JOURNAL OF PHYSICAL ORGANIC CHEMISTRY
J. Phys. Org. Chem. **12**, 703–707 (1999)

Photosensitized oxygenation of some benzyl sulfides. The role of persulfoxide

Sergio M. Bonesi, Mauro Freccero and Angelo Albini*

Department of Organic Chemistry, University of Pavia, via Taramelli 10, 27100 Pavia, Italy

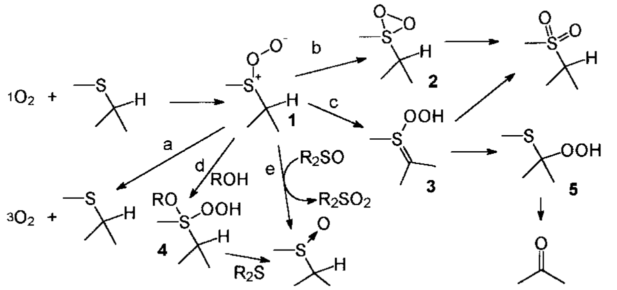
Received 3 November 1998; revised 26 April 1999; accepted 26 April 1999

ABSTRACT: Benzyl ethyl sulfide (**6a**) is photo-oxidized to benzaldehyde in benzene, whereas diethyl sulfide is known to give inefficiently the sulfoxide under these conditions. Oxidative C—S cleavage is the main process also with benzhydryl ethyl sulfide (**6c**), but not with α-methylbenzyl ethyl sulfide (**6b**), which mainly gives the sulfoxide. The carbonyl derivatives reasonably arise from *S*-hydroperoxy ylides (**3**). Consistently with this finding, calculations at the PM3 level suggest that the first intermediate, the persulfoxide (**1**), undergoes intramolecular hydrogen transfer when an activated α-hydrogen is available and gives **3**. This is the case for the above benzyl sulfides ($\Delta H^{\neq}$ for the process decreases with decreasing C—H BDE). However, only some of the persulfoxide conformations are correctly oriented for this rearrangement, and this may slow this process and make other reactions compete, as happens with **6b**. Copyright © 1999 John Wiley & Sons, Ltd.

KEYWORDS: single oxygen; sulfides; photochemistry; oxidation

INTRODUCTION

The photosensitized oxygenation of sulfides is currently rationalized as involving an adduct, the persulfoxide **1**, as the first-formed intermediate.[1] This is a weakly bound adduct, and the main (≥95%) fate of this species in aprotic media is chemically unproductive decay to the ground-state components (Scheme 1, path a), so that under these conditions sulfides are essentially physical quenchers of $^1O_2$. On the basis of a thorough kinetic analysis, Foote[1d] suggested that a small fraction of **1** undergoes isomerization to a further intermediate, for which a possible structure was that of thiadioxirane **2** (path b). The second intermediate is an electrophile; it can be trapped with sulfides (to give sulfoxides) and possibly it rearranges to a sulfone. Recent computations by Jensen *et al.*[2] and McKee[3] do not support the intermediacy of **2**, while suggesting that another rearrangement, intramolecular hydrogen transfer to give the hydroperoxy ylide **3**, is possible (path c). Calculations show that further rearrangement of **3** to the sulfone is viable,[2,3] it has been considered that **3** may be involved in oxygen transfer to sulfides (viz. that it is the second intermediate as proposed by Foote), but this has found no clear support.[2]



Scheme 1

Further processes attributed to the persulfoxide are intermolecular reactions, viz addition of alcohols to give a hydroperoxyalkoxy sulfide (**4**, path d), an important reaction because this is what makes the photo-oxidation efficient in alcohols, and oxygen transfer to sulfoxides (path e), a mechanistically interesting process which allows recognition of the nucleophilic character of this species (as opposed to the electrophilic second intermediate).[1]

