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LIGHT INDUCED AND DYE ACCELERATED REDUCTIONS OF PHENACYL ONIUM SALTS BY 1,4-DIHYDROPYRIDINES

by

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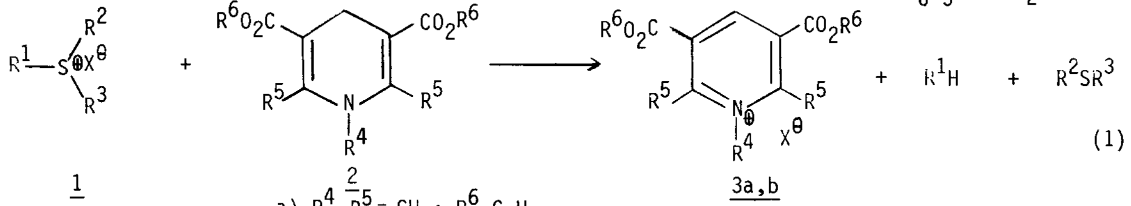
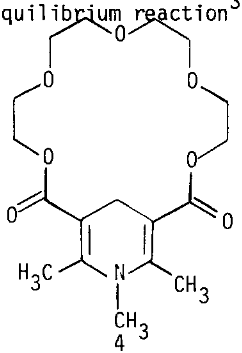
New examples of reductions by synthetically accessible 1,4-dihydropyridines, NAD(P)H mimics, are steadily being found[1]. Our efforts in this area have centered about our previous discovery[2] of the reduction at sp^3 carbon of various sulfonium salts 1 by 1,4-dihydropyridines 2 (eq. 1). The rate of reduction, at least for phenacyl sulfonium salts (R^1 = $C_6H_5C(O)CH_2$) was greatly increased on using 4, an effect that is ascribed to complexation of the sulfonium salt by the "crown ether" segment of 4 in a fast equilibrium reaction[3].



a) $R^4=R^5=CH_3$; $R^6=C_2H_5$
b) $R^4=R^6=CH_3$; $R^5=H$

(1)



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The efficiencies of these, as well as other reductions with N-substituted 1,4-dihydropyridines, can be lessened greatly, however, by isomerization of the 1,4-dihydropyridine to its 1,2-isomer by pyridinium salt 3 (eq. 2) formed on hydride transfer to a substrate[4]. This auto-

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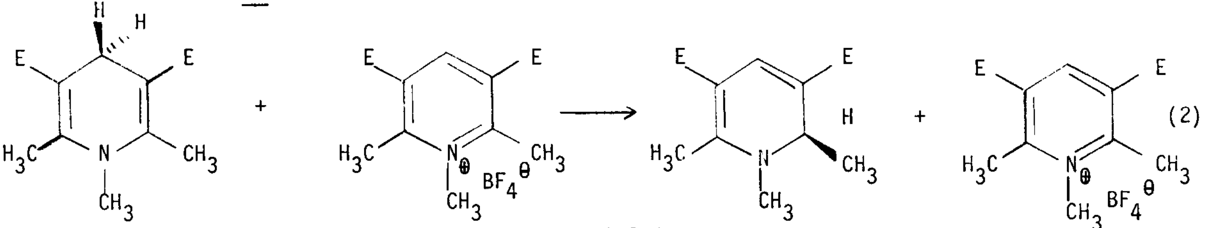
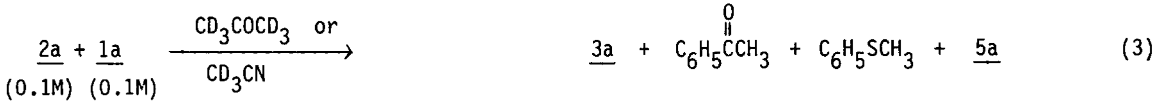
catalytic reaction increases in rate as the concentration of pyridinium salt (arising from reduction of a substrate) increases. With sluggish substrates the greater part of the 1,4-dihydropyridine will be consumed by isomerization to the 1,2-isomer which reaction in the case of the "Hantzsch" esters 2a is irreversible.



2a 3a $E \equiv CO_2C_2H_5$ 5a 3a

We report here means of increasing greatly the rate of hydride transfer to phenacyl sulfonium (and other) salts. An example is given in equation 3.



