

Phosphonium tosylates as solvents for the Diels–Alder reaction with 1,3–cyclopentadiene

Petra Ludley and Nazira Karodia*

Department of Chemical and Forensic Sciences, University of Bradford,
Bradford, BD7 1DP, UK,
E-mail: n.karodia@bradford.ac.uk

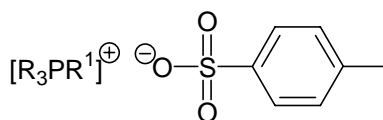
Abstract

A number of phosphonium tosylates have been investigated as solvents for the Diels–Alder reactions of cyclopentadiene with methyl vinyl ketone and methyl acrylate.

Keywords: Diels–Alder reaction, phosphonium tosylates, cyclopentadiene

Introduction

The Diels–Alder reaction is a very useful reaction because it is one of the most effective methods for constructing six-membered rings, for example in the synthesis of natural products. In general, the reactions of 1,3–cyclopentadiene with dienophiles result in mixtures of two stereoisomers, the *endo* and the *exo* product. The reaction is usually catalysed by Lewis acids, which improve the reaction rate as well as the stereoselectivity. Among other methods is the use of supercritical carbon dioxide $scCO_2$ as solvent,¹ catalysts such as a cationic palladium (II) complex² and lithium perchlorate–diethyl ether mixtures.³ Recently ionic liquids, usually imidazolium salts, have been used as solvents for the Diels–Alder reaction.^{4–6}



	A	B	C	D	E
R	Ph	Ph	Ph	<i>n</i> -Bu	Oct
R ¹	Et	<i>n</i> -Bu	Oct	Et	Et

Figure 1

We have reported that phosphonium tosylates (Figure 1) are very good solvents for the Diels–Alder reaction of isoprene with oxygen-containing dienophiles.⁷ The reaction proceeds with high regioselectivity, even without the use of Lewis acids as catalysts. The reaction temperatures are moderate and the solvents can be reused. This class of ionic solvent has also been used very

successfully in catalytic hydroformylation reactions⁸ and transfer hydrogenation reactions.⁹ Some of the advantages of phosphonium tosylates as solvents are high thermal stability, tolerance towards air and moisture and low vapour pressures. They are non-corrosive and solid at room temperature, making them easy to handle and to separate from the products.

Results and Discussion

We now report the results of our study into the reaction of 1,3-cyclopentadiene **1** with the dienophiles methylvinyl ketone (MVK) **2a** and methyl acrylate **2b** in phosphonium tosylates as ionic solvents (Figure 2).

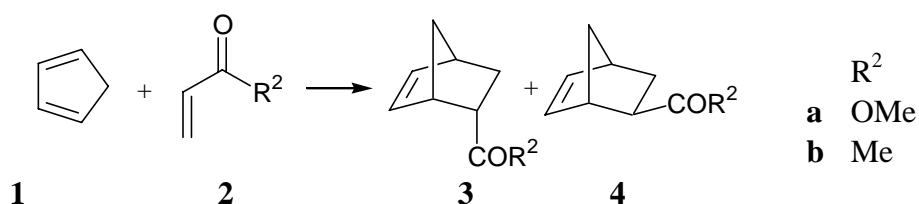


Figure 2

In a typical reaction, the diene (2.5 mmol) and the dienophile (2.5 mmol) were added to the phosphonium tosylate (1 g). The mixture was sealed in a tube and stirred at the temperature specified in Tables 1 and 2. After the reaction was finished the product was either distilled from the reaction mixture or the product was extracted into diethyl ether or petroleum ether (bp. 40–60 °C) and the phosphonium salt was removed by filtration. In some cases, the product had to be purified by vacuum distillation which did not alter the isomer ratio. The solvents were removed *in vacuo* and the resulting product mixtures were analysed by ¹H-NMR (270 MHz, in CDCl₃). The pure ionic solvents were dried and may be reused.

The reaction of 1,3-cyclopentadiene and MVK was studied in phosphonium salts **A–E**, at reaction temperatures between 0–80 °C for either two or 24 hours. The results are presented in Table 1.