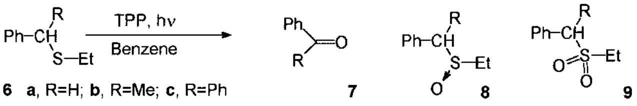
Although there is a general consensus on the role of **1**, there is no direct identification of such an intermediate or of a rearranged isomer. A way to tackle this problem is to study a chemical process directly related to these intermediates. This is difficult with dialkyl sulfides, since in aprotic media the photooxygenation is very inefficient and mainly gives the sulfoxide. This is not mechanistically indicative since, as mentioned above, it is not clear whether this may arise directly from **1** or **3**, while it is formed much more efficiently in protic solvents, where a secondary intermediate, presumably adduct **4**, is involved. Products different from sulfoxides have been

---

Correspondence to: Angelo Albini, Department of Organic Chemistry, University of Pavia, via Taramelli 10, 27100 Pavia, Italy.

Contract/grant sponsor: CNR.
Contract/grant sponsor: MURST.

CCC 0894–3230/99/090703–05 $17.50



Scheme 2

Table 1. Products from the tetraphenylporphine photosensitized oxidation of benzyl sulfides in benzene

Substrate	R	Relative reactivity	Product yield (%) 7	8	9
6a	H	3.5	80	3	8
6b	Me	1.8	10	70	5
6c	Ph	2.8	60	9	22
Et_2S		1	Et_2SO (90%)		

reported for some thiazolidines, which give the corresponding α-hydroperoxides (see formula **5**).[4] Calculations support that this arises by shift of the OOH group from ylide **3**.[2,3] A related reaction has been reported for some benzyl sulfides, where the products actually obtained are aldehydes, presumably resulting from the fragmentation of **5** (Scheme 1).[5,6]

The mechanism of benzyl sulfide photo-oxidation has received little experimental study and has not as yet been considered computationally. We thought that a detailed investigation was a unique opportunity to understand the reactivity of the persulfoxide, since the cleavage to aldehydes appears to depend on the rearrangement of this intermediate and should provide information on its structure. Therefore, we began the study of this reaction through a kinetic analysis of the oxidation of benzyl ethyl sulfide.[7] A further way of exploring the mechanism could be to test the sensitivity of the reaction to substitution at the key α-position. Here we report the photo-oxygenation of three benzyl sulfides and compare the experimental results with a semiempirical computational study energy surface of the corresponding persulfoxides.

RESULTS

Photoreactions

Tetraphenylporphine (TPP) photosensitized oxygenation of benzyl ethyl sulfide (**6a**) in benzene mainly gave benzaldehyde (**7a**) with virtually no sulfoxide (**8a**) and only a little sulfone (**9a**) at the beginning of the reaction. The proportion of the sulfoxide grew somewhat during the course of the reaction, but did not alter the predominance of benzaldehyde (see Scheme 2). In Table 1 the yields obtained at ca 25% conversion are reported (see Experimental). These were measured by gas chromatography (GC) when the products were stable to this technique (this is not the case for sulfoxide **8b;** see below and Experimental) and ^1H NMR spectroscopy. The irradiation of the sulfides was carried out under the same conditions for a different time until a ca 25% conversion was reached. In this way, a reactivity order was established. As an example, Table 1 shows that the oxidation of **6a** was much more efficient than that of diethyl sulfide under the same condition.

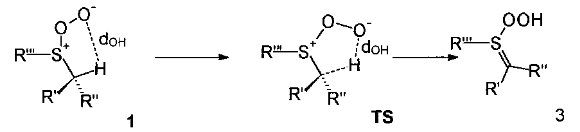
The TPP photo-oxidation of α-methylbenzyl ethyl sulfide (**6b**) in benzene gave only a small amount of acetophenone (**7b**), the main product being by far sulfoxide **8b**, accompanied by some sulfone **9b**. With benzhydryl ethyl sulfide (**6c**) the oxidative cleavage was again predominant, with benzophenone (**7c**) as the main product, a considerable amount of sulfone (**9c**) and a small amount of sulfoxide (**8c**).

