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Titanium-Induced Reductive Coupling of Carbonyls to Olefins

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Active titanium metal, produced in a finely divided form by reduction of $TiCl_3$ with either potassium or lithium, will reductively couple ketones and aldehydes to olefins. Although the intermolecular coupling works best when two identical carbonyls are coupled to a symmetrical product, unsymmetrical couplings can also be carried out in certain cases. The unsymmetrical coupling of a diaryl ketone with another partner is particularly efficient, and a mechanism to account for this is proposed. Intramolecular dicarbonyl coupling to form rings is also possible, and the combination $TiCl_3$/Zn–Cu works best. Rings of size 4–16 and 22 are prepared in high yield. The nature of the active titanium metal is studied by scanning electron microscopy, and a mechanistic proposal accounting for all observed results is presented. It is believed that the coupling reaction occurs on the surface of the active titanium particle.

Recently, three separate research groups independently observed that low-valent titanium reagents ($TiCl_4$/Zn,[1] $TiCl_3$/Mg,[2] $TiCl_3/LiAlH_4$[3]) would reductively dimerize ketones and aldehydes to olefins. Two of these reagent systems[1,2] were reported to be effective only for aryl ketones, while our $TiCl_3/LiAlH_4$ reagent gave excellent yields in both aryl and alkyl cases.[3] Subsequently, a number of research groups used our method to prepare a variety of interesting olefins,[4-9] but, as we have reported,[10] the $TiCl_3/LiAlH_4$ reagent gives capricious results depending on the exact batches of reagents used. Although we have been unable to discover the reason for these capricious coupling results, we have found that the $TiCl_3/LiAlH_4$ reagent does reproducibly effect numerous other organic reductions.[11] We have also found that the carbonyl coupling reaction can be reproducibly carried out using active titanium metal prepared by reducing $TiCl_3$ with 3 equiv of potassium.[10] The results of our study of this Ti^0-induced coupling reaction are presented herein.

Intermolecular Carbonyl Couplings. Significant developments have occurred recently in the preparation of metals in highly active forms.[12,13] Rieke and co-workers, for example, have described a general method for the preparation of highly active metals in finely divided form by reduction of the metal halide with potassium in tetrahydrofuran (THF). Magnesium prepared by this method shows extraordinary reactivity in Grignard reagent formation.[14] We therefore reduced a slurry of $TiCl_3$ in THF with 3 equiv of potassium and observed that the resultant black slurry reductively coupled carbonyl compounds to olefins in high yield. Since the reaction is a heterogeneous one, excess titanium reagent is required and we therefore optimized conditions to find the most efficient procedure. Our results using cyclododecanone as substrate are shown in Table I.

As can be seen in the table (run 2 vs. run 1), heating the reaction for prolonged periods did not increase the yield. The use of either 1 equiv of potassium per $TiCl_3$ (run 4) or 2 (run 3) rather than the theoretical 3 gave markedly lower yields of product. Use of dimethoxyethane (DME) as solvent rather than THF had little effect. Addition of KI to the mixture[14] prior to reduction had little effect. The optimum ratio of $TiCl_3$/K/ketone was 1:3.5:0.25. It became clear in the course of these optimization experiments that material was being lost during aqueous workup, and we therefore developed a nonaqueous filtration procedure for workup (run 13; see Experimental Section). This modification allowed us to isolate excellent yields (90%) reproducibly.

With optimum conditions established, the coupling of other aliphatic ketones and aldehydes was examined and our results are given in Table II. The coupling reaction is general for aliphatic ketones and aldehydes, and good yields of products are usually obtained. Cycloalkanones of varying ring sizes couple well, and highly hindered olefins (tetraisopropylethylene) can be made in modest yields. The one obvious problem revealed by the results in Table II is that diaryl ketones (fluorenone, benzophenone) couple well, but the products do not survive. The tetraarylethylenes produced reduce further to tetraarylethanes.

It is clear that this Ti^0-induced coupling procedure is an effective one, but the use of potassium to reduce the metal halide, as recommended by Rieke, is a potentially hazardous process. We therefore examined the use of other less reactive alkali metals and were surprised to discover that lithium metal proved as effective as potassium even at temperatures far below its melting point. Thus, heating a slurry of $TiCl_3$ and 3 equiv of Li in DME for 1 h produced a black slurry which effectively coupled carbonyl compounds to olefins. This is a most surprising result for several reasons. In the first place, one would expect the solid lithium pieces to become coated on the surface and rapidly inactivated. This does not appear to happen, however, perhaps due to mechanical agitation by the stirrer. More surprising is the fact that, although the reduction of $TiCl_3$ to Ti^0 is incomplete (much unreacted lithium is recovered), the coupling still proceeds well. We do not know whether lithium is recovered because the $TiCl_3$ is reduced only to Ti(II) rather than Ti^0 or if Ti^0 is actually produced. Considering, however, both the fact that Ti(II) ($TiCl_3$ + 1 equiv of K; run 4, Table II) does not effectively couple alkyl ketones and the fact that Li is a stronger reducing agent than K, we feel that Ti^0 is probably the active species in the $TiCl_3$/Li reduction. When we investigated the reactivity of $TiCl_3$/Li for carbonyl coupling, we found that it was generally as effective as $TiCl_3$/K but was somewhat less reactive in that diaryl ke-

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Table I. Reductive Coupling of Cyclododecanone

run	molar ratio $TiCl_3$/K/ketone	solvent	time,[a] h	yield,[b] %
1	1:3:0.5	THF	18	59
2	1:3:0.5	THF	40	56
3	1:2:0.5	THF	16	38
4	1:1:0.5	THF	16	28
5	1:3:0.5	THF	15	64
6	1:3:0.5	DME	15	49
7	1:3:0.25	THF	16	67
8	1:3.5:0.25	THF	17	76
9	1:4.7:0.25	THF	13	71
10	1:3:0.25	THF[c]	15	77
11	1:3:0.25[d]	THF	16	67
12	1:3:0.25[e]	THF	16	68
13	1:3:0.25	THF	16	90[f]

[a] Heating at reflux subsequent to addition of ketone. [b] Isolated yield after aqueous workup and column chromatography. [c] Solvent deoxygenated prior to reaction. [d] KI (0.25 equiv) added prior to potassium. [e] $AlCl_3$ (1.0 equiv) added prior to potassium. [f] Isolated yield after nonaqueous workup and column chromatography.

tones gave good yields of olefin without over reduction. Some results are shown in Table III.

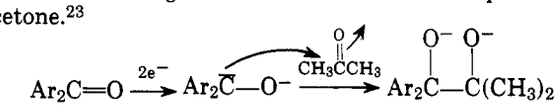
Both the $TiCl_3$/K procedure and the $TiCl_3$/Li procedure are effective. We did however examine several other possibilities. Neither Al^0, Fe^0, V^0, Cr^0, Zn^0 (all prepared by potassium reduction of their chlorides), nor commercial titanium powder had any activity. Of the systems we examined, active Ti^0 was unique.

Mixed Couplings. Thus far, we have considered only the symmetrical coupling of two identical ketones. From a synthesis point of view, it would of course be more useful to be able to effect a mixed coupling of two different ketones, yielding an unsymmetrical olefin. In practice, this mixed coupling reaction is unlikely to be successful unless certain conditions are met. We have already demonstrated that the carbonyl coupling proceeds through an intermediate pinacol dimerization,[3,10] and it is generally accepted that pinacol dimerization occurs via anion radicals.[15] The synthesis of unsymmetrical olefins by our method would therefore require a mixed pinacol reaction. Although little literature is available on mixed pinacol couplings, it appears that one generally obtains a nearly statistical mixture of the three possible products.[16-20] It was therefore our expectation that a mixed carbonyl coupling reaction could probably be carried out in a synthetically useful manner only when one carbonyl component was used in excess and when the olefin dimer of that component could be readily removed from the product mixture. Acetone is the obvious choice as the component to be used in excess, and the results of some mixed couplings between acetone and other ketones are shown in Table IV.[21]

In all cases examined, the isopropylidene products could be isolated in synthetically useful yields, and since the isopropylidenecycloalkane functionality is commonly found among sesquiterpenes, this mixed coupling reaction may prove quite useful. Further, the synthesis and spectroscopic study of *vic*-diisopropylidene compounds such as that derived from pulegone (entry 12, Table IV) has been an active field recently,[22] and the present synthesis is efficient.

Careful examination of the results in Table IV reveals an interesting fact. Although dialkyl ketones and monoaryl ketones give an approximately statistical ratio of products, the diaryl ketones benzophenone and fluorenone give only cross coupled products. This is surprising when one considers that the reduction potentials of both benzophenone and fluorenone are 1.0–1.5 V less negative than that of acetone.[23] One would therefore expect their anion radicals to form more rapidly than that of acetone, leading predominantly to symmetrical coupling. Since this is not the case, we believe it unlikely that the mixed pinacol coupling of acetone with diaryl ketones is a radical process.

An alternative mechanistic hypothesis is to assume that the initially formed diaryl ketyl further reduces to a dianion and the dianion effects a nucleophilic addition to acetone. Support for this hypothesis comes from the fact that the second reduction potential of benzophenone and fluorenone to give dianions is less negative than the first reduction potential of acetone.[23]



If this suggestion is correct, then the mixed pinacol coupling of diaryl ketones with other ketones should be a general process, not limited to cases where one inexpensive component is used in excess. We should be able to obtain good yields of mixed coupled product whenever one component of the reaction reduces to a dianion before the other component reduces to a radical anion. We have carried out several such reactions successfully, and our results are given in Table V.

