ACCOUNTS OF CHEMICAL RESEARCH

VOLUME 7 NUMBER 9 SEPTEMBER, 1974

Organic Chemistry of Low-Valent Titanium

John E. Mc Murry

Thimann Laboratory, University of California, Santa Cruz, California 95064

Received February 7, 1974

Titanium is one of the more abundant metals in the earth's crust (0.6%), but its chemistry is little known compared to that of many other metals.[1] It is most often encountered in the 4+ oxidation state where TiO_2, under the name titania, is used commercially as a white pigment and where the rapidly hydrolyzed $TiCl_4$ is used as "smoke" by sky-writers. Titanium also has well-defined 2+ and 3+ oxidation states, however. The rather uncommon 2+ state has no aqueous chemistry since it is oxidized by water, but the binary halides are well known, and titanocene is an object of much current interest in nitrogen-fixation studies. The 3+ oxidation state is much better known and is commercially available as the trichloride in both solid, anhydrous, form and as a 20% aqueous solution. These violet solutions are fairly rapid, mild reducing agents which are used in volumetric analysis [$Ti^{3+} + H_2O = TiO^{2+}(aq) + 2H^+ + e^-$; $E° = -0.1$ V].

Ti(III) has an interesting history as a reducing agent in organic chemistry: it was well known in the early 1900's but was then more or less forgotten until a decade ago. Knecht and Hibbert, for example, published a series of early papers[2] on the ability of aqueous $TiCl_3$ solutions to reduce nitro arenes to amino arenes. They showed that the reaction was useful, not only as a preparative synthetic method but also as an analytical tool for the quantitative determination of aromatic nitro groups in unknown substances.[3] The procedure still survives in texts on functional group analysis.[4] The same authors showed a short time later that aqueous $TiCl_3$ was capable of effecting rapid reduction of quinones to hydroquinones, and once again they worked out a quantitative analytical procedure based on their method.[5] In 1922, Macbeth demonstrated[6] a further aspect of the reducing power of Ti(III) when he showed that both N–Br and N–Cl bonds in a variety of substrates were readily reduced.

Still other reports appearing occasionally in the literature through the first half of this century demonstrated that cinnamic acid type double bonds could be reduced to the saturated analogs,[7] that azo groups were reduced to hydrazines,[8] and that acetylenic diphenylcarbinols were coupled by action of aqueous $TiCl_3$ to the symmetrical diacetylenic tetraphenylethanes.[9] These results, collected in Table I, show a remarkably wide range of action and suggest that Ti(III) deserves a careful new look as a potentially useful reagent in organic synthesis.

Presumably, part of the driving force for these reactions (all are carried out in aqueous solution) involves stabilization of the oxidized Ti(IV) state as TiO_2. Realizing this, and presupposing a valency change II → IV, van Temelen and Schwartz in 1965 added an entire new dimension to the chemistry of titanium by reductively coupling allylic and benzylic alcohols to the dimeric symmetrical hydrocarbons.[10] Experimentally, an alkoxide anion was added to 0.5 equiv of $TiCl_4$ to produce a dichlorotitanium(IV) dialkoxide. Reduction with potassium metal to the titanium(II) dialkoxide, followed by heating, gave coupled hydrocarbon plus TiO_2. A similar coupling could be effected by treating a monochlorotitanium(III) dialkoxide with methyllithium as reducing agent.[11] Although the process is limited both by moderate yields and by the fact that the alkoxide must be allylic or benzylic, it is nevertheless quite clever in conception. The mechanism[12] involves ho-

John E. Mc Murry is Associate Professor of Chemistry at University of California, Santa Cruz. He was born in New York City in 1942. He received his B.A. degree from Harvard College and the Ph.D. from Columbia University (with Gilbert Stork). His research interests are centered on new synthetically useful reactions and their application to the synthesis of natural products.

---

(1) For a general discussion of titanium chemistry, see F. A. Cotton and G. Wilkinson, "Advanced Inorganic Chemistry," 3rd ed, Interscience, New York, N. Y., 1972, pp 807–818.

(2) E. Knecht and E. Hibbert, *Chem. Ber.*, **36**, 166 (1903).

(3) E. Knecht and E. Hibbert, *Chem. Ber.*, **40**, 3819 (1907).

(4) C. L. Wilson and D. W. Wilson, Ed., "Comprehensive Analytical Chemistry," Vol. IB, Elsevier, New York, N. Y., 1960, pp 390–393.

(5) E. Knecht and E. Hibbert, *Chem. Ber.*, **43**, 3455 (1910).

(6) I. A. Black, E. L. Hirst, and A. K. Macbeth, *J. Chem. Soc.*, 121, 2527 (1922).