Using solvent **D** at 0 °C results in the best *endo* selectivity (90:10) with the yield improving with time (entries 8 and 9). Reactions in solvent **E** under the same conditions give very similar selectivity with improved yields (entries 14 and 15). This compares to 84:16 for benzene under similar conditions.¹⁰ The selectivity is better in ethylammonium nitrate (91:9) but the yield for the reaction at 25 °C only results in a 45% yield after 72 h.¹¹

When using ethyltriphenylphosphonium tosylate **A** as solvent for the reaction at 80 °C the yield only improves slightly when the reaction time is increased from 2 to 24 hrs (entries 1 and 2). What is more remarkable is that the selectivity for the *endo* product decreases from 75:25 to 50:50. When the reaction temperature was raised from 80 to 90 °C the yield improved to 99% but at the same time the *endo* selectivity decreased to 65:35 (entry 3). Similar observations are made when the tosylate **B** is used. At 40 °C the reaction is already virtually complete and the selectivity

is good, but after 2 hours at 90 °C both isomers are produced in equal amounts (entry 5). A similar observation is made for solvent **C**.

Overall there is a clear correlation of temperature and time with the *endo* selectivity of the reaction for all solvents. The *exo* isomer is formed in larger amounts as the reaction temperature and reaction time are increased.

This suggests that initially the *endo* isomer is formed. This isomer then undergoes a retro-Diels–Alder reaction to give the starting materials, cyclopentadiene and MVK. These then react again to form the thermodynamically more stable *exo* Diels–Alder product. This conforms with observations in conventional organic solvents.

Table 1. Reactions of cyclopentadiene **1** with MVK **2a** in quaternary phosphonium tosylates

Entry	Solvent	Time/h	T/°C	Yield (%) ^a	<i>endo/exo</i> ^b
1	A	2	80	78	75:25
2	A	24	80	84	50:50
3	A	2	90	99	65:35
4	B	2	40	98	80:20
5	B	2	90	99	50:50
6	C	2	40	89	85:15
7	C	2	80	87	65:35
8	D	2	0	19	90:10
9	D	24	0	70	85:15
10	D	2	RT	74	85:15
11	D	24	RT	99	85:15
12	D	2	80	85	55:45
13	D	24	80	89	50:50
14	E	2	0	33	88:12
15	E	24	0	79	85:15
16	E	24	RT	91	80:20
17	E	2	80	91	65:35
18	E	24	80	92	50:50

^a Isolated yield.

^b Ratio of isomers determined by ¹H-NMR.

The reaction of 1,3-cyclopentadiene and methyl acrylate was studied in phosphonium tosylates **A**, **B**, **D** and **E** solvents at reaction temperatures between 0 °C and 120 °C for 24 hours. The results are presented in Table 2.

As before an increase in reaction temperature results in a loss of *endo* selectivity with the effect being more subtle in this case. Generally the yield improves with longer reaction time and with higher temperature. The reaction in solvent **A** at 120 °C gives the overall best yield, but also the lowest *endo* selectivity (entry 2).

Reaction in tosylates **D** and **E** at 0 °C give the best selectivity with an *endo/exo* ratio of 80:20 (entry 4). This compares to 79:21 for CH₂Cl₂ (22 °C)¹², 75:25 for benzene (20 °C),¹⁰ 87:13 (6.7)

for EAN (25 °C),¹² 82:18 (4.3) for [emim][BF₄] (20 °C)⁴ and 84:16 (5.25) for EMIC–AlCl₃ (20 °C).⁶

Table 2. Reactions of cyclopentadiene **1** with methyl acrylate **2b** in quaternary phosphonium tosylates

Entry	Solvent	Time/h	T/°C	Yield (%) ^a	<i>endo/exo</i> ^b
1	A	24	80	86	75:25
2	A	24	120	99	70:30
3	B	24	80	43	75:25
4	D	24	0	44	80:20
5	D	24	RT	58	80:20
6	D	24	80	96	75:25
7	E	24	0	55	80:20
8	E	24	RT	67	80:20
9	E	24	80	78	75:25

^a Isolated yield.

^b Ratio of isomers determined by ¹H-NMR.

Phosphonium tosylates prove to be very useful solvents for the Diels–Alder reaction. The reactions of cyclopentadiene, especially with methyl vinyl ketone show *endo* selectivity enhancement compared to nonpolar organic solvents as well as good yields. The reaction conditions are moderate and the solvents can be reused.

We continue to investigate phosphonium salts as potential solvents for organic synthesis.

Acknowledgements

We would like to thank Dr. F. H. Ludley for helpful discussions.

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