The problem of mixed couplings thus remains only partially solved. A procedure is still not available to cleanly couple any desired pair of carbonyl compounds.

Intramolecular Couplings. Another type of unsymmetrical couplings which might have great synthetic potential is the intramolecular coupling of a dicarbonyl compound to form a cycloalkene. Such a procedure, were it to be successful, might be considered the formal reverse of a double bond ozonolysis.

Table II. Coupling of Carbonyl Compounds with $TiCl_3$/K

entry	registry no.	carbonyl	$\xrightarrow{TiCl_3/3K}$	product	registry no.	yield,[a] %
1	110-62-3	Valeraldehyde		5-Decene (70% trans/30% cis)		77
2	112-31-2	Decanal		10-Eicosene	66587-45-9	60
3	120-92-3	Cyclopentanone		Cyclopentylidenecyclopentane		40
4	108-94-1	Cyclohexanone		Cyclohecylidenecyclohexane		85
5	502-42-1	Cycloheptanone		Cycloheptylidenecycloheptane		86
6	502-49-8	Cyclooctanone		Cyclooctylidenecyclooctane		70
7	700-58-3	Adamantanone		Adamantylideneadamantane		91
8	565-80-0	Diisopropyl ketone		Tetraisopropylethylene		37
9	830-13-7	Cyclododecanone		Cyclododecylidenecyclododecane	53416-00-5	90
10	566-88-1	Cholestanone		Cholesterylidenecholestane	66673-25-4	85
11	486-25-9	Fluorenone		9,9′-Bifluorene		85
12	119-61-9	Benzophenone		Tetraphenylethane		80

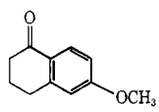
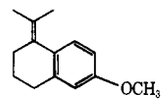
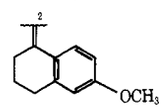
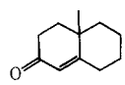
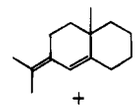
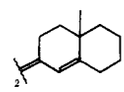
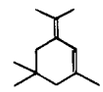
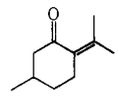
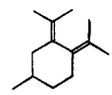
[a] Isolated yield.

Table III. Coupling of Carbonyl Compounds with $TiCl_3$/Li

entry	carbonyl[b]	$\xrightarrow{TiCl_3/3Li}$	product[c]	yield,[a] %
1	Cyclohexanone		Cyclohexylidenecyclohexane	79
2	Cycloheptanone		Cycloheptylidenecycloheptane	85
3	Cyclododecanone		Cyclododecylidenecyclododecane	65
4	Adamantanone		Adamantylideneadamantane	82
5	Benzaldehyde		Stilbene	97
6	Acetophenone		2,3-Diphenyl-2-butene (10% cis/90% trans)	94
7	Benzophenone		Tetraphenylethylene	96
8	Retinal		β-Carotene	95

[a] Isolated yield after column chromatography. [b] Registry no.: benzaldehyde, 100-52-7; acetophenone, 98-86-2; retinal, 116-31-4. [c] Registry no.: *cis*-2,3-diphenyl-2-butene, 782-05-8; *trans*-2,3-diphenyl-2-butene, 782-06-9.

Table IV. Mixed Coupling Between Acetone and Other Ketones (Acetone/Ketone = 4:1)

entry	registry no.	ketone	$\xrightarrow{TiCl_3/3Li}$	products	registry no.	yield,[a] %
1		Adamantanone		Isopropylideneadamantane	20441-18-3	63
				Adamantylideneadamantane		12
2	98-53-3	4-*tert*-Butylcyclohexanone		4-*tert*-Butylisopropylidenecyclohexane	14033-75-1	55
				Bi-4-*tert*-butylcyclohexylidene		22
3		Cycloheptanone		Isopropylidenecycloheptane	7087-36-7	50
				Cycloheptylidenecycloheptane		26
4		3-Cholestanone		3-Isopropylidenecholestane	1176-53-0	54
				3-Cholesterylidenecholestane		29
5	83-33-0	1-Indanone		1-Isopropylideneindane	61370-23-8	71
				1-Indanylidene-1-indane		24
6		Acetophenone		2-Methyl-3-phenyl-2-butene	769-57-3	65
				2,3-Diphenyl-2-butene		16
7		Benzophenone		1,1-Diphenyl-2-methylpropene	781-33-9	94
				Tetraphenylethylene		Trace
8		Fluorenone		Isopropylidenefluorene	19326-47-7	84
				Bifluorenylidene		0
9	1078-19-9			 + 	61370-24-9	85 9
10	826-56-2			 + 	61370-26-1	67 26
11	78-59-1				50523-39-2	63
12	89-82-7				66587-46-0	55

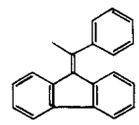
[a] Isolated yield after column chromatography.

We have reported in a preliminary communication[24] that the intramolecular dicarbonyl coupling is in fact successful, and our results are given in Table VI.

Our initial results in attempting intramolecular dicarbonyl coupling were discouraging in that rather low yields of cycloalkenes were produced under conditions that worked well for intermolecular couplings. We discovered, however, that when high dilution conditions were used (36-h addition of dicarbonyl to $TiCl_3$/Zn–Cu via syringe pump) much better yields were obtained. We also discovered that, although the coupling could be carried out with $TiCl_3$/Li, better yields were obtained when zinc–copper couple was used as the reducing agent. This reagent is readily and safely prepared (see Experimental Section), and we now prefer it for all carbonyl couplings, both intermolecular and intramolecular.

As can be seen from Table VI, the cyclization is general for

Table V. Mixed Carbonyl Coupling of Diaryl Ketones with Other Partners (Ratio of Ketones 1:1)

entry	registry no.	ketones	$TiCl_3/3Li$ →	products	registry no.	yield,[a] %
1		Benzophenone		1,1-Diphenyl-2-methylpropene		81
		Acetone		Tetraphenylethylene		14
2		Benzophenone		Cyclohexylidenediphenylmethane	30125-24-7	78
		Cyclohexanone		Tetraphenylethylene		19
				Cyclohexylidenecyclohexane		6
3		Benzophenone		1,1-Diphenyl-1-heptene	1530-20-7	84
	66-25-1	Hexanal		Tetraphenylethylene		9
				6-Dodecene		8
4		Benzophenone		3-Cholesterylidenediphenylmethane	66673-26-5	82
		3-Cholestanone		Tetraphenylethylene		14
				3-Cholesterylidene-3-cholestane		15
5		Benzophenone		Tetraphenylethylene		90
	815-24-7	Di-*tert*-butyl ketone				
6		Fluorenone		Isopropylidenefluorene		74
		Acetone		Bifluorenylidene		8
7		Fluorenone		Cycloheptylidenefluorene	61370-29-4	77
		Cycloheptanone		Bifluorenylidene		7
				Cycloheptylidenecycloheptane		17
8		Fluorenone				
		Acetophenone			61370-30-7	70
				2,3-Diphenyl-2-butene		15
				Bifluorenylidene		8

[a] Isolated yield after column chromatography.

both aldehydes and ketones. Most remarkable, however, is the fact that excellent yields of cycloalkene are obtained for all ring sizes, including the difficult medium size rings and the very large 22-membered ring. To compare the titanium dicarbonyl cyclization to other methods,[25] the Thorpe–Ziegler dinitrile cyclization[26] is reported to fail for ring sizes 9–13. The acyloin cyclization of diesters is much better,[27] but it shows a dip in yield for ring sizes 9–11.

As an example of the potential utility of the method, we undertook a synthesis of the natural product civetone (**6**), a 17-membered ring olefinic ketone. Civetone has been synthesized several times previously[28] by other workers, but it nevertheless appeared to be a good target for synthesis by our reaction. The route used is shown in Scheme I.

We were surprised to learn that the key coupling step occurred with partial removal of the ketal protecting group during the reaction. The ethylene ketal, in particular, was almost totally removed, and we therefore resorted to use of the somewhat more stable catechol ketal **3**. This proved more stable, and civetone ketal **5** was isolated in 70% yield. This compares favorably with the yield reported for civetone synthesis by the acyloin reaction.[28]

Reduction of 1,2-Diols. The deoxygenation of 1,2-diols to olefins is a useful synthetic transformation which can be carried out by various methods.[29] Since the carbonyl coupling reaction proceeds through the intermediacy of a pinacol dianion, we examined the reaction of diols with active Ti^0. The deoxygenation is quite successful,[10] and our attempts at optimizing reaction yields are given in Table VII. Some results on different diols are given in Table VIII.