(7) P. Karrer, Y. Yen, and T. Reichstein, *Helv. Chim. Acta*, **13**, 1308 (1930).

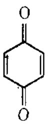
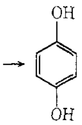
(8) N. R. Large, F. J. Stubbs, and C. Hinshelwood, *J. Chem. Soc.*, 2736 (1954).

(9) R. S. Sweet and C. S. Marvel, *J. Amer. Chem. Soc.*, **54**, 1184 (1932).

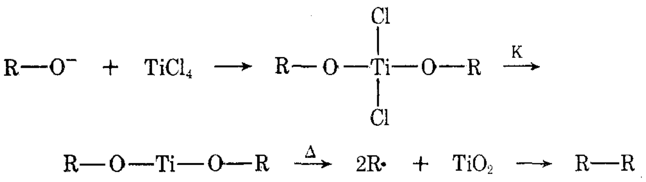
(10) E. E. van Tamelen and M. A. Schwartz, *J. Amer. Chem. Soc.*, **87**, 3277 (1965).

(11) K. B. Sharpless, R. P. Hanzlik, and E. E. van Tamelen, *J. Amer. Chem. Soc.*, **90**, 209 (1968).

Table I
Some Reactions of Aqueous Ti(III)

		Ref
$C_6H_5NO_2$ **1**	→ $C_6H_5NH_2$ **2**	1,2
 3	→  4	4
$CH_3CONHBr$ **5**	→ CH_3CONH_2 **6**	5
C_6H_5NHCl **7**	→ **2**	5
$C_6H_5CH{=}CHCOOH$ **8**	→ $C_6H_5CH_2CH_2COOH$ **9**	6
$C_6H_5N{=}NC_6H_5$ **10**	→ $C_6H_5NHNHC_6H_5$ **11**	7
$t\text{-}BuC{\equiv}CCPh_2OH$ **12**	→ $t\text{-}BuC{\equiv}CCPh_2CPh_2C{\equiv}C\text{-}t\text{-}Bu$ **13**	8

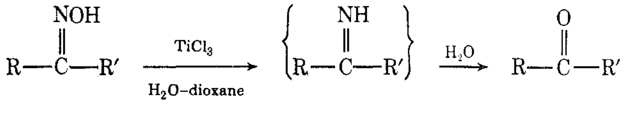
molysis of allylic C-O bonds with expulsion of TiO_2 and coupling of the resultant carbon radicals.



$$R{-}O^- + TiCl_4 \longrightarrow R{-}O{-}\overset{Cl}{\underset{Cl}{Ti}}{-}O{-}R \xrightarrow{K} R{-}O{-}Ti{-}O{-}R \xrightarrow{\Delta} 2R\cdot + TiO_2 \longrightarrow R{-}R$$

Reaction of Ti(III) with Oximes

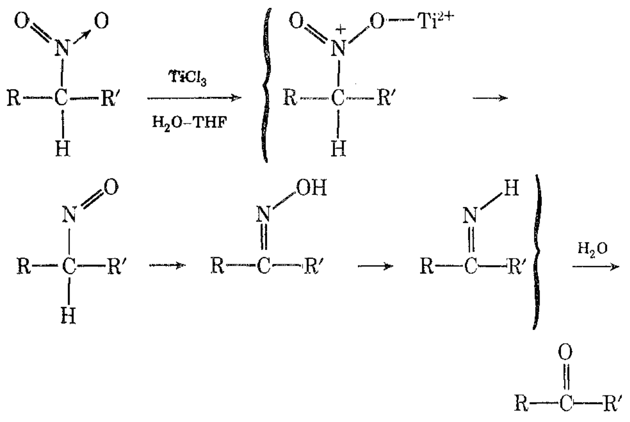
Our own interest in titanium chemistry was fired by a short note published in 1971 by Timms and Wildsmith.[13] These authors, faced with the synthetic problem of transforming the complex antibiotic erythromycin into erythromycylamine, chose to examine the action of buffered, aqueous $TiCl_3$ on erythromycin oxime. After a very short reaction time, they isolated erythromycin imine. Ti(III) had effected a deoxygenation but had not further reduced the C=N double bond. Since imines are rapidly hydrolyzed to ketones at low pH, the reaction was developed into a mild, rapid, and efficient deoximation procedure (acetophenone oxime → acetophenone, 96%).



