

Oxygen Atom Transfer With Niobocene Ketenes; Baeyer-Villiger Chemistry with Unusual Regioselectivities

Maria C. Fermin and Joseph W. Bruno*

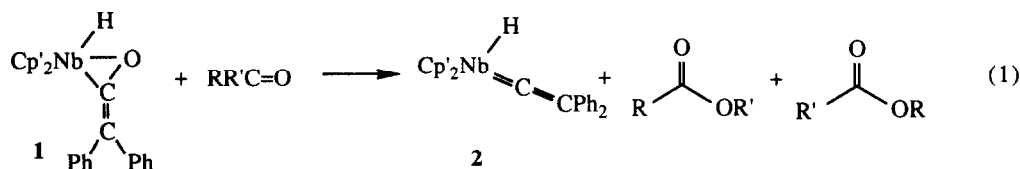
Hall-Atwater Laboratories, Wesleyan University, Middletown, CT 06459

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Abstract: Niobocene ketene complex **1** has been utilized as an oxygen atom transfer reagent, converting ketones and aldehydes to esters and carboxylic acids. The steric properties of compound **1** give rise to a series of relative migratory aptitudes that differs from those seen for peracids. The process may be rendered catalytic in **1** with methyltrifluoromethyldioxirane (**4**).

Oxygen atom transfer processes are of considerable importance in inorganic chemistry, biochemistry, and synthetic organic chemistry, and have been the subject of several recent reviews.¹ Organic reactions of note include epoxidation^{1b} and the Baeyer-Villiger conversion of ketones to esters;^{1d} these processes are typically carried out using oxometal species or peroxyacids, but the use of other reagents is also known.² We recently reported a novel example of ligand-based oxygen atom transfer involving the formal scission of the carbon-oxygen bond of a niobium-bound ketene ligand (**1**, Cp' = η^5 -C₅H₄SiMe₃), and identified the resulting product as a vinylidene species (**2**).^{3a} Compound **1** converts nitriles or isocyanates, a process involving C-to-N migration in the case of nitriles. Carbon-to-heteroatom migrations are also central to the Baeyer-Villiger reaction,^{1d} so we chose to investigate the potential of **1** in reactions with organic carbonyls. Such processes are indeed facile; herein we report the use of **1** in stoichiometric and catalytic Baeyer-Villiger (BV) reactions occurring under mild conditions.

For stoichiometric oxidations (eq. 1), an equimolar amount of carbonyl compound was added to a



solution of **1**^{3b} in THF, diethyl ether, or toluene. Infrared analysis indicated that the reactions are complete in 4-8 hrs at 25° C; conversions are typically greater than 95% (but see below). Organic products were removed by vacuum distillation and identified by comparison of their IR, ¹H NMR, and GC-mass spectra with those of commercial samples. The reactions and products are specified in Table 1.

Several comments are in order regarding the scope and regiochemistry of the reaction. Entries 1-4 in Table 1 show that **1** reacts readily with acyclic dialkyl ketones at ambient temperature, compounds that are often relatively unreactive toward peracids.^{1c-e} Entries 5-7 show reactions of three acetophenones and are of interest in the context of relative migratory aptitudes. Acetophenone gives methyl benzoate as the major product here, whereas most BV reactions give exclusively phenyl acetate.^{1d,4} We surveyed the effect of acceptor (entry 6) or donor (entry 7) substituents; in both cases we found *only* the benzoate product. These results show that aryl groups do not compete well with methyl as a migrating group, and that both donating and withdrawing *para* substituents increase the ratio of alkyl migration. The reaction of

benzophenone (entry 8) shows that phenyl is indeed a poor migrating group; this reaction proceeds slowly and gave only partial conversion to ester after 4 days in refluxing toluene. We have also verified that **1** converts benzonitrile and 1,4-dicyanobenzene to the corresponding isocyanate and diisocyanate, respectively; hence, the conversion in entry 6 shows that the ketone reaction is considerably faster than is nitrile oxidation.

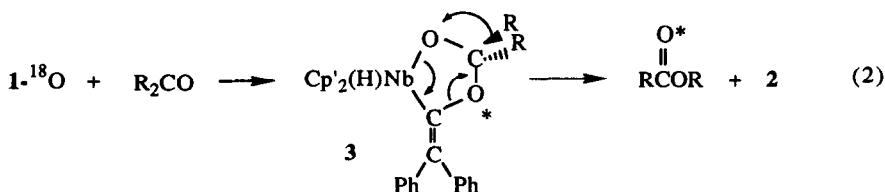
Table 1. Reactions of **1** with Ketones and Aldehydes^a

<u>Reactant</u>	<u>Products (ratios)</u>
1. ⁱ PrCOMe	ⁱ PrCOOMe (72%) + MeCOO ⁱ Pr (28%)
2. ^t BuCOMe	MeCOO ^t Bu (97%) + ^t BuCOOMe (3%)
3. MeCOEt	EtCOOMe (54%) + MeCOOEt (46%)
4. ⁱ PrCOEt	ⁱ PrCOOEt (59%) + EtCOO ⁱ Pr (41%)
5. PhCOMe	PhCOOMe (85%) + MeCOOPh (15%)
6. (4-CN-Ph)COMe	(4-CN-Ph)COOMe
7. (4-MeO-Ph)COMe	(4-MeO-Ph)COOMe
8. PhCOPh ^b	PhCOOPh
9. MeC(O)COMe	MeC(O)COOMe
10. 4-MeO-PhCHO	4-MeO-PhCOOH
11. MeCHO	MeCOOH

^aReactions run in THF or Et₂O at 25° C except as noted. ^bReaction run in refluxing toluene; conversion ca. 60% after 4 days.

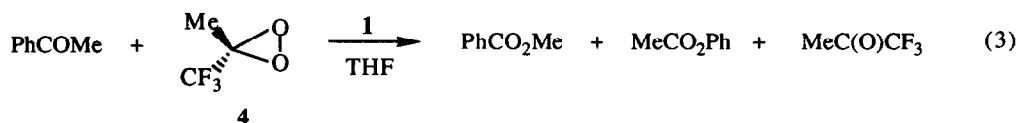
The reaction in entry 9 is also unusual. α,β -Diketones give predominantly acid anhydrides in their reactions with BV reagents,⁵ whereas **1** yields only methyl pyruvate. We have also determined the tendency of **1** to oxidize aldehydes, and entries 10 and 11 show that carboxylic acids result; we see no evidence for the production of aryl formates (the Dakin reaction), as is often seen with electron-rich aryl groups.⁶ Finally, **1** gives no reaction with cyclohexanone, cyclopentanone, or cyclobutanone; this again differs from other BV reactions, in which lactone formation is usually *more* facile than is the oxidation of acyclic ketones.^{1c-e} From these data we can formulate an order of migratory aptitudes for reactions with **1**; these decrease as 3° > Me > 1° ≥ 2° > Ar, with acetyl coming somewhere after Me. This may be compared to the order seen in other BV reactions, for which migratory aptitudes usually decrease as 3° > 2° ≈ Ar > 1° > Me.^{1c-e}

In view of the unusual regiochemistries seen in Table 1, we deemed ¹⁸O-labelling studies important here. Hence **1**-¹⁸O was prepared^{3a} and reacted with acetophenone; the resulting methyl benzoate contained label only in the carbonyl position (eq. 2), as established by IR and GC-MS studies. This differs from other BV reactions, in which labelled peracid yields ester with label in the opposite position.^{1c-e} This result also disproves the intermediacy of a dioxirane,⁷ since this would lead to equal populations of label in



both oxygen positions. We thus invoke dioxaniobacycle **3** in the chemistry,⁸ such that R migrates to the ketone-derived oxygen (eq. 2). Stable trioxaplating cycles have been isolated in the reactions of platinum peroxides with ketones,⁹ and in one case such species have been implicated in a catalyzed BV reaction.^{9c} The function of the niobium center is to provide an electron-deficient oxygen for migration, then act as a good leaving group. This is also the role of the carboxylate in peracid-induced BV reactions, in which the transition state contains an electron-deficient migrating group;¹⁰ hence the normal order of migratory aptitude parallels the ability of the substituents to stabilize a positive charge. In **3**, the metallacycle ring constitutes the equatorial plane of the bent metallocene, and the C-to-O migration would require the migrating group to move above this plane; this will induce a steric interaction with the ring SiMe₃ substituents. Hence, we believe the regiochemical preferences in Table 1 result from a steric bias that works to counteract the usual electronic requirement. Others have shown that steric effects induced by large peroxides or substrates may exert a similar effect on migratory aptitudes,¹¹ although rarely to the extent seen with **1**.

We reported^{3a} that vinylidene **2** could be converted back to **1** with the use of methyltrifluoromethyldioxirane (**4**)¹² as an oxygen atom donor. For this reason, we attempted the catalytic reaction depicted in eq. 3, in which **4** serves as the oxygen source and **1** is the catalyst. These reactions were run



at 25° C in THF with 0.1 molar equivalents of **1** per equivalent of acetophenone in the presence of excess **4** (which must be periodically replenished during the course of the reaction), and control reactions showed there was no reaction between **4** and acetophenone under these conditions in the absence of **1**. The reaction did indeed proceed to complete conversion to methyl benzoate and phenyl acetate, which were produced in the same 85:15 ratio for virtually the entire reaction; this is consistent with catalysis by **1**, which we have also found to catalyze the oxidation of isonitriles to isocyanates with **4**. The catalytic processes require ca. 2 days to reach completion; however, there is no apparent loss of catalytic activity for **1** during this time and the mass balance is quite good, since the sum of ketone and ester concentrations during the reaction is consistently $\geq 95\%$ of the starting ketone concentration. Clearly these reactions are very slow, and we are currently pursuing convenient derivatives of **1** which can operate efficiently; the goal here is to combine useful catalytic rates with the novel oxidation selectivities observed.

In conclusion, ketene complex **1** engages in facile oxygen atom transfer processes by which ketones or aldehydes are converted to esters or acids, respectively. These reactions are related to peracid-induced Baeyer-Villiger reactions, but involve substantially different regioselectivities and relative migratory aptitudes. ¹⁸O-labelling studies and the occurrence of C-to-O migration during the process are consistent with metallacyclic intermediate **3**, in which the original ketone oxygen is imparted with the electron-deficient character required to support migration. The nature of the ketene ligand is important in inducing oxygen transfer, as it ensures there is no tendency for the C-O scission reaction to produce unreactive niobium oxide and the unstable free vinylidene.¹³ In addition, the $\eta^2\text{-C,O}$ bonding mode gives rise to the 3-membered Nb-O-C ring that provides the weak C-O and Nb-O bonds needed for facile transfer.¹⁴ The reactions between carbonyls and dioxirane **4** may be made catalytic, a process in which **1** serves to mediate a reaction between two electrophilic species. Further studies on the scope and mechanism of these and related atom transfer reactions are in progress.

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