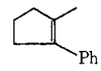
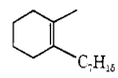
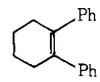
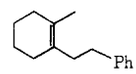
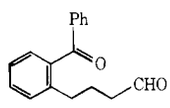
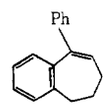
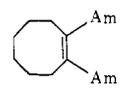
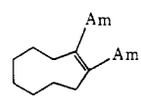
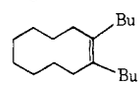
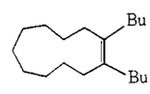
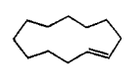
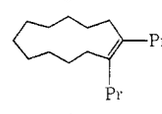
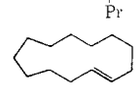
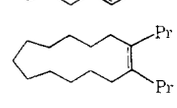
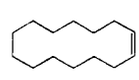
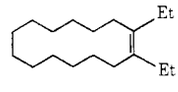
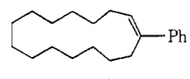
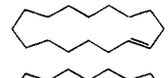
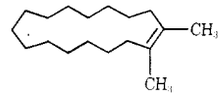
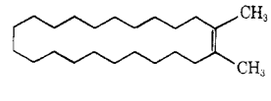
There are several interesting features of the reaction displayed in these tables. The use of 3 equiv of potassium to reduce the diol (runs 4 and 5, Table VII) led to considerably lower yields of product than did the use of 4.5 equiv. We assume that this is due to the necessity of first removing the acidic hydroxyl protons to form the pinacol dianion. A further point is that both cyclic and acyclic diols reduced in good yield, including the trans diaxial glycol 2β,3α-dihydroxy-3β-methyl-5α-cholestane (entry 2, Table VIII). *trans*-9,10-Decalindiol (entry 7, Table VIII), however, did not reduce. From a synthetic point of view, the good yields and generality observed make this reaction a potentially useful one. From the mechanistic point of view, these results have clear implications as to the exact nature of the carbonyl coupling process.

Mechanism of the Titanium-Induced Carbonyl Coupling. One can conceive of many possible mechanisms to account for the carbonyl coupling reaction, and we depict four such likely possibilities in Scheme II.

The intermediate pinacol can reduce in one of several ways, and it should be possible, by a proper choice of experiments, to distinguish between them. In path A, we assume that the pinacol forms a five-membered ring intermediate with both oxygens bound to the same titanium atom [presumably Ti(II)]. This intermediate can further react either by a concerted path A_1, giving olefin and TiO_2, or it can react by a nonconcerted path A_2, in which the two C–O bonds are broken at different times. It should be possible to distinguish between these by looking at the reduction of a diol of known stereochemistry, and entries 4 and 5 in Table VIII do just this. When both *meso*- and *dl*-5,6-dihydroxydecane were reduced with $TiCl_3/K$, mixtures of *cis*- and *trans*-5-decene were produced, indicating the nonconcerted nature of the reaction. It was rather surprising to us that a different mixture was observed in the two cases, indicating perhaps that the reaction lies on the borderline of being concerted. We have, however, verified the results and carried out a control experiment, showing that both *cis*- and *trans*-5-decene are stable to reaction conditions.

An alternative explanation accounting for the observed mixture of cis and trans products would be to postulate that our starting diols were undergoing isomerization by reverse pinacol reaction prior to deoxygenation. Such reverse pinacol reactions have been reported,[30-31] and it is possible that such a process is occurring here and thus hiding a concerted deoxygenation.

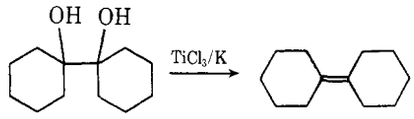
Table VI. Intramolecular Dicarbonyl Coupling

entry	registry no.	dicarbonyl	$TiCl_3/Zn$–Cu →	product	registry no.	yield,[a] %
1	495-71-6	$PhCO(CH_2)_2COPh$				87
2	6303-82-8	$CH_3CO(CH_2)_3COPh$				70
3	66587-47-1	$CH_3CO(CH_2)_4COC_7H_{15}$			66587-48-2	79
4	3375-38-0	$PhCO(CH_2)_4COPh$				95
5	63521-73-3	$CH_3CO(CH_2)_4COCH_2CH_2Ph$			63521-79-9	50
6	63521-74-4				21855-89-0	80
7	31335-02-1	$AmCO(CH_2)_6COAm$			66587-49-3	67
8	31335-05-4	$AmCO(CH_2)_7COAm$			66587-50-6	68
9	31335-01-1	$BuCO(CH_2)_8COBu$			63521-82-4	75
10	63521-75-5	$BuCO(CH_2)_9COBu$			63521-83-5	76
11	38279-34-4	$CHO(CH_2)_{10}CHO$			1501-82-2	76
12	7029-25-6	$PrCO(CH_2)_{10}COPr$			66587-35-7	71
13	63521-76-6	$CHO(CH_2)_{11}CHO$			6573-70-2	52
14	31335-04-3	$PrCO(CH_2)_{11}COPr$			66587-36-8	65
15	63521-77-7	$CHO(CH_2)_{12}CHO$			6568-33-8	71
16	31335-00-9	$EtCO(CH_2)_{12}COEt$			66587-37-9	75
17	63521-78-8	$CHO(CH_2)_{13}COPh$			63521-84-6	80
18	6812-43-7	$CHO(CH_2)_{14}CHO$			6568-44-1	85
19	34959-20-1	$CH_3CO(CH_2)_{14}COCH_3$			66587-38-0	90
20	34689-16-2	$CH_3CO(CH_2)_{20}COCH_3$			66587-39-1	83

[a] Isolated yield.

This is clearly not the case, however. We have shown conclusively in other studies[32] that the pinacol coupling of simple aliphatic carbonyl compounds is not readily reversible, and we have also run the *meso*- and *dl*-5,6-dihydroxydecane reductions to partial completion and examined the recovered diols. The recovered diols showed no isomerization. We feel

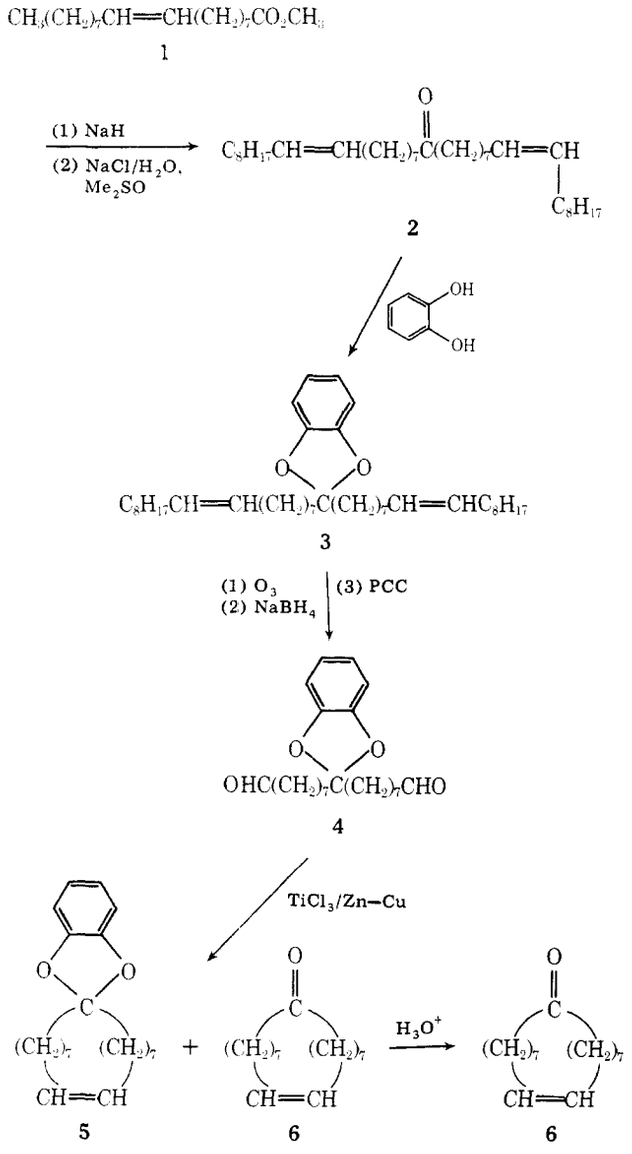
Table VII. Deoxygenation of Bicyclohexyl-1,1'-diol to Cyclohexylidenecyclohexane with $TiCl_3/K$



run	molar ratio $TiCl_3$/K/diol	rxn temp, °C	rxn time, h	diol recovered,[a]	olefin,[a] %
1	1:4.5:0.25	65	16	0	85
2	1:4.5:0.25	65	1.25	61	24
3	1:4.5:0.25	20	16	78	14
4	1:3.0:0.25	65	17	28	59
5	1:3.0:0.125	65	18	37	49
6	1:3.1:0.25[b]	65	13	46	43

[a] Isolated yield after column chromatography. [b] Diol added as dipotassium salt.