The efficiency of the photo-oxidation for the sulfides tested decreased in the order **6a** > **6c** > **6b** > Et_2S. Thus, the introduction of a phenyl group α to the sulfur atom makes photo-oxidation of alkyl sulfides more efficient, while directing it towards oxidative C—S bond fragmentation rather than to the sulfoxidation consistently observed with dialkyl sulfides. However, introducing a further α-substituent again affects both efficiency and competition between the above two processes in a non-intuitively obvious way: a second α-phenyl simply slows the reaction, but with an α-methyl slowing is more marked and the main product is the sulfoxide.

Table 2. Conformations of the persulfoxide **1** and activation energy for the transition state leading to **3** (see Scheme 3)

Conformer	R′	R″	R‴	**1**, ΔH_f (kcal mol^{-1})	$d_{O—H}$ (Å)	TS, $\Delta H^{\neq}$ (kcal mol^{-1})	$d_{O—H}$ (Å)
1d[a]	H	H	Me	4.68	3.15	19.1	1.32
1a α	Ph	H	Et	31.40	2.90	15.9	1.33
β				30.07	3.21	16.0	1.33
1b α	Ph	Me	Et	28.88	4.57	—	—
β				28.12	3.05	13.9	1.34
γ				27.98	3.10	13.8	1.33
δ				27.71	3.74	—	—
1c α	Ph	Ph	Et	64.37	3.01	12.2	1.34
β				63.20	4.72	—	—

[a] The energy data for **1d** and the related TS reproduce well those previously reported by Ishiguro *et al.*[8]



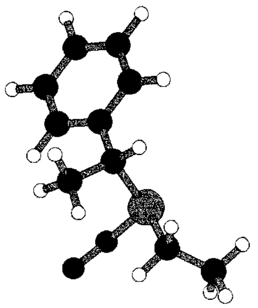
Scheme 3

Computational analysis

The above-mentioned calculations by Jensen *et al.*[2] [MP2/6–31G(d) and advanced levels] and McKee[3] (B3LYP/6–31 + G and advanced levels) on the Me_2S–$^1O_2$ system showed that ylide **3** is slightly stablized with respect to persulfoxide **1** and is separated by a barrier of only a few kcal mol^{-1}. Benzyl substitution was difficult to manage at this level of theory. However, in 1996 Ishiguro *et al.*[8] reported a study of the Me_2S–$^1O_2$ system at the PM3 level and also found the rearrangement to ylide **3** to be a viable path. Given the difficulty of using *ab initio* methods, we thus felt it worthwhile to perform a PM3 study on benzyl sulfides **6a–c**, since this would give at least qualitative information on the difference of such substrates with respect to aliphatic sulfides.

