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AN EFFICIENT INTERMOLECULAR CARBON-CARBON BOND FORMATION VIA SmI_2-PROMOTED ANION RADICAL ALKYLATION[1)]

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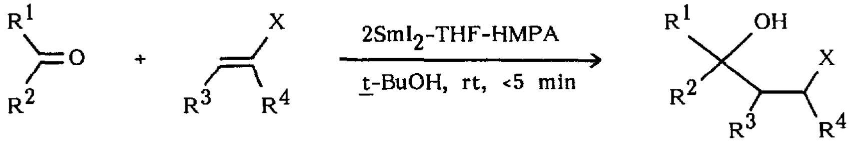
Summary: Anion radicals generated from the corresponding ketones with the efficient one electron transfer system, SmI_2-THF-HMPA, attacked a variety of activated olefins at room temperature affording the corresponding addition products in good to excellent yields, some of which are hardly accessible by the conventional nucleophilic alkylation of ketones.

Several methods have been known for intramolecular ketone-olefin reductive coupling.[2-5)] Most of them are, however, not effective to entropically less-favored intermolecular reactions.[3c,6)] Recently we found that the addition of HMPA dramatically accelerates the electron transfer process of SmI_2 in THF,[7,8)] and now we report that the reduction system (SmI_2-THF-HMPA) is highly useful also for the generation of ketyls and their intermolecular addition to a variety of activated olefins[9,10)] under extremely mild conditions. (Eq. 1)



(1)

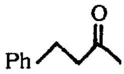
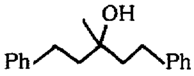
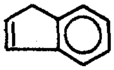
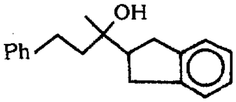
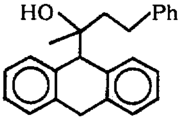
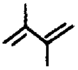
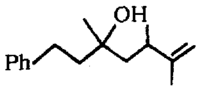
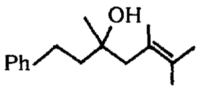
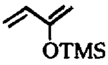
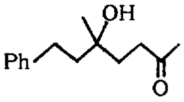
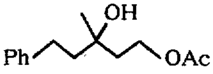
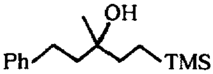
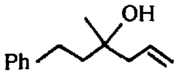
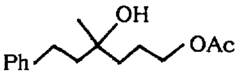
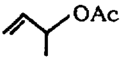
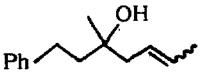
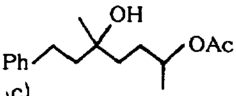
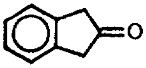
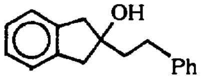
X = Ph, CH=CHR, OAc, CH_2OAc, TMS, CO_2R,[6e)] etc.

The reactions were carried out as follows: A SmI_2-THF solution[8)] (0.1 mol dm^{-3}, 3 ml) was added to a mixture of ketones[11)] (0.15 mmol), olefins (0.3 mmol), t-BuOH or i-PrOH (0.3 mmol), and HMPA[12)] (0.2-0.3 ml) at room temperature under nitrogen atmosphere. The reactions could easily be monitored by the color change from purple[7a)] to colorless. After 5 min, a 3% aqueous hydrochloric acid solution (4-5 drops), hexane (3 ml), and silica gel (ca. 1 g) was added and the resulting mixture was stirred for 5 min. Filtration followed by chromatographic purification gave the corresponding coupling products. The results are summarized in the Table.

Unactivated olefins such as allylbenzene did not react at all.[13)] However, conjugated ones such as styrene, indene, anthracene, or 1,3-butadiene reacted almost instantaneously to afford the coupling products in excellent yields (run 1-4). The silyl dienol ether, prepared from methyl vinyl ketone, was attacked on its less electronegative site, regioselectively.

The reactions with some nonconjugated terminal olefins[14)] such as vinyl acetate, vinyltrimethylsilane, or allylic acetates also proceeded smoothly (run 6-9), whereas the reactions with the electron-rich double bond of ethyl vinyl ether did not[13)] in accordance with the general

Table. Intermolecular Ketone-Olefin Reductive Coupling with SmI_2-THF-HMPA System[a)]

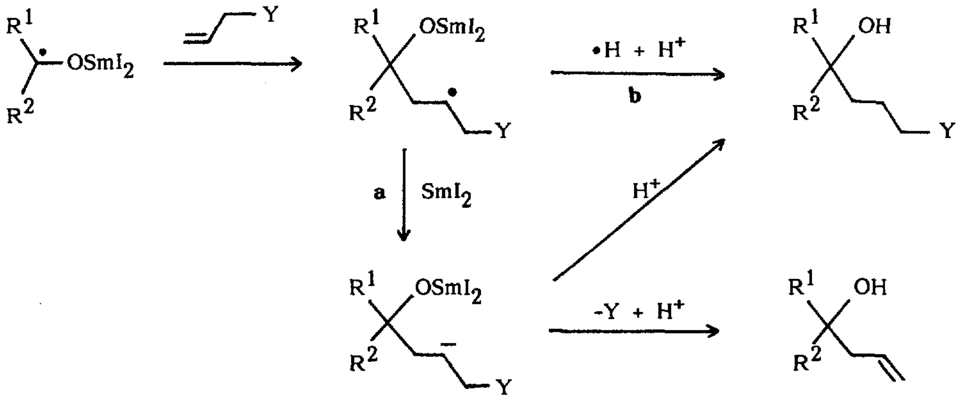
Run	Ketone	Olefin	Product	Yield(%)[b)]
1				97
2	"			85
3	"			95
4	"		 +  (2 : 1)[c)]	99
5	"			49[d)]
6	"			62
7	"			93
8[e)]	"		 +  (79 : 21)[c)]	79
9	"		 +  (26 : 74)[c)]	88
10				71