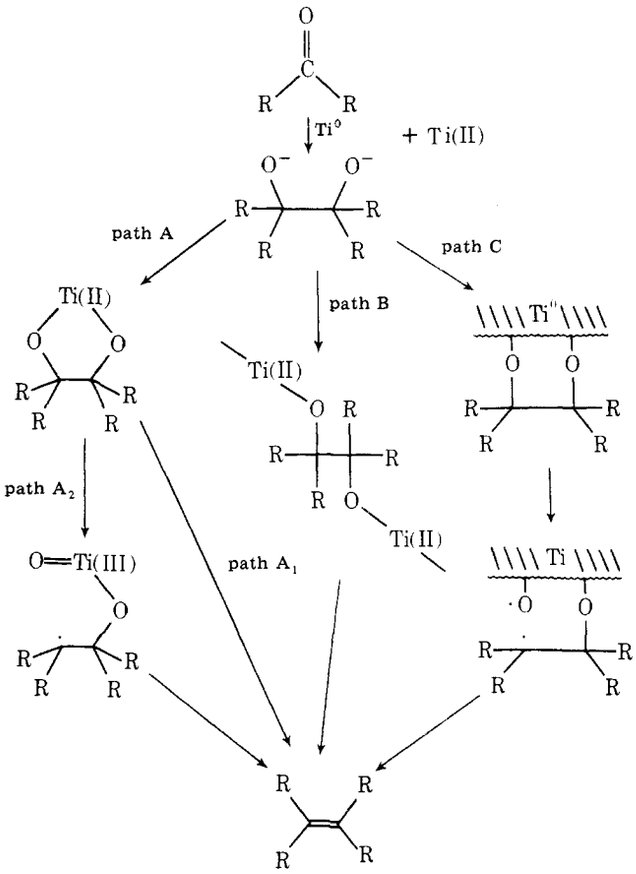
Scheme I. Synthesis of Civetone (6)



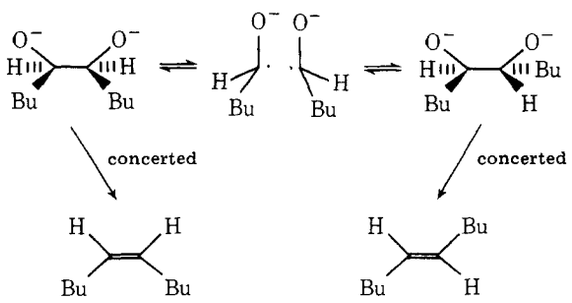
that these results rule out path A_1 as a possible deoxygenation mechanism.

Path B differs from path A in that a five-membered ring is not present and the two oxygens are bound to different titanium atoms. The path B intermediate would presumably further react, giving olefin by a nonconcerted path. Entries 6 and 7 (Table VIII) were designed to distinguish between path A_2 and path B. Reduction of *cis*-9,10-decalindiol (entry

Scheme II

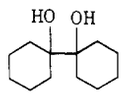
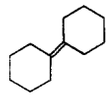
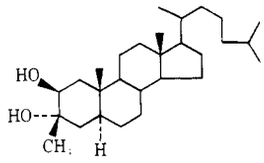
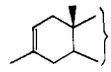
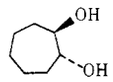
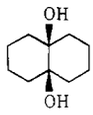
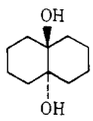
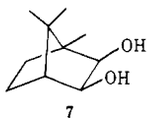
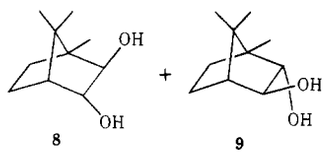


6) proceeds smoothly to yield the expected 1,2,3,4,5,6,7,8-octahydronapthalene. Reaction of the isomeric *trans*-9,10-decalindiol under identical conditions, however, gives no



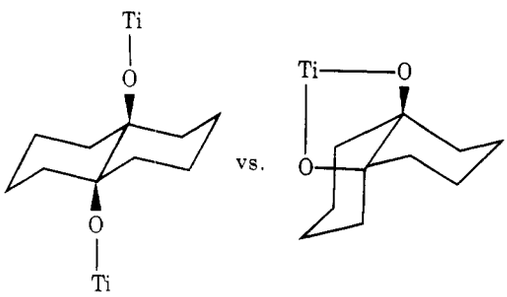
olefinic product. The only obvious difference between the two diol substrates is that in the cis isomer the oxygen atoms can

Table VIII. Reduction of Some Diols with $TiCl_3/K$

entry	registry no.	diol	product	yield, %
1	2888-11-1			85
2	28809-87-2			80[a]
3	13553-19-0			55[b]
4	3266-25-9	*meso*-BuCH(OH)CH(OH)Bu	5-Decene (40% cis/60% trans)	75[b]
5	59367-33-8	*dl*-BuCH(OH)CH(OH)Bu	5-Decene (9% cis/91% trans)	80[b]
6	28795-95-1			80[b]
7			No reaction	
8		 7		78[b]
9		 8 9		60[b]

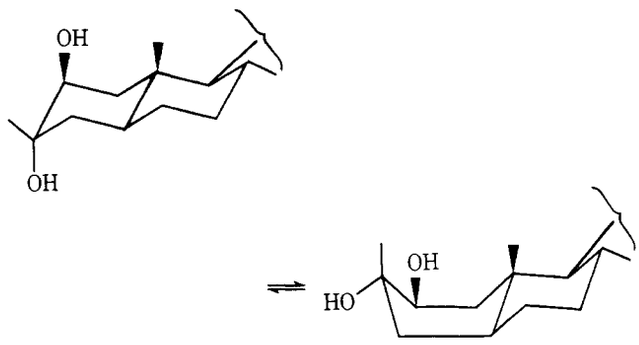
[a] Isolated yield after column chromatography. [b] GLC yield relative to internal standard.

both bond to a common surface or single titanium atom while in the trans isomer this is not possible. We conclude therefore that path B does not represent a viable choice of reaction mechanism.



At first glance, one might consider it surprising that a trans diaxial glycol such as the 2α,3β-dihydroxy steroid in entry 2 of Table VIII reacts so readily since in the chair conformer the oxygens can not bond to a common point. The logical explanation of this reduction, however, is that reaction occurs through the A ring boat conformer.

The final mechanistic possibility we would like to consider is path C of Scheme II. This is rather poorly defined in comparison to paths A and B, but we would like to consider the chance that the deoxygenation reaction may actually be occurring on the surface of an active titanium particle in a heterogeneous process. Such a process would be analogous to the acyloin condensation which is thought to occur on the surface of molten sodium droplets.[27] Path C differs from path A in



that the two oxygens bond to a common surface rather than to a common atom, and both are compatible with the results of the isomeric decalindiol reactions. Paths A_2 and C should be distinguishable, however, by employing a classic test for the presence or absence of a five-membered ring intermediate. Entries 8 and 9 of Table VIII accomplish this.

Previous studies have shown a large difference in the reaction rates of cis diol 7 and trans diols 8 and 9 with various reagents assumed to form five-membered ring intermediates. For example, cis glycol 7 undergoes cleavage with lead tetraacetate at 20 °C very quickly (second order rate constant $k = 2.5 \times 10^4$ mol^{-1} L min^{-1}) in contrast to the reaction with trans diols 8 and 9, which proceeded too slowly at 20 °C to be measured ($k = 0.38$ mol^{-1} L min^{-1} at 50 °C.[33] The explanation for this difference is that the cis diol can easily form a five-membered ring lead alkoxide while the trans diols have their hydroxyls rigidly held too far apart to accommodate a five-

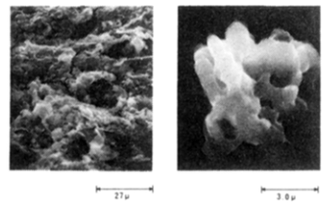


Figure 1. The surface of the active titanium reagent as examined by scanning electron microscopy.

membered ring. If the titanium deoxygenation reaction also proceeds through a five-membered ring (path A), we would expect cis diol **7** to reduce at a much faster rate than trans diols **8** and **9**. If, however, the hydroxyls need only approach a common broad surface (path C), both cis and trans diols should reduce. Treatment of cis diol **7** and a 70:30 mixture of trans diols **8** and **9** in side by side experiments gave the results shown in Table IX.

Aliquots were periodically removed, and yields of 2-bornene were determined by GLC. The table clearly shows that both *cis*- and *trans*-camphanediols were reduced at approximately the same rate and were complete after 5 h. These results strongly suggest to us that the deoxygenation of diols does not require the formation of a five-membered ring intermediate. We therefore conclude that the reaction occurs by the route shown in path C of Scheme II; i.e., the deoxygenation of diols occurs in a heterogeneous process on the surface of an active titanium particle (see Scheme III).

Nature of the Titanium Reagent. With the knowledge that the carbonyl coupling reaction is occurring on the active titanium surface, we were curious as to the nature of the particles. We therefore prepared the active reagent and examined it by scanning electron microscopy. The results are shown in Figure 1. The titanium evidently forms aggregates of widely varying shapes and sizes. A highly pebbled "Swiss cheese" type of surface is present giving what must certainly be an extremely high surface-to-mass ratio. The wide variation in particle shape and size, however, makes a simple calculation of surface area impossible.