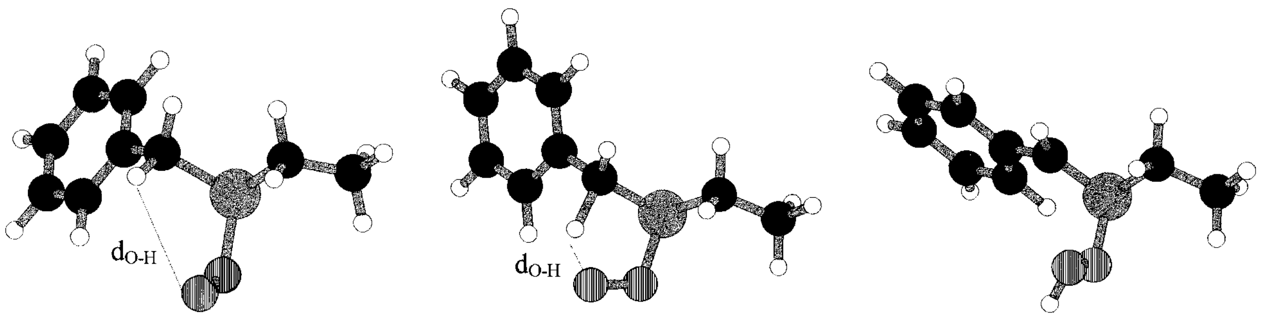
We first carried out the calculation on dimethyl persulfoxide (**1d**). The conversion to ylide **3d** involved, as reported by Ishiguro *et al.*[8] a sizeable barrier ($\Delta H^{\neq} =$ 19 kcal mol^{-1}, see Table 2). This should be compared with the 5.8–7.8 kcal mol^{-1} obtained by CCSD(T) 6–31 G(d) or 6–3111 + G(2df) methods[2] and with the 9–12.6 kcal mol^{-1} obtained with the B3LYP/a(+2PC) or the QCISD(T)/a methods.[3] Apparently there is a scaling factor of ca 2. However, we observed that the minimum located by the PM3 computation corresponded favourably with that found for the persulfoxide using more advanced methods[2,9] and had the O—O bond roughly bisecting the Me—S—Me angle and 3 Å distance between the α hydrogen and the persulfoxide oxygen ($d_{O—H}$, see Table 2 and Scheme 3). Therefore, we felt that any difference with substitution observed by the PM3 method should be indicative of the reactivity order.

Owing to the lower symmetry, more stable conformations were expected for the currently considered benzyl persulfoxides than for the dimethyl derivative. Indeed, two minima were located for persulfoxide **1a** (α and β in Table 2). In both of them, the geometry (angle of the O—O bond with respect to the sulfide moiety, $d_{O—H}$) was close to that calculated for the single minimum of **1a** (see Scheme 3, Table 2). For both conformers, conversion to ylide **3a** occurred smoothly via a transition state (TS) where the hydrogen was equidistant between the oxygen and the carbon atom, again similarly to the Me_2S case, but $\Delta H^{\neq}$ was considerably smaller, 16 rather than 19 kcal mol^{-1} (see Table 2). As for ylide **3a**, this showed an S—CH distance of 1.60 Å (compared with 1.84 Å for the S—CH_2 distance in persulfoxide **1a**) and the dihedral angle CH_2—S—C(Ph)—H was 160°. This evidence supported the double bond nature of the S—CH bond. The geometry of the persulfoxide (conformation α), the corresponding transition state and the resulting ylide are shown in Fig. 1 as an example.



1b (α)

A further decrease in symmetry led to four minima for persulfoxide **1b** and these are arranged in order of increasing stability in Table 2. It can be seen that conformers β and γ were similar to those discussed above ($d_{O—H} \approx 3$ Å) and the TS for the rearrangement to the ylide was lowered by a further 2 kcal mol^{-1}. However, conformations α and δ, although of similar energy and again with the O—O bond bisecting the R—S—R angle,



1a (α) **TS** **3a**

Figure 1. Geometries of **1a** (α conformation), the TS and **3a**

had the outer oxygen closer to the α-methyl than to the α-hydrogen (see Fig. 2). The search for a TS leading to **3b** gave no result in this case.

Finally, two minima were located for persulfoxide **1c** (Table 2). Conformer α had a short O—H distance and the $\Delta H^{\neq}$ for conversion to the ylide was diminished by a further 2 kcal mol^{-1} with respect to **1b**, while the slightly less energetic conformer β had $d_{O—H} = 4.7$ Å and no accessible TS for rearrangement to the ylide.

Previous calculations, both *ab initio*[2,3] and at the PM3 level,[8] showed the viability of the rearrangement of the ylide **3d** to the α-hydroperoxy sulfide (and hence to a carbonyl derivative after C—S bond cleavage) or, presumably through a higher barrier, to the sulfone (see Scheme 1). In view of the multiplicity of paths, it appeared that semiempirical calculations on the benzyl derivatives could add little to this point and were therefore not investigated further.