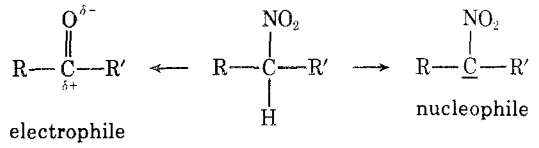
$$R{-}\overset{NOH}{\overset{\|}{C}}{-}R' \xrightarrow[H_2O\text{-dioxane}]{TiCl_3} \left\{R{-}\overset{NH}{\overset{\|}{C}}{-}R'\right\} \xrightarrow{H_2O} R{-}\overset{O}{\overset{\|}{C}}{-}R'$$

Reaction of Ti(III) with Nitro Compounds

We immediately recognized that a simple and useful extension of this reaction might be possible if a nitro compound were to undergo similar deoxygenation. Monodeoxygenation might lead to an oxime or nitroso tautomer, and further reaction would give an imine which would hydrolyze to a carbonyl.

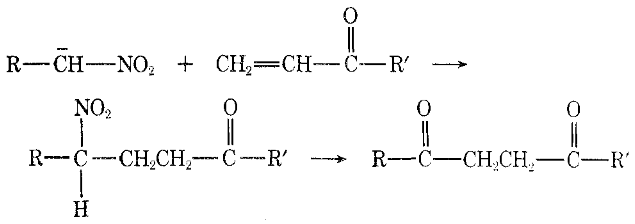


The net transformation, nitro → carbonyl, is of importance in synthetic chemistry since it greatly extends the nitro group's utility. In nitronate salts, the carbon next to nitro is nucleophilic (CH_3NO_2; pK_a = 9) and nitro compounds thus serve as excellent donors in the Michael reaction. Similarly, nitro olefins are themselves good Michael acceptors. By changing the functionality nitro → carbonyl, the polarity of the carbon changes from nucleophilic to electrophilic, thus allowing a whole new range of reactions to be carried out.



$$R{-}\overset{O^{\delta-}}{\overset{\|}{\underset{\delta+}{C}}}{-}R' \longleftarrow R{-}\overset{NO_2}{\underset{H}{C}}{-}R' \longrightarrow R{-}\overset{NO_2}{\underline{C}}{-}R'$$

We were interested in this transformation from the point of view that nitronate anions might serve as "carbonyl anion" equivalents[14] and might therefore provide a general synthesis of 1,4-diketones according to



$$R{-}\bar{C}H{-}NO_2 + CH_2{=}CH{-}\overset{O}{\overset{\|}{C}}{-}R' \longrightarrow R{-}\overset{NO_2}{\underset{H}{C}}{-}CH_2CH_2{-}\overset{O}{\overset{\|}{C}}{-}R' \longrightarrow R{-}\overset{O}{\overset{\|}{C}}{-}CH_2CH_2{-}\overset{O}{\overset{\|}{C}}{-}R'$$

Although other methods do exist for carrying out the conversion,[15] none are sufficiently mild and general to be routinely applicable. We therefore treated a THF solution of 5-nitro-2-heptanone with aqueous $TiCl_3$. After 6-hr stirring at room temperature, vpc analysis indicated disappearance of starting material and presence of a single new product. After work-up, 2,5-heptanedione was isolated in 85% yield. The feasibility of the new method had therefore been established, and we began a study of its scope and mechanism.[16] Some results are given in Table II.

It quickly became apparent that, although simple primary and secondary nitro compounds both underwent transformation to the corresponding aldehydes and ketones in good yields, our conditions were too vigorous (pH <1) for acid-sensitive functional groups to survive. Thus, ketal **20** was deketalized, cyclohexene **23** underwent bond migration, and hexanal was isolated only as its aldol dimer (**22**). Clearly, milder conditions were necessary, and this was achieved by

---

(12) E. E. van Tamelen, B. Akermark, and K. B. Sharpless, *J. Amer. Chem. Soc.*, **91**, 1552 (1969).

(13) G. H. Timms and E. Wildsmith, *Tetrahedron Lett.*, 195 (1971).

(14) See D. Seebach, *Angew. Chem., Int. Ed. Engl.*, **9**, 639 (1969), for a discussion of carbonyl anion equivalents.

(15) See J. E. Mc Murry, J. Melton, and H. Padgett, *J. Org. Chem.*, **39**, 259 (1974), for a list of methods.

(16) J. E. Mc Murry and J. Melton, *J. Org. Chem.*, **38**, 4367 (1973).