Scheme III

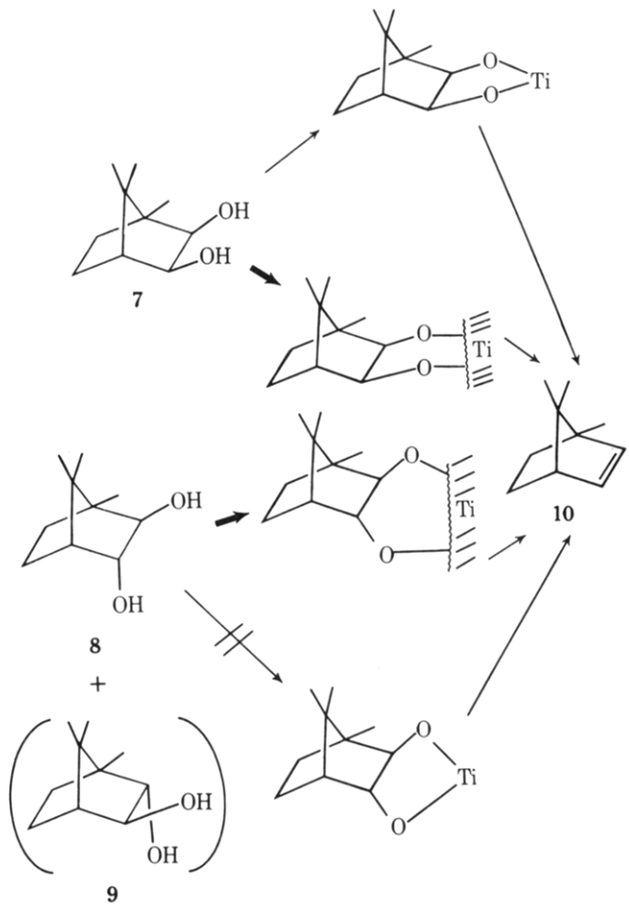


Table IX. Deoxygenation of *cis*- and *trans*-Camphanediols with $TiCl_3/K$ in THF

run	time, h	% yield[a] from cis diol **7**	% yield[a] from trans diols **8,9**
1	0.5	51	29
2	1	76	33
3	5	81	60

[a] GLC yield determined relative to internal standard.

Reaction of Ti^0 with Other Functional Groups. We have spent considerable time investigating the reactions of other functional groups with Ti^0, but to date our efforts have not been fruitful. One can imagine, for example, that Ti^0 might react with esters to give an acyloin reaction, and the product enediolate might then deoxygenate, yielding an acetylene.[34]

$$RCO_2R' \xrightarrow{Ti^0} \underset{\displaystyle O^- \quad O^-}{RC{=}CR} \longrightarrow RC{\equiv}CR$$

We found, however, that treatment of esters with Ti^0 led only to complex mixtures of products containing only small (2–3%) amounts of acetylene. Ethyl valerate, for example, gave only about 2% of 5-decyne along with 5-decene and various oxygen-containing products. Attempted acyloin-type cyclization of a 1,16-diester gave none of the desired cyclohexadecyne, but rather a mixture containing cyclohexadecene, cyclohexadecane, cyclohexadecanol, 2-hydroxycyclohexadecanone, and other products.

In similar reactions, we have also treated acids, acid chlorides, α-bromo ketone enolates, α-phenylsulfenyl ketone enolates, and α-diketones with Ti^0, but in no case were useful results obtained. A control experiment in which 5-decyne was treated with Ti^0 established that acetylenes are slowly reduced. A successful acetylene synthesis is therefore unlikely unless its rate is rapid.

Table X reports the results of some other reactions with Ti^0. Saturated alcohols do not react with Ti^0, and imines (entries 3 and 5) react poorly. Thioketones (entry 6) react well, as might be expected, and surprisingly, a free aliphatic acyloin (entry 7) also reacts cleanly, although the product is, unexpectedly, the dimer resulting from coupling of cyclotetradecanone.

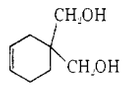
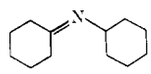
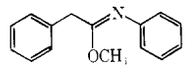
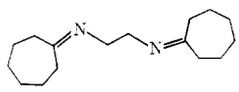
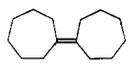
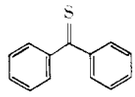
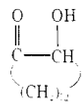
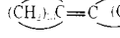
Summary

It is clear from the results presented that active titanium metal is an efficient reagent for coupling ketones and aldehydes to olefins. The reactions work well both inter- and intramolecularly. In special cases, even mixed couplings can be carried out in good yield. Ti^0 will also reduce diols to olefins, and we believe the reaction occurs on the surface of active metal particles. Unfortunately, however, Ti^0 does not react cleanly with other reducible functional groups and it therefore appears that its use is limited to cases where functional groups other than alcohols, ethers, and olefins are not present.

Experimental Section

General. Melting points were obtained on a Thomas-Hoover unimelt apparatus. Proton NMR spectra were recorded on a Varian A56/60A (60 MHz) or a Jeolco Minimar (60 MHz) instrument. Chemical shifts are reported in δ (ppm) downfield from internal tetramethylsilane. IR spectra were recorded on Perkin-Elmer 237 or 337

Table X. Reaction of Some Functional Groups with $TiCl_3$/Li

entry	registry no.	starting material	product	yield, %
1		Cholesterol	No reaction	
2			No reaction	
3			No reaction	
4	19813-45-7		Mixture	
5	66587-40-4			14
6	1450-31-3		Tetraphenylethylene	90
7	54561-32-9			80

grating spectrophotometers. Gas chromatography/mass spectroscopy was performed on a Finnigan Model 4000 instrument operating at a 70 eV ionization potential and employing a 3% OV-1 on Chromosorb W glass column (4 ft × 0.25 in). $TiCl_3$ was obtained from Alfa Inorganics and was transferred under an inert atmosphere in a glovebag or a Schlenk apparatus.

The phrase "usual workup procedure" used below means that the reaction mixture was cooled to room temperature, diluted with water, and extracted several times with ether. The combined ether extracts were washed with saturated brine, dried ($MgSO_4$), and concentrated by solvent removal at the rotary evaporator.

General Procedure for Intermolecular Coupling Using $TiCl_3$/K. Potassium metal (1.92 g, 49 mmol) was washed with hexane to remove oil and was added to a stirred slurry of $TiCl_3$ (2.15 g, 14 mmol) in 75 mL of dry tetrahydrofuran (THF) at room temperature under an inert atmosphere. After refluxing for 40 min, the black mixture was cooled and a solution of ketone or aldehyde (3.5 mmol) in 5 mL of THF was added. After a further 16 h at reflux, the reaction mixture was cooled to room temperature and transferred by syringe to a sintered glass filtration tube (medium frit) under an inert atmosphere. The mixture was vacuum filtered, and the filter cake was washed with hexane. The filtrate was then concentrated by solvent removal at the rotary evaporator to yield the crude product. The black filter cake was carefully quenched by the slow dropwise addition of methanol and was allowed to stand until gas evolution ceased. This must be done with caution under an inert atmosphere since the filter cake is pyrophoric when exposed to air. In this manner, the following reactions were carried out.

5-Decene from Valeraldehyde. A 77% yield was obtained as determined by GLC analysis (20% SF-96 on GC-22 "Super Support"; 5 ft × 0.25 in) using 1-dodecene as an internal standard. The cis/trans ratio of the product was determined by the method outlined in the accompanying paper[11] and was found to be approximately 70% trans to 30% cis.

10-Eicosene[35] from Decanal. A 60% yield was obtained by column chromatographic isolation: NMR ($CDCl_3$) δ 5.3 (m, 2 H), 2.0 (m, 4 H), 0.8–1.5 (m, 34 H); mass spectrum, *m/e* (relative intensity) 280 (M^+, 100).

Cyclopentylidenecyclopentane from Cyclopentanone. A 40% yield was isolated as an oil by column chromatography: mass spectrum, *m/e* 136 (M^+); NMR spectrum corresponds to that reported.[36]

Cyclohexylidenecyclohexane from Cyclohexanone. An 85% yield was isolated by column chromatography, mp 52–53 °C (lit.[37] mp 53.5–54.5 °C).

Cycloheptylidenecycloheptane from Cycloheptanone. An 86% yield was isolated as an oil by column chromatography: mass spectrum, *m/e* 192 (M^+); NMR spectrum corresponds to that reported.[36]

Cyclooctylidenecyclooctane from Cyclooctanone. A 70% yield was isolated by column chromatography, mp 39–40 °C (lit.[36] mp 39–41 °C).

Adamantylideneadamantane from Adamantanone. A 91% yield was isolated by column chromatography, mp 183–185 °C (lit.[38] mp 184–187 °C).

Tetraisopropylethylene from Diisopropyl Ketone. A 37% yield was isolated by chromatography, mp 118–120 °C (lit.[5] mp 116–117 °C).

Cyclododecylidenecyclododecane from Cyclododecanone. A 90% yield was isolated by column chromatography: mp 150–152 °C; NMR ($CDCl_3$) δ 1.8–2.3 (m, 8 H), 1.2–1.6 (m, 36 H); mass spectrum, *m/e* (relative intensity) 332 (M^+, 100). Anal. Calcd for $C_{24}H_{44}$: C, 86.67; H, 13.33. Found: C, 86.53; H, 13.45.

3-Cholesterylidene-3-cholestane from 3-Cholestanone. An 85% yield was isolated by column chromatography: mp, decomposition at ca. 310 °C. Anal. Calcd for $C_{54}H_{92}$: C, 87.49; H, 12.51. Found: C, 87.66; H, 12.75.

9,9′-Bifluorene from Fluorenone. An 85% yield was isolated by column chromatography, mp 244–246 °C (lit.[39] mp 246 °C).

Tetraphenylethane from Benzophenone. An 80% yield was isolated by column chromatography, mp 207–209 °C (lit.[40] mp 209–210 °C).

