

## Oxygen–Carbon $\beta$ -Bond Effects in Radical Reactions

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Oxygen bonded to the  $\beta$ -carbon of a carbon radical has a marked stabilising effect; this permits radical reactions not seen, except at much higher temperatures, in non-oxygenated model compounds.

$\alpha$ -Bond effects [see (1)] are well known in free radical chemistry. For example oxygen (2) and nitrogen (3) free radicals are strikingly stabilised in this way.<sup>1</sup>

$\beta$ -Bond effects have been clearly demonstrated for  $\beta$ -bromine–carbon bonds by rate increases and by stereochemical considerations.<sup>2,3a</sup> Unsymmetrical bridging [as in (4)] is frequently postulated.<sup>2,3a</sup> Similar chemical evidence is not available for bridging by elements in the first row of the Periodic Table, nor is it expected theoretically.<sup>3</sup> However, preferred conformational effects in e.s.r. spectra have been seen in radicals with  $\beta$ -oxygen functionality.<sup>3b</sup>

We draw attention to recent experimental work, which we have supplemented, for  $\beta$ -bond stabilisation of carbon radicals by oxygen. These results are shown in Table 1. We comment as follows.

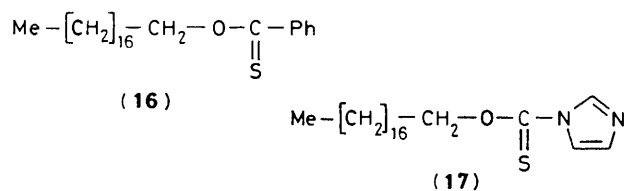
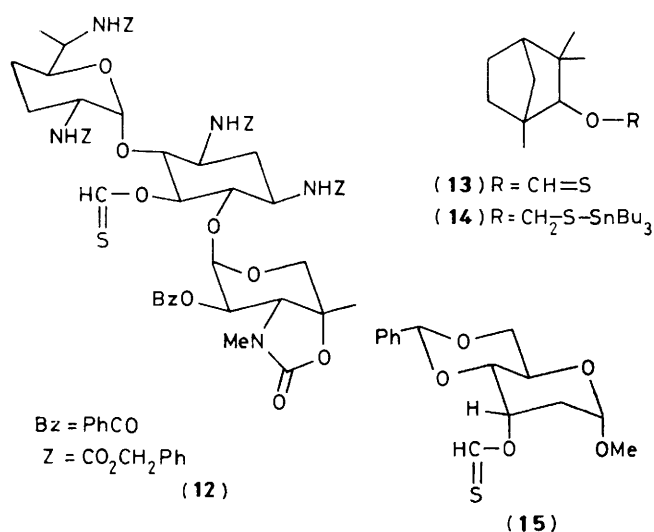
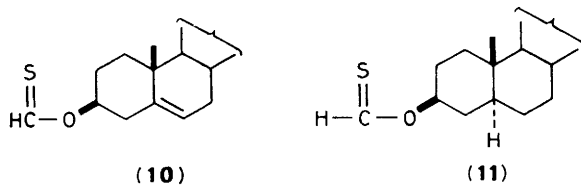
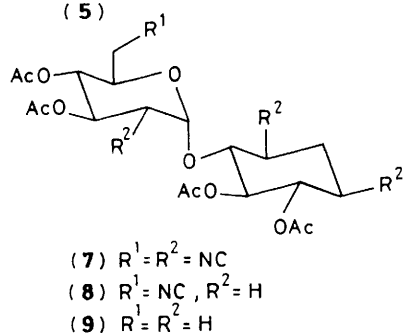
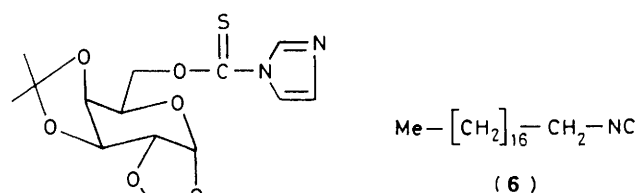
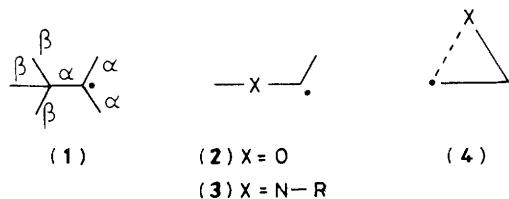
The tin hydride reduction of *O*-thiocarbonyl derivatives of secondary alcohols<sup>4</sup> is by now a well known process giving high yields at 110 °C in toluene. In contrast, primary alcohols can only be deoxygenated at much higher temperatures.<sup>5</sup> Entries 1 and 2 in Table 1 are illustrative. Unexpected, then, is

the observation<sup>6</sup> that the primary derivative (5) gives 31% of deoxygenation at 110 °C. A similar result is implied in a recent communication.<sup>7</sup>

We have observed the same phenomenon in our radical deamination studies.<sup>8,9</sup> Thus (see Table 1, entries 4 and 5) radical reduction<sup>8</sup> of the isonitrile (6) is not seen at 110 °C, but proceeds in good yield at 140 °C. In contrast<sup>9</sup> (see Table 1, entry 5), reduction of the tetraisonitrile (7) removes *all* four isonitriles at 80 °C, and the temperature had to be lowered to 70 °C before the primary isonitrile group was retained.

Table 1

Entry	Substrate, R-X	Solvent	Temp./°C	R-H %	Ref.
1	(16)	Toluene	110	None	4
		Xylene	130	84	5
2	(17)	Toluene	110	None	4
		Xylene	130	81	5
3	(5)	Toluene	110	31	6
4	(6)	Toluene	110	None	8
		Xylene	140	81	
5	(7)	Benzene	70	(8) 63	9
		Benzene	80	(9) 81	
6	(10)	Toluene	110	None	4
7	(11)	Toluene	110	9	
		Xylene	140	24	
8	(12)	Toluene	110	78	10
9	(13)	Toluene	110	None	
		None	110	None	
10	(15)	Toluene	110	29	



We noted previously that cholesterol thioformate (**10**) was not reduced to the hydrocarbon at 110 °C. In agreement cholestanol thioformate (**11**) (see Table 1, entry 7) gives only 9% of cholestane at 110 °C and even at 140 °C affords only 24% of hydrocarbon. In contrast, Daniels and McCombie<sup>10</sup> have reported that the thioformate derivative (**12**) from gentamicin C<sub>2</sub> (see Table 1, entry 8) is deoxygenated in good yield at 110 °C.

Clearly, these results show that  $\beta$ -bonded oxygen has a marked effect in stabilising carbon radicals and thus permitting homolytic bond fission not seen otherwise. Another explanation, that of steric assistance to fission, can be discarded. Fenchol thioformate (**13**) (mixed isomers) did not give the hydrocarbon on reduction (see Table 1, entry 9). The tin derivative (**14**) was isolated (54%) instead using toluene as solvent. The fenchol system is at least as hindered as (**12**).

Finally, we studied a thioformate where radical bridging is not possible, because the  $\beta$ -oxygen is part of another ring. The thioformate (**15**) was reduced at 110 °C with significant deoxygenation (29%). Also formed were the tin derivative [as (**12**)] (25%), the starting alcohol (18%) (probably formed by hydrolysis of the tin derivative), and the starting alcohol formate (8%).

The conclusion to be drawn is that  $\beta$ -bonds (to oxygen) have a marked effect on radical reactions, which is not due to oxygen-bridging. The phenomenon may be the  $\beta$ -analogue of the  $\alpha$ -effects studied elegantly by Deslongchamps.<sup>11</sup> In this case the stereochemical (orbital) arrangement of the  $\beta$ -atom will be of importance.<sup>12</sup> However, the results with compounds (**12**) and (**15**) show that equatorial oxygen is also stabilising. In addition, extensive studies<sup>6,13</sup> on deuterium atom transfer in tin deuteride reductions do not indicate that  $\beta$ -oxygen directs radical configuration as does  $\beta$ -bromine.<sup>2,3</sup>

In fact, the totality of the evidence on  $\beta$ -bond participation in radical reactions would seem to be explained by the absence of bridging but the presence of a  $\beta$ -effect which increases rate and may influence stereochemistry. The geometry of  $\beta$ -substituted radicals may show preferred rotational conformers,<sup>3b</sup> but without significant angular deformation.  $\delta$ -Bridging by

sulphur is, however, well established,<sup>14</sup> but here angular deformation is not required.

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