π-(2-Methoxyallyl)nickel Bromide, a Reagent for the Introduction of the Acetonyl Functional Group into Organic Substrates[1]

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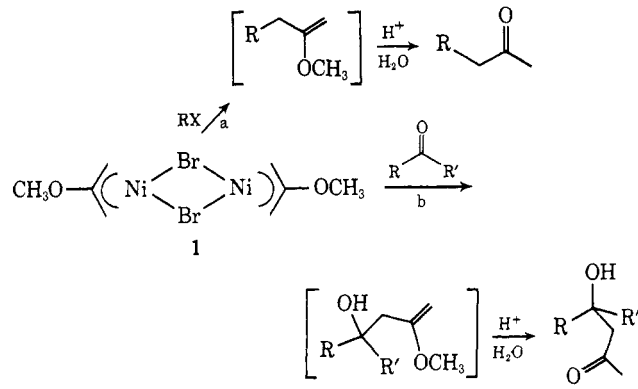
Abstract: π-(2-Methoxyallyl)nickel bromide (**1**) has been synthesized and characterized for the first time. It is prepared in high yield by the reaction of 2-methoxyallyl bromide and nickel carbonyl or bis(1,5-cyclooctadiene)nickel in benzene. It reacts with a variety of organic substrates including halides, ketones, and aldehydes to introduce the acetonyl functional group. These reactions proceed in high yield under mild conditions (25° in DMF) with high specificity. The scope of reactivity and the synthetic utility of this new complex are discussed.

π-Allylnickel halide complexes are reagents which afford mild and selective methods for carbon–carbon bond formation and are finding increasing application in organic synthesis.[2] They are readily prepared in high yield by the reaction between allylic halides and nickel carbonyl or bis(1,5-cyclooctadiene)nickel in benzene solvent.[2] The resulting red solids are purified by crystallization and are stable in the absence of air for at least 1 year. Thus, a large quantity of the desired complex can be prepared in one reaction and stored for long periods, and portions can be used and handled like other discrete, moderately air-sensitive solid reagents. In polar, coordinating solvents such as DMF or HMPA, π-allylnickel halide complexes react with organic halides to replace the halogen with the allyl group,[3] with ketones and aldehydes to produce homoallylic alcohols,[4] and with quinones to produce allylquinones.[5] However, they are unreactive toward esters, acid chlorides, amides, nitriles, and alcohols,[6] thus offering a degree of selectivity not available with the corresponding allylmagnesium, -zinc, or -lithium reagents. Furthermore, these unreactive functional groups may be incorporated into the nickel-complexed allyl group, allowing the introduction of functionalized allyl groups into reactive organic substrates. For example, π-(2-carbethoxyallyl)nickel bromide has been reacted with ketones and aldehydes to produce α-methylene-γ-butyrolactones.[4] The recently reported preparation of 2-methoxyallyl bromide[7] suggested the possibility of synthesizing π-(2-methoxyallyl)nickel bromide (**1**). This complex is of interest because it offers the possibility of introducing the acetonyl moiety (after facile hydrolysis of the initially formed enol ether) into reactive organic substrates under mild, neutral conditions (Scheme I) with both the unusual

Scheme I



reactivity patterns (aryl, vinyl, allyl halides > alkyl halides > aldehydes > ketones) and the selectivities characteristic of π-allylnickel halide complexes. The potentially broad synthetic applicability of complex **1** prompted a thorough investigation of both its preparation and its reactions with organic substrates.

Results and Discussion

Preparation and Characterization of π-(2-Methoxyallyl)nickel Bromide (1). Complex **1** is most conveniently prepared by the reaction of 2-methoxyallyl bromide with excess nickel carbonyl in refluxing benzene. The fact that the 2-methoxyallyl bromide available by published methods[7] is contaminated with ~30% of a mixture of the vinyl bromide, bromoacetone, and the bromoketal (which cannot be removed by distillation) does not interfere, since nickel carbonyl reacts *only* with the allylic bromide, and the other impurities are removed in a subsequent step (recrystallization). The 2-methoxyallyl bromide requires a somewhat higher temperature (80°) to react with nickel carbonyl than is necessary for allyl bromide (50°) or 2-carbethoxyallyl bromide (30°). However, at this temperature the reaction proceeds smoothly to produce **1** in 75% yield (based on allylic bromide) after crystallization from ether at −78°.

Complex **1** can also be prepared by the reaction of the allylic bromide with bis(1,5-cyclooctadiene)nickel in benzene at 4°, but yields from this procedure are variable. Frequently catalytic decomposition of the

(1) A portion of this work was introduced in preliminary form at the Sixth International Conference on Organometallic Chemistry, University of Massachusetts, Amherst, Mass., August 13–17, 1973.

(2) For recent reviews, see (a) M. F. Semmelhack, *Org. React.*, **19**, 115 (1972); and (b) R. Baker, *Chem. Rev.*, **73**, 487 (1973).