General Procedure for Intermolecular Coupling Using $TiCl_3$/Li. Lithium wire (0.328 g, 47.3 mmol) and $TiCl_3$ (2.405 g, 15.6 mmol) were slurried in 40 mL of dry dimethoxyethane (DME) under an argon atmosphere, and the mixture was refluxed for 1 h. After cooling, a solution of ketone in 10 mL of DME was added. After a further 16 h at reflux, the reaction mixture was cooled to room temperature, diluted with petroleum ether, and filtered through a small pad of Florisil on a sintered glass filter. The residue was cautiously quenched by the slow addition of methanol. The filtrate was concentrated by removal of solvent at the rotary evaporator to yield the crude product. In this manner, the following reactions were carried out.

Cyclohexylidenecyclohexane from Cyclohexanone. A 79% yield was isolated by column chromatography. The product was identified by comparison with the sample prepared above.

Cycloheptylidenecycloheptane from Cycloheptanone. An 85% yield was isolated by column chromatography. The product was identified by comparison with the sample prepared above.

Cyclododecylidenecyclododecane from Cyclododecanone. A 65% yield was isolated by column chromatography. The product was identified by comparison with the sample prepared above.

Adamantylideneadamantane from Adamantanone. An 82% yield was isolated by column chromatography. The product was identified by comparison with the sample prepared above.

Stilbene from Benzaldehyde. A 97% yield was isolated by column chromatography. The product (trans) was identified by comparison with an authentic sample.

2,3-Diphenyl-2-butene from Acetophenone. A 94% yield was isolated by column chromatography. NMR spectroscopy of the resulting oil showed it to be a 90:10 mixture of isomers. The major isomer showed an NMR methyl absorption at δ 2.14 while the minor isomer had a methyl absorption at δ 1.87. According to the literature

assignments[41] therefore, our mixture is 90% *Z* and 10% *E*. We believe, however, that these assignments are almost certainly wrong and should be reversed since analogous compounds (stilbene and stilbestrol) are known to prefer an *E* geometry.

Tetraphenylethylene from Benzophenone. A 96% yield was isolated by column chromatography, mp 221–222 °C (lit.[42] mp 222 °C).

β-Carotene from Retinal. A 95% yield of crude material was isolated by column chromatography. This dark red solid was homogeneous by TLC, but by comparison with published UV spectra[43] it was shown to be a mixture of double-bond isomers.

General Reaction Procedure for Mixed Carbonyl Coupling Using $TiCl_3$/Li. Lithium wire (0.45 g, 65 mmol) was added to a stirred slurry of $TiCl_3$ (2.87 g, 18.6 mmol) in 30 mL of DME under an argon atmosphere, and the mixture was refluxed for 1 h. The black slurry was then cooled to room temperature, and the two carbonyl components (4.65 mmol total) in 5 mL of DME were added. The mixture was stirred for 2 h at room temperature and then refluxed for 16 h. After cooling to room temperature, the reaction was diluted with pentane and filtered through a small pad of Florisil. Evaporation of solvent from the filtrate gave the crude product. In this manner, the following reactions were carried out.

Adamantanone with 4 equiv of acetone gave isopropylideneadamantane[44] as an oil (63%): NMR (CCl_4) δ 2.87 (m, 2 H), 1.77 (m, 12 H), 1.63 (s, 6 H); mass spectrum, *m/e* 176 (M^+).

4-*tert*-Butylcyclohexanone with 4 equiv of acetone gave isopropylidene-4-*tert*-butylcyclohexane[45] as an oil (55%): NMR (CCl_4) δ 2.83–2.53 (2 H), 1.95–1.0 (7 H), 1.63 (s, 6 H), 0.87 (s, 9 H); mass spectrum, *m/e* 180 (M^+).

Cycloheptanone with 4 equiv of acetone gave isopropylidenecycloheptane[46] as an oil (50%): NMR (CCl_4) δ 2.22 (m, 4 H), 1.65 (s, 6 H), 1.52 (m, 8 H); mass spectrum, *m/e* 138 (M^+).

Cholestanone with 4 equiv of acetone gave 3-isopropylidenecholestane as white crystals (54%): mp 94–96 °C (lit.[47] mp 95–97 °C); mass spectrum, *m/e* 412 (M^+).

1-Indanone with 4 equiv of acetone gave 1-isopropylideneindane[48] as an oil (71%): NMR (CCl_4) δ 7.4 (m, 1 H), 7.05 (m, 3 H), 2.77 (m, 4 H), 2.02 (s, 3 H), 1.83 (s, 3 H); mass spectrum, *m/e* 158 (M^+).

Acetophenone with 4 equiv of acetone gave 2-methyl-3-phenyl-2-butene[49] as an oil (65%): NMR (CCl_4) δ 7.13 (m, 5 H), 1.95 (m, 3 H), 1.82 (s, 3 H), 1.58 (m, 3 H); mass spectrum, *m/e* 146 (M^+).

Benzophenone plus acetone gave 1,1-diphenyl-2-methyl-1-propene[50] as an oil (94%): NMR (CCl_4) δ 7.12 (s, 10 H), 1.78 (s, 6 H); mass spectrum, *m/e* 208 (M^+).

Fluorenone plus acetone gave isopropylidenefluorene[51] as an oil (84%): NMR (CCl_4) δ 7.6 (m, 4 H), 7.13 (m, 4 H), 2.40 (s, 6 H).

6-Methoxy-1-tetralone with 4 equiv of acetone gave 1-isopropylidene-6-methoxytetralin as an oil (85%): NMR (CCl_4) δ 7.08 (m, 1 H), 6.55 (m, 2 H), 3.72 (s, 3 H), 2.47 (m, 4 H), 1.88 (s, 3 H), 1.78 (s, 3 H), 1.68 (m, 2 H); mass spectrum, *m/e* 202 (M^+).

4a-Methyl-4,4a,5,6,7,8-hexahydronapthalen-2(3*H*)-one with 4 equiv of acetone gave 2-isopropylidene-4a-methyl-2,3,4,4a,5,6,7,8-octahydronapthalene as an oil (67%): NMR (CCl_4) δ 6.0 (m, 1 H), 2.2 (m, 4 H), 1.7 (s, 6 H), 1.5 (m, 8 H), 1.07 (s, 3 H); mass spectrum, *m/e* 190 (M^+).

Pulegone with 4 equiv of acetone gave 1,2-diisopropylidene-4-methylcyclohexane as an oil (55%): NMR (CCl_4) δ 2.6 (m, 2 H), 2.1–1.2 (3 H), 1.68 (s, 6 H), 1.50 (s, 6 H), 0.9 (m, 5 H); mass spectrum, *m/e* 178 (M^+).

Isophorone with 4 equiv of acetone gave isopropylidene-3,5,5-trimethyl-2-cyclohexene[52] as an oil (63%): NMR (CCl_4) δ 6.1 (m, 1 H), 1.95 (m, 2 H), 1.73 (m, 9 H), 1.17 (m, 2 H), 0.88 (s, 6 H); mass spectrum, m/e 164 (M^+).

Benzophenone with cyclohexanone gave cyclohexylidenediphenylmethane (78%): mp 83–84 °C (lit.[53] mp 83–83.5 °C); NMR (CCl_4) δ 7.13 (10 H), 2.23 (m, 4 H), 1.58 (m, 6 H); mass spectrum, *m/e* 248 (M^+).

Benzophenone with hexanal gave 1,1-diphenyl-1-heptene[54] as an oil (84%): NMR (CCl_4) δ 7.17 (s, 10 H), 6.03 (t, 1 H, J = 7 Hz), 2.1 (m, 2 H), 1.7–0.65 (9 H); mass spectrum, *m/e* 250 (M^+).

Benzophenone with 3-cholestanone gave 3-cholesterylidenediphenylmethane (82%): mp 106–109 °C; NMR (CCl_4) δ 7.12 (m, 10 H), 0.93 (s), 0.83 (s), 0.67 (s); mass spectrum, *m/e* 536 (M^+).

Fluorenone plus cycloheptanone gave cycloheptylidenefluorene (77%): mp 123.5–124.5 °C; NMR (CCl_4) δ 7.67 (m, 4 H), 7.23 (m, 4 H), 3.05 (m, 4 H), 1.72 (m, 8 H); mass spectrum, *m/e* 260 (M^+).

Fluorenone plus acetophenone gave fluorenylidene-1-phenylethane (70%): mp 112–113.5 °C; NMR (CCl_4, Δ —/]9–6/67 (7 H), 7.43 (s, 5 H), 6.23 (d, 1 H, J = 8 Hz), 2.72 (s, 3 H); mass spectrum, *m/e* 268 (M^+).

General Procedure for Intramolecular Dicarbonyl Coupling with $TiCl_3$/Zn–Cu. The Zn–Cu couple was prepared by adding zinc dust (9.81 g, 150 mmol) to 40 mL of deoxygenated water and adding $CuSO_4$ (0.75 g, 4.7 mmol). The black suspension was agitated by purging with a stream of N_2 gas for 10 min and was then filtered under N_2. After washing with deoxygenated water, acetone, and ether, the couple was dried under vacuum and then stored under an inert atmosphere.