DISCUSSION

The present data show that the oxidation of benzyl sulfides in an aprotic solvent is considerably more efficient than that of diethyl sulfide and finally leads to oxidative C—S bond cleavage. The literature proposal that this reaction is initiated by intramolecular hydrogen transfer competing with persulfoxide dissociation to the components is supported by calculations showing that the barrier to this process is substantially decreased when a α-phenyl substituent is present. This is support for the role of ylide **3** in the photo-oxidation of sulfides that would be difficult to obtain in the reaction of dialkyl sulfides, since in that case the yield of sulfone, possibly formed via **3**, is very low in an aprotic solvent, where the main products is the sulfoxide, formed much more efficiently in protic media.

As for the mechanism of such an intramolecular step, the original report suggested that this is a proton abstraction by the negatively charged outer oxygen atom of the persulfoxide.[5] Both *ab initio* and the present PM3 calculations show indeed that there is substantial charge separation in the persulfoxide. However, Table 2 shows that the energy of the TS for hydrogen transfer dropped monotonically with increasing substitution at the α-carbon and, despite the large scaling factor between the semiempirical and *ab initio* calculated $\Delta H^{\neq}$, the effect was sufficiently large and consistent to ensure that the trend was real. The stabilization of the TS was strictly proportional to the decrease in the α-C—H homolytic bond dissociation energy (BDE), while it is doubful that phenyl or methyl substituents would substantially increase the α-hydrogen acidity. Furthermore, we found previously that the efficiency of photooxidative C—S bond cleavage in both the 4-nitro- and the 4-methoxy-substituted derivatives was similar to that of parent benzyl ethyl sulfide,[7] suggesting that polar factors are not determinant. Thus, to the extent that such a distinction is meaningful, the rearrangement of persulfoxide **1** to ylide **3** should be envisaged as radical hydrogen transfer rather than proton transfer (peroxy radicals are known as poor hydrogen abstractors; however, an intramolecular process may be sufficiently fast) On the other hand, persulfoxides, like in general mesomeric 1,3-dipoles,[10] can be considered as diradical as well as charge-localized zwitterions. Hence it is suggested that rearrangement to ylide **3** is significant when a radical-stabilizing (phenyl) group is present in the α position.

The introduction of a second α substituent further decreases $\Delta H^{\neq}$ for rearrangement, but on the other hand increases the number of persulfoxide configurations, and for some of these there is no accessible path to the ylide. Since *ab initio* calculations (to which our PM3 data should be scaled) suggest that the barrier for hydrogen transfer is below 10 kcal mol^{-1}, i.e. of the same order of magnitude as rotation barriers, and collapse of the persulfoxide to the components encounters in every case a small barrier, it is expected that the presence of conformations unable to rearrange significantly diminishes the overall efficiency of rearrangement. Hence the two effects above operate in opposite directions.

This may explain the result with sulfide **6b**, with which the overall reaction is slower than with **6a** and gives much more sulfoxide, despite the fact that two out of four conformations of persulfoxide **1b** rearrange to the ylide through a TS lying lower than those from **1a**. We attribute this fact to the overwhelming effect of adding two roughly equally populated, but unproductive, conformations, which decreases the overall rate for hydrogen transfer (path c) and increases the proportion of both decay to the ground-state components (path a) and other chemical processes leading to the sulfoxide.

With **1c** the ratio of productive vs unproductive conformations remains the same as with **1b** (1:1), but the further decrease of $\Delta H^{\neq}$ favours rearrangement to **3c**. As a result, the oxidation of sulfide **6c**, although not as efficient as that of **6a**, mainly gives the ketone.