(3) E. J. Corey and M. F. Semmelhack, *J. Amer. Chem. Soc.*, **89**, 2755 (1967).

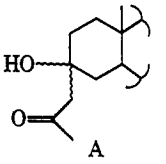
(4) L. S. Hegedus, S. D. Wagner, K. Siirala-Hansen, and E. L. Waterman, in preparation. See ref 3 for the first report of this type of reaction.

(5) L. S. Hegedus, E. L. Waterman, and J. Catlin, *J. Amer. Chem. Soc.*, **94**, 7155 (1972).

(6) These substrates were unreactive with an array of π-allylnickel halide complexes under reaction conditions sufficiently severe to cause thermal decomposition of the nickel complex. A report of full details of these experiments is in preparation.[4]

(7) C. Greenwood and H. M. R. Hoffmann, *J. Org. Chem.*, **37**, 611 (1972).

Table I. Reaction of π-(2-Methoxyallyl)nickel Bromide (1) with Organic Substrates[a]



A

Substrate	Time, hr	Temp, °C	Product	Yield, %[b]
Iodobenzene	3	25	1-Phenyl-2-propanone	73
6′-Bromopapaverine (**3a**)	16	25	6′-Acetonylpapaverine (**3b**)	73
Cyclohexyl iodide	24	25	Cyclohexylacetone	88
2-Iodooctane	5	25	4-Methyl-2-decanone	83
Geranyl bromide	10	25	Geranylacetone	58[c]
2-Carbethoxy-3-bromopropene	10	25	5-Carbethoxy-5-hexen-2-one	84
trans-β-Bromostyrene	1	25	*trans*-5-Phenyl-4-penten-2-one	87[d]
cis-β-Bromostyrene	1	25	*cis*-5-Phenyl-4-penten-2-one	84[d]
1-Bromo-1-propene	1	25	4-Hexen-2-one	12
			3-Hexen-2-one	71
Benzyl bromide	24	25	4-Phenyl-2-butanone	82
	6	40		
Benzaldehyde	24	25	4-Phenyl-4-hydroxy-2-butanone	67
	1	50		
Heptaldehyde	24	25	4-Hydroxy-2-decanone	65[e]
	4	50		
5α-Cholestan-3-one	24	25	A	76[f]
	1	50		

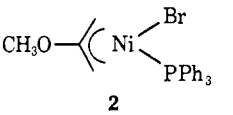
[a] Reactions were run in DMF solvent. [b] Reported yields are of isolated products purified by distillation or chromatography. No attempt to maximize yields has been made. [c] Substantial amounts (34%) of bigeranyl were obtained. [d] This reaction was >95% stereospecific. [e] About 30% of 3-decen-2-one, from elimination of H_2O during purification, was obtained. [f] The ratio of β to α acetonyl isomers was 2.1:1.

$(COD)_2Ni$ to metallic nickel results after only a few drops of the allylic halide has been added. On other occasions substantial amounts of unidentified impurities are observed. Since the procedure based on nickel carbonyl is reliable, easy to carry out, and produces high yields of easily purified complex, it is the method of choice for the production of complex **1**.

π-(2-Methoxyallyl)nickel bromide (**1**) as prepared in the above manner is a brick red, microcrystalline solid (mp 96–98° dec, argon filled, sealed capillary), soluble in benzene, ether, THF, DMF, and chloroform but insoluble in alkanes such as pentane or cyclohexane. Like most π-allylnickel halide complexes, it is moderately air sensitive as a solid but decomposes in solution immediately upon exposure to air. It can be stored as a solid in the absence of air for at least six months.

The mass spectrum of the complex has a parent ion cluster of peaks at *m/e* 416, 418, 420, 422, and 424 with ratios 6:18.5:18:7:1, as expected for $C_8H_{14}Br_2Ni_2O_2$.[8] The nmr spectrum (benzene–TMS) of the complex consists of an AB quartet [δ_A 1.31 (2 H, protons anti to CH_3O) and δ_B 2.53 (2 H, protons syn to CH_3O, J_{AB} = 2.5 Hz)] and a singlet [δ 3.29 (3 H, CH_3O)]. This is a typical spectrum for this type of complex.[9] The infrared spectrum was also typical.[10]

Treatment of a benzene solution of complex **1** with 1 equiv of triphenylphosphine led to immediate precipitation of the orange triphenylphosphine-π-(2-methoxyallyl)nickel bromide (**2**) (mp 173–174° dec, argon filled, sealed capillary) resulting from the bridge-splitting reaction characteristic of π-allylnickel halide complexes.[11] Complex **2** also had infrared and nmr spectra



2

typical of this type of complex. Both complexes **1** and **2** had acceptable elemental analyses.

Reactions of Complex 1 with Organic Substrates. Having developed methods to produce large quantities of complex **1** in high yield, its utility as a carbon–carbon bond-forming reagent in organic synthetic transformations was next examined. The general approach is summarized in Scheme I, and the experimental results are collected in Table I. The reactions were carried out by the addition of the substrate to a DMF solution of complex **1** under an argon atmosphere. The disappearance of starting material was followed by tlc. Upon completion the reaction mixture was partitioned between ether and aqueous HCl (3%). The ether phase was washed several times with 3% HCl to ensure complete hydrolysis of the initially formed enol ether (Scheme I). After drying and removal of solvent under vacuum, the crude material (usually >90% of the desired product) was purified by distillation or chromatography.

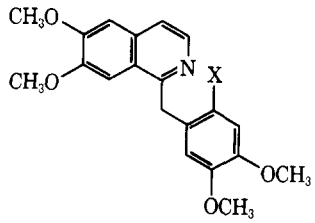
As is observed with other π-allylnickel halide complexes, **1** is generally reactive with organic halides (Scheme I, path a). Thus, iodobenzene is converted to 1-phenyl-2-propanone in 3 hr at 25°, while 6′-bromopapaverine (**3a**) requires longer reaction times (16 hr) to convert to 6′-acetonylpapaverine (**3b**). Alkyl iodides are similarly reactive, converting to the corresponding ketones in high yield at 25°. Allylic halides have been reported to react with π-allylnickel halide complexes to give all possible coupling products because of rapid equilibration of the allylic bromide with the π-allyl-

(8) The calculated ratio of peaks for a species containing two nickel atoms with isotopes 58 (68%) and 60 (26%) and two bromine atoms with isotopes 79 (50%) and 81 (50%) is 6.8:18.7:18.1:7.2:1.

(9) E. O. Fischer and H. Werner, "Metal π Complexes," Elsevier, Amsterdam, 1966, p 177.

(10) M. F. Semmelhack, Ph.D. Thesis, Harvard University, 1967, p 109.

(11) G. Wilke, *Angew. Chem., Int. Ed. Engl.*, **5**, 159 (1966).



3a, X = Br
b, X = CH_2COCH_3

nickel halide complex.[12] Indeed, **1** reacts with geranyl bromide to produce geranyl acetone, as well as a substantial amount (34%) of bigeranyl, from symmetric coupling of geranyl bromide. However, with 2-carbethoxy-3-bromopropene, **1** reacts to give *exclusively* the cross-coupled product, 5-carbethoxy-5-hexen-2-one, indicating that in this case halogen–metal exchange does *not* occur to any great extent. Vinyl bromides are quite reactive toward **1**, reacting to completion in less than 1 hr at 25°, to produce β,γ-unsaturated ketones. Furthermore, with the β-bromostyrenes, the reaction is >95% stereospecific, with *cis*-β-bromostyrene yielding *cis*-5-phenyl-4-penten-2-one, and the trans bromide producing the trans ketone. On the other hand, extensive β,γ to α,β rearrangement of the double bond is observed in the product from 1-bromo-1-propene (mixture of cis and trans isomers). This probably results during the acid hydrolysis of the enol ether and could possibly be avoided by careful control of conditions for this step. Finally, benzyl bromide reacts sluggishly with **1**, to produce the corresponding ketone in high yield.

The reaction of **1** with organic carbonyl compounds was also examined. Although less reactive than most of the organic halides studied, benzaldehyde and *n*-heptaldehyde react to give the corresponding 4-hydroxy-2-ketones (Scheme I, path b) in moderate yields. Similarly, 5α-cholestan-3-one produces a 2.1:1 mixture of the α and β isomers of the corresponding hydroxy ketones. In contrast to base-catalyzed condensations, *in situ* elimination of H_2O to form conjugated enones is *not* a major pathway. Furthermore, esters, amides, acid chlorides, and nitriles are *unreactive* toward **1**,[6] allowing a degree of specificity not available with base-catalyzed acetonylations of ketones and aldehydes.

Thus, π-(2-methoxyallyl)nickel bromide is a useful reagent for the introduction of the acetonyl functional group into organic halides, aldehydes, and ketones under essentially neutral, very mild conditions, in high yield. Because of its unusual order of reactivity, and specificities, it is a powerful complement to existing methods for this type of synthetic transformation.

Experimental Section

General. All melting points are uncorrected. Infrared (ir) spectra were measured with a Perkin-Elmer Model 337 spectrometer. Nuclear magnetic resonance (nmr) spectra were measured with a Varian Associates Model A60A with TMS internal standard. Mass spectra were measured with an Associated Electronics Industries MS-12 mass spectrometer. Layer chromatography was performed using Brinkman silica gel PF254 analytical and preparative plates, visualized by uv light. Microanalyses were performed by Midwest Microanalytical Laboratory, Indianapolis, Ind. All manipulations of the nickel complex were carried out under an argon atmosphere.

