones without noticeable formation of intermediate enol addition compound,[13] and entries E and H establish the superiority of this method on the Wittig reaction.[14]

The intermediate metallacycles 2 were almost quantitatively formed[15] and can be isolated in good yields. ^{1}H NMR affords interesting information on their geometry and on the stereoselectivity of the insertion reaction. Table II summarizes relevant spectral data of spiro compounds **2C–H**.[16] The $N(SiMe_3)_2$, $SiMe_2$, and CH_2 protons of **2D**, **2E**, and both **2Cα** and **2Cβ** were equivalent, the six-membered ring containing the tetrahedral uranium atom appeared also to be quite planar at room temperature, and the broadening of these signals in **2E–H** spectra could be due to a dramatic increase of the steric crowding around the nitrogen atom.[11]

2C and **2H** were, in fact, mixtures of the two expected diastereoisomers in the ratio α/β, 2/1 and 20/1, respectively, whereas only one diastereoisomer was obtained for the bimetallic compound **2G**. The stereochemistry of this insertion reaction is under investigation and will be discussed elsewhere.

Acknowledgment. We thank D. Arnoult for his technical assistance.

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[13] About 3% of the F and G starting ketones were recovered after workup even if a large excess of 1 was used. ^{1}H NMR monitoring of the reaction showed the complete consumption of the ketone whereas an additional broad singlet appeared near the $N(SiMe_3)_2$ signals of **2F** (δ 2.51) and **2G** (δ 3.96). This singlet could be attributed to the 54 equiv of $N(SiMe_3)_2$ protons of the enol addition compounds (yields determined by comparison of intensities of signals of the $N(SiMe_3)_2$ protons: 3–5 %).

[14] Greenwald, R.; Chaykovsky, M.; Corey, E. J. *J. Org. Chem.* **1963**, *28*, 1128.

[15] Based on ^{1}H NMR analysis of the crude product.

[16] Cyclanic protons of **2F** and **2G** appeared as poorly resolved multiplets. All other signals of cyclanic, cyclopentadienyl, aromatic, and alkyl protons were well resolved, and the chemical shift dispersion (40–50 ppm) allowed observation and assignment of every resonance even at 100 MHz.

Synthesis of Diacids and Keto Acids by Ruthenium Tetraoxide Catalyzed Oxidation of Cyclic Allylic Alcohols and α,β-Unsaturated Ketones

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In the course of synthesizing both enantiomers of the pheromone grandisol,[1] we needed to oxidatively cleave tertiary, allylic alcohol 1 to the known keto acid 2. This transformation has been reported by Zurflüh et al.,[2] who employed osmium tetraoxide and sodium periodate in a two-phase system of ether and water[3] to obtain a 51% isolated yield of keto acid 2. In our hands, the reaction gave erratic results with yields as low as 30%. In 1981, the Sharpless group reported a much improved method for cleaving simple olefins with a catalytic amount of ruthenium tetraoxide and a stoichiometric amount of sodium periodate.[4] Before Sharpless reported his results, catalytic ruthenium oxidations were troublesome and erratic.[5] As an extension of his work, we report the oxidative cleavage of cyclic allylic alcohols and α,β-unsaturated ketones.

In all of the reactions reported here, one or more carbon atoms are excised from a mono- or bicyclic compound, leaving either a keto acid or a diacid. There are many possible paths from the starting compound to the final, isolated product, and indeed there may be no one predominant path. In any event, the following reactions are probably occurring. First, any lower valence forms of ruthenium are oxidized to the tetraoxide. The initial olefin

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[1] Webster, F. X.; Silverstein, R. M. *J. Org. Chem.*, in press.

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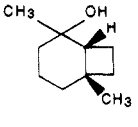
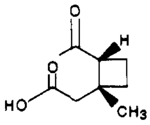
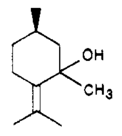
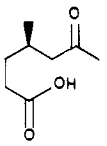
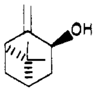
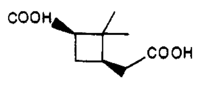
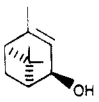
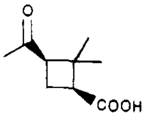
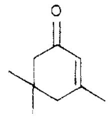
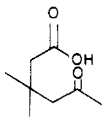
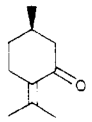
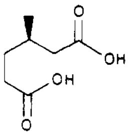
[5] Berkowitz, L. M.; Rylanders, P. M. *J. Am. Chem. Soc.* **1958**, *80*, 1261.