Certainly, the final result depends on the following reaction of ylide **3**, in addition to its rate of formation. The *ab initio* analysis by Jensen *et al.*[2] suggests that a possible path is backward rearrangement to **1**. The fact that no deuterium loss occurs on recovered sulfide after partial photooxidation of the α,α-d_2-benzyl ethyl sulfide[7] militates against a role of such a path with benzyl derivatives. However, the fact sulfide **6c**, for which the yield of C—S cleavage is somewhat lower gives a higher yield of sulfone **9c** may indicate that the competition between the reactions of **3** is also affected by substituents. The rearrangement to the ylide and the following conformation-dependent chemistry of this intermediate may have a role also with other sulfides. In particular, this may be the case for the Pummerer rearrangement reported by Ando and co-workers with thiolanes[11] and thiazolidines[4] (in the former case, attributed by the authors to the acidity of the α-hydrogen). This process seems to be favoured with five-membered cyclic sulfides.

CONCLUSION

Benzyl sulfides are photo-oxidized more easily than dialkyl sulfides, and are cleaved to aldehydes or ketones. The experimentally determined relative efficiency of this fragmentation agrees with the computational prediction about the ease of the rearrangement of the initially formed oxygen adduct, persulfoxide **1**, to ylide **3**, in turn the likely intermediate for the observed carbonyl derivatives. The **1**→**3** conversion can be viewed as a hydrogen atom transfer process, and its probability is determined by the α-C—H BDE and the proportion of correctly oriented conformations of **1**. This is *per se* not definitive evidence that this is the mechanism operating. Another possibility is that **3** is formed through a separate path, e.g. via a concerted reaction directly from the sulfide and singlet oxygen, analogously to the alkene ene reaction; this is e.g. the path indicated at the MP2/6—31 G(d) level, although there is no experimental support.[2] At any rate, the present evidence suggests that if **1** is the intermediate it has an as yet overlooked diradicalic character.

EXPERIMENTAL

Materials. Benzene for the photo-oxygenation was distilled over calcium hydride before use. The sulfides **6a–c**[12–14] were prepared from the corresponding halides through published procedures. Likewise, samples of the corresponding sulfoxides **7a–c**[15–17] and sulfones **8a–c**[13,17,18] for comparison with the photoproducts were prepared by 3-chlorobenzoic acid oxidation according to the general procedure.[19]

Photoreactions. The photo-oxidations were carried out using 0.01 M solutions of the appropriate sulfide in benzene in the presence of tetraphenylporphine. The solutions were contained in rubber-stoppered Pyrex tubes. These were exposed to four phosphor-coated 15 W lamps (Applied Photophysics) emitting from 350 to 700 nm while a stream of oxygen saturated with benzene was passed in to the solution through a needle.

The products were determined by GC on the basis of calibration curves. A Hewlett-Packard Model 5890 instrument equipped with an Innowax column (30 m × 0.25 mm i.d., 0.5 μm film thickness) was used, with He as the carrier gas. The injector pressure was constant (12 psi). The temperature program was 50–140 °C (5 °C min^{-1}), 140–250 °C (25 °C min^{-1}), 7 min final hold. Sulfoxide **8b** was converted to α-methylstyrene under these conditions, so in this case the yields were determined by ^{1}H NMR spectroscopy.

Computational details. PM3[20] calculations were carried out with the HyperChem program (version 5.0). Persulfoxide conformational minima were fully optimized. Transition structures were located using the algorithm eigenvector following. Transition structures have only one negative eigenvalue (first-order saddle point) with the corresponding eigenvector involving the formation of an O—H bond and the cleavage of the benzylic C—H bond.

Acknowledgements

Financial support by CNR, Rome and MURST, Rome is gratefully acknowledged. S.M.B. thanks FOMEC for a fellowship.

REFERENCES

1. (a) E. L. Clennan, *Sulfur Rep.* **19**, 171 (1996); (b) W. Ando and T. Takada, in *Singlet* O_2, edited by A. A. Frimer, Vol. **3**, p. 1. CRC, Boca Raton, FL (1985); