Short Communication

Selectivity in Diimide Reductions of Conjugated Enynes

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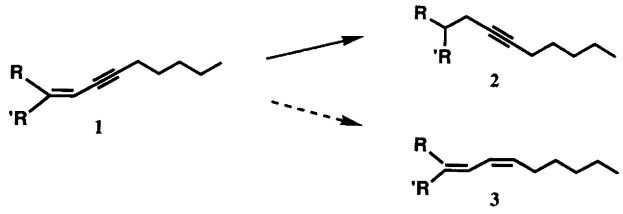
Methyl (2*E*,4*Z*)-2,4-decadienoate is a pheromone component of the six-spined spruce bark beetle *Pityogenes chalcographus*. The geometrical isomers of this compound have been synthesized and tested for their synergistic inhibitory effects.[1,2] In order to synthesize the (*Z*,*Z*)-isomer **3**



(R=COOMe, 'R=H) we tried to reduce the triple bond in methyl (*Z*)-2-decen-4-ynoate (**4**, Table 1) with diimide. Methyl 4-decynoate (**2**, R=COOMe, 'R=H) was formed instead of the expected product **3**. However, the latter was obtained by reduction of **4** using a Lindlar catalyst.[2] Further studies revealed that the presence of the carbonyl group has little or no effect on the selectivity, since even after exchange of the ester substituent in **4** for an alkyl group (e.g. **5**, Table 1, entry 3), diimide still showed a preference for reduction of the double bond, although the reaction rate was lower. The latter was evidenced from a comparative reduction experiment wherein **4** and **5** were mixed in the same reaction vessel and the product, acetylene **2**, was more rapidly formed from **4**. Furthermore, when the diimide reacted with methyl sorbate or methyl (2*Z*,4*Z*)-2,4-decadienoate, it was observed that the α,β double bond was reduced faster than the γ,δ double bond. From these observations, one can conclude that the carbonyl group, to some extent, activates the double bond in **1** (R=COOMe, 'R=H) towards diimide. A consequence of this is that the acetylene **2** (R=COOMe, 'R=H) is obtained in higher yield in entry 2 than in entry 3, since the competing subsequent reduction of **2** has less time to proceed.

A survey of the literature indicated that very few comparative reductions of olefins versus acetylenes had been reported. Rao *et al.*[3] reported that diimide reduction of oleic acid [(*Z*)-9-octadecenoic acid] in dioxane, benzene or rectified spirit, is faster than the reduction of the corresponding acetylene, stearolic acid (9-octadecynoic acid), whereas Koch[4] reported that the reduction rates of methyl oleate and methyl stearolate are equal in acetonitrile. Both authors used hydrazine hydrate for the oxidative generation of diimide.

A comparison of the diimide reduction of the (*Z*)-enyne **4** and its corresponding (*E*)-isomer **6** revealed that the reduction proceeded more slowly for the (*Z*)-isomer **4**. This observation is in accordance with previous reports that (*E*)-double bonds react more rapidly with diimide than (*Z*)-double bonds.[5–10]

It must be noted that the reactions yielded mixtures, and the major acetylenic products had to be isolated from over-reduced material by chromatographic methods.[11] The present method might therefore be of limited interest for large-scale synthesis. On the other hand, there are a number of biologically active compounds which contain an enyne moiety, for example: histrionicotoxin, laurencin, (*Z*)-hexadec-13-en-11-ynyl acetate, esperamicin and calichemicin.[12–17] It might be of interest selectively to transform these natural products to their acetylenic analogues for structure–activity test. In this case, diimide reduction seems to be the method of choice. Furthermore, with deuterium- and tritium-diimide, it should be possible to prepare labelled acetylenic compounds which are difficult to achieve by other methods.

In conclusion, the reduction procedure using diimide is an expedient method for the selective reduction of a double bond in a conjugated enyne system and is complementary to the Lindlar triple bond reduction.

Experimental

The composition of the reaction mixtures was analysed by GLC after various reaction times.

In a typical experiment, dipotassium azodicarboxylate (2.5 equiv., 0.5 mmol) and acetic acid (2.5 equiv., 0.5 mmol) in methanol (1 ml) were added to a stirred methanolic solution (2 ml) of the enyne (0.2 mmol). The mixture

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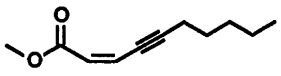
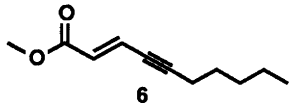
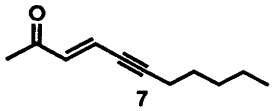
Table 1. Results from reductions of conjugated enynes.[a]

Entry	Enyne 1	Reagent	Acetylene 2	Diene 3	Remaining starting material	Over-reduced material	Other diene isomers
1	 4	Lindlar's/H_2	0	70	<1	>19	10
2	 4	HN=NH	54	5	16	25	0
3	 5	HN=NH	42	2.5	45	10.5	0
		HN=NH	36	2.5	16	45.5	0
4	 6	HN=NH	64	3	18	15	0
5	 7	HN=NH	0[b]	0	0	0	0

[a]Values given in the table are GLC yields (percentage of integrated area) and show the composition of the reaction mixture at a stage of the reduction when the yield of the acetylene **2** is close to optimum. [b]Disproportionation of diimide gives hydrazine which reacts with the keto group to yield a hydrazone.

was stirred at room temperature until the yellow colour disappeared. The reaction was monitored by GLC and new batches of the reagents were added subsequently until 15–20 % of the starting material remained. After neutralization (aq. $NaHCO_3$), the reaction products were extracted into pentane, dried, concentrated *in vacuo* and chromatographed on silica gel.[11] For the products obtained after reduction of the dialkyl enyne **4**, silica gel impregnated with 10 % caffeine was used. The reduction products were identified using GLC/MS, ^1H and ^{13}C NMR spectroscopy.

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