The rapid photomediated alkenylation of 2-alkyl-1,3-dioxolanes with alkynes: a stereoelectronically assisted chain reaction

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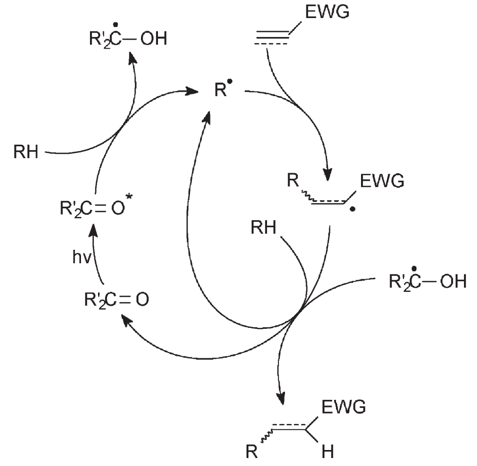
The photomediated reaction of alkynes such as DMAD with 1,3-dioxolanes leads to remarkably rapid alkenylation; evidence is presented that these reactions occur *via* a chain mechanism.

Involving unactivated systems such as cycloalkanes and ethers, and moderately activated systems such as 1,3-dioxolanes, in carbon–carbon bond formation is synthetically challenging. Although the problem is often addressed through the use of reactions based on carbon radicals, many of these suffer from the disadvantage that they involve undesirable reagents such as peroxides, tin hydrides, *etc.*, and/or in many cases require the synthesis of an appropriate radical precursor. It has been demonstrated however that the most direct route for the creation of the key carbon radicals, C–H bond cleavage, is accessible by exploiting the well-established ability of triplet state ketones to participate in hydrogen abstraction.[1,2] This photochemical production of carbon radicals can also be achieved using supported photomediators and solar radiation, features that enhance its attractiveness from the clean/green chemistry perspective.[3] Although there is the expectation that pinacol formation should be the inevitable outcome in such reaction systems, this process is not competitive in many cases and the available evidence indicates that this photochemical route to carbon radicals can be synthetically useful for simple molecules in which the options for hydrogen abstraction are limited for reasons of symmetry or substitution. Thus the reaction of cycloalkanes with alkenes and alkynes carrying electron withdrawing groups (EWGs) produces alkylated[4] and alkenylated[2] products, respectively.

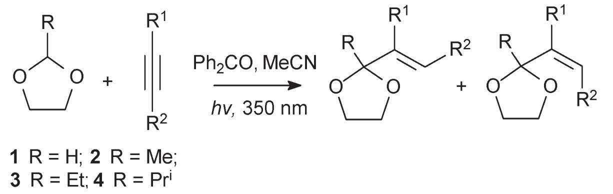
There is little uncertainty about most of the mechanistic steps involved in these reactions: initial formation of the triplet state of the ketone (the photomediator); hydrogen abstraction from the substrate generating a carbon radical; and addition of this nucleophilic radical to an alkene or alkyne carrying an EWG (Scheme 1). The final step in the process, product formation through hydrogen abstraction by an alkyl or alkenyl radical, could however involve two possible hydrogen donors. If the ketyl radical formed in the first step of the process provides the hydrogen atom then this completes the cycle and the absorption of a further photon of UV light is required for further reaction. On the other hand, if it is provided by a molecule of substrate then this opens up the intriguing possibility that the reaction could proceed *via* a chain mechanism.



Scheme 1

It has already been shown that 1,3-dioxolanes and 2-substituted-1,3-dioxolanes can participate in this photomediated process, the resulting radicals adding to α,β-unsaturated aldehydes,[5] ketones[6,7] and esters[8] in a synthetically useful way. The corresponding thermal process, based on radical initiators such as AIBN or benzoyl peroxide, is much less efficient with, in some cases, rearrangement of the dioxanyl radical being competitive with its addition to the unsaturated system.[6] The present communication reports on the remarkably rapid photomediated reaction between 2-alkyl-1,3-dioxolanes and electron deficient alkynes (Scheme 2), and presents quantum yield data which suggest that the efficiency of these reactions is at least in part due to the operation of a chain mechanism.

