Tetrahedron Letters, Vol. 34, No. 43, pp. 6875-6876, 1993
Printed in Great Britain

0040-4039/93 $6.00 + .00
Pergamon Press Ltd

A Three Component Free Radical Coupling Reaction: Vicinal Dialkylation of α,β-Unsaturated Ketones and Esters

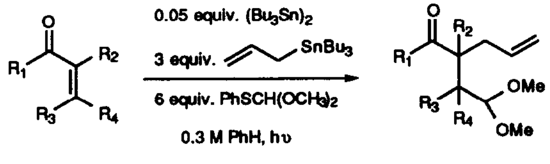
Gary E. Keck* and Cheryl P. Kordik

Department of Chemistry
University of Utah
Salt Lake City, Utah 84112

Abstract: A three component free radical coupling reaction that produces vicinal dialkylated ketones and esters has been investigated. The products possess versatile functionality that is easily manipulated into a variety of other functional groups.

A three component free radical coupling reaction is a potentially powerful synthetic strategy, particularly when the products produced contain functionality well suited for further elaboration into a variety of other functional groups. There are several precedents for such a reaction. A reaction has been reported in the literature that achieved this goal, but was limited to acyclic olefinic substrates that contained two strongly electron-withdrawing groups such as carboethoxy and cyano.[1] More recently, Toru *et. al.* demonstrated a radical mediated vicinal dialkylation of α,β-unsaturated cyclic ketones with alkyl halides and allylplumbanes.[2]

We have undertaken the investigation of a one-pot vicinal dialkylation of a variety of α,β-unsaturated carbonyl compounds with allylstannane and dimethoxy(phenylthio)methane[3] via free radicals (Eq. 1). From a mechanistic point of view, this case appeared especially promising since the initially formed electron rich dimethoxymethyl radical[4] should react much more rapidly with an electron deficient olefin than with the relatively nucleophilic allylstannane. The electron deficient α-carbonyl radical so produced, conversely, should react readily with allylstannane.



Eq. 1

The results are shown in Table 1.[5,6] In a typical experiment, a 0.3 to 0.5 M degassed benzene solution of 2-cyclopenten-1-one, 0.05 equiv. of hexabutylditin, 3 equiv. of allylstannane and 6 equiv. of dimethoxy(phenylthio)methane was irradiated with a sun lamp for 12 h. The resultant solution was concentrated and subjected to flash chromatography on silica to give a 69% yield of 2-allyl-3-dimethoxymethyl-1-cyclopentanone (Entry 1). As indicated in the table, both α,β-unsaturated ketones and ester substrates produced the desired products (Entries 1-4, 5-6). With the cyclic enones, the 5-membered ring cases gave higher yields than the corresponding 6-membered ring substrate (Entry 1, 4). When the substrates have additional substitution on the olefin, a substituent α to the carbonyl is better tolerated than one β (Entry 2, 3). This seems reasonable as the initial attack occurs at the β-position which would suggest that steric hindrance would be more detrimental at this position. When the solvent is changed from benzene to toluene there is essentially no change in the yield of the reaction (Entry 1 vs. 7) However, if a 450W Hanovia UV lamp is used for the irradiation instead of a sun lamp the yield is lowered significantly (Entry 1 vs. 8). Also, the presence of hexabutylditin appears to mediate the reaction as the yield drops slightly when it is absent (Entry 4 vs. 9).

Table 1. Vicinal Dialkylation of α,β-Unsaturated Ketones and Esters

Entry	α,β-Unsaturated Compound	Yield[a]	Isomer Ratio[b,c]	Method[d]
1	2-cyclopenten-1-one	69 %	8:1[b]	A
2	2-methyl-2-cyclopenten-1-one	51 %	3:1[c]	A
3	3-methyl-2-cyclopenten-1-one	28 %	3:1[c]	A
4	2-cyclohexen-1-one	33 %	4:1[b]	A
5	methyl acrylate	42 %	n.a.	A
6	methyl crotonate	46 %	2:1[c]	A
7	2-cyclopenten-1-one	67 %		B
8	2-cyclopenten-1-one	55 %		C
9	2-cyclohexen-1-one	11 %		D

a: isolated yields b: determined by GC c: determined by NMR d: A=standard conditions as described in the text B= 0.3 M toluene C= 450 W Hanovia UV lamp D= no hexabutylditin

In all cases where there was a possibility for the formation of diastereoisomers, a mixture was indeed obtained. With 2-cyclopenten-1-one (Entry 1) and 2-cyclohexen-1-one (Entry 4) the predominant isomer was *trans* in agreement with literature precedent.[2]

The yields of the reaction are moderate. However the yields when the percentage conversion of starting material is considered are higher. For example, the reaction with the substrate 3-methyl-2-cyclopenten-1-one (Entry 3) produces a 28% isolated yield, but the yield based on recovered starting material is 58%, a substantial increase. We are currently working on this yield and conversion problem by reevaluating our choice of acetal free radical precursor. These results will be reported in due course.[7]

References and Notes:

1. Mizuno, K.; Ikeda, M.; Toda, S.; Otsuji, Y. *J. Am. Chem. Soc.* **1988**, *110*, 1288.
2. Toru, T.; Watanabe, Y.; Tsusaka, M.; Gautam, R. K.; Tazawa, K.; Bakouetila, M.; Yoneda, T.; Ueno, Y. *Tetrahedron Lett.* **1992**, *28*, 4037.
3. Shiner, C.S.; Tsunoda, T.; Goodman, B.A.; Ingham, S.; Lee, S.; Vorndam, P.E. *J. Am. Chem. Soc.* **1989**, *111*, 1381.
4. The addition of acetal radicals (generated photochemically via H abstraction from acetals with ^{3}n-p* benzophenone) has been described. See Fraser-Reid, B.; Hicks, D.R.; Walker, D.L.; Iley, D.E.; Yunker, M.B. *Tetrahedron Lett.* **1975**, 297.
5. All new compounds were fully characterized by spectroscopic techniques (^{1}H NMR, ^{13}C NMR, IR) and their molecular formulas established by microanalysis.
6. In some cases the reaction can be done under thermal conditions. A typical procedure for thermal initiation: A 0.3 M degassed benzene solution of ethyl cinnamate, 0.5 equiv AIBN, 3 equiv allylstannane and 6 equiv of dimethoxy(phenylthio)methane was heated at 80 C for 12 h. The solution was cooled to room temperature, concentrated and subjected to flash chromatography on silica to provide 25% of the product.
7. Financial support of this research by the National Science Foundation (CHE8312729) is gratefully acknowledged.

(Received in USA 22 June 1993; accepted 26 August 1993)