A stirred slurry of $TiCl_3$ (1.03 g, 6.7 mmol) and Zn–Cu (1.0 g, 15.4 mmol) in 20 mL of DME was refluxed under argon for 1 h. The dicarbonyl compound (0.30 mmol) in 20 mL of DME was added by a motor driven syringe pump over 9 h, and the reaction was further refluxed for 12 h. An additional 0.30 mmol (0.60 mmol total) of dicarbonyl compound in 20 mL of DME was added over 9 h followed by a further 12-h period of reflux. The reaction mixture was then cooled to room temperature and filtered through a Florisil pad. Concentration by solvent removal at the rotary evaporator gave the crude product. In this manner, the following reactions were carried out.

1,2-Diphenylcyclobutene from 1,4-Diphenylbutane-1,4-dione. An 87% yield was isolated by column chromatography, mp 49–50.5 °C (lit.[55] mp 50.5–52 °C).

1-Methyl-2-phenylcyclopentene from 1-Phenylhexane-1,5-dione. A 70% yield was isolated by distillation, bp 53–58 °C (0.14 mm) [lit.[56] bp 66–67 °C (2 mm)].

1-Methyl-2-heptylcyclohexene from Tetradecane-2,7-dione. A 79% yield was isolated by distillation: bp 37 ° (0.26 mm) [lit.[57] bp 78–80 °C (1.8 mm)]; mass spectrum, *m/e* 194 (M^+).

1,2-Diphenylcyclohexene from 1,6-Diphenylhexane-1,6-dione. A 95% yield was isolated by distillation, mp 46–47 °C (lit.[7] mp 48–48.5 °C).

1-Methyl-2-(2-phenylethyl)cyclohexene from 1-Phenylnonane-3,8-dione. A 50% yield was isolated by Kugelrohr distillation: bp 75–80 °C (0.1 mm); mass spectrum, *m/e* 200 (M^+).

3-Phenylbenzocycloheptene was isolated from the corresponding keto aldehyde in 80% yield by Kugelrohr distillation: bp 110–115 °C (0.6 mm) [lit.[58] bp 182 °C (15 mm)]; mass spectrum, *m/e* 220 (M^+).

1,2-Diamylcyclooctene from Octadecane-6,13-dione. A 67% yield was isolated by distillation: bp 70–75 °C (0.15 mm); mass spectrum, *m/e* 250 (M^+).

1,2-Diamylcyclononene from Nonadecane-6,14-dione. A 68% yield was isolated by distillation: bp 70–74 °C (0.25 mm); mass spectrum, *m/e* 264 (M^+).

1,2-Dibutylcyclodecene from Octadecane-5,14-dione. A 75% yield was isolated by distillation: bp 61–63 ° (0.25 mm); mass spectrum, *m/e* 250 (M^+).

1,2-Dibutylcycloundecene from Nonadecene-5,15-dione. A 76% yield was isolated by distillation: mp 80.5–82.5 °C; mass spectrum, *m/e* 264 (M^+).

Cyclododecene from Dodecanedialdehyde. A 76% yield was isolated by distillation: bp 50–55 °C (0.25 mm) [lit.[59] bp 76 °C (4 mm)]; mass spectrum, *m/e* 166 (M^+).

1,2-Dipropylcyclododecene from Octadecane-4,15-dione. A 71% yield was isolated by distillation: bp 71–74 °C (0.7 mm); mass spectrum, *m/e* 250 (M^+).

Cyclotridecene from Tridecanedialdehyde. A 52% yield was isolated by distillation: bp 50–53 °C (0.1 mm) [lit.[60] bp 122–126 °C (10 mm)]; mass spectrum, *m/e* 180 (M^+).

1,2-Dipropylcyclotridecene from Nonadecane-4,16-dione. A 65% yield was isolated by distillation: bp 65–68 °C (0.12 mm); mass spectrum, *m/e* 264 (M^+).

Cyclotetradecene from Tetradecanedialdehyde. A 71% yield was isolated by distillation: bp 55–60 °C (0.05 mm) [lit.[61] bp 136–138 °C (13 mm)]; mass spectrum, *m/e* 194 (M^+).

1,2-Diethylcyclotetradecene from Octadecane-3,16-dione. A 75% yield was isolated by distillation: bp 63 °C (0.1 mm); mass spectrum, *m/e* 250 (M^+).

1-Phenylcyclopentadecene from 1-Phenylpentadecane-1,15-dione. An 80% yield was isolated by Kugelrohr distillation: bp 121–128 °C (0.15 mm); mass spectrum, *m/e* 284 (M^+).

Cyclohexadecene from Hexadecanedialdehyde. An 85% yield was isolated by Kugelrohr distillation: bp 110–115 °C (0.25 mm) [lit.[60] bp 105 °C (0.15 mm)]; mp 49–50.5 °C; mass spectrum, *m/e* 222 (M^+).

1,2-Dimethylcyclohexadecene from Octadecane-2,17-dione. A 90% yield was isolated by distillation: bp 66–68 °C (0.1 mm); mass spectrum, *m/e* 250 (M^+).

1,2-Dimethylcyclodocosane from Tetracosane-2,23-dione. An 83% yield was isolated by distillation: bp 125–128 °C (0.15 mm); mass

spectrum, *m/e* 334 (M^+).

Ketone 2. Methyl oleate (30.0 g, 100 mmol) was dissolved in 180 mL of dry DME and added to NaH (7 g of a 57% dispersion in mineral oil; 166 mmol). The mixture was refluxed for 20 h under an inert atmosphere and then acidified with dilute HCl. Workup in the usual way gave the β-keto ester product (22.3 g, 80%): IR (film) 1750 and 1715 cm^{-1}; NMR ($CDCl_3$) δ 0.86 (t, 3 H), 1.92 (m, 8 H), 2.45 (m, 2 H), 3.37 (m, 1 H), 3.63 (s, 3 H), 5.27 (t, 4 H).

This β-keto ester was decarbomethoxylated[62] without further purification. The crude β-keto ester (22.3 g, 40 mmol) was added to a solution of NaCl (2.3 g, 40 mmol) and 2.1 mL of water in 30 mL of Me_2SO. The solution was heated to 145 °C under an inert atmosphere for 8 h and then cooled to room temperature. Workup in the usual way gave ketone **2** (19 g, 95%), homogeneous by TLC: IR (film) 1725 cm^{-1}; NMR (CCl_4) δ 0.86 (m, 6 H), 1.26 (CH_2 envelope, 44 H), 1.80–2.46 (m, 12 H), 5.22 (t, 4 H).

Ketal Dialdehyde 4. Ketone **2** (2 g, 4 mmol) and catechol (1.76 g, 16 mmol) were combined with triethyl orthoformate (6 mmol) in 20 mL of benzene. A small amount of *p*-toluenesulfonic acid catalyst was added, and the reaction was stirred for 16 h at room temperature. After quenching with $NaHCO_3$, the reaction was worked up in the usual way to give ketal **3** (75%): NMR (CCl_4) δ 0.86 (m, 6 H), 1.26 (CH_2 envelope, 48 H), 1.66–2.33 (m, 8 H), 5.22 (t, 4 H), 6.53 (s, 4 H).

Ketal **3** (1.78 g, 3.0 mmol) was dissolved in 25 mL of dichloromethane at −78 °C, and a dilute stream of ozone (Welsbach ozonator) was passed through. The reaction was monitored by TLC, and when starting material was consumed excess ozone was removed by purging with nitrogen. The solution was warmed to room temperature, and $NaBH_4$ (0.76 g, 20 mmol) in 10 mL of 50% aqueous ethanol was added. The reaction was stirred overnight at room temperature and then acidified and worked up in the usual way. Column chromatography on silica gel gave a dihydroxy ketal (340 mg, 30%). This material was dissolved in 5 mL of dichloromethane and added to a solution of pyridinium chlorochromate (700 mg, 3.3 mmol) in 5 mL of dichloromethane. After stirring for 2 h at room temperature under an inert atmosphere, the reaction mixture was worked up in the usual way to provide ketal dialdehyde **4** (236 mg, 75%) as an oil: IR (film) 2720 and 1715 cm^{-1}; NMR ($CDCl_3$) δ 1.29 (CH_2 envelope, 24 H), 2.37 (t, 4 H), 6.71 (s, 4 H), 9.70 (t, 2 H).

Civetone (6). Ketal dialdehyde **4** (236 mg, 0.63 mmol) was dissolved in 40 mL of DME. Half of this solution was added via a motor driven syringe pump over a 9-h period to a refluxing slurry of $TiCl_3$ (1.3 g, 8.4 mmol) and Zn–Cu (1.1 g, 16.2 mmol) in 15 mL of DME. After addition was complete, the reaction was refluxed for 12 h, and the remaining half of the dialdehyde solution was added over a further 9-h period. After dialdehyde addition was complete, the reaction was refluxed for 12 h and then cooled to room temperature and filtered through a Florisil pad. Concentration gave 195 mg of crude product which was deketalized by acid treatment. This crude cyclization product, levulinic acid (3 mL), and 0.3 mL of 1 N HCl were dissolved in 3 mL of chloroform and heated to 70 °C for 72 h. Workup in the usual way and column chromatography on neutral alumina gave civetone[63] as a mixture of cis and trans isomers (33%): IR (film) 1705 cm^{-1}; NMR ($CDCl_3$) δ 5.4 (m, 2 H); mass spectrum, *m/e* 250.