Table I. Results from the Oxidative Cleavage of Various Substrates

substrate	reaction conditions		product	yield of isolated, pure product, %
	time, h	equiv of $NaIO_4$		
 1	5	5.5	 2	60
 3	24	5	 4	66
 5	5	5	 6	76
 7	5	5.5	 8	78
 9	24	5.5	 10	86
 11	5	5	 12	92

reacts with and is cleaved by RuO_4. The compound now must contain vicinal oxygen atoms in unspecified oxidation states. The compound is cleaved again by the well-known periodate reaction with the loss of one or more carbon atoms. Finally, any remaining aldehyde groups are oxidized to acids. The main difference between our procedure and the one described by Sharpless is the excision of one or more carbon atoms in our procedure.

The mildness of the reaction is best illustrated with the reaction of allylic alcohol **1** to produce the cis-vicinal-substituted cyclobutane **2**. Zurflüh et al.[2] have shown that this compound is easily isomerized to the trans compound. Since ruthenium/periodate cleavage of allylic alcohol **1** gives only *cis*-**2**, we assume that the stereochemistry of the starting materials is conserved in the product of all cases tested. The other easily epimerized cyclobutanes, **6** and **8**, were found to be pure compounds by ^{13}C NMR spectrometry.

Besides the allylic alcohol **1**, we chose several other allylic alcohols and α,β-unsaturated ketones to define the scope and limitations of the reaction. Table I, summarizing the results of our survey, shows that the reaction is quite general and yields range from good to excellent. The alcohols in Table I are listed in order of decreasing propensity toward dehydration and, as can be seen, the yields increase accordingly. The last two entries, both enones, gave excellent yields.

The oxidation of the allylic alcohol **3** (from the addition of ethereal methyllithium to (+)-pulegone) gave a 66% yield of an optically active keto acid **4** ((+)-4-methyl-6-oxoheptanoic acid) that had been previously synthesized[6] in six steps (without a reported yield) from (+)-pulegone. The oxidation of (+)-*trans*-pinocarveol (**5**) yielded (−)-*cis*-pinic acid (**6**) ((−)-3-carboxy-2,2-dimethylcyclobutaneacetic acid), which had been recently reported as a natural product[7] and synthesized in two steps from α-pinene in unspecified yield.[8] We assume a cis configuration for pinic acid on the basis of stereochemical conservation and agreement of our ^1H NMR spectrum with that of racemic *cis*-pinic acid (mp 101–102 °C) prepared by Subramanian and Krishna Rao.[7] Grandperrin[9] and Lewis and Hedrick[10] reported a mp of 79–80 °C and a rotation of $[\alpha]_D$ −1.9° (*c* 0.6, $CHCl_3$) for "optically pure" (−)-*cis*-pinic acid. Although we obtain the product in 76% yield and record the highest optical rotation to date ($[\alpha]^{24}_D$ −4.9° (*c* 0.3, $CHCl_3$)), our compound is an oil despite the ^{13}C NMR evidence for chemical purity. *trans*-Verbenol (**7**) gave a 78% yield of (+)-*cis*-pinononic acid (**8**) ((+)-*cis*-3-acetyl-2,2-dimethylcyclobutanecarboxylic acid), which had been previously synthesized by the ozonolysis of verbenone in 35% yield.[11]

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[6] Joulain, D. *Riv. Ital. Essenze, Profumi, Piente Off., Aromi, Saponi, Cosmet., Aerosol* **1976**, *58*, 479; *Chem. Abstr.* **1976**, *86*, 95852.

[7] Subramanian, L. R.; Krishna Rao, G. S. *Tetrahedron* **1969**, *25*, 1749.

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[9] Grandperrin, M. *Ann. Chim. (Paris)* **1936**, *6*, 5.

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The enone isophorone (**9**) gave 3,3-dimethyl-5-oxohexanoic acid (**10**) in 86% yield.[12] Pulegone (**11**) gave a 92% yield of optically pure 3-methyladipic acid (**12**), which had been previously synthesized in unspecified yield by ozonization of pulegone.[13] A comparison of substrates **3** and **11** suggests a useful strategy: Oxidation with RuO_4 of an enone produces a dicarboxylic acid, whereas prior conversion of an enone with an alkyllithium to a tertiary allylic alcohol produces a keto acid with two different functional groups for further elaboration. (Cf. **12** with **4**.)