Materials. DMF was distilled from calcium hydride and stored under an argon atmosphere. Benzene (Fisher, reagent grade) was used without further purification. Nickel carbonyl was purchased from Matheson in 1 lb lecture bottles. Bis(1,5-cyclooctadiene)nickel was prepared by the method of Semmelhack.[2a] The method of Greenwood and Hoffmann[7] was followed to prepare 2-methoxyallyl bromide. 2-Carbethoxyallyl bromide was prepared by the method of Ferris.[13] *cis*-β-Bromostyrene was prepared by the procedure of Grovenstein and Lee[14] and purified by recrystallization from pentane at −45°. 6′-Bromopapaverine was prepared by the procedure of Spath and Lang.[15] All other substrates were commercial materials purified by standard methods.

Preparation of π-(2-Methoxyallyl)nickel Bromide (1). (a) From 2-Methoxyallyl Bromide and Nickel Carbonyl. *CAUTION!! Nickel carbonyl is an exceedingly toxic, volatile (bp 43°) liquid. All operations involving this compound must be carried out in an efficient draft hood.*[16]

Benzene (380 ml) was placed in a 1-l. three-necked flask containing a large magnetic stirring bar and fitted with a stopcock, a serum cap, and a cold finger condenser filled with a salt–ice mixture and vented through an empty trap to prevent suck-back, and then a trap filled with concentrated HNO_3 to decompose any nickel carbonyl which escaped from the reaction vessel. The system was thoroughly flushed with argon. With the system open to the trap, nickel carbonyl (38.5 ml)[17] was added *via* syringe, and the mixture was heated to 50°. The 2-methoxyallyl bromide (~70% pure) (16 g, ~75 mmol) was added, and the mixture was heated to reflux with rapid stirring. A deep red color rapidly developed, and CO evolution began.

After 0.75 hr at reflux, the mixture was very dark red, and CO evolution had slowed considerably. The solution was cooled to 25° and the condenser replaced with a stopper. The solution was evaporated to dryness under aspirator vacuum through a −78° trap followed by a −196° trap.[18] The red-brown nonvolatile residue was taken up in argon-saturated ether and filtered under a positive pressure of argon, and the residue on the filter was washed with ether until the washes were colorless. The dark red filtrate was concentrated under aspirator vacuum until a brick red precipitate began to form. The solution was then cooled to −78° to complete crystallization, and the supernatant was removed through a syringe needle attached to an aspirator. After drying under vacuum, the yield was 12.9 g (80%) of a brick red solid: mp 96–98° (sealed capillary); ir (KBr), 2980 (w), 2940 (w), 1720 (w), 1480 (s), 1470 (s), 1460 (s), 1432 (m), 1332 (s), 1260 (w), 1186 (w), 1060 (s), 950 (w), 896 (m), 820 (s) cm^{-1}; nmr (benzene–TMS) AB quartet, δ_A 1.31 (2 H, protons anti to OCH_3) and δ_B 2.53 (2 H, protons syn to OCH_3, J_{AB} = 2.5 Hz), singlet, δ 3.29 (3 H, OCH_3); mass spectrum, parent ion cluster *m/e* 416, 418, 420, 422, 424, ratio 6:18.5:18:7:1.

Anal. Calcd for $C_8H_{14}Br_2Ni_2O_2$: Ni, 27.99; Br, 38.15. Found: Ni, 27.62; Br, 38.00.

(b) From 2-Methoxyallyl Bromide and Bis(1,5-cyclooctadiene)-nickel. Bis(1,5-cyclooctadiene)nickel (2.63 g, 9.60 mmol) was suspended in argon-saturated benzene (40 ml) in a 100-ml two-neck flask fitted with a stopcock and a dropping funnel and was cooled to 4°. The 2-methoxyallyl bromide (1.45 g, 9.6 mmol) in 5 ml of benzene was added dropwise to the stirred slurry. A deep red color developed immediately, and some metallic nickel separated. The mixture was allowed to warm to 25° and was stirred at this temperature for 0.5 hr. It was then filtered under argon and concentrated to ~20 ml under aspirator vacuum, and petroleum ether (75 ml) was added. The resulting red slurry was cooled to −20° to complete crystallization, and the supernatant was removed with a syringe. After drying under vacuum the yield was 1.00 g (55%) of a brick red solid.

(12) E. J. Corey, M. F. Semmelhack, and L. S. Hegedus, *J. Amer. Chem. Soc.*, **90**, 2416 (1968).

(13) T. Ferris, *J. Org. Chem.*, **20**, 780 (1955).

(14) E. Grovenstein and D. E. Lee, *J. Amer. Chem. Soc.*, **75**, 2639 (1953).

(15) E. Spath and N. Lang, *Chem. Ber.*, **54**, 3064 (1921).

(16) See ref 2a, p 160 for detailed information on the handling and toxic effects of nickel carbonyl.

