Tetrahedron Letters,Vol.23,No.29,pp 2957-2960,1982 0040-4039/82/292957-04$03.00/0
Printed in Great Britain

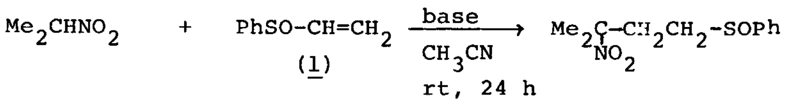
CONJUGATE ADDITION OF ALKYL GROUPS TO α,β-UNSATURATED SULFOXIDES VIA MICHAEL ADDITION OF NITROPARAFFINS AND SUBSEQUENT DENITRATION WITH TRIBUTYLTIN HYDRIDE

Noboru Ono,* Hideyoshi Miyake, Akio Kamimura, Nobuo Tsukui, and Aritsune Kaji*
Department of Chemistry, Faculty of Science, Kyoto University,
Kyoto 606, Japan

Summary: Michael addition of nitroparaffins to α,β-unsaturated sulfoxides is well effected in the presence of DBU. The nitro group in the adduct is replaced by hydrogen with Bu_3SnH without influence to the sulfinyl function. The overall reactions provide an efficient method for the conjugate addition of alkyl groups to α,β-unsaturated sulfoxides.

Recently we have reported an efficient method for the direct replacement of aliphatic nitro group by hydrogen or deuterium with Bu_3SnX (X = H, D).[1)] In this paper we report a new method for the conjugate addition of alkyl groups to α,β-unsaturated sulfoxides via Michael addition of nitroparaffins and the subsequent denitration with Bu_3SnH. This may provide some syhthetic utility, for good and general methods for the conjugate addition to α,β-unsaturated sulfoxides have not been available so far.[2)]

Two problems exsist for the desired transformations, namely, α,β-unsaturated sulfoxides are less reactive as Michael acceptors than the corresponding carbonyl compounds and the sulfinyl function is readily eliminated under reducing or thermal conditions. First problem can be resolved simply by using DBU as a base for a catalysis of Michael addition. Effectiveness of this base is well demonstrated in the reaction of 2-nitropropane with phenyl vinyl sulfoxide (1). Results are summarized below.

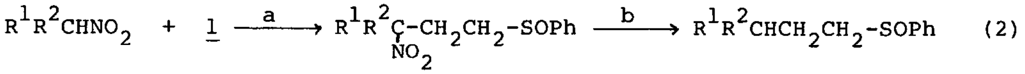


$$Me_2CHNO_2 + \underset{(1)}{PhSO\text{-}CH{=}CH_2} \xrightarrow[CH_3CN,\ rt,\ 24\ h]{base} Me_2\underset{NO_2}{C}\text{-}CH_2CH_2\text{-}SOPh$$

base (1 eq)	yield, %
Et_3N	0
KF,reflux	10
t-BuOK	15
TMG*	60
DBU	95

* tetramethy guanidine

Michael addition of other nitroparaffins to 1 was similarly well effected by DBU. The procedure of this reaction is very simple. The solution of nitroparaffins (10 mmol), 1 (10 mmol), and DBU (10 mmol) in CH_3CN (10 ml) was kept at room temperature for 24 h without stirring. The usual precautions for protecting the reaction from moisture and air were unnecessary. Pure products (2) were obtained in good yields after the usual work up and column chromatography. Heating the mixture of 2 (10 mmol), Bu_3SnH (13 mmol), and AIBN (3 mmol) in benzene (10 ml) at 80°C for 2 h resulted in the clean denitration without affecting the sulfinyl function giving 3 in good yields. Thus the second problem also simply resolved.[3)]



$$R^1R^2CHNO_2 + \underline{1} \xrightarrow{a} R^1R^2\underset{NO_2}{C}\text{-}CH_2CH_2\text{-}SOPh \xrightarrow{b} R^1R^2CHCH_2CH_2\text{-}SOPh \quad (2)$$

