Tetrahedron Letters,Vol.26,No.11,pp 1453-1456,1985
Printed in Great Britain

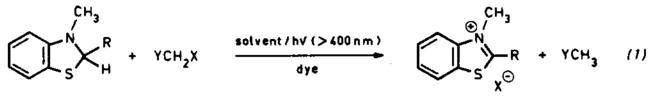
0040-4039/85 $3.00 + .00

3-METHYL-2,3-DIHYDROBENZOTHIAZOLES AS REDUCING AGENTS. DYE ENHANCED PHOTOREACTIONS.

Sabir H. Mashraqui and Richard M. Kellogg*
Department of Organic Chemistry, University of Groningen
Nijenborgh 16, 9747 AG Groningen, The Netherlands

SUMMARY: Various types of electron deficient saturated carbon atoms are reduced in a visible light initiated process by N-alkyl-2,3-dihydrobenzothiazoles; these reactions are accelerated in the presence of $Ru(bipy)_3Cl_2$. The same ring system can act as an enolate carrier under electrophilic conditions.

The redox chemistry of flavines and dihydropyridines has been extensively studied in conjunction with the enzymic processes mediated by these types of cofactors.[1] Although not as extensively explored, it is also well established that heterocycles such as benzoimidazoline, benzothiazoline, and other related compounds are subject to oxidation by air, peroxides, peracids, and other oxidizing agents.[2] The potential to reduce is clearly available in such systems. This anticipation finds support in the recent work of Chikashita, et. al., who used 2-phenylbenzoimidazoline and 2-phenylbenzothiazoline for the reduction of unsaturated substrates with concomitant oxidation of the heterocycles.[3,4] We report herein that under the influence of light and certain dyes, 3-methyl-2-aryl or alkyl-2,3-dihydrobenzothiazole (1a-c) reduce activated halides, sulfonium salts, and certain pyridinium salts.[5] The overall reaction, illustrated for the reduction of saturated carbon, is shown in eq. 1.[6]



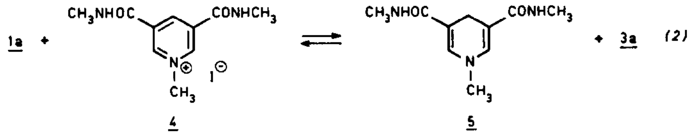
1 2 3a-c

a) $R = C_6H_5$
b) $R = C_6H_4\text{-}4\text{-}OCH_3$
c) $R = CH_3$

Compound 1a under conditions of electrophilic catalysis, heat, or light has in our hands little tendency to reduce nonactivated carbonyl groups although the highly reactive ethyl phenylglyoxylate in CD_3CN is reduced smoothly to ethyl mandelate in 70% yield in the presence of $Mg(ClO_4)_2 \cdot 2H_2O$ with formation of 3a.[7] On the other hand, the type of conversion summarized in eq. 1 goes well as documented in the Table. The effect of visible light is much enhanced by certain dyes, the best of which, in accord with observations reported by us earlier,[8,9] is $Ru(bipy)_3Cl_2$ (bipy = 2,2-bipyridyl). Pertinent data on the effect of this and other dyes, as well as the effect of structural variation in the hydride acceptors are given in the Table. For the cases of < 100% conversion the theoretical amounts of unreacted 2 were detected. However, over a period of a number of hours of irradiation any unreacted benzothiazine undergoes some decomposition via undetermined pathways.

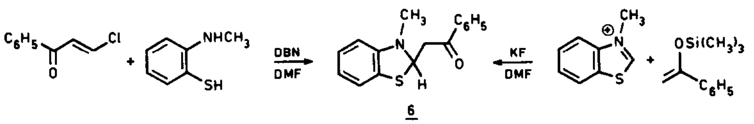
Several points deserve emphasis: a) the reductions are accelerated by light but relatively inefficient thermal initiation is also possible (compare entries 1, 5 and 6). Only at 55° does slow (but clean) reduction of 2a by 1a occur in the dark;[5] b) these reductions can be inhibited by additives that are good electron traps. In the photoinduced reduction of 2a by 1a with Ru(bipy)$_3$Cl$_2$(5.10^{-3}M) in CD$_3$CN 1,4-dinitrobenzene (DNB), also 5·10^{-3}M, completely inhibits the reduction; c) increased electron deficiency at the carbon to be reduced leads to higher rates of reduction. Comparison of entries 7 and 8 and of entries 9 and 10 underscores this point. Bromide, chloride, and sulfide (entry 13) are acceptable leaving groups but not ammonium (entry 14).[10] d) although not illustrated in the Table, considerable structural variation can be tolerated in 1. For example 1b is qualitatively as good a reductant as 1a, and the 2-methyl derivative 1e reacts only slightly less rapidly.