(17) Nickel carbonyl was transferred by inverting the lecture bottle and running a slight excess into an erlenmeyer flask. It was rapidly withdrawn into a syringe and added to the reaction vessel. Any excess nickel carbonyl was poured into concentrated HNO_3 to decompose it. Large amounts of nickel carbonyl are more safely decomposed by treatment with a solution of I_2 in benzene. All manipulations were carried out in an efficient hood.

(18) The trapped volatile material was treated with excess I_2 to decompose nickel carbonyl.

Preparation of Triphenylphosphine-π-(2-methoxyallyl)nickel Bromide (1). Triphenylphosphine (0.29 g, 1.10 mmol) in 5 ml of ether was added to complex **1** (0.23 g, 0.55 mmol) in 10 ml of ether under an argon atmosphere at 25°. An orange precipitate formed immediately. After stirring at 25° for 0.5 hr, the slurry was allowed to settle, and the supernatant was removed with a syringe. After washing with 10 ml of ether and drying under vacuum, the yield of **2** was 0.50 g (97%): mp, 173–174° dec (sealed capillary); ir (KBr) 3080 (w), 1489 (m), 1482 (m), 1460 (m), 1440 (s), 1434 (s), 1336 (m), 1330 (s), 1092 (m), 1070 (s), 818 (s), 755 (s), 744 (s), 699 (s), 692 (s) cm^{-1}; nmr ($CDCl_3$–TMS) δ 2.08 (2 H, broad singlet), 2.93 (2 H, CH_2 broad singlet), 3.28 (3 H, OCH_3 singlet), 7.5 (15 H, aromatic multiplet).

Anal. Calcd for $C_{22}H_{22}BrNiOP$: Ni, 12.42; Br, 16.92. Found: Ni, 12.00; Br, 17.20.

General Procedure for the Reaction of 1 with Organic Substrates. Reactions were carried out in a 100-ml one-neck flask with a side arm capped with a serum cap containing a magnetic stirring bar and fitted with a stopcock. The reaction flask was flushed with argon and placed in a nitrogen-filled glove bag along with the flask containing complex **1**. The desired amount of **1** (1–2 mmol) was transferred into the reaction flask through the side arm (in the glove bag), the side arm was recapped with the serum cap, and the reaction flask was removed from the glove bag. The complex was dissolved in argon-saturated DMF (30 ml solvent/mmol complex) giving a deep red solution.[19] Liquid reactants (1.8–3.6 mmol) were directly added to the reaction flask, while solid reactants were dissolved in a minimum amount of DMF and added as solutions. With organic halides as reactants, the solution turned emerald green upon completion, whereas with ketones and aldehydes, it turned brown-orange. Upon completion, the reaction mixture was poured into a separatory funnel containing 50 ml of aqueous 3% HCl and 50 ml of ether and was thoroughly shaken. The aqueous phase was washed with three 20-ml portions of ether, and the combined ether extracts were washed with three 50-ml portions of aqueous 3% HCl to ensure complete hydrolysis of the enol ether and complete removal of DMF. The organic phase was dried over anhydrous $MgSO_4$ and solvent was removed under vacuum. The crude product, usually more than 90% pure, was purified by silica gel preparative layer chromatography or distillation.

1-Phenyl-2-propanone. Iodobenzene (0.20 g, 1.00 mmol) was added to **1** (0.23 g, 0.55 mmol) in 15 ml of DMF, and the resulting mixture was stirred for 3 hr at 25°, during which time it changed from a deep red to an emerald green color. After routine isolation and evaporative distillation pure 1-phenyl-2-propanone (98 mg, 73%) was obtained: ir and nmr spectra identical with those of authentic material; 2,4-DNP, mp 151°, undepressed by addition of authentic material (lit.[20] 154°).

6′-Acetonylpapaverine (3b). A solution of 6′-bromopapaverine (**3a**) (0.20 g, 0.48 mmol) in 5 ml of DMF was added to **1** (0.20 g, 0.48 mmol) in 10 ml of DMF. The resulting solution was stirred for 16 hr at 25°. The reaction mixture was then poured into 50 ml of aqueous 3 *N* HCl to hydrolyze the crude enol ether. The acid was neutralized by addition of Na_2CO_3 and the resulting suspension extracted with three 50 ml portions of chloroform. The combined chloroform extracts were washed with four 75-ml portions of water and dried over anhydrous magnesium sulfate. After removal of solvent under vacuum, the crude yellow solid was recrystallized from ether at −20°, producing 0.138 g (73%) of 6′-acetonylpapaverine, as white needles: mp 125–125.5°; ir ($CHCl_3$), 3.29, 3.31, 3.38, 3.39, 4.16, 5.85 (C=O), 6.12, 6.20, 6.35, 6.62, 6.72, 6.80, 6.94, 7.02, 7.88, 8.10, 8.42, 8.61, 9.05, 9.55, 10.00, 11.55; nmr ($CDCl_3$–TMS) δ 2.12 (s, 3H; $CH_3C(=O)$); 3.66, 3.82, 3.90, 4.00 (s, 3 H each, CH_3O); 3.75 (s, 2 H, $-CH_2C(=O)$); 4.48 (s, 2 H, CH_2Ph); 6.55, 6.68, 7.08, 7.32 (s, 1 H each, aromatic); AB quartet δ_A 7.41, δ_B 8.40 (J_{AB} = 6.0 Hz, 2 H, isoquinoline system).

Anal. Calcd for $C_{23}H_{25}NO_5$: C, 69.86; H, 6.37; N, 3.54. Found: C, 69.62; H, 6.57; N, 3.62.

Cyclohexylacetone. Iodocyclohexane (0.18 g, 0.86 mmol) was added to **1** (0.24 g, 0.58 mmol) in 15 ml of DMF, and the resulting mixture was stirred at 25° for 24 hr. After routine isolation and evaporative distillation (0.1 mm, 30°) 0.106 g (88%) of pure cyclohexylacetone was obtained: ir (neat) and nmr (CCl_4–TMS) spectra identical with those reported for this compound (ir spectrum, Sadtler No. 19103; nmr spectrum, Sadtler No. 2152M); semicarbazone mp 166° (lit.[21] 165–166°).

4-Methyl-2-decanone. Neat 2-iodooctane (0.174 g, 0.72 mmol) was added to **1** (0.20 g, 0.48 mmol) in 15 ml of DMF, and the resulting mixture was stirred for 5 hr at 25°. After routine isolation and evaporative distillation (120° (20 mm)) pure 4-methyl-2-decanone (0.10 g, 83%) was obtained as a colorless liquid: ir (neat) 5.81 μ (s, C=O); nmr (CCl_4–TMS) δ 0.90 (m, 6 H, CH_3CH), 1.22 (s, 10 H, $-CH_2-$), 1.50 (m, 1 H, CH), 2.03 (s, 3 H, CH_3CO), 2.18 (m, 2 H, CH_2CO); 2,4-dinitrophenylhydrazone mp 57° (lit.[22] 55–57°).

Anal. Calcd for $C_{11}H_{22}O$: C, 77.58; H, 13.02. Found: C, 77.32; H, 12.98.

Geranylacetone. Geranyl bromide (0.19 g, 0.87 mmol) was added to **1** (0.24 g, 0.57 mmol) in 15 ml of DMF. After 10 hr at 25°, the crude product was isolated as usual. Separation by tlc (silica gel, developed twice with 3:1 pentane–ether) gave two bands: R_f 0.75; 47.5 mg (34%) colorless liquid; ir (neat) 3.38, 3.42, 3.50, 6.90, 7.28 μ (–CH–); nmr (CCl_4–TMS) δ 1.58, 1.65 (broad, overlapping singlets, 18 H, $CH_3C=C$), 2.00 (m, 12 H, CH=C), 5.05 (m, 4 H, CH=C).[23] The material was bigeranyl (2,6,11,15-tetramethyl-2,6,10,14-hexadecatetraene) from coupling of the geranyl bromide:[24] R_f 0.50; 105 mg (58%) colorless liquid; ir (neat) 3.38, 3.42, 3.51 (CH), 5.81 μ (C=O), identical with that reported[25] for pure material; nmr (CCl_4–TMS) δ 1.55, 1.66 (m, 9 H, $CH_3C=C$)[c] 2.00 (m, 6 H, $CH_2C=C$), 2.04 (s, 3 H, CH_3CO); 2.29 (m, 2 H, CH_2CO), 5.05 (m, 2 H, CH=C). This compound was geranyl acetone (6,10-dimethyl-5,9-undecadien-2-one).

5-Carbethoxy-5-hexen-2-one (Ethyl-2-methylene-5-oxohexanoate). Neat 2-carbethoxyallyl bromide (0.175 g, 0.91 mmol) was added to **1** (0.26 g, 0.61 mmol) in 15 ml of DMF, and the resulting mixture was stirred for 10 hr at 25°. After routine isolation and purification by preparative layer chromatography (silica gel, developed with 5:1 pentane–ether, R_f 0.30) pure 5-carbethoxy-5-hexen-2-one (155 mg, 84%) was obtained as a colorless liquid: ir (neat) 3.35, 3.40 (CH), 5.80 (COOEt), 5.86 (C=O), 6.14 μ (C=C); nmr (CCl_4–TMS) δ 1.29 (t, 3 H, J = 7.0 Hz, CH_3 of OEt), 2.04 (s, 3 H, CH_3CO), 2.51 (s, 4 H, $=CCH_2CH_2CO$), 4.12 (q, 2 H, J = 7.0 Hz, CH_2O), 5.54 (s, 1 H, HC=C), 6.04 (d, 1 H, J = 2 Hz, HC=C). Analysis by glpc (10 ft × 0.25 in., 10% SE 30 on Chromosorb W, acid washed, 60–80 mesh, 145°) showed one peak, with a retention time of 10.4 min. A sample was collected for elemental analysis.