Table II
Reaction of Some Nitro Compounds with Aqueous $TiCl_3$ (pH <1)

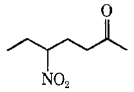
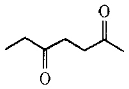
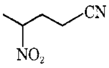
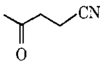
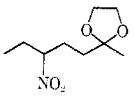
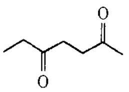
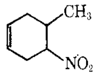
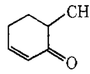
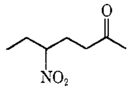
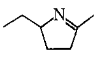
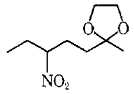
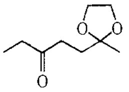
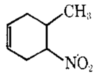
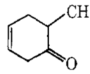
			% yield
 **14**	→	 **15**	85
$C_6H_5CH_2NO_2$ **16**	→	C_6H_5CHO **17**	80
 **18**	→	 **19**	55
 **20**	→	 **15**	40
$CH_3(CH_2)_4CH_2NO_2$ **21**	→	$CH_3(CH_2)_4CHOHCH(CHO)(CH_2)_3CH_3$ **22**	74
 **23**	→	 **24**	35

Table III
Reaction of Nitro Compounds with Buffered Aqueous $TiCl_3$ (pH 6)

			% yield
 **14**	→	 **25**	20
 **20**	→	 **26**	70
$CH_3(CH_2)_4CH_2NO_2$ **21**	→	aldol dimer **22** + $C_6H_{13}N(\rightarrow O){=}NC_6H_{13}$ **27**	45 20
 **23**	→	 **28**	

carrying out the reaction in buffered solution (pH $\simeq$6). Some results are given in Table III.

Although a marked improvement was noted in some examples (ketal **20** was not cleaved; cyclohexene **23** did not undergo bond migration), several other examples were much worse at pH $\simeq$6. Thus, nitro ketone **14** gave pyrroline **25** as the only isolable product, and 1-nitrohexane gave some azoxy-*n*-hexane (**27**) as by-product in addition to hexanal dimer. Certainly any mechanism we propose must account for these nitrogen-containing products.

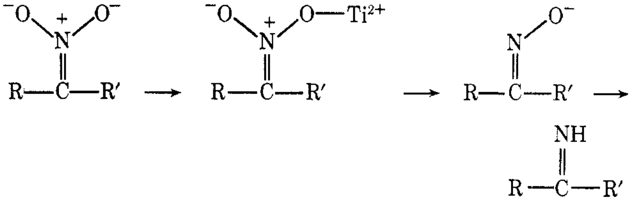
After considering possible reaction mechanisms, it occurred to us that the reaction might be improved by first forming the nitronate anions and then treating these salts with buffered aqueous $TiCl_3$. Under these conditions, reaction occurred within minutes, and good yields were found in all cases (Table IV). Our synthetic goal of developing a mild, general, and efficient method of transforming a nitro group into a carbonyl had therefore been realized through use of aqueous Ti(III).

Table IV
Reaction of Nitronate Anions with Buffered Aqueous $TiCl_3$

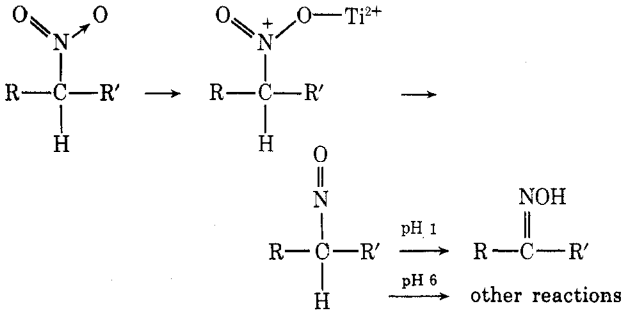
			% yield
14	→	**15**	90
20	→	**26**	70
18	→	**19**	90
$CH_3(CH_2)_4CH_2NO_2$ **21**	→	$CH_3(CH_2)_4CHO$ **29**	45
23	→	**28**	60
$C_6H_5CH_2CH_2NO_2$ **30**	→	$C_6H_5CH_2CHO$ **31**	70

Mechanism of Nitro Reduction

As mentioned above, we have carried out two basic kinds of reactions: reactions on free nitro compounds at different pH's and reactions on nitronate anions. The reaction of nitronate anions is the more straightforward, and we consider it to be exactly analogous to oxime reduction



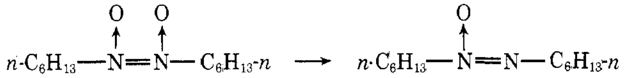
Reduction of free nitro compounds is more complex, and the major question involves timing of the C=N formation. We believe that our product data are best explained by the following mechanism involving formation of a discrete nitroso intermediate



It has been shown that the rate of tautomerization of nitroso compounds to oximes is pH dependent and acid catalyzed.[17] At low pH (Table II), tautomerization is fast, and reductions go normally through the oxime. At neutral pH, however (Table III), tautomerization is slow, so the nitroso intermediate lives long enough to give side reactions. The most common side reaction of nitroso compounds is dimerization to azodioxy compounds, and, since this reaction is sterically sensitive, one would expect primary compounds to dimerize fastest.

