Cationic Hydrogenation of Benzyl Alcohols and Arylethylenes using Acridane Derivatives as Hindered NADH Models

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Secondary and tertiary benzyl alcohols and arylethylenes are efficiently reduced by acridane derivatives (**1**) in the presence of trifluoroacetic acid in dichloromethane.

In steroid biosynthesis, reduction of double bonds usually involves[1] protonation and reduction of the incipient carbenium ion catalysed by enzymes possessing NADH as cofactor. We report a reaction in which benzyl alcohols (**2**) and arylethylenes (**3**) are reduced cleanly at room temperature when acridane derivatives (**1**)[2] are employed as hindered NADH models.

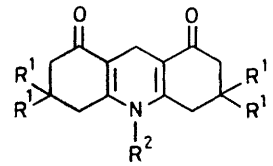
Reductions of numerous functional groups have been carried out using *N*-benzyl-1,4-dihydronicotinamide (**4a**) or 3,5-diethoxycarbonyl-2,6-dimethyl-1,4-dihydropyridine [(**4b**), 'Hantzch ester'] as NADH models.[3] However, these models are rapidly destroyed in acidic media or when heated, the enamine moiety in (**4**) being too reactive and exposed.[4] We found that compounds (**1**) are sufficiently stable towards heat and strong acid to be suitable NADH models for reactions requiring such experimental conditions. [The tricyclic structure seems to protect the enamine moiety in (**1**).]

Trialkylsilanes have been used for reducing carbenium ions, generated from alcohols or olefins by treatment with acids such as trifluoroacetic acid or Lewis acids.[5] We found that benzyl alcohols (**2**) and arylethylenes (**3**) undergo smooth reduction in dichloromethane at room temperature (Table 1), when treated with an equimolar amount of (**1**) and trifluoroacetic acid or boron trifluoride–diethyl ether (5 mol. equiv.). Benzyl alcohols capable of dehydration [*e.g.* (**2**; Ar = R^1 = Ph, R^2 = Me)] are reduced slowly, giving predominantly the dehydration product [e.g. (**3a**)]. However, if the latter is isolated and reduced as above the required product is obtained in good yield. The acridane derivative (**1**) can be regenerated from the oxidized product (**5**) with alkaline sodium dithionite

Table 1. Reduction of the alcohols (**2**) and olefins (**3**) with the acridine derivative (**1a**).

Compound	Ar	R^1	R^2	R^3	% Yield[a]	Time
(**2a**)	Ph	Ph	Ph	—	89	15 min
(**2b**)	Ph	*p*-MeO C_6H_4	*p*-MeO C_6H_4	—	86	30 min
(**2c**)	Ph	*p*-MeO C_6H_4	Ph	—	87	30 min
(**2d**)	*p*-MeO C_6H_4	*p*-MeO C_6H_4	*p*-MeO C_6H_4	—	85	30 min
(**2e**)	Ph	Ph	H	—	87	2 h
(**2f**)	Ph	*p*-MeO C_6H_4	H	—	87	2 h
(**3a**)	Ph	Ph	H	H	90	24 h
(**3b**)	*p*-MeO C_6H_4	H	H	Ph	85	24 h
(**3c**)	Ph	Ph	H	Ph	90	24 h

[a] Yield of $ArCHR^1R^2$ [from (**2**)] or $ArCHR^1CHR^2R^3$ [from (**3**)].

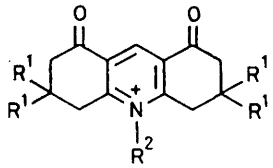


(**1**)

a, $R^1 = R^2 = H$
b, $R^1 = Me$, $R^2 = H$

$ArCR^1{=}CR^2R^3$

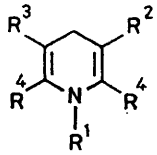
(**3**)



(**5**)

$ArCR^1R^2OH$

(**2**)



(**4**)

a, $R^1 = PhCH_2$, $R^2 = CONH_2$, $R^3 = R^4 = H$
b, $R^1 = H$, $R^2 = R^3 = CO_2Et$, $R^4 = Me$

or borohydride.[6] Compound (**1b**) although much more hindered than (**1a**) was equally reactive albeit more stable to acidic conditions. The reaction possibly involves a carbenium ion intermediate.

Except for catalytic hydrogenolysis, most other deoxygenating methods for alcohols involve two steps, *i.e.* derivatization, followed by alkali metal–amine,[7] tributylstanane,[8] trialkylsilane,[9] or electrochemical[10] reduction. This one step process is convenient and similar to the corresponding biological process of deoxygenation, *e.g.* formation of deoxy-sugars[11] and the reduction of trisubstituted double bonds in steroids. Hindered NADH models such as (**1b**) are useful electron sources in which the electron donor moiety (enamine in 1,4-dihydropyridine) is suitably protected from the electrophilic environment. Similar reductions of ethers, epoxides, *etc.* will be reported shortly.

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