Pergamon

SCIENCE @ DIRECT®

Tetrahedron Letters 44 (2003) 3001–3003

TETRAHEDRON
LETTERS

# $I_2$ as an efficient catalyst in ionic Diels–Alder reactions of α,β-unsaturated acetals

Subhash P. Chavan,* Pallavi Sharma, G. Rama Krishna and Mahesh Thakkar

*Division Of Organic Chemistry: Technology, National Chemical Laboratory, Pune-411008, India*

Received 22 October 2002; revised 29 January 2003; accepted 7 February 2003

**Abstract**—A variety of protected and unprotected α,β-unsaturated aldehydes react with 1,3-dienes in the presence of $I_2$ to give the corresponding cycloadducts. © 2003 Elsevier Science Ltd. All rights reserved.

The Diels–Alder reaction[1] finds immense utility in the synthetic arena by virtue of its operational simplicity, generality and stereoselective construction of six-membered rings. Although the Diels–Alder reaction is a very powerful tool for six-membered ring annulation, it is often limited by polymerization of the diene as well as dienophiles under the reaction conditions. A useful variant of the Diels–Alder reaction, developed by Gassman et al.[2] employs acetals or orthoesters of the α,β-unsaturated dienophile so as to avoid the problem of polymerisation or isomerisation under thermal conditions. Thus, in the Lewis acid-catalysed ionic Diels–Alder reaction, powerful dienophiles are generated by transient formation of a carbocation, the most powerful carbon-based electron-withdrawing group known, adjacent to the vinyl moiety which finally gives a neutral adduct. Thus the masked dienophiles furnish 4π+2π cycloadducts in high yields and under milder reaction conditions.

A number of acids and Lewis acids, viz. TfOH,[2a] TMSOTf,[2b] $BF_3 \cdot Et_2O$,[2c] $CF_3SO_3H$,[2d] $CF_3SO_3Si(CH_3)_3$,[2e] $TiCl_4$–$Ti(O^iPr)_4$,[3] electro-generated acid,[4] $LiClO_4$,[5] Nafion-H[6a] and recently $InCl_3$[6b] have been studied as catalysts to effect 4π+2π cycloaddition reactions. A variety of protic acids are also known to catalyse the reaction.

Recently our group has reported the use of $FeCl_3$ and $FeCl_3$ adsorbed on silica gel[7] as an efficient catalyst in the ionic Diels–Alder reaction. In continuation of our efforts in search of a better catalyst, we found that $I_2$ had the potential to catalyse this reaction. In the presence of iodine the reaction goes to completion within 15–30 min and shows high selectivity in almost all the cases.

$I_2$ has been reported earlier in the context of Diels–Alder reactions wherein it activates substrates like *N*-allyl enamides and lactam derivatives,[8a] anilide and maleimide derivatives[8b] via the formation of cationic intermediates arising from iodolactonisation, to give the cycloadducts. In all the above, the presence of a suitably placed olefin is critical and crucial for the success of the reaction. Aditionally, an excess (2 equiv.) of iodine has to be employed to effect the Diels–Alder reaction.

Herein we report that iodine can also catalyse all kinds of masked α,β-unsaturated dienophiles bearing no activating group, with equal ease. It was observed that the Diels–Alder reactions of acrolein acetal were efficiently catalysed by iodine to furnish the adducts in 15–30 min, with high selectivity.

Thus, when a mixture of the 2,2-dimethylpropylene acetal of acrolein **3** and cyclopentadiene (1:2) in dry dichloromethane at 0°C was treated with 0.1 equiv. of $I_2$, the adduct **8** was obtained in excellent yield after quenching the reaction with $Et_3N$ and purification by column chromatography. The product was obtained as a mixture of *endo* and *exo* isomers 12.6:1. The doublets at $\delta$ 3.7 and $\delta$ 4.2 in the $^1H$ NMR spectrum indicated the ratio of *endo* and *exo* isomers.

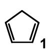
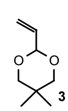
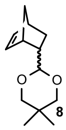
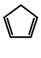
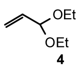
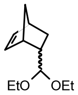
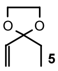
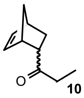
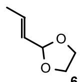
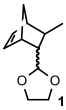
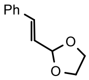
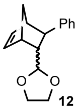
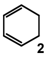
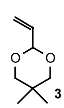
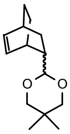
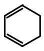
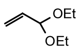
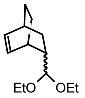
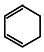
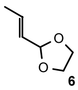
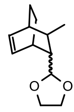
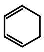
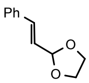
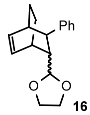
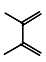
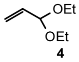
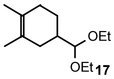
To demonstrate the generality of our protocol a variety of protected α,β-unsaturated dienophiles substituted at various positions were subjected to reaction with both cyclic and acyclic dienes. Moderate to excellent yields were obtained as shown in Table 1. As shown in Table

---

* Corresponding author.

