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NAD(P)$^+$-NAD(P)H MODEL. 41. REDUCTION OF SULFONATE BY A MODEL OF NAD(P)H

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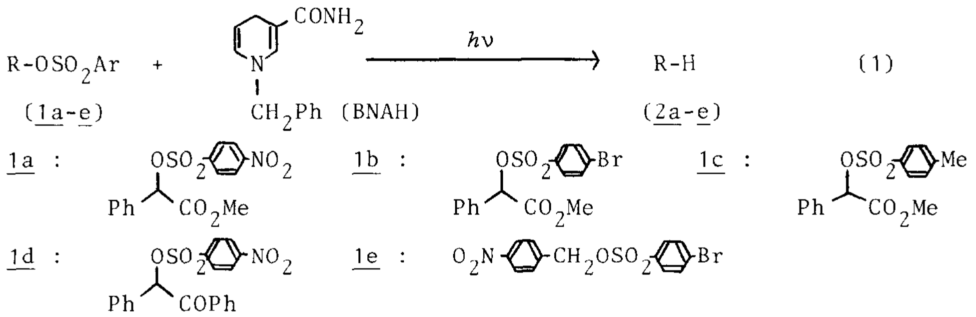
Summary : Carbon-oxygen bonds in sulfonate esters are reduced to the corresponding carbon-hydrogen bonds by an NAD(P)H model compound under irradiation with visible light. Tracer experiments with deuterium have revealed that this reduction proceeds through radical intermediates (1).

New examples for reductions by NAD(P)H model compounds are steadily being found (2). Our efforts in this area have been centered on the reduction at sp^3 carbon of various benzyl sulfonate esters, 1a-e, by 1-benzyl-1,4-dihydronicotinamide (BNAH), an NAD(P)H model compound (eq. 1).



For example, *p*-bromobenzenesulfonate ester of methyl mandelate, 1b, was reduced to give methyl phenylacetate by BNAH under irradiation in pyridine or acetonitrile. Results are summarized in Table 1. The chemoselectivity in the reduction is important. Thus the ester group in 1a-c, the keto group in 1d, or the nitro group in 1e was not reduced.

The followings are characteristics of the reduction and provide important information to discuss on the mechanism.

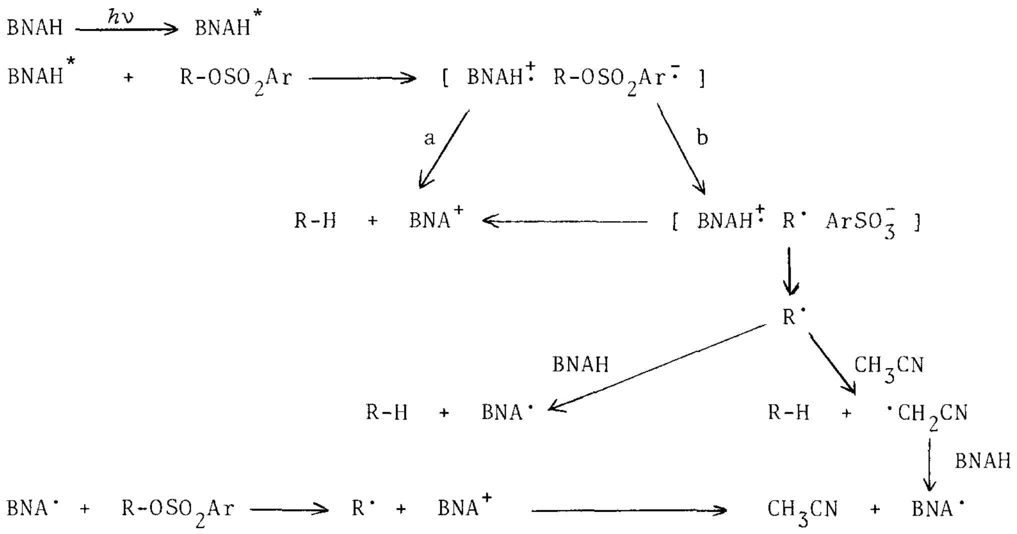
a) The reduction is accelerated remarkably by the addition of a visible-light sensitizer such as tris(2,2'-bipyridyl)ruthenium(II) dichloride or tetraphenylporphine.

b) The reduction is inhibited by the presence of *m*-dinitrobenzene, 2,3,5,6-tetramethylnitrosobenzene, or oxygen. The reaction under oxygen atmosphere affords methyl benzoylformate (47% yield) as a main product.

c) Isotope distributions shown in Table 2 indicate that hydrogens of acetonitrile are involved in the reduction pathway.

These observations cannot be interpreted by a mechanism with hydride transfer from an NAD(P)H model compound but strongly suggest that the reduction proceeds through a mechanism involving one electron transfer process. A proposed mechanism is shown in scheme 1 (3).

Scheme 1.



The reduction is initiated by one-electron transfer from the photoactivated BNAH to a substrate. Then the anion radical from the sulfonate abstracts a hydrogen atom from $BNAH^{+\cdot}$ in a solvent cage (path a) or is degraded to give a free radical, R· (path b). Easy formation of a free radical from anion radical of benzylic sulfonate is known (4). The free radical,R·, abstracts a hydrogen atom from $BNAH^{+\cdot}$ or escapes from the solvent cage. In the latter case, R$^\cdot$ abstracts a hydrogen atom from BNAH or acetonitrile (5). The extent of deuterium incorporation in the product increases when pyridine is added to the system. For example, in the reaction with 1e, the deuterium content in the product increases from 0% to 7.3% when the solvent is changed from acetonitrile-d_3 to an acetonitrile-d_3 - pyridine mixture. The role of pyridine seems to abstract a proton from the one-electron transfer intermediate (BNAH$^{+\cdot}$ R-$OSO_3Ar^{-\cdot}$). It is known that BNAH$^{+\cdot}$ is readily deprotonated by a base to yield BNA$^\cdot$ (6).

The production of methyl benzoylformate in the reaction under oxygen atmosphere suggest that a free radical, R$^\cdot$, is invoved in the reaction. Rearrangement of a peroxy radical ($R_2CHOO^\cdot$) to a ketone is known (7). The role of photosensitizer such as Ru^{2+} or tetraphenylporphine may be to excite BNAH, but the detail is ambiguous presently. Further study on the mechanism is now under progress.

Table 1. Reduction of Sulfonates

Substrate	Product	Yield,%$^{a)}$	Solvent$^{b)}$	Condition$^{c)}$
1a	$PhCH_2CO_2Me$	17	acetonitrile	A
1a	"	64	pyridine	A
1a	"	36	acetonitrile	B
1b	"	70	pyridine	A
1c	"	37	pyridine	A
1d	$PhCOCH_2Ph$	75	pyridine	A
1e	$MeC_6H_4NO_2$	68	acetonitrile	A

a) Based on 1. [BNAH] = 0.15mmol. [1] = 0.05mmol. b) 8cm^3. c) Irradiation with (A) a high pressure mercury lamp (500W) with a filtered solution of 2,3-dihydro-5,7-dimethyl-1,4-diazepine perchlorate (the solution is transparent above 350nm (8)), and (B) under normal room light in the presence of 1×10^{-3} mol dm^{-3} of $Ru(bpy)_3^{2+}$ under argon atmosphere at room temperature.

Table 2. Deuterium Distribution in the Product

Substrate[a)]	Condition[b)]	Product Distribution	
		d_0	d_1
1a	BNAH-h_2 / CD_3CN	94.8	5.2
1b	BNAH-h_2 / CD_3CN	98.1	1.9
1b	BNAH-h_2 / CD_3CN-pyridine[c)]	77.4	22.6
1b	BNAH-d_2[d)] / CH_3CN	56.8	43.2
1c	BNAH-h_2 / CD_3CN	98.3	1.7
1d	BNAH-h_2 / CD_3CN	83.6	16.4
1e	BNAH-h_2 / CD_3CN	100	0
1e	BNAH-h_2 / CD_3CN-pyridine[c)]	92.7	7.3
1e	BNAH-d_2[d)] / CH_3CN	26.8	73.2

a) [Substrate] = 0.02mmol. b) [BNAH] = 0.05mmol. Solvent = 2cm^3.

c) CD_3CN = pyridine = 1cm^3. d) Deuterium content = 96.2%.

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$$BNA^{\cdot} + CD_3CN \longrightarrow BNAD + {}^{\cdot}CD_2CN$$
$${}^{\cdot}CD_2CN + BNAH \longrightarrow CHD_2CN + BNA^{\cdot}$$

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