Pergamon

Tetrahedron Letters 42 (2001) 5963–5965

TETRAHEDRON LETTERS

Thermal- and microwave-assisted hydrogenation of electron-deficient alkenes using a polymer-supported hydrogen donor

Bimbisar Desai and Timothy N. Danks*

Department of Chemistry, University of Surrey, Guildford, Surrey GU2 7XH, UK

Received 21 May 2001; accepted 28 June 2001

Abstract—Under microwave conditions hydrogenation of olefinic substrates may be achieved in excellent yields using a hydrogen donor supported on an ion-exchange resin and Wilkinson's catalyst.

In this paper we wish to report a simple procedure for catalytic hydrogenation reactions using a recyclable, polymer-supported transfer hydrogenation source.

Recent environmental constraints have led to the development of clean and easily recycled reagents for use in synthetic chemistry. This need has led to the development and use of reagents that are supported on a solid matrix. Also, because of the development of robotic systems for chemical synthesis in many industrial sectors, the need for solid-supported reagents has increased considerably. Such supports facilitate easy removal of the residues from the reaction mixture without release of the residues into the environment. They allow work-up procedures to be simplified where simple filtration rather than extraction, etc., is required. Reagents supported on organic polymers and within and/or on the surface of inorganic matrices have all been reported.[1]

Microwave-assisted organic chemistry has also experienced considerable growth over the past decade. Notable contributions from many groups have been detailed in several recent reviews.[2] Laboratory scale catalytic transfer hydrogenation[3] plays a key role in organic synthesis. Typically a catalyst (e.g. Pd/C, $RhCl(PPh_3)_3$, etc.) and a hydrogen source, such as ammonium formate, is used for the hydrogenation reactions. Although efficient, these reactions are often troublesome since ammonium formate can sublime and block the reaction apparatus. Also the reactions lead to release of ammonia and, whilst on a small scale this does not create any serious problems, on a larger scale this release may become more significant.

Microwave-assisted catalytic transfer hydrogenation, has also been achieved.[4] In most cases, under microwave conditions, Pd/C catalyst, and ammonium formate as the hydrogen donor are used. Hydrogenolysis has been shown to proceed with a similar level of efficiency under microwave conditions.[5]

During our studies on microwave-assisted hydrogenation reactions we reported how use of the di-formate salt of tetramethylethylene diamine provided an ideal alternative to ammonium formate for isotopic labelling of alkenes using Wilkinson's catalyst.[6]

In this note we wish to report the use of polymer-supported formates (PSF) for the reduction of alkenes using Wilkinson's catalyst. As far as we are aware this paper represents the first example of a polymer-supported transfer hydrogenation source for alkenes. The procedure does not result in sublimation and in principle, may also be easily adapted for parallel hydrogenation protocols and is also of potential use in robotic synthesizers.

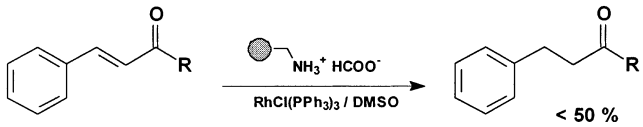
Initially Wilkinson's catalyst and polymer-supported formate derived from (aminomethyl)polystyrene (0.6 mmol/g) was used as a hydrogen source in our reactions. Conversion of the resin to the formate form was achieved by washing with a 20% solution of formic acid in dichloromethane. After filtration and drying under vacuum the resulting activated resin was used directly in a hydrogenation reaction.

Keywords: microwaves; hydrogen donor; hydrogenation; ion-exchange resin.

* Corresponding author. E-mail: t.danks@surrey.ac.uk

0040-4039/01/$ - see front matter
PII: S0040-4039(01)01157-1

A mixture of formylated (aminomethyl)polystyrene, Wilkinson's catalyst and *E*-3-phenylpropenoic acid in a minimum quantity of DMSO (0.5 ml) was irradiated at 100 W for 30 s. Filtration and removal of the solvent led to the isolation of white crystals, which were identified as the reduction product 3-phenylpropanoic acid by comparison of spectroscopic data with literature values. Similarly, when the corresponding methyl and ethyl esters were used as a substrate, the reaction led to the formation of the corresponding saturated esters. Attempts to increase the yield of these reactions by either increasing the quantity of hydrogen donor or prolonging the irradiation time led either to degradation or no significant increase in yield.

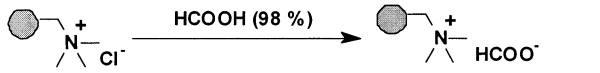


1 R = OH
2 R = OCH_3
3 R = OCH_2CH_3

4 R = OH
5 R = OCH_3
6 R= OCH_2CH_3

In view of the relatively low yields of the reduction products and the relatively high cost of (aminomethyl)-polystyrene the use of a different support for formate was investigated. There are several reports of the use of relatively inexpensive Amberlite® and Amberlyst® ion-exchange resins as a support for reagents.[1] In view of these reports we decided to support formate on these resins and use the resulting material in catalytic hydrogenation reactions.

The hydrogen donor was prepared by washing Amberlite (IRA 938 Cl^- form) resin with formic acid (98%) and subsequently with water until no further chloride was eluted. The resulting solid was dried under vacuum over P_2O_5. The resin thus obtained was ready for further application in hydrogenation reactions.[7]



Amberlite® IRA 938 Cl^- form **Amberlite® IRA 938 $HCOO^-$ form**

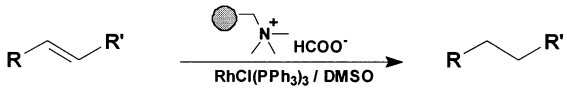
A mixture of Amberlite® IRA 938-supported formate, Wilkinson's catalyst and *E*-3-phenylpropenoic acid in a minimum quantity of DMSO was irradiated at 100 W for 30 s. After filtration, extraction and removal of the solvent, white crystals identified as 3-phenylpropanoic acid were isolated in excellent yield. When the identical reaction was performed under thermal conditions (70°C, 3 h) the reaction required considerably longer and resulted in a reduced reaction yield.