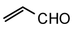
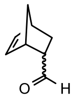
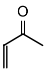
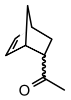
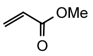
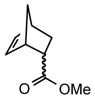
0040-4039/03/$ - see front matter © 2003 Elsevier Science Ltd. All rights reserved.
doi:10.1016/S0040-4039(03)00387-3

**Table 1.**

| Entry | Diene | Dienophile | Product | Method | Yield(%)<br>(*endo*:*exo*)[1i] |
|---|---|---|---|---|---|
| 1. |  1 |  3 |  8 | 1a | 80[1e]<br>(12.6:1) |
| 2. |  |  4 |  9 | 1b | 70[1f]<br>(8.3:1) |
| 3. |  |  5 |  10 | 1d | 85[1e]<br>(10:1) |
| 4. |  |  6 |  11 | 1a | 45[1f]<br>(3.5:1) |
| 5. |  |  7 |  12 | 1c | 67[1f]<br>(21:1) |
| 6. |  2 |  3 |  13 | 1a | 73<br>(42.3:1) |
| 7. |  |  4 |  14 | 1a | 73[1g,1h] |
| 8. |  |  6 |  15 | 1a | 61[1g,1h] |
| 9. |  |  7 |  16 | 1c | 48[1h] |
| 10. |  |  4 |  17 | 1a | 43 |

1a) Diene:dienophile, 2:1, $I_2$ (0.1 equiv.), 15-30 min, DCM, 0°C; 1b) diene:dienophile, 2:1, $I_2$ (<0.05 equiv.), 15 min, DCM, 0°C; 1c) diene:dienophile, 2:1, $I_2$ (0.2 equiv.), DCM (stored over $K_2CO_3$ overnight) 0°C, overnight; 1d) corresponding hydrolysed product was obtained; 1e) reported in Ref. 4; 1f ) reported in Ref. 6b; 1g ) reported in Ref. 2a; 1h) only the *endo* isomer was obtained; 1i) determined by proton NMR spectroscopy.

**Table 2.**

| Entry | Diene | Dienophile | Product | Method | Yield(%)<br>(*endo*:*exo*)[2c] |
|---|---|---|---|---|---|
| 1. |  |  |  | 2a | 74<br>(5.8:1) |
| 2. |  |  |  | 2b | 77<br>(11:1) |
| 3. |  |  |  | 2a | 40<br>(97.3:2.7) |

2a) Diene:dienophile (2:1), $I_2$ (0.05 equiv.); DCM; 0°C; 15 to 30 min; 2b) diene:dienophile (2:1); $I_2$ (0.1 equiv.); DCM; 0°C; 15 to 30 min; 2c) determined by proton NMR spectroscopy; 2d) determined by GC.

1, acetals of both ketones and aldehydes participated smoothly to give appreciable yields. It is noteworthy that the yield from the reaction of **3** with cyclopentadiene in the presence of $I_2$ is far better than that reported using electro-generated acids.[4]

As shown in entries 7–9 reaction with cyclohexadiene resulted in almost exclusive formation of *endo* isomers in all cases. The protocol developed works equally well for both acyclic and cyclic acetals. Variously substituted dienophiles react to different exents to furnish the corresponding cycloadducts in varying yields, although the selectivity remains unaffected.

Interestingly, it was observed that under the above mentioned reaction conditions, $I_2$ also effectively catalyses the Diels–Alder reaction of unprotected dienophiles (Table 2), which are known to undergo polymerisation under most of the reported reaction conditions, in good to moderate yields.

In conclusion, this study clearly demonstrates the efficiency of $I_2$ to catalyse ionic Diels–Alder reactions of protected dienophiles as well as those of unprotected dienophiles with dienes for cycloadduct formation with high selectivity and good yields over short reaction times.

## Acknowledgements

We thank the CSIR, New Delhi (India) for the award of fellowships to P.S., G.R.K. and M.T. Funding from YSA (CSIR), New Delhi, India to S.P.C. is gratefully acknowledged.

## References

1. Martin, J. G.; Hill, R. K. *Chem. Rev.* **1961**, *61*, 537–562.

2. (a) Gassman, P. G.; Singleton, D. A.; Wilwerding, J. J.; Chavan, S. P. *J. Am. Chem. Soc.* **1987**, *109*, 2182–2184; (b) Gassman, P. G.; Chavan, S. P. *J. Org. Chem.* **1988**, *53*, 2392–2394; (c) Gassman, P. G.; Chavan, S. P. *J. Chem. Soc. Chem. Commun.* **1989**, 837–839; (d) Gassman, P. G.; Chavan, S. P.; Fertel, L. B. *Tetrahedron Lett.* **1990**, *31*, 6489–6492; (e) Gassman, P. G.; Chavan, S. P. *Tetrahedron Lett.* **1989**, *29*, 3407–3410.
3. Samakia, T.; Berliner, M. A. *J. Org. Chem.* **1994**, *59*, 6890–6891.
4. Inokuchi, T.; Tanigawa, S.; Toru, S. *J. Org. Chem.* **1990**, *55*, 3958–3961.
5. Greico, P. A.; Collins, J. L.; Handy, S. T. *Synlett* **1995**, 1155–1157.
6. (a) Vankar, P. S.; Reddy, M. V.; Kumareswaran, R.; Pitre, S. V.; Roy, R.; Vankar, Y. D. *Tetrahedron* **1999**, *55*, 1099–1110; (b) Reddy, G.; Kumareswaran, R.; Vankar, Y. D. *Tetrahedron Lett.* **2000**, *41*, 10333–10336.
7. Chavan, S. P.; Sharma, A. K. *Synlett* **2001**, 667–669.
8. (a) Kitagawa, O.; Aoki, K.; Inoue, T.; Taguchi, T. *Tetrahedron Lett.* **1995**, *36*, 593–596; (b) Kitagawa, O.; Izawa, H.; Sato, K.; Dobashi, A.; Taguchi, T. *J. Org. Chem.* **1998**, *63*, 2634–2640.