Tetrahedron Letters, Vol.31, No.20, pp 2857-2860, 1990
Printed in Great Britain

0040-4039/90 $3.00 + .00
Pergamon Press plc

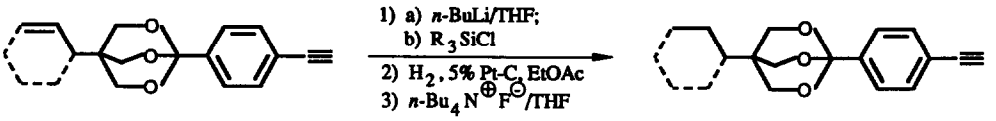
SELECTIVE CATALYTIC HYDROGENATION OF AN OLEFIN MOIETY IN THE PRESENCE OF A TERMINAL ALKYNE FUNCTION

Christopher J. Palmer* and John E. Casida

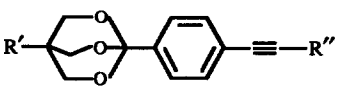
Pesticide Chemistry and Toxicology Laboratory, Department of Entomological Sciences

University of California, Berkeley, California 94720 U.S.A.

Summary: Protection of a terminal alkyne as a (trimethyl- or triisopropylsilyl)alkyne permits selective catalytic hydrogenation of a mono- or disubstituted olefin moiety without reducing the alkyne function.



1-(4-Ethynylphenyl)-4-propyl-2,6,7-trioxabicyclo[2.2.2]octane (1) is a highly potent insecticide and $GABA_A$ receptor antagonist[1]. The need for [^{3}H]1 at high specific activity in order to better understand its metabolism and receptor site interactions prompted consideration of a method to add tritium to alkene 2, the 4-allyl analog, without affecting the alkyne function.



No.	R′	R″	No.	R′	R″
1		H	6		$SiMe_3$
2		H	7		$Si(i\text{-}Pr)_3$
3		$SiMe_3$	8		$Si(i\text{-}Pr)_3$
4		$SiMe_3$	9		H
5		CMe_3			

The best method for introducing tritium at the required high specific activity is reduction with a metal hydride, e.g. sodium borotritide, or with tritium gas over a cata-

lyst, e.g. palladium on carbon[2]. It is very difficult to selectively induce double bonds to undergo addition reactions, such as reduction, in the presence of the more reactive triple bonds[3]; consequently, there are few examples in the literature. Although selective reduction is reported for a simple conjugated enyne using a molybdic hydride complex[4], this method is not suitable for radiolabeling. It is possible to protect an alkynyl group as an (alkyne)dicobalt(hexacarbonyl) complex which renders the coordinated triple bond inert to addition reactions. Selective transformation of a double bond can then be achieved, e.g. reduction with diimide or hydroboration, but these procedures are also not suitable for labeling at high specific activity. Unfortunately catalytic hydrogenation of a double bond is not feasible because the (alkyne)dicobalt(hexacarbonyl) complex is an effective catalyst poison[5]. Whereas terminal alkenes undergo catalytic hydrogenation faster than terminal alkynes[6], when the two are reduced competitively the alkyne is preferentially hydrogenated because of its higher heat of adsorption which enables it to displace the olefin from the catalyst surface[7-9]. Terminal triple bonds are reduced faster than internal ones and both are reduced faster than terminal or internal double bonds in competitive processes[10]. While there are numerous reports of semi-hydrogenation of alkynes to alkenes, i.e. selective alkyne reduction, there appear to be none of selective catalytic hydrogenation of alkenes in the presence of alkynes.

The selectivity of functional group reduction was examined with the reactant (prepared by procedures analogous to those in reference 1) (30 mg) in dry ethyl acetate (20 ml) containing triethylamine (0.1 ml) (to prevent acid-catalyzed trioxabicyclooctane ring opening) and 5% platinum on carbon (5 mg) stirred vigorously under 1 atmosphere of hydrogen. Platinum was chosen as the catalyst since this metal tends to exhibit a relatively low selectivity towards semi-hydrogenation of triple bonds [7,9,11], suggesting that it may be more favorable towards olefin reduction than other metals. The products were isolated by filtration through celite and solvent evaporation and identified by ^{1}H NMR (Table).