This is evidently exactly what happens in the 1-nitrohexane reduction.

$$\underset{\mathbf{21}}{CH_3(CH_2)_4CH_2NO_2} \longrightarrow \underset{\mathbf{32}}{CH_3(CH_2)_4CH_2N{=}O} \longrightarrow$$



$$\underset{\mathbf{33}}{n\text{-}C_6H_{13}{-}\overset{\overset{O}{\uparrow}}{N}{=}\overset{\overset{O}{\uparrow}}{N}{-}C_6H_{13}\text{-}n} \longrightarrow \underset{\mathbf{27}}{n\text{-}C_6H_{13}{-}\overset{\overset{O}{\uparrow}}{N}{=}N{-}C_6H_{13}\text{-}n}$$

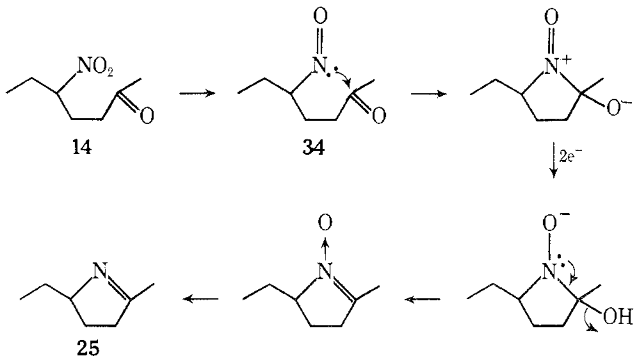
---

(17) M. H. Palmer and E. R. R. Russell, *Chem. Ind. (London)*, 157 (1966).

Table V
Deoxygenation of Sulfoxides with Aqueous $TiCl_3$

			% yield
$Ph_2S{\rightarrow}O$ **35**	→	$(Ph)_2S$ **36**	91
$(PhCH_2)_2S{\rightarrow}O$ **37**	→	$(PhCH_2)_2S$ **38**	78
$PhCH_3S{\rightarrow}O$ **39**	→	$PhSCH_3$ **40**	80
$(n\text{-}Bu)_2S{\rightarrow}O$ **41**	→	$(n\text{-}Bu)_2S$ **42**	68

The observed azoxy-*n*-hexane (**27**) must be derived by further reduction of the nitroso dimer **33**. Similarly, formation of pyrroline **25** can be explained as arising from nitroso intermediate **34**. In this case, the nitroso intermediate is trapped internally, by addition to the carbonyl before it can tautomerize. Further reduction gives the observed pyrroline product.



14 **34** **25**

Reaction of Aqueous $TiCl_3$ with Sulfoxides

As mentioned previously, titanium has a strong affinity for oxygen, and this undoubtedly is partly responsible for its remarkable ability to cleave N-O bonds. This deoxygenating ability might well be expected to extend to other systems (X-O), where X = S or P, and this expectation is at least partially realized as shown in a recent note by Ho.[18] Sulfoxides do in fact deoxygenate cleanly and in high yield to the corresponding sulfides. Some of Ho's results are given in Table V.

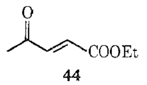
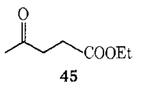
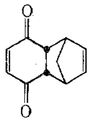
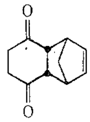
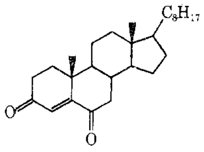
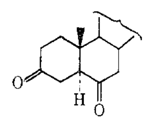
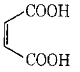
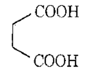
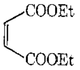
We have been less fortunate, however, in our attempts to deoxygenate phosphine oxides. Triphenylphosphine oxide, for example, has resisted all attempts at reduction by Ti(III).[19]

$$Ph_3P{\rightarrow}O \xrightarrow{Ti(III)}\!\!\!\!\!\!\!/\;\; Ph_3P$$

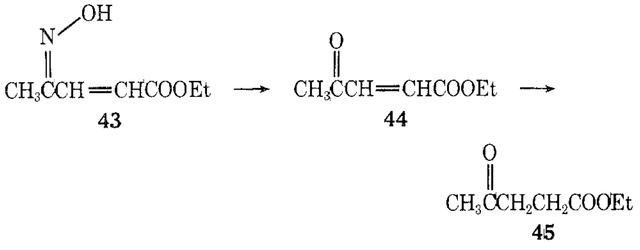
Reaction of Aqueous $TiCl_3$ with Enedicarbonyl Compounds

In connection with some other work, we recently treated ethyl 4-oximino-2-pentenoate (**43**) with aqueous $TiCl_3$ according to the original Timms–Wildsmith deoximation procedure. The sole product of the reaction was the saturated keto ester, ethyl levulinate (**45**). The simplest rationalization of this result is to assume that initial deoximation occurs normally to give ethyl 4-oxo-2-pentenoate (**44**) and that Ti(III) is capable of effecting rapid further reduction of enedicarbonyl compounds to their saturated analogs.