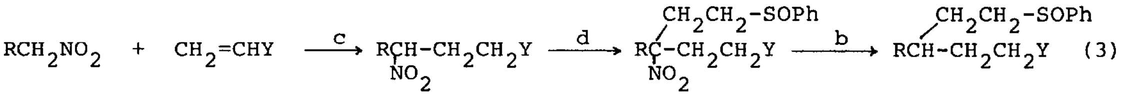
(2) (3)

Results

(a) DBU (1 eq)/CH_3CN, rt, 24 h, (b) Bu_3SnH/benzene, 80°C, 2 h

R^1	R^2	yield of 2, %	yield of 3, %
Me	Me	95	93
$PhCH_2$	Me	98	94
Me_2CHCH_2	Me	90	91
$Me_2C{=}CHCH_2CH_2$	Me	81	84

The present method has some merits over that using organometallic reagents. Compared to organometallic reagents, nitroparaffins are easy to handle and available from various sources such as alkyl halides, amines, ketones, oximes, hydrocarbons or carboxylic acids.[4)] Furthermore, nitroalkanes undergo Michael addition to various α,β-unsaturated esters, ketones, nitriles or sulfones under mild conditions.[4)] Considering them, the sequences of eq 2 provide a useful synthetic operation Some examples are presented here. Michael addition of nitroparaffins to methyl vinyl ketone or methyl acrylate was effected in the presence of TMG (0.1 eq) to give the adduct 4. Compound 4 underwent further Michael addition to 1 in the presence of DBU to give 5. The nitro group in 5 was selectively replaced by hydrogen with Bu_3SnH to give 6.



$$RCH_2NO_2 + CH_2{=}CHY \xrightarrow{c} R\underset{NO_2}{C}H\text{-}CH_2CH_2Y \xrightarrow{d} R\overset{CH_2CH_2\text{-}SOPh}{\underset{NO_2}{C}}\text{-}CH_2CH_2Y \xrightarrow{b} R\overset{CH_2CH_2\text{-}SOPh}{C}H\text{-}CH_2CH_2Y \quad (3)$$

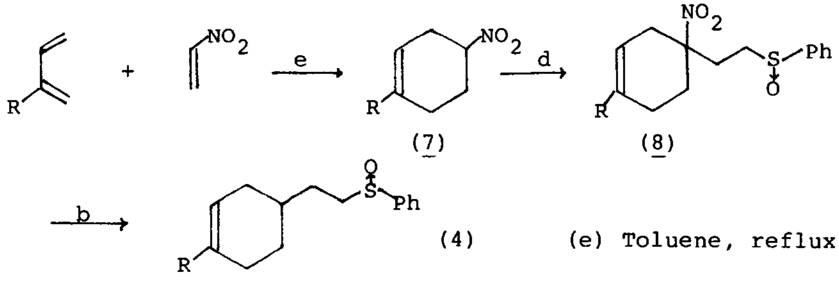
(4) (5) (6)

(c) TMG (0.1 eq)/CH_3CN, rt, 24 h (d) 1, DBU (1 eq), rt, 24 h

Results

R	Y	yield of 4, %	yield of 5, %	yield of 6, %
Me	C(=O)Me	76	79	90
Me_2CH	C(=O)Me	72	72	70
Me	COOMe	72	80	88

Further important applications of the present procedure can be demonstrated in the regioselective construction of six membered rings via Diels-Alder reactions of nitroolefins and the sequences of eq 2. For example, nitroethylene is an excellent dienophile and undergoes the regioselective Diels-Alder reactions under relatively mild conditions with unsymmetrical dienes. The reaction of nitroethylene with isoprene or myrcene gave the adduct 7 in good yields regioselectively, which was further converted to 9 via the sequences of eq 2. It should be emphasized again that the sulfinyl function was unchanged under the conditions for denitration. The similar transformations might be possible by using acrylonitrile or phenyl vinyl sulfone, but it is probably very difficult to remove the cyano or sulfonyl function without affecting the sulfinyl function. In this regard the nitro group is far superior to the cyano or sulfonyl group as an activating or controlling element in these reactions.