***meso*-5,6-Decanediol.** A solution of *cis*-5-decene (0.269 g, 1.92 mmol) and osmium tetroxide (0.5 g, 1.97 mmol) in 15 mL of pyridine was stirred at room temperature for 2 h. A solution of sodium sulfite (0.9 g) in 17 mL of 14% aqueous pyridine was added, and the reaction was stirred for an additional 45 min. The mixture was diluted with chloroform, and the organic layer was drawn off and concentrated. The residue was taken up in ether and washed with aqueous cupric sulfate to remove residual pyridine. After drying (K_2CO_3), removal of solvent gave the product (0.25 g, 76%), pure by GLC (5% Carbowax 20M on Chromosorb P; 12 ft × 0.25 in), mp 134–135.5 °C (lit.[64] mp 130–132 °C).

***dl*-5,6-Decanediol.** A solution of 85% *m*-chloroperbenzoic acid (2.03 g, 10.1 mmol) in 20 mL of dichloromethane was added dropwise to *cis*-5-decene (1.34 g, 9.6 mmol) in 50 mL of dichloromethane at room temperature. After stirring for 16 h, the mixture was washed with 10% aqueous sodium sulfite and 10% aqueous potassium carbonate and then dried ($MgSO_4$) and concentrated. The crude epoxide was stirred in 50 mL of 70% aqueous THF containing 2 drops of sulfuric acid at 60 °C for 4 h. Workup in the usual way gave the diol (1.28 g, 77%); mp 49–51 °C; NMR ($CDCl_3$) δ 2.3 (s, 2 H), 3.7–4.0 (m, 2 H); IR (neat) 3350 cm^{-1}; mass spectrum, *m/e* (relative intensity) 174 (M^+, 1), 117 (100). Anal. Calcd for $C_{10}H_{22}O_2$: C, 68.92; H, 12.72. Found: C, 68.73; H, 12.95.

2-*exo*,3-*exo*-Camphanediol (7). The method of Robertson[65] was used. Camphorquinone (2.0 g, 12.0 mmol) in 20 mL of ether was added dropwise over 15 min to a stirred solution of $LiAlH_4$ (0.49 g, 13.0 mmol) in 30 mL of ether at room temperature. After refluxing for 1.5 h, the reaction was cooled to room temperature and cautiously quenched by the addition of wet ether. The mixture was then filtered, and the filtrate was dried ($MgSO_4$) and concentrated. Chromatography on 60 g of Florisil gave product **7** (1.40 g, 68%): mp 257–259 °C (lit.[66] mp 259–261 °C); NMR spectrum was in agreement with published data.[66]

2-*exo*,3-*endo*-Camphanediol (8). A solution of borane in THF (50 mL of a 1 M solution; 50 mmol) was added dropwise over 30 min to a solution of camphor enol silyl ether[67] (11.2 g, 50.0 mmol) in 50 mL of dry THF. The reaction was stirred for 2 h at 0 °C and then at 35 °C for 2 h. After cooling at 0 °C, 16 mL of 30% hydrogen peroxide and 16 mL of 3 N sodium hydroxide were added. The reaction was warmed to 35 °C for 1.5 h and then cooled to room temperature and worked up in the usual way. The product consisted of a 70:30 mixture (NMR integration) of two diols whose spectral properties corresponded to those reported[66] for **9** and **8**. We believe, however, based on our method of synthesis in which camphor enol silyl ether should be hydroborated from the less hindered endo face, that the literature assignments should be reversed and that the major product (70%) is the 2-*exo*,3-*endo* diol **8** while the minor product is the 2-*endo*, 3-*exo* diol **9**.

General Reaction Procedure for the Reduction of Diols Using $TiCl_3$/K. A stirred slurry of $TiCl_3$ (1.103 g, 7.15 mmol) in 40 mL of dry THF was refluxed for 1.5 h with potassium (1.3 g, 33.2 mmol) under an inert atmosphere. The black suspension was then cooled slightly, and diol (1.8 mmol) in 5 mL of THF was added. After a further 16 h at reflux, the reaction mixture was cooled and quenched by the slow addition of methanol. The quenched mixture was diluted with water, extracted with ether, and worked up in the usual way. In this manner, the following reactions were carried out.

Cyclohexylidenecyclohexane from Bicyclohexyl-1,1'-diol.[68] An 85% yield of product was isolated by column chromatography. The product was identified by comparison with an authentic sample obtained above.

Cycloheptene from *trans*-Cycloheptane-1,2-diol. A 55% yield of product was obtained as judged by GLC (20% SF-96 on GC-22 "Super Support"; 5 ft × 0.25 in) using cyclooctene as an internal standard.

3-Methylcholest-2-ene from 3β-Methylcholestane-2β,3α-diol. An 80% yield of product was isolated by column chromatography. Identification was made by comparison with an authentic sample.

5-Decene from *dl*-5,6-Dihydroxydecane. An 80% yield of 5-decene was obtained as judged by GLC (5% Carbowax 20M on Chromosorb P; 4 ft × 0.25 in) using 1-dodecene as an internal standard. The cis/trans product ratio was determined by the method described in the accompanying paper[11] and was found to be 9% cis to 91% trans.

5-Decene from *meso*-5,6-Dihydroxydecane. A 75% yield of 5-decene was obtained as judged by GLC (5% Carbowax 20M on Chromosorb P; 4 ft × 0.25 in) using 1-dodecene as an internal standard. The cis/trans product ratio was determined by the method described in the accompanying paper,[11] and was found to be 40% cis to 60% trans.

1,2,3,4,5,6,7,8-Tetrahydronaphthalene from *cis*-9,10-Dihydroxydecalin.[69] An 80% yield of product was determined as isolated by column chromatography. Identification was made by comparison with an authentic sample.

2-Bornene from 2-*exo*,3-*exo*-Camphanediol (7). This reduction was carried out on 0.335 g (1.97 mmol) of diol in the presence of 0.340 g of 1-decene, serving as an internal GLC standard. An 81% yield of product was obtained after a 5-h reaction time. The reaction was followed by withdrawing aliquots at given intervals and analyzing by GLC.

2-Bornene from 2-*exo*,3-*endo*-Camphanediol (8) and 2-*endo*,3-*exo*-Camphanediol (9). This reduction was carried out in the same manner as the previous one, and its course was followed by removing aliquots at intervals. After 5 h, a 60% yield was obtained.

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Registry No.—**1**, 112-62-9; **2**, 504-54-1; **3**, 66587-41-5; **4**, 66587-42-6; *cis*-**5**, 66587-43-7; *trans*-**5**, 66652-56-0; *cis*-**6**, 542-46-1; *trans*-**6**, 1502-37-0; **7**, 56614-57-4; **8**, 56614-58-5; **9**, 13837-85-9; *cis*-5-decene, 7433-78-5; camphorquinone, 465-29-2; camphor enol silyl ether,

56613-17-3; acetone, 67-64-1; (Z,Z)-2-(7-hexadecenyl)-11-eicosenoic acid methyl ester, 66587-44-8.

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Role of Silver(II) in Silver-Catalyzed Oxidations by Peroxydisulfate[1]

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In Ag^+-catalyzed oxidations of organic substrates by peroxydisulfate, both $SO_4^{-}\cdot$ and Ag(II) are present as oxidants and may show quite different selectivity patterns, yielding quite different products. Ag(II) is shown to oxidize alcohols to alkoxy radicals, but at a slower rate than its known decarboxylation of acids. Contrary to some previous reports, rates of acid decarboxylation appear quite sensitive to acid structure and also to pH. In the oxidation by Ag(II) of aromatic molecules with side-chain –OH or –COOH functions, reaction may involve either side-chain attack or ring oxidation to a radical cation, the relative importance of the two paths depending on structure. The contribution of Ag(II) to the overall oxidation is shown to increase with the Ag/substrate ratio and to vary inversely with the rate of the $SO_4^{-}\cdot$ substrate reaction. The rate of the reaction $SO_4^{-}\cdot + Ag^+ \rightarrow SO_4^{2-} + Ag(II)$ is estimated as $\sim 3 \times 10^9$.

Silver ion is a well-known catalyst for peroxydisulfate ($S_2O_8^{2-}$) oxidations, the first report being by Marshall in 1900,[2] and a number of reveiws covering earlier work are available.[3–5] The initial steps usually postulated for such oxidations are the one-electron redox processes

$$S_2O_8^{2-} + Ag^+ \rightarrow SO_4^{2-} + SO_4^{-}\cdot + Ag(II) \quad (1)$$

$$SO_4^{-}\cdot + RH \rightarrow SO_4^{2-} + R\cdot + H^+ \quad (2)$$

$$SO_4^{-}\cdot + Ag^+ \rightarrow SO_4^{2-} + Ag(II) \quad (3)$$

although in some interpretations Ag(III) has also been proposed as an intermediate. Reactions 1 and 2 are quite analogous to the initial steps in the Fenton's reagent oxidation of organic substrates by Fe^{2+}–H_2O_2 or Fe^{2+}–$S_2O_8^{2-}$ [6] but differ in that while Fe^{3+} is able to oxidize intermediate substrate radicals, Ag(II) is a considerably stronger oxidizing agent and capable of oxidizing suitable substrates as well. As a conse-

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