a) The reactions were carried out at room temperature for 5 min under an atmosphere of nitrogen. For the standard procedure, see the text. b) Isolated yield. c) Determined by ^1H NMR (400 MHz) analysis. d) After acidic workup. e) Inverse addition procedure without proton source. See the text.

trend of the reactivity of alkyl radicals having high SOMO levels.[10a)] The high reactivity of vinylsilane as a radical acceptor is attributable to the property of silicon atom which may stabilize the radical at its α-position through p-σ* interaction.[15)] The unusually high reactivity of allylic acetates in the present reaction may be explained by considering the extra activation of the double bond by the coordination of the acetoxyl group to highly oxophilic samarium(III) ion.

The present reaction seemed to proceed through successive two electron transfer process (route **a** in Scheme 1); the ketyl formation followed by its addition to the double bond yielding an alkyl radical, which then accepts one more electron to produce an anion species. Therefore, the presence of a good leaving group at β-position of the carbanion (e.g. Y = OAc) was expected to cause β-elimination to yield the allylated product.[16)] In fact, such elimination was observed in the reaction of run 9. However, substantial amount of the non-eliminated product (δ-acetoxy alcohol) was formed even when a ketone was added to a solution of allyl acetate and SmI_2 in THF (inverse addition) in the absence of a proton source (run 8), where exclusive β-elimination is highly expected. This fact seems to indicate that the hydrogen abstraction (route **b**) is competing with the sencond electron transfer (route **a**).

Scheme 1.



It is noteworthy that the neutral compounds such as silyl dienol ether, vinyl acetate, or allylic acetates can be used as a homoenolate anion equivalent (run 5), β-acetoxy anion equivalent (run 6), or γ-acetoxy anion equivalents (e.g. run 9), respectively, which are not easily accessible by the conventional methodologies.[17)] Because of the extremely mild reaction conditions, even an easily enolizable ketone (2-indanone) afforded the alkylated product in good yield (run 10).

References and Notes

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7) Our previous studies with SmI_2-THF-HMPA reduction system: a) Reduction of organic halides, J. Inanaga, M. Ishikawa, and M. Yamaguchi, Chem. Lett., 1485 (1987); b) Barbier-type reaction, K. Otsubo, K. Kawamura, J. Inanaga, and M. Yamaguchi, ibid., 1487 (1987); c) γ-Lactone synthesis, see ref. 6e; d) Regioselective reduction of α,β-epoxy esters, K. Otsubo, J. Inanaga, and M. Yamaguchi, Tetrahedron Lett., 28, 4437 (1987); e) Deoxygenation of organoheteroatom oxides, Y. Handa, J. Inanaga, and M. Yamaguchi, J. Chem. Soc., Chem. Commun., in the press; f) Deoxygenation of α-oxygenated esters, K. Kusuda, J. Inanaga, and M. Yamaguchi, Tetrahedron Lett., in the press. For the use of this system by other groups, see ref. 2b, and 2c.

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9) For the reaction with α,β-unsaturated esters by the present reduction system, see ref. 6e.

10) For the intermolecular formation of aliphatic C-C bonds via alkyl radical reactions, see a) B. Giese, "Radicals in Organic Synthesis: Formation of Carbon-Carbon Bonds" in "Organic Chemistry Series" ed by J. E. Baldwin, Pergamon Press (1986); b) M. Ramaiah, Tetrahedron, 43, 3541 (1987); c) D. P. Curran, Synthesis, 417 (1988).

11) Generally, aldehydes gave the coupling products in lower yields than ketones because of the simple reduction leading to the corresponding primary alcohols. For example, the reaction of cyclohexanecarboxaldehyde with styrene gave the coupling product (57%) and cyclohexylmethyl alcohol (36%).

12) Different from the reaction with α,β-unsaturated esters (ref. 6d and 6e), the addition of HMPA is crucial for the present reaction: In the absence of HMPA little coupling product was obtained.

13) When the desired addition reaction of ketyls to olefins did not take place, simple reduction of ketones to alcohols proceeded slowly.

14) Internal acyclic olefins such as crotyl acetate, cinnamyl acetate, or 1-phenyl-1-propene showed poor or modest reactivity. For example, the reaction of 4-phenyl-2-butanone with 1-phenyl-1-propene afforded the corresponding coupling product in 42% yield.

15) E. W. Colvin, "Silicon in Organic Synthesis", Butterworths, London (1981), p. 12. The LUMO level of vinyltrimethylsilane has been reported to be considerably low: J. C. Giordan, J. Am. Chem. Soc., 105, 6544 (1983).

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