Experimental Section

General. All of the substrates, except **1** and **3**, are commercially available. The chemical purity of all substrates was checked by ^{13}C NMR, which showed no detectable impurities (<2%). Mass spectra were obtained on a Finnigan 4000 (quadrupole) by direct inlet to the source with an ionizing voltage of 70 eV. Both ^{1}H and ^{13}C NMR spectra were obtained on a Varian XL-100. Unless otherwise noted, all NMR samples were run in $CDCl_3$ with Me_4Si as internal reference. Optical rotations were obtained on Perkin-Elmer 141 polarimeter. Melting points are uncorrected.

(+)-3-Acetyl-2,2-dimethylcyclobutaneacetic Acid ((+)-*cis*-Pinononic Acid (8)). The oxidation of *trans*-verbenol (**7**) is representative. A stock solution was prepared from ruthenium chloride trihydrate (Aldrich), which contained 1.92 mg of $RuCl_3$/mL of H_2O. (+)-*trans*-Verbenol (**7**) ($[\alpha]^{24}_{\mathrm{D}}$ +5.7° (*c* 0.5, $CHCl_3$)) (760 mg, 5 mmol) was dissolved in 10 mL of CCl_4 and 10 mL of acetonitrile in a 100-mL, three-neck flask equipped with a condenser and magnetic stirrer. Sodium periodate (5.88 g, 27.5 mmol) was suspended in the solution with vigorous magnetic stirring. The standard rutherium chloride solution (15 mL; 28.8 mg, 0.14 mmol of $RuCl_3$) was added in one portion, and vigorous stirring was continued for 5 h. Sufficient water was then added to dissolve the separated sodium iodate. The solution was extracted with 3 × 50 mL of CH_2Cl_2, and the organic extracts were combined, dried (Na_2SO_4), and evaporated. The residue, which contained highly colored ruthenium species, was dissolved in 50 mL of diethyl ether and filtered through Celite. If necessary (usually not), residual color may be removed by stirring the ether solution with a small amount of solid $NaHSO_3$. Evaporation of the ether left 664 mg (78%) of (+)-*cis*-pinononic acid: mp 99–100 °C (CCl_4); ^{1}H NMR δ 0.98 (s, 3 H), 1.48 (s, 3 H), 1.90 (m, 1 H), 2.09 (s, 3 H), 2.44–3.01 (m, 3 H), 10.87 (s, 1 H); ^{13}C NMR δ 18.06, 18.86, 30.00, 30.31, 44.95, 45.01, 52.99, 177.89, 206.79; MS, *m/z* (relative intensity) 43 (100), 55 (26), 71 (18), 82 (22), 95 (9), 100 (8), 109 (5) 124 (2), 152 (1), 170 (<1); $[\alpha]^{25}_{\mathrm{D}}$ +18.2° (*c* 1.4, $CHCl_3$).

(+)-4-Methyl-6-oxoheptanoic Acid (4). 1,5-Dimethyl-2-(1-methylethylidene)cyclohexan-1-ol (**3**) (1.13 g, 6.0 mmol) [from (+)-pulegone (**11**); Givaudan Corp.; $[\alpha]_{\mathrm{D}}$ +23.7° (neat)] gave 0.73 g of **4** (66%) as an oil: ^{1}H NMR δ 0.95 (d, *J* = 7 Hz, 3 H), 1.62 (m, 2 H), 2.10 (m, 1 H), 2.18 (s, 3 H), 2.40 (m, 4 H), 11.25 (s, 1 H); ^{13}C NMR δ 18.84, 28.09, 29.72, 30.90, 31.11, 50.04, 178.01, 208.43; MS, *m/z* 43 (100), 55 (16), 58 (23), 69 (12), 73 (4), 83 (4), 85 (4), 97 (2), 112 (1), 125 (1), 140 (1), 158 (1); $[\alpha]^{25}_{\mathrm{D}}$ +9.3 ° (*c* 2.3, $CHCl_3$).