Table VI
Reduction of Enedicarbonyl Compounds with Aqueous $TiCl_3$

			% yield
 **44**	→	 **45**	84
 **46**	→	 **47**	95
 **46**	→	 **49**	86
 **50**	→	 **51**	45
 **52**	↛		

This result is hardly unexpected in view of Karrer's 1930 experiments on cinnamic acid,[7] but it has not been noticed or used previously by synthetic chemists.



$$\overset{\overset{\displaystyle N\diagup OH}{\|}}{CH_3C}CH{=}CHCOOEt \longrightarrow \overset{\overset{\displaystyle O}{\|}}{CH_3C}CH{=}CHCOOEt \longrightarrow \overset{\overset{\displaystyle O}{\|}}{CH_3C}CH_2CH_2COOEt$$

43 **44** **45**

We carried out a short study of the reaction which showed it to be mild, efficient, and remarkably simple to use.[20] Some results are given in Table VI.

The reaction, which is usually complete within 15 min at room temperature, works well for diketones, keto esters, and diacids, but fails for diesters.[21]

Reduction of α-Halo Ketones with Aqueous $TiCl_3$

Perhaps the most commonly used low-valence transition metal ion is chromous ion.[22] Cr(II) is a strong reducing agent often used by synthetic organic chemists to effect the elimination of vicinal dihalides to olefins and to reduce α-halo ketones. By analogy, Ti(III) might also be capable of doing such reductions. Should this be the case, use of Ti(III) would certainly be attractive since it is commercially available whereas Cr(II) must be prepared freshly each time. We therefore tested an acetone solution of 2-bromocyclohexanone with aqueous $TiCl_3$ and, after the violet Ti(III) color had disappeared, we isolated

---

(18) T.-L. Ho and C. M. Wong, *Syn. Commun.*, **3**, 37 (1973).

(19) J. E. Mc Murry and J. Melton, unpublished results.

(20) L. C. Blaszczak and J. E. Mc Murry, *J. Org. Chem.*, **39**, 258 (1974).

(21) This is presumably a reflection of the more negative reduction potential of esters *vs.* ketones: H. O. House and M. J. Umen, *J. Amer. Chem. Soc.*, **94**, 5495 (1972).

(22) J. R. Hanson and E. Premuzic, *Angew. Chem., Int. Ed. Engl.*, **7**, 247 (1968).

Table VII
Some Reductions of α-Halo Ketones with Aqueous $TiCl_3$[24]

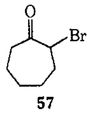
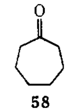
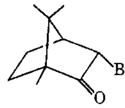
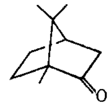
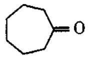
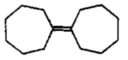
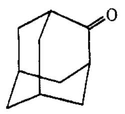
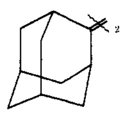
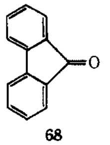
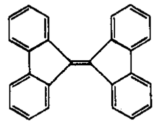
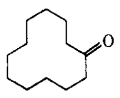
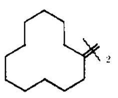
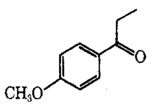
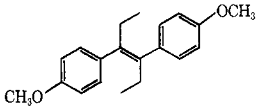
			% yield
PhCOCHClPh 53	→	$PhCOCH_2Ph$ 54	95
$C_6H_5COCH_2Br$ 55	→	$C_6H_5COCH_3$ 56	100
 57	→	 58	86
 59	→	 60	84

Table VIII
Reductive Coupling of Carbonyl Compounds with $LiAlH_4$–$TiCl_3$

			% yield
Ph_2CO 61	→	$(Ph)_2C{=}C(Ph)_2$ 62	95
 63	→	 64	95
 65	→	 66	85
PhCHO 17	→	*trans*-PhCH=CHPh 67	85
 68	→	 69	95
 70	→	 71	80
 72	→	 73	95

a near-quantitative yield of cyclohexanone.[23] A more complete study of the reaction was independently undertaken and published by Ho.[24] Some results from his communication are given in Table VII.