Direct hydrogenation of 2 is rapid giving as expected ethynyl reduction to vinyl and ethyl groups preferentially over reduction of the allyl substituent. It appeared that protection of the terminal ethynyl group with a bulky, easily-removable moiety such as trimethylsilyl might make the alkyne less reactive to hydrogenation and permit selective reduction of the alkene function[12]. This proved to be the case as hydrogenation of 3 pro-

ceeded slowly but with complete specificity for olefin reduction to give 4. After 4 h olefin reduction was complete, with longer times resulting in some reduction of the alkyne. Similar hydrogenation of the corresponding carbon compound 5 gives slightly slower but completely specific olefin reduction. The apparent resistance to hydrogenation conferred to the alkyne function by the trimethylsilyl group is therefore most probably due to a steric effect. It is interesting to note that silylation does not totally inhibit alkyne hydrogenation, which does occur after olefin consumption, but rather permits olefin hydrogenation to proceed first indicating that perhaps chemisorption by the catalyst is more favorable for the olefin than the silylated ethynyl function.

Selective reduction of a disubstituted olefin is even more difficult to achieve. Thus, compound 6 with a cyclohexenyl moiety is very slowly but not specifically reduced at the olefin substituent. However, the desired specificity is obtained using a more bulky silyl group, i.e. (triisopropylsilyl)ethynyl compound 7 is reduced almost exclusively to 8 after 5.5 h. Finally, desilylation with tetrabutylammonium fluoride[1] quantitatively converted compounds 4 and 8 to 1 and 9, respectively.

The easy addition and removal of the appropriate silyl protecting group makes this an attractive route to achieve the desired selective catalytic hydrogenation of an olefin in the presence of a terminal alkyne. It offers a suitable method to convert 2 to [^{3}H]1 in high yield and at high specific activity.

Acknowledgements. This study was supported in part by National Institutes of Health Grant 5 PO1 ES00049.

Extent of Functional Group Reduction in the Catalytic Hydrogenation of Trioxabicyclooctanes

Compound	Time, h	Extent of reduction, % Olefin	Alkyne[a]
2	0.1	45	90
	0.25	85	100
3	4	100	0
	18	100	15
5	4	80	0
6	4	10	trace
	6	35	25
	18	100	50
7	5.5	100	<5
	24	100	20

[a]Sequential formation of $-CH{=}CH_2$ and $-CH_2CH_3$ from 2 and of $-CH{=}CHSiR_3$ and $-CH_2CH_2SiR_3$ from 3, 6 and 7.

References

1. C.J. Palmer and J.E. Casida, J. Agric. Food Chem. 37, 213 (1989).
2. L.E. Feinendegen, "Tritium-Labeled Molecules in Biology and Medicine", Academic Press, New York (1967).
3. D.A. Ben-Efraim, p. 804 in "The Chemistry of the Carbon-Carbon Triple Bond", Part 2, S. Patai, Ed., Wiley, New York (1978).
4. H. Kondo and A. Miyake, Japan Patent 69 10,245, Chem. Abstr. 71, 60659x (1969).
5. K.M. Nicholas and R. Pettit, Tetrahedron Lett. 37, 3475 (1971).
6. G.C. Bond and P.B. Wells, Advances in Catalysis 15, 91 (1964).
7. P.B. Wells, Chem. & Ind., 1742 (1964).
8. G.C. Bond, pp. 281-309 in "Catalysis by Metals", Academic Press, New York (1962).
9. G.C. Bond, G. Webb, P.B. Wells and J.M. Winterbottom, J. Catalysis 1, 74 (1962).
10. N.A. Dobson, G. Eglinton, M. Krishnamurti, R.A. Raphael and R.G. Willis, Tetrahedron 16, 16 (1961).
11. L. Crombie, J. Chem. Soc., 3510 (1955); G.C. Bond, D.A. Dowden and N. Mackenzie, Trans. Faraday Soc. 54, 1537 (1958).
12. Trimethylsilyl groups have been used to protect terminal alkynes from hydrogenation during the semi-hydrogenation of internal alkynes to olefins. For a review see W.P. Weber, pp. 139-144 in "Silicon Reagents for Organic Synthesis", Springer, New York (1983).

(Received in USA 16 January 1990)