(−)-3-Carboxy-2,2-dimethylcyclobutaneacetic Acid ((−)-*cis*-Pinic Acid, 6). (+)-*trans*-Pinocarveol [IFF; $[\alpha]^{24}_{\mathrm{D}}$ +52.7° (*c* 0.8, $CHCl_3$)] (**5**) (500 mg, 3.2 mmol) gave 460 mg (76%) of **6**. The following changes in the standard procedure were made. After the reaction was completed, the pH was lowered to 2 with 1 N HCl. Since the final traces of ether could not easily be removed, the product was dissolved in dilute $NaHCO_3$, acidified, and extracted with 3 × 20 mL of CH_2Cl_2. This treatment gave pure **6** as an oil:[9] ^{1}H NMR δ 1.02 (s, 3 H), 1.23 (s, 3 H), 1.70–2.50 (m, 5 H), 2.74 (t, *J* = 7 Hz, 1 H), 11.63 (s, 2 H); ^{13}C NMR δ 17.61, 24.31, 29.96, 35.18, 38.01, 43.00, 46.17, 178.93, 179.21; MS, *m/z* (relative intensity) 42 (100), 45 (48), 55 (36), 69 (65), 82 (43), 100 (71), 114 (29), 124 (2), 140 (10), 150 (1), 16 8 (3); $[\alpha]^{25}_{\mathrm{D}}$ −4.9 (*c* 0.3, $CHCl_3$).

3,3-Dimethyl-5-oxohexanoic Acid (10). Isophorone (**9**) (1.11 g, 3.0 mmol) gave 1.09 g (86%) of **10** as an oil: ^{1}H NMR δ 1.00 (s, 6 H), 2.02 (s, 3 H), 2.38 (s, 2 H), 2.49 (s, 2 H), 11.34 (s, 1 H); ^{13}C NMR δ 27.81, 31.62, 32.23, 44.19, 52.04, 177.50, 208.41; MS, *m/z* (relative intensity) 43 (100), 58 (19), 70 (4), 83 (12), 101 (7), 112 (4), 125 (1), 140 (1), 158 (4).

(+)-3-Methyladipic Acid (12). (+)-Pulegone (1.07 g, 7.0 mmol) gave 1.03 g (92%) **12** as a solid: mp 85–87 °C; ^{1}H NMR δ 1.03 (d, *J* = 6 Hz, 3 H), 1.40–2.20 (m, 3 H), 2.35 (m, 4 H), 10.6 (s, 2 H); ^{13}C NMR (Me_2SO) δ 19.57, 29.71, 31.61, 31.78, 41.40, 174.05, 174.76; MS, *m/z* (relative intensity) 41 (100), 45 (64), 55 (78), 59 (39), 69 (19), 73 (12), 83 (22), 101 (13), 114 (15), 142 (2), 160 (<1); $[\alpha]^{25}_{\mathrm{D}}$ +9.5° (*c* 0.8, $CHCl_3$).

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Halide Exchange Reactions between Aryl Halides and Alkali Halides Catalyzed by Nickel Metal

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The application of metal powders in organic and organometallic synthesis has attracted considerable interest in recent years.[1-4] However, most of the investigations were focused on activated metal powders prepared by special methods. There is little work concerning the reactivities of less active, but readily available, metal powders. Such work is important because these less active powders may be more selective and easier to handle than the activated ones. In a previous report, we have demonstrated that activated nickel and cobalt powders from nickel and cobalt amalgams, respectively, react with aryl halides and benzyl halides to yield the corresponding biaryls and bibenzyls.[4] The activated nickel powders prepared by other methods[1a,b,2] also showed similar activities toward aryl bromides and aryl iodides. To compare the reactivities of these activated metals with less active ones, we investigated the reactions of aromatic halides with commercial nickel and cobalt powders. We report here the results of the exchange reactions between aryl halides and alkali metal halides mediated by these commercial metal powders. The nickel powder selectively catalyzes the aromatic halide exchanges without causing further reaction to give coupling products. The cobalt powder, however, does not exhibit any activity toward aryl halide.

Aryl halides generally do not undergo halide exchange reactions in the absence of a suitable transition metal complex. Finkelstein-type halide exchanges between aryl iodide (or bromide) and cuprous bromide (or chloride) to yield the corresponding aryl bromide (or chloride)[5] were the earliest reported. The reactions are of limited synthetic

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