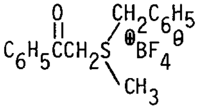
$$\underset{(0.1M)}{\underline{2a}} + \underset{(0.1M)}{\underline{1a}} \xrightarrow[CD_3CN]{CD_3COCD_3 \text{ or}} \underline{3a} + C_6H_5\overset{O}{\overset{\|}{C}}CH_3 + C_6H_5SCH_3 + \underline{5a} \qquad (3)$$

	conditions	$t_{\frac{1}{2}}$	yield			
A.	60^o, dark	10 hr	34%	38%	37%	52%
B.	25^o, dark	72 hr	0%	0%	0%	0%
C.	25^o, room light	48 hr	100%	100%	100%	0%
D.	25^o, room light, TPP	3 hr	100%	100%	100%	0%
E.	25^o, room light, eosin	1 hr	100%	100%	100%	0%
F.	25^o, room light, $[Ru(II)(bipy)_3Cl_2]$	0.3 hr	100%	100%	100%	0%

Normal room lighting (neon fluorescent lamps at ca. 2 m distance) and Pyrex reaction vessels were used. The added dyes (TPP = meso-tetraphenylporphine, eosin as disodium salt, Ru(II)-$(bipy)_3Cl_2$ = ruthenium (II) tris(2,2'-bipyridyl)dichloride[5]) were present in ca. 10^{-3}M concentration. The progress of the reduction was monitored by ^{1}H-NMR spectroscopy; yields are accurate within ± 5%. Other groups have observed that visible light can have an accelerating effect on reductions[6] but to the best of our knowledge rate enhancements, especially of the magnitude reported here, using dyes have not been reported previously.

Using $Ru(II)(bipy)_3$ as sensitizer phenacyl trimethylammonium and triphenylphosphonium salts are reduced to acetophenone and the corresponding amine or phosphine. Yields of acetophenone are not quantitative, however (60% for the ammonium salt and 16% for the phosphonium salt).

The following points have bearing on the mechanism of reduction of phenacyl sulfonium salts: a. phenacyl dimethyl, phenacyl phenyl methyl, and phenacyl diphenyl sulfonium salts react in the presence of light (no sensitizer) at similar rates indicating that structural effects at the sulfonium center are not great; b. benzyl sulfonium salts were reduced in poor yield to toluene and alkyl sulfonium salts scarcely react; this indicates a structural need for the phenacyl substituent. Acetonyl sulfonium salts are reduced to acetone and sulfide slowly but cleanly. The salt 6 reacts smoothly but gives only acetophenone rather than toluene, the ylide 7 fails to react eliminating this as an intermediate; c. one equivalent of 1,4-dinitrobenzene, a known electron acceptor[7], completely quenches the reaction of 1a with 2a with or without Ru(II)(bipy)$_3$Cl$_2$ (or



$C_6H_5\overset{O}{\overset{\|}{C}}CH_2\overset{\oplus}{S}(CH_2C_6H_5)(CH_3)\ \overset{\ominus}{BF_4}$

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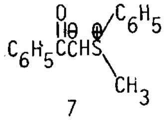

$C_6H_5\overset{O}{\overset{\|}{C}}\overset{\ominus}{C}H\overset{\oplus}{S}(C_6H_5)(CH_3)$

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other dyes); hydroquinone causes an induction period in reduction[8]; e. the reaction can have chain character under the proper conditions. In the dark in CD$_3$COCD$_3$ at 55°, under which conditions little spontaneous reaction occurs, 2a reduced 1a quantitatively to acetophenone on addition of the radical initiator, azo-bis-isobutyronitrile (AIBN). Chain lengths, defined as moles of product per mole of AIBN, are at least 10.

These observations suggest that the light induced reactions proceed through a mechanism (or mechanisms) involving one electron transfer steps. In this regard the electrochemical reductions of sulfonium salts via one-electron steps have been described[9]. The most remarkable aspect, of course, of the reactions reported here is the large accelerating effect of dyes. The most effective, Ru(II)(bipy)$_3$Cl$_2$, is known to donate an electron to an acceptor on irradiation in the 450 nm charge transfer band[10]; eosin, on the other hand, can be an efficient hydrogen abstractor[11] (dyes like chlorophyll and methyl orange that usually act only as photochemical sensitizers without entering into physical reaction have no effect on the light induced reaction of 1a with 2a). Detailed mechanistic investigation will be needed to ascertain with certainty whether the dyes are involved in an electron transfer capacity.

Examples of reductions wherein 1,4-dihydropyridines appear to be involved in one-electron transfer reactions are becoming more commonplace. Bruice has speculated extensively on the biochemical implications of such processes[12]. We have preliminary evidence indicating that visible light enhances greatly the rate of reduction of aliphatic ketones by 1,4-dihydropyridines in a manner similar to that seen with sulfonium salts.[13]

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