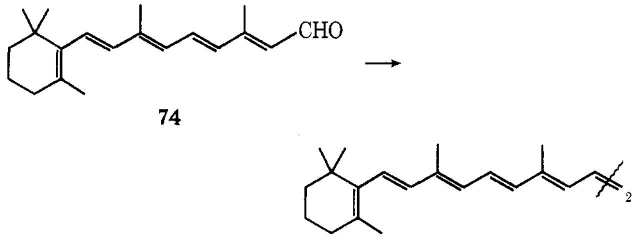
We have not actively pursued the question of whether Ti(III) is an effective reagent for reductive elimination of vicinal dihalides. In one experiment, we treated cholesterol dibromide with aqueous $TiCl_3$ and isolated a moderate yield of cholesterol. The reaction deserves study in more detail, however.

Reductive Coupling of Carbonyls to Olefins with $LiAlH_4$–$TiCl_3$

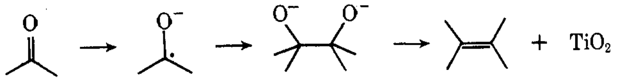
It is well known that the reactivity of $LiAlH_4$ as a reducing agent can be greatly modified by addition of transition metal salts. We therefore thought it would be of interest to investigate a reagent prepared from $LiAlH_4$ and $TiCl_3$. Such a reagent, since it is derived both from a good hydride donor and a good electron donor, might be expected to show unique reducing ability.

We therefore added 1 equiv of powdered $LiAlH_4$ to a stirred slurry of 2.5 equiv of fresh anhydrous $TiCl_3$ in THF. After addition of a THF solution of 1 equiv of benzophenone, followed by overnight reflux, we isolated a 96% yield of tetraphenylethylene. Such a result is precedented only by the recent report of Sharpless[25] on the reductive coupling of aromatic ketones with low-valent tungsten reagents, and it opens up a wide new area of titanium chemistry for exploration. In our initial studies, we have found that the reaction works well both for saturated and for unsaturated ketones.[26] Some results are given in Table VIII.

From a practical point of view, the reaction is probably limited to the synthesis of symmetrical olefins (although one can imagine carrying out a mixed reaction where one cheap reagent is used in excess), but even so it should prove valuable. β-Carotene (75), for example, is a symmetrical polyolefin of commercial importance as a nontoxic yellow food-coloring agent. After subjecting retinal (74) to treatment with the $LiAlH_4$-$TiCl_3$ reagent, we isolated β-carotene in 85% yield. Since the reagent is basic, multiple unsaturation in the substrate is quite compatible with the coupling reaction. A further example of possible commercial importance is the synthesis of dimestrol (73), a precursor of diethylstilbestrol, in high yield from *p*-methoxypropiophenone.


74
75

The course of the reaction can be readily accounted for if one assumes that Ti(II) species are involved. Ti(II) is a strong reducing agent [$Ti^{2+} \rightarrow Ti^{3+} + e^-$; $E° \simeq 0.37$ V] and should be capable of effecting pinacol reduction of a ketone to an intermediate coupled diol. Further reduction, either through formation of a cyclic Ti(II) complex followed by concerted loss of TiO_2 or by stepwise loss of the oxygens, then gives the product olefin.



Evidence in support of this hypothesis comes from observation of the black color characteristic of Ti(II) species[10] and from the fact that, when we allowed the reaction of benzophenone or cyclododecanone to proceed only to partial completion, the corresponding pinacols could be isolated as by-products. van Tamelen has already shown that the 1,2-diol, *meso-*

---

(23) L. C. Blaszczak and J. E. Mc Murry, unpublished results.

(24) T.-L. Ho and C. M. Wong, *Syn. Commun.*, **3**, 237 (1973).

(25) K. B. Sharpless, M. A. Umbreit, M. T. Nieh, and T. C. Flood, *J. Amer. Chem. Soc.*, **94**, 6538 (1972).