The reactions were carried out by irradiating a solution of the alkyne (1 mmol), the 1,3-dioxolane (20 mmol) and the photomediator benzophenone (0.4 mmol), in acetonitrile (20 cm^3), using a Rayonet reactor equipped with 350 nm lamps. The reactions were monitored by GC. The reactivity of 1,3-dioxolane **1** itself is unremarkable and it affords modest yields of addition products with a range of electron-deficient alkynes (Table 1). Reaction generally occurs regiospecifically at the 2-position, although propiolate esters give small amounts of products resulting from reaction at the 4-position.



1 R = H; **2** R = Me;
3 R = Et; **4** R = Pr^i

Scheme 2

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Table 1 The photomediated reaction of alkynes with dioxolanes

	1			**2**			**3**			**4**		
Alkyne	Time[a]	Yield[b]	$E : Z$[c]	Time[a]	Yield[b]	$E : Z$[c]	Time[a]	Yield[b]	$E : Z$[c]	Time[a]	Yield[b]	$E : Z$[c]
$R^1 = H$, $R^2 = CO_2Me$	60	32	1.3 : 1	15[d]	52	1 : 7.7	30	50	1 : 7.3	15	75	1 : 12.2
$R^1 = H$, $R^2 = SO_2Tol$	22	39	10 : 1	15	60	*E* only	15	46	*E* only	25	27	*E* only
$R^1 = H$, $R^2 = Ph$	3960[e]	3	1 : 2	570[f]	19	1 : 1.7	—	—	—	—	—	—
$R^1 = R^2 = CO_2Me$	25	42	1 : 3.1	15	89	5.1 : 1	15	74	6.2 : 1	25	70	10.4 : 1
$R^1 = R^2 = CO_2Bu^t$	—	—	—	15	64	4.0 : 1	15	79	4.4 : 1	30	53	5.5 : 1

[a] Time in minutes for complete reaction of alkyne, unless otherwise indicated. [b] Combined isolated yield of *E* and *Z* isomers (%). [c] GC. [d] Reaction time determined by monitoring product formation as alkyne co-eluted with solvent. [e] 88% conversion. [f] 75% conversion.

A remarkable enhancement in reactivity is observed however when an alkyl group is introduced at the 2-position of the dioxolane (Table 1). Thus the reaction of 2-methyl-1,3-dioxolane **2** with dimethyl acetylenedicarboxylate (DMAD) is complete in 15 min and gives the alkenylated products in a combined isolated yield of 89%. A GC determination of the yield suggests that this reaction is essentially quantitative. Although the effect of dioxolane substitution is less pronounced in reactions involving monosubstituted alkynes, it can even be observed in the reactions of styrene (Table 1). 2-Ethyl- and 2-isopropyl-1,3-dioxolane, **3** and **4**, respectively, behave in a parallel fashion, although the reactivity of the latter is lower, presumably because of the steric bulk of the isopropyl group.

It is reasonable to look for an explanation of the relative reactivities of the substituted and unsubstituted dioxolanes in terms of the hydrogen abstraction process which generates the key dioxolanyl radical, as the abstraction of α-hydrogens from ethers by photochemically generated *tert*-butoxyl has been shown to be subject to a stereoelectronic effect which is related to the size of the torsion angle (θ) between the α-C–H bond and the p-type lone-pair on the oxygen.[9,10] Thus a small value for θ facilitates interaction between the developing half-filled orbital and the oxygen's p-type lone-pair, resulting in enhanced rates of C–H bond cleavage. High reactivity was predicted[9] for the C_2–H bond(s) in **1** and **2** on the basis of measured values (Drieding models) for θ of 30° with both oxygen atoms. This prediction was confirmed by EPR spectroscopy, with **1** actually being found to be the more reactive. The reactivity of the related 2-methyl-1,3-dioxane in this context was interpreted in terms of a preferred conformation in which the methyl group is equatorial.[10] Although 5-membered rings would be expected to be more conformationally mobile, the results reported here can be rationalised in terms of 2-alkyl-1,3-dioxolanes also having a more clearly defined conformational preference. A DFT (B3LYP/6-31G*) optimisation of the minimum energy geometry derived from an MM based conformational search procedure[11] shows that dioxolane **1** and 2-alkylated-1,3-dioxolanes **2–4** prefer half-twist conformations. This indicates that, although 1,3-dioxolane is presumably conformationally mobile, its C_2 hydrogens actually have a favourable stereoelectronic relationship with one of the oxygens in its minimum energy form (Table 2). The key point however in terms of the remarkable reactivity reported here for **2**, which as indicated above is assumed to exhibit a conformational preference, is the fact that abstraction of the C_2 hydrogen will be significantly accelerated by both oxygen atoms (θ = 7.1, 9.5°). Although this inverts the relative reactivity of **1** and **2** suggested by the EPR spectral data,[7] it is clearly entirely consistent with their behaviour in terms of the photomediated reaction with alkynes reported here. The C_2 hydrogens in the other 2-alkyl-1,3-dioxolanes considered in this study also enjoy favourable stereoelectronic relationships with both oxygen atoms. The importance of this type of stereoelectronic effect in these systems is underlined by the fact that, whereas small amounts of a C_4 alkenylated product are obtained in the reaction of **1** with propiolate esters, no such products are obtained in the reactions of **2–4** with any of the alkynes used. This effect has also been observed in the reactions of these dioxolanes with alkenes.[8] This can be rationalised on the basis that two of the C_4/C_5 hydrogens in **1** have, uniquely, almost coplanar relationships with p-type lone-pairs on the oxygen atoms.

The enhanced stereoelectronic effect operating in 2-alkyl-1,3-dioxolanes influences their reactivity in another way. As indicated above, the suggested mechanism (Scheme 1) allows for the operation of a chain process involving hydrogen transfer from a second molecule of dioxolane to the initially formed alkenyl radical, a process which in the case of the 2-alkyl-1,3-dioxolanes is now seen to be stereoelectronically facilitated. Quantum yield measurements using a valerophenone actinometer[12,13] provide evidence for the availability of such a route to product formation and indicate that the reactivity of dioxolane–alkyne combinations depends on the extent to which product formation involves this chain process. Thus, whereas the most reactive combination, 2-methyl-1,3-dioxolane–DMAD, occurs with a quantum yield which is much greater than unity (Φ = 4.8), the reaction of 1,3-dioxolane with methyl propiolate involves a quantum yield which is less than one (Φ = 0.5), with that for 2-methyl-1,3-dioxolane–methyl propiolate being intermediate between the two (Φ = 1.4).

Although the above analysis provides a rationale for the effect of substitution in the 2-position on the reactivity of 1,3-dioxolanes in their reactions with alkynes, the reactivity of the system in general is also dependent on the nature of the unsaturated

Table 2 α-C–H/O(p-type lone pair) torsion angles (°) in optimised[a] 1,3-dioxolane structures

Torsion angle	**1**, R = H	**2**, R = Me	**3**, R = Et	**4**, R = Pr^i
H_2O_1	16.1	7.1	11.5	15.3
$H_2'O_1$	43.2	—	—	—
H_2O_3	43.2	9.5	7.5	5.5
$H_2'O_3$	16.1	—	—	—
H_4O_3	61.0	68.1	68.9	68.6
$H_4'O_3$	1.2	7.7	8.8	8.5
H_5O_1	1.2	27.4	22.4	18.8
$H_5'O_1$	61.0	33.2	38.0	41.5

[a] B3LYP/6-31G* optimisation using a starting geometry generated by an MM based conformational search.[11]

molecule involved. Thus **1** and **2** exhibit comparable reactivities in their reactions with α,β-unsaturated aldehydes.[5] Despite this complexity the results clearly indicate that the photomediated generation of carbon radicals by direct hydrogen abstraction can be remarkably efficient and warrants further investigation.

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