The standard redox potential for 1a is approximately -330 ± 10 mV in CD$_3$CN. This is determined by equilibration with pyridinium salts of known redox potential by the method described by us previously.[10] A typical (nonphotochemical) equilibration is shown in eq. 2; the reduction potential of 5 is virtually identical to that of 1a.[11,12]



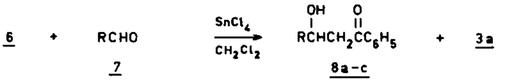
(2)

These types of heterocycles can be used in acid catalyzed enolate transfer in illustration of a principle, which we have discussed previously in other context.[13] Compound 6 is obtained readily by either of the routes shown in eq. 3. Modest yields of the



(3)

aldol condensation products (8) are obtained in the presence of a stoichiometric amount of SnCl$_4$ (eq. 4). The limitation in this process, as illustrated with 6, is competitive rates of fragmentation, after complexation with the electrophile, at C-2 of the C-2/enolate C-C bond (desired), and the C-2/S bond (undesired).



$$\underline{6} + RCHO \xrightarrow[CH_2Cl_2]{SnCl_4} RCH(OH)CH_2C(O)C_6H_5 + \underline{3a}$$ (4)

7

8a-c

a) R = C_6H_5
b) R = C_6H_4-4-NO_2
c) R = $(CH_3)_2CH$

cmpd	yield(%)
8a	35
8b	45
8c	25

In summary we have demonstrated that compounds 1 can be mild, selective reducing agents under completely neutral conditions. The mechanism of these reductions must surely involve an electron transfer chain as established in similar reactions of 1,4-dihydropyridines.[8,9,14] In addition the potential for mediation of carbon-carbon bond formation by electrophilic catalysis under mild conditions is opened with compounds like 6.

TABLE

Reductions of Saturated Carbon Centers by 2,3-Dihydrobenzothiazole 1a[a]

Entry	Hydride acceptor	Photocatalyst	Time (hr)	% Reduct.
1	$C_6H_5COCH_2Br$ (2a)	$Ru(bipy)_3Cl_2$	1.3	>95[b]
2	$C_6H_5COCH_2Br$ (2a)	Rose Bengal	1.3	65[b]
3	$C_6H_5COCH_2Br$ (2a)	Eosin	1.3	35[b]
4	$C_6H_5COCH_2Br$ (2a)	Meth.Blue	1.3	10[b]
5	$C_6H_5COCH_2Br$ (2a)	None	1.3	< 5[b]
6	$C_6H_5COCH_2Br$ (2a)	None	20(55°)	95[b]
7	$BrCH_2CN$ (2b)	$Ru(bipy)_3Cl_2$	40	>95[c]
8	$BrCH(CN)_2$ (2c)	$Ru(bipy)_3Cl_2$	0.7	>95[d]
9	$BrCH_2CO_2C_2H_5$ (2d)	$Ru(bipy)_3Cl_2$	70	75-85
10	$BrCH(CO_2C_2H_5)_2$ (2e)	$Ru(bipy)_3Cl_2$	1	100[f]
11	$ClCH_2COCH_3$ (2d)	$Ru(bipy)_3Cl_2$	60	50[g]
12	$BrCH_2SO_2C(CH_3)_3$ (2e)	$Ru(bipy)_3Cl_2$	90	>95[h]
13	$C_6H_5COCH_2S(C_6H_5)CH_3^+,BF_4^-$ (2f)	$Ru(bipy)_3Cl_2$	40	90[i]
14	$C_6H_5COCH_2N(CH_3)_3^+,ClO_4^-$ (2f)	$Ru(bipy)_3Cl_2$	40	0[j]

a) Temperature ± 20° unless otherwise noted; concentrations 1 and 2 in CD_3CN 0.1M, concentration sensitizer 0.005M; irradiation provided by two fluorescent lamps held ± 20 cm from Pyrex NMR tubes. Conversions calculated by repeated integration of ^1H NMR spectra; b) $C_6H_5COCH_3$ product; c) CH_3CN product; d) $CH_2(CN)_2$ product; e) $CH_3CO_2C_2H_5$ product; f) $CH_2(CO_2C_2H_5)_2$ product; g) CH_3COCH_3 product; h) $CH_3SO_2C(CH_3)_3$ product; i) $C_6H_5COCH_3$ and $C_6H_5SCH_3$ products; j) No reaction.

Acknowledgement. Partial support of this work was provided by the Netherlands Foundation for Scientific Research (Z.W.O.) administered by the Office for Chemical Research (S.O.N.) in the form of fellowship to S.H.M.

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14. In the reaction of 1a with 2a trace amounts (2-3%) of $(C_6H_5COCH_2)_2$ are isolated. Coupling of free phenacyl fragments is indicated.

(Received in UK 18 January 1985)