Pergamon

Tetrahedron Letters 39 (1998) 5413–5416

TETRAHEDRON
LETTERS

Sonochemical Synthesis of Norbornane Derivatives Using Allene Cyclopentadiene Diels–Alder Cycloaddition

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Received 19 February 1998; revised 13 May 1998; accepted 15 May 1998

***Abstract*: The dienophilic reactivity of allenic trichloromethyl sulfoxides under ultrasound irradiation has been investigated. A considerable rate enhancement has been observed for cycloaddition of the unsubstituted and γ-monosubstituted allenyl trichloromethyl sulfoxides to cyclopentadiene. With the corresponding γ,γ-disubstituted allenic sulfoxides, a competing 1,2- to 1,3-diene isomerization is observed.**

Diels-Alder cycloaddition reactions have drawn a great deal of mechanistic and synthetic attention in recent years, owing to their extensive application in the construction of ring systems which are frequently required for the synthesis of natural products, drugs and other biologically active compounds.[1] There are several disadvantages in the conventional preparation of the Diels-Alder products, namely, (i) the reaction time is occasionally too long, and (ii) unsuitable in the presence of some functional groups. Unactivated allenes are indeed resistant to [4+2] cycloaddition reactions. However, allenes which are activated by a sulfonyl group,[2] especially trichloromethyl sulfonyl group[3] undergo smooth Diels-Alder reaction. In contrast, trichloromethyl allenyl sulfoxides are very sluggish in reactivity. Although the propadiene trichloromethyl sulfoxide reacts with cyclopentadiene when heated in acetonitrile under reflux,[3] the methyl and phenyl substituted allenes fail to react under these conditions. Therefore, an alternative approach is required to overcome this barrier.

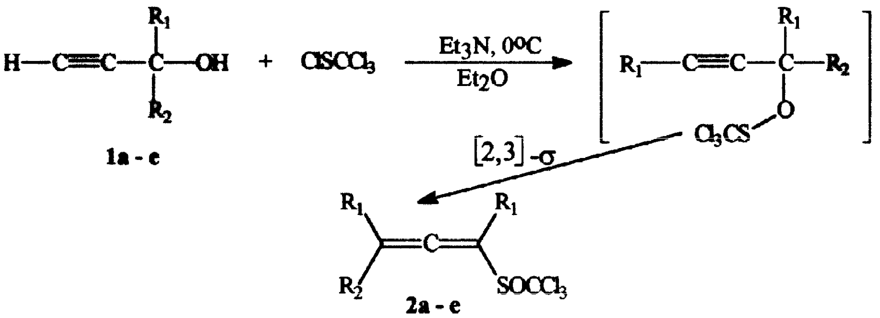
Recently, the application of ultrasound to organic synthesis was proven to be a versatile methodology for the preparation of organic molecules.[4] The success and advantages of sonochemical reactions include higher yields, improved selectivity and milder reaction conditions when compared with conventional chemical methods. The chemical effects of ultrasound arise from acoustic cavitation: formation, growth, and implosive collapse of bubbles in the liquid.[5] The implosive collapse of the bubble generates localised hot spots through adiabatic compression or shock wave formation within the gas phase of the collapsing bubble. The conditions formed in these hot spots have been experimentally determined, with transient temperatures of ~5000 K, pressures of 1800 atm and cooling rates in excess of 10^{10} K/s[5]. These extreme conditions attained during bubble collapse have been exploited to trigger the organic reactions. Therefore, it leads to the conclusion that the sonochemical method may be a suitable substitute for reactions that require high temperatures and pressures.

Although the use of ultrasound would thus appear as an important substitute for thermal Diels-Alder cycloaddition reactions, its application to organic synthesis is rather limited in the literature. Furthermore, there is still some controversy regarding the utility of ultrasound in Diels-Alder cycloaddition reactions.[4b] To the best of our knowledge, the application of ultrasound to allene cycloaddition has not been explored so far.

0040-4039/98/$19.00
PII: S0040-4039(98)01016-8

Herein, we report the use of ultrasound assisted construction of methylene norbornane derivatives using allene cyclopentadiene [4+2] cycloaddition reactions at near room temperature.

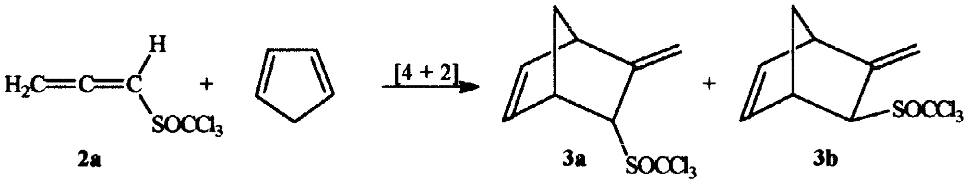
The allenic trichloromethyl sulfoxides **2a-e** required for the present study were prepared by the well-known reaction of the appropriate propargyl alcohol with trichloromethanesulfenyl chloride and *in situ* [2,3]-sigmatropic rearrangement of the corresponding sulfenate esters[6] (eq. 1).



(1)

a, $R_1 = R_2 = H$ c, $R_1 = H, R_2 = Ph$ e, $R_1 = Me, R_2 = Ph$
b, $R_1 = H, R_2 = Me$ d, $R_1 = R_2 = Me$

Having prepared sulfoxides **2a-2e**, we next examined their Diels-Alder cycloaddition under ultrasound irradiation conditions. We have thus found that allenyl trichloromethyl sulfoxide **2a** reacted with cyclopentadiene at 0° C in acetonitrile under ultrasound irradiation (eq. 2, Table 1). The *endo* (**3a**) and *exo* (**3b**) isomers have been obtained in a 9:1 ratio, respectively, as determined by ^{1}H and ^{13}C NMR spectra.[7] The *endo-exo* assignment was confirmed by COSY experiments.

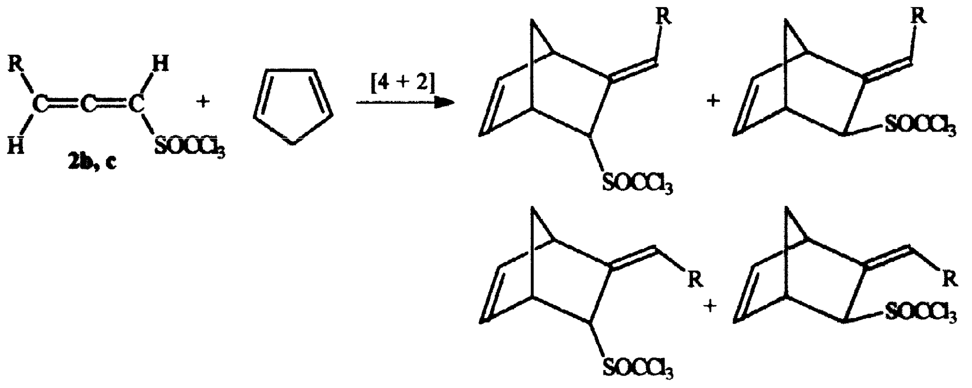


(2)

In the reaction between allenes **2b**, **2c** and cyclopentadiene four isomers are formed (**4**, **5**,eq.3). The presence of four isomers in the reaction mixture was ascertained by appropriate DEPT experiments. In the products only the bridge carbon (C-7) carries two hydrogens. Consequently, one would expect only one methylene signal in the DEPT spectra. However, there are four signals for bridge carbon, which indicates the presence of four isomers. There is no product formed when the reaction was carried out in absence of ultrasound irradiation in two hours.

Table 1. Diels-Alder cycloaddition of allenes to cyclopentadiene

Dienophile	Reaction Condition		Yield (%)		Product	Mass	
	time (h)	Temp.(° C)	Sonication	Normal	Formula	Theoretical	Found
2a	1	0	85	8	$C_9H_9SOCl_3$	269.943	269.941
2b	2	25	78	0	$C_{10}H_{11}SOCl_3$	283.959	283.955
2c	2	25	63	0	$C_{15}H_{13}SOCl_3$	345.975	345.972

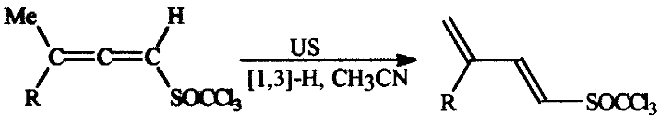


4, R = CH3; 5, R = Ph

(3)

During an extended period of time in the absence of ultrasound, allenes **2b** and **2c** underwent polymerisation. Further, all the above allenes reacted regioselectively with cyclopentadiene. There is no product observed corresponding to β,γ-double bond acting as dienophile, in accordance with previous experience[2,3].

Not surprisingly, γ,γ-dimethyl (**2d**) and, γ-methyl-γ-phenyl (**2e**) allenes did not react with cyclopentadiene. This may be due to steric reasons, as previously suggested.[3] However, a competitive reaction has been observed, namely, isomerization by 1,3-hydrogen shift which leads to the formation of thermodynamically stable 1,3-butadiene derivatives (**6**, 7, eq.4). Although such cumulated to conjugated diene isomerization have been reported before[8] we are not aware of such reaction under ultrasonic conditions. It is interesting to note that though compounds **6** and 7 have a trichloromethyl activated double bond, they are not reactive enough to enter into [4+2] cycloaddition reaction with cyclopentadiene. In other words, cumulated double bond of allene does have influence in the reactivity of allene as a dienophile.



2d, e

6, R = Me
7, R = Ph

(4)

Recently, Caulier and Reisse[9] demonstrated that increase in the rate of Diels-Alder cycloaddition could be due to the sonochemical formation of inorganic acids when halogenated solvents are used as the reaction medium. However, choosing non-halogenated solvents can eliminate such an effect. Further, in order to assess the possibility of any acid catalysed acceleration of rate, control experiments were carried out in the presence of 2,6-lutidine. The results show that there is no change in the yield of the product when 2,6-lutidine is added to the sonication mixture. The results obtained from the present study indicate that sonochemical irradiation may have a positive effect on the Diels-Alder cycloaddition of allenic trichloromethyl sulfoxides. We are now investigating the generality of this reaction to other allenes.

General Procedure: A solution of 1 mmol allene and 1.5 mmol cyclopentadiene (freshly distilled) in dry acetonitrile (10 ml) was exposed to high intensity ultrasound radiation by employing a direct immersion titanium horn (Misonix XL sonifier; 1.13 cm diameter Ti horn, 20 kHz, 100 Wcm^{-2})[10] under argon at a pressure of roughly 2 atmospheres. A flat bottom Pyrex glass vessel (total volume 15 ml) was used for the ultrasound irradiation, which had a silicon rubber septum for gas bubbling or sample extraction. The solutions to be irradiated were purged with argon gas, and were kept under argon throughout the experiment. The sonication cell was kept immersed in an automatic cold bath (Julolab cooler) during the entire sonication.

Acknowledgement: We thank Dr. Hugo E. Gottlieb for his valuable help in analysing ^{13}C and 2D NMR spectra. One of us (CPR) acknowledges the financial assistance from the Bar-Ilan University.

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7. **3a**: ^1H NMR: (600 MHz, $CDCl_3$) δ : 1.62 (1H, dtt, J = 9, 1.5, 0.5 Hz), 1.78 (1H, dt, J = 9, 2 Hz), 3.43 (1H, m), 3.52 (1H, m), 4.21 (1H, dtd, J = 3.5, 2.5, 2.0), 5.07 (1H, d, J = 2 Hz), 5.22 (1H, dd, J = 2.5, 1.0 Hz), 6.16 (1H, ddq, J = 5.5, 3.5, 0.5 Hz), 6.46 (1H, ddt, J = 5.5, 3.0, 0.5 Hz). ^{13}C (300 MHz, $CDCl_3$) δ : 45.39 (C-1), 48.99 (C-7), 51.40 (C-4), 67.60 (C-2), 107.80 (CCl_3), 134.09 (C-5), 135.55 (C-6), 146.95 (C-3). **3b**: 1.76 (1H, ddd, J = 9.5, 2.0, 1.5 Hz), 1.83 (1H, dtt, J = 9.5, 1.5, 0.5 Hz), 3.37 (1H, m), 3.56 (1H, ddd, J = 2.5, 2.0, 0.5 Hz), 3.70 (1H, m), 5.12 (1H, d, J = 2.0 Hz), 5.37 (1H, dd, J = 2.5, 1.0 Hz), 6.22 (1H, ddt, J = 5.5, 3.0, 0.5), 6.36 (1H, ddt, J = 5.5,3.0, 0.5 Hz). 43.51 (C-1), 48.90 (C-7), 49.51 (C-4), 63.64 (C-2), 107.45 (CCl_3), 110.06 (C-8), 135.21 (C-6), 140.22 (C-5), 147.40 (C-3).
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10. The use of the immersion probe means that there is the possibility of contamination of the reaction mixture with titanium metal (by erosion), and also $TiCl_3$ by surface reaction with the chloro groups on the reagents. The possibility (though remote) of some form of catalysis by such materials was removed by preliminary sonification of the allene in the absence of cyclopentadiene, followed by conventional reaction of the pre-sonicated material with added cyclopentadiene. We thank the referee for the suggestion of this control experiment.