It should be noted that after separation of the Amberlite® at the end of the reaction the polymer-supported formate salt was easily regenerated and could be reused in further hydrogenation reactions. In total, five reaction/regeneration cycles were possible before there was an appreciable decrease in the reaction yield.

In order to explore the scope of this reaction, a range of alkenes were treated with formate and Wilkinson's catalyst under identical conditions. The results of these experiments are presented in Table 1. In each case a thermal comparison for each reaction is presented. This allows the influence of the microwave irradiation on the reaction yield to be better understood.

Interestingly for pentenoic acid (Table 1, entry 6) there is a particularly noticeable improvement by the application of microwave irradiation. In all other cases the reactions show an increase in yield of between 10 and 25% by application of microwave irradiation. The greatest saving, however, is the dramatically reduced reaction times and solvent volumes for the microwave-assisted processes.

Table 1. Hydrogenation of alkenes using polymer-supported formate and Wilkinson's catalyst under microwave and thermal conditions



1 - 8 **9 - 16**

Entry	Alkene	R	R′	Product[a]	Yield (%)	
					Microwave[b]	Thermal[c]
1	**1**	Ph	CO_2H	**9**	95	80
2	**2**	Ph	CO_2Me	**10**	90	75
3	**3**	Ph	CO_2Et	**11**	80	62
4	**4**	Ph	CHO	**12**	95	70
5	**5**	Ph	$COCH_3$	**13**	95	88
6	**6**	Et	CO_2H	**14**	95	50
7	**7**	Ph	CN	**15**	95	95
8	**8**	Ph	$CON(CH_3)_2$	**16**	95	70

[a] All products gave satisfactory spectroscopic data.
[b] All microwave irradiations were carried out at 100 W for 30 s.[8]
[c] All thermal reactions were performed at 70°C for 3 h in DMSO.

In conclusion, it has been shown that a formate supported on an Amberlite® resin may be used as a polymer-supported source for transfer hydrogenation reactions using Wilkinson's catalyst under thermal and microwave conditions.

The application of this chemistry for catalytic reduction of electron-rich alkenes, debenzylations, and asymmetric hydrogenation reactions is currently under investigation.

Acknowledgements

We thank the Personal Chemistry AB for financial support and provision of a MW-10 Microwell microwave reactor.

References

1. (a) Ley, S. V.; Baxendale, I. R.; Bream, R. N.; Jackson, P. S.; Leach, A. G.; Longbottom, D. A.; Nesi, M.; Scott, J. S.; Store, R. I.; Taylor, S. J. *J. Chem. Soc., Perkin Trans. 1* **2000**, 3815; (b) Kirschning, A.; Monenschein, H.; Wittenberg, R. *Angew. Chem., Int. Ed.* **2001**, *40*, 650.
2. (a) Caddick, S. *Tetrahedron* **1995**, *51*, 10403; (b) Deshayes, S.; Liagre, M.; Loupy, A.; Luche, J. L.; Petit, A. *Tetrahedron* **1999**, *55*, 10851; (c) de la Hoz, A.; Díaz-Ortiz, A.; Moreno, A.; Langa, F. *Eur. J. Org. Chem.* **2000**, 3659; (d) Loupy, A.; Petit, A.; Hamelin, J.; Texier-Boullet, F.; Jacquault, P.; Mathe, D. *Synthesis* **1998**, 1213.
3. (a) Rylander, P. N. *Hydrogenation Methods*; Academic Press: Orlando, FL, 1985; (b) James, B. R. *Homogenous Hydrogenation*; Wiley: NewYork, 1973.
4. Banik, B. K.; Barakat, K. J.; Wagle, D. R.; Manhar, M. S.; Bose, A. K. *J. Org. Chem.* **1999**, *64*, 5746.
5. (a) Anwer, M. K.; Sherman, D. B.; Roney, J. G.; Spatola, A. F. *J. Org. Chem.* **1989**, *54*, 1284; (b) Anwer, M. K. *Tetrahedron Lett.* **1985**, *26*, 1381; (c) Rajagopal, S.; Spatola, A. F. *Appl. Catal. A* **1997**, *152*, 69.
6. Al-Qahtani, M. H.; Cleator, N.; Danks, T. N.; Garman, R. N.; Jones, J. R.; Stefaniak, S.; Morgan, A. D.; Simmonds, A. J. *J. Chem. Res.* **1998**, *26*, 400.
7. Resin loading was determined as 2.5 mmol g^{-1} by potentiometric titration after releasing the formate as formic acid by washing with dil. HCl.
8. In a typical experiment, *E*-3-phenylpropenoic acid (0.025 g, 0.16 mmol), Amberlite® IRA 938-supported formate (0.200 g) and Wilkinson's catalyst (0.04 g, 0.0043 mmol) were suspended in a reaction tube using DMSO (0.5 ml) as the solvent. The mixture was irradiated with microwaves at 100 W for 30 s. On cooling the mixture was diluted with dichloromethane (5 ml) and filtered. The filtrate was washed with water (2×5 ml). The organic fraction was dried over magnesium sulfate ($MgSO_4$) and the solvent removed under reduced pressure to give a reddish-orange residue which was purified by filtration through a plug of alumina to give 3-phenylpropanoic acid as white crystals (0.024 g, 95%).