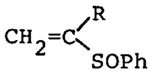


(7) (8) (9) (4)

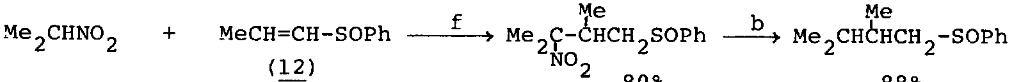
(e) Toluene, reflux, 4 h

Results	R	yield of 7, %	yield of 8, %	yield of 9, %
	Me	86	93	91
	$Me_2C{=}CHCH_2CH_2$	71	82	83

Michael addition of nitroparaffins to α,β-unsaturated sulfoxides is not limited to 1. Other sulfoxides such as 10-12 can serve as Michael acceptors. Among them, 1-propenyl phenyl sulfoxide (12) is the least reactive. The reaction of 2-nitropropane with 12 required the rather drastic conditions (f)



$CH_2{=}C(R)SOPh$ R = Ph (10) R = C_5H_{11} (11)



$$Me_2CHNO_2 + \underset{(12)}{MeCH{=}CH\text{-}SOPh} \xrightarrow{f} \underset{80\%}{Me_2\underset{NO_2}{C}\text{-}\overset{Me}{C}HCH_2SOPh} \xrightarrow{b} \underset{88\%}{Me_2CH\overset{Me}{C}HCH_2\text{-}SOPh} \quad (5)$$

(f) DBU (1 eq), rt, 48 h, no solvent

Finally, as the sulfinyl function has been used widely for the preparation of various important compounds such as aldehydes or olefins, the reactions presented in this paper find wide application in organic synthesis.

References and notes

(1) N. Ono, H. Miyake, R. Tamura, and A. Kaji, Tetrahedron Lett., 1705 (1981). The first useful method for the replacement of the nitro group by hydrogen was found by N. Kornblum et al, (N. Kornblum, S. C. Carlson and R. G. Smith, J. Am. Chem. Soc., 101, 647 (1979), where CH_3SNa was used as a reducing agent The same compounds were treated with Bu_3SnH by D. D. Tanner et al. to give the similar results to those obtained by using CH_3SNa. (D. D. Tanner, E. V. Blackburn, and G. E. Diaz, J. Am. Chem. Soc., 103, 1557 (1981)). However, the reagent CH_3SNa is too strong nucleophile for the use of the denitration from the compounds of Michael addition of nitroparaffins. We have found that Bu_3SnH is highly selective reagent and can be used for the denitration in variuos cases.

(2) In general, RMgX + CuX or R_2CuLi undergoes the facile conjugate addition to α,β-unsaturated carbonyl compounds, but there are some difficulties in the case of the conjugate addition to α,β-unsaturated sulfoxides. For example, RMgX reduces α,β-unsaturated sulfoxides to the corresponding sulfides in the presence of CuX. (G. H. Posner and P. W. Tang, J. Org. Chem., 43, 4131 (1978)). R_2CuLi undergoes the conjugate addition to p-chlorophenyl vinyl sulfoxide, but the yields are rather low (30-75%). (H. Sugihara, R, Tanikaga, K. Tanaka, and A. Kaji, Bull. Chem. Soc. Jpn., 51, 655 (1976)). These difficulties arises from the instability of α-sulfinyl carbanions, therefore the additional activating groups generally require for the facile conjugate addition of RMgX or R_2CuLi to α,β-unsaturated sulfoxides.

(3) As the sulfinyl functions are readily eliminated under the conditions of desulfonylation or decyanation using Na-Hg or K-HMPA, the denitration without affecting the sulfinyl function promises a potent synthetic utility.

(4) Houben-Weyl, "Methoden der Organischen Chemie" 4 th Ed., E. Muller, Ed., Vol. X, part 1, Georg Thieme Verlag, Stuttgart, 1971. D. Seebach, E. W. Colvin, F. Lehr, and T. Weller, Chimia, 33, 1 (1979). N. Ono and A. Kaji, Yuki Gosei Kagaku Kyokaishi, 38, 115 (1980).

(Received in Japan 8 April 1982)