(26) J. E. Mc Murry and M. P. Fleming, *J. Amer. Chem. Soc.*, **96**, 4708 (1974).

hydrobenzoin, is reduced to *trans*-stilbene by a $TiCl_3$–CH_3Li reagent[11] [presumably *via* Ti(II)], and we have further demonstrated that treatment of either benzpinacol (76) or the dilithium salt of cyclododecanone pinacol (77) with the $LiAlH_4$–$TiCl_3$ reagent also yields the corresponding olefins. Thus, the reagent affords a method for the reduction of 1,2-diols to olefins and competes favorably with other methods of doing the transformation.[27]

76, R = R′ = Ph
77, R,R′ = -$(CH_2)_{11}$-

One further observation which should be made is that, if $LiAlH_4$ is serving merely to reduce Ti(III) to Ti(II), then other reagent systems producing Ti(II) might also effect the coupling reaction. There have in fact been two recent reports on the use of $TiCl_4$–Zn[28] and $TiCl_4$–Mg[29] reagents to couple aromatic ketones. Both reagents fail for aliphatic ketones, however. We ourselves have also found that a variety of reducing agents, including $LiBH_4$, LiH, and CaH_2, will reduce either $TiCl_3$ or $TiCl_4$ to a reagent which will couple aromatic ketones.

The coupling of aliphatic ketones is considerably more difficult, however, and in our experience only the $LiAlH_4$–$TiCl_3$ reagent has performed satisfactorily. The rate-determining step in the coupling must involve loss of oxygen from the pinacol (pinacol formation must be faster than subsequent deoxygenation since pinacols can be isolated as intermediates). Certainly the deoxygenation should be easier in aromatic cases than in aliphatic cases since the C–O bond involved is benzylic. We have no explanation for the enhanced reactivity of the $LiAlH_4$–$TiCl_3$ system, but studies are in progress to further elucidate the matter.

Conclusion

The organic chemistry of low-valent titanium has undergone a renaissance in the past decade, but, as indicated at several places in the text, much work remains yet to be done. A study of the reduction of other species with S–O bonds is not complete, and the reductive elimination of vicinal dihalides and alkoxy halides needs more examination. Most exciting at the moment, however, is the continuing study of $LiAlH_4$–$TiCl_3$, and many questions remain to be answered: Can the reagent be used to form rings from 1,5- and 1,6-diketones (a "reverse ozonolysis")? Is the diol to olefin reduction stereospecific? Do epoxides reduce to olefins, and, if so, is the reaction stereospecific? Do other functional groups such as alkyl halides and acyloins reduce? Do allylic and benzylic alcohols couple to symmetrical hydrocarbons with the reagent? Low-valency titanium reagents undoubtedly hold many new surprises for the organic chemist, and with the wide range of reactions already discovered, it seems quite doubtful that titanium chemistry will sink into obscurity again.

I am fortunate to have had the assistance of three able and energetic graduate students, Mr. Jack Melton, Dr. Larry Blaszczak, and Mr. Michael Fleming, on parts of this work. Partial support was provided by a fellowship grant from the Alfred P. Sloan Foundation and by a research grant from the National Science Foundation (GP 28173).

---

(27) See K. B. Sharpless and T. C. Flood, *J. Chem. Soc., Chem. Commun.*, 370 (1972), and references therein.
(28) T. Mukaiyama, T. Sato, and J. Hanna, *Chem. Lett.*, 1041 (1973).
(29) S. Tyrlik and I. Wolochowicz, *Bull. Soc. Chim. Fr.*, 2147 (1973).

Propellanes as Stereochemical Models

David Ginsburg

Department of Chemistry, Israel Institute of Technology, Haifa, Israel

Received January 14, 1974

"The world is chiral and clinal; enjoy symmetry wherever you find it." Although V. Prelog offered this advice to my daughter, I too have followed it. The result is esthetically pleasing and chemically exciting. Without doubt propellanes are fine models for stereochemical studies in which symmetry is a cardinal component. The following Account constitutes an attempt to prove this thesis.

When the tetraenic propellane ether **1** was treated with iron pentacarbonyl, a single product, **2**, was obtained in high yield.[1] But we were equally pleased when we obtained five distinct products upon treatment of **1** with $Fe_2(CO)_9$. These were separated by column chromatography, and it turned out that this time **2** was accompanied by two isomeric bis-$Fe(CO)_3$ derivatives and two mono-$Fe(CO)_3$ derivatives.

From the viewpoint of symmetry this is perhaps

David Ginsburg was born in New York, N. Y., and educated there and in Palestine. After 5 years in industry in the United States, he went to Israel where, from 1948 to 1954, he was at the Weizmann Institute. He then moved to the Technion-Israel Institute of Technology. Professor Ginsburg has served as a Visiting Professor at Brandeis University, the University of Zurich, New York University, University of Saskatchewan, Weizmann Institute, McGill University, and Oxford University. Throughout his career, his research interests have remained in the areas of stereochemistry and alkaloids.

---

(1) J. Altman, E. Cohen, T. Maymon, J. B. Petersen, N. Reshef, and D. Ginsburg, *Tetrahedron*, **25**, 5115 (1969).