Anal. Calcd for $C_9H_{14}O_3$: C, 63.51; H, 8.29. Found: C, 63.28; H, 8.22.

***trans*-5-Phenyl-4-penten-2-one.** Pure *trans*-β-bromostyrene (0.23 g, 1.27 mmol) was added to **1** (0.35 g, 0.85 mmol) in 15 ml of DMF and stirred for 1 hr at 25°. After routine isolation and purification by preparative layer chromatography (silica gel, 4:1 pentane–ether, R_f 0.42) pure material (176 mg, 87%) was obtained. This product was identical in all respects with material synthesized by an independent method.[26]

***cis*-5-Phenyl-4-penten-2-one.** The reaction was run exactly as in the preceding case, starting with *cis*-β-bromostyrene, to give 170 mg (84%) of pure product: ir (neat) 3.30, 3.36, 3.48 μ (CH), 5.86 (C=O), 6.03, 6.30, 6.40, 6.72, 6.95, 7.10, 7.24, 7.38, 7.65, 8.10, 8.40, 8.50, 9.10, 9.70, 10.90, 13.10, 14.40 (cis, –CH=CH–); nmr (CCl_4–TMS) δ 2.02 (s, 3 H, CH_3CO), 3.30 (doublet of doublets, 2 H, J = 9.0 and 2.0 Hz, $=CCH_2CO-$), 5.6–6.1 and 6.5 (m, 2 H, *cis*-CH=CH), 7.20 (s, 5 H, aromatic). Upon standing, this compound slowly isomerized to the trans isomer.

4-Hexen-2-one and 3-Hexen-2-one. Neat 1-bromo-1-propene (0.15 g, 1.27 mmol) was added to **1** (0.35 g, 0.85 mmol) in 15 ml of DMF, and the mixture was stirred at 25° for 1 hr. After routine isolation the crude material (80 mg, 83%) was examined spectrally: ir (neat) 5.85 (C=O), 5.95 (conj C=O), 6.15 μ (C=C). The nmr spectrum (CCl_4–TMS) showed the product to be a 1:6 mixture of β,γ and α,β unsaturated ketones, by integration of the δ 2.05 singlet (CH_3CO of β,γ unsaturated ketone) compared with the δ 2.18 singlet (CH_3CO of α,β unsaturated ketone). This experiment demonstrated that simple vinyl bromides were reactive toward **1**, but that double bond rearrangements were facile. Analytical glpc (10 ft × 0.25 in., 10% SE 30 on Chromosorb W, acid washed,

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105°) showed two components, retention times 4.2 and 5.1 min, in a ratio of 1:6. These components were separated by preparative glpc under the above conditions. The peak with retention time 4.2 min was due to 4-hexen-2-one:[27] ir ($CHCl_3$), 3.31, 3.38, 3.42 (CH), 5.86 (C=O), 6.80–7.0 (broad), 7.10, 7.38 μ; nmr (CCl_4–TMS) δ 1.70 (m, 2 H, CH_3C=C), 2.05 (s, 3 H, CH_3CO), 3.00 (m, 2 H, =CCH_2-CO), 5.50 (m, 2 H, CH=CH).

The peak with retention time 5.1 min was due to 3-hexen-2-one;[28] ir ($CHCl_3$) 3.31, 3.38, 3.41 (CH), 5.98 (C=O), 6.16 (C=C), 6.85, 7.02, 7.36, 7.80, 7.95, 8.20, 8.40, 10.30 μ; nmr ($CDCl_3$–TMS) δ 1.08 (t, J = 7.0 Hz, 3 H, CH_3), 2.20 (m, 2 H, CH_2C=C), 2.25 (s, 3 H, CH_3CO), 6.10, (d, J = 16.0 Hz, 1 H, =CHCO), 6.90 (doublet of triplets, J = 16.0 and 6.0 Hz, 1 H, CH=CCO).

4-Phenyl-2-butanone. Benzyl bromide (0.16 g, 0.91 mmol) was added to **1** (0.26 g, 0.61 mmol) in 15 ml of DMF, and the mixture was stirred at 25° for 24 hr then heated to 40° for 6 hr. After routine isolation and evaporative distillation (115° (13 mm)) 0.14 g (82%) of 4-phenyl-2-butanone, a colorless liquid, was obtained. Its spectra were identical to those reported for authentic material (ir, Sadtler No. 13494, nmr, Sadtler No. 10232); 2,4-dinitrophenylhydrazone mp 122–123° (lit.[29] 123°).

4-Phenyl-4-hydroxy-2-butanone. Benzaldehyde (0.95 g, 0.89 mmol) was added to **1** (0.25 g, 0.59 mmol) in 15 ml of DMF, and the resulting solution was stirred at 25° for 24 hr and 50° for 1 hr. After routine isolation and purification by preparative layer chromatography (silica gel, 4:1 pentane–ether, R_f 0.62) 0.96 g (66.5%) of a colorless liquid was obtained: ir (neat) 2.92 (OH), 5.85 (C=O), 6.25–6.33, 6.67, 6.90, 13.3, 14.3 μ (aromatic); nmr (CCl_4–TMS) δ 2.00 (s, 3 H, CH_3CO), 2.65 (m, 2 H, CH_2CO), 3.78 (broad s, 1 H, OH), 4.95 (m, 1 H, PhCHOH), 7.20 (s, 5 H, aromatic); 3,5-dinitrobenzoate mp 128–129° (lit.[30] 128–129°).

4-Hydroxy-2-decanone. *n*-Heptaldehyde (0.11 g, 0.96 mmol) was added to **1** (0.27 g, 0.64 mmol) in 15 ml of DMF and the resulting mixture was stirred at 25° for 24 hr and at 50° for 4 hr. After routine isolation and purification by preparative layer chromatography (silica gel, 5:1 pentane–ether, R_f 0.40) 0.11 g (65%) of a colorless liquid was obtained: ir (neat) 2.90 (OH), 3.39, 3.51, 3.50 (CH), 5.86 μ (C=O); nmr (CCl_4–TMS) δ 0.90 (m, 3 H, CH_3), 1.30 (broad s, 10 H, $-CH_2-$), 2.10 (s, 3 H, CH_3CO), 2.46 (d, J = 7.0 Hz, 2 H, CH_2CO), 3.52 (broad s, 1 H, OH), 3.90 (m, 1 H, CHOH); semicarbazone mp 112–113° (lit.[31] 112.5–113°).

3-Acetonyl-5-α-cholestan-3-ol. A solution of **1** (0.29 g, 0.69 mmol) in 15 ml of DMF was added to 5-α-cholestan-3-one (0.26 g, 0.69 mmol), and the resulting mixture was stirred for 24 hr at 25° and 1 hr at 50°. After routine isolation, the crude material was purified by preparative layer chromatography (silica gel) developing three times with 1:1 pentane–ether. Two major bands were obtained.

Band 1: R_f 0.36, 155 mg white crystalline solid; mp 111–112°; ir ($CHCl_3$) 2.85 (OH), 3.41, 3.50 (CH), 5.88 (C=O), 6.82, 6.92, 7.11, 7.23, 7.31, 8.60, 9.50 μ; nmr ($CDCl_3$–TMS) δ 0.64 (s, 3 H, C-18 methyl), 0.74 (s, 3 H, C-19 methyl), 0.84 (d, 6 H, J = 7.0 Hz, C-25 methyls), 0.90 (d, 3 H, J = 7.0 Hz, C-20 methyl), 0.92–1.90 (m, 31 H, ring and chain $-CH_2-$ and $-CH-$), 2.18 (s, 3 H, CH_3CO), 2.56 (s, 2 H, CH_2CO), 3.44 (s, 1 H, α-OH).[32] This material was the pure β acetonyl isomer[33] in 51% yield.

Anal. Calcd for $C_{30}H_{52}O_2$: C, 81.02; H, 11.79. Found: C, 80.75; H, 11.82.

Band 2: R_f 0.30; 74 mg white solid; mp 120–122°; ir ($CHCl_3$) identical with material in band 1; nmr ($CDCl_3$–TMS) δ 0.64 (s, 3 H, C-18 methyl), 0.83 (s, 3 H, C-19 methyl), 0.86 (d, 6 H, J = 7.0 Hz, C-25 methyls), 0.90 (d, 3 H, J = 7.0 Hz, C-20 methyl), 0.92–1.90 (m, 31 H, ring and chain $-CH_2-$ and $-CH-$), 2.21 (s, 3 H, CH_3CO), 2.77 (s, 2 H, CH_2CO), 4.00 (s, 1 H, β-OH).[32] This material was the pure α acetonyl isomer[33] in 24.4% yield.

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(33) This structure assignment is based on the following arguments: (a) a 3-β-hydroxy group causes a 0.04 ppm downfield shift in the C-19 methyl absorption (N. S. Bhacca and D. H. Williams, "Applications of NMR Spectroscopy in Organic Chemistry," Holden-Day, San Francisco, Calif., 1964, p 190); since the compound in band 2 had the C-19 methyl absorption shifted 0.07 ppm downfield the OH must be β, and thus the acetonyl group α; (b) the C-19 methyl absorption for 3-β-cholestanol (Sadtler No. 9962) is δ 0.83, identical with that for the band 2 product, again indicating that the OH is β and the acetonyl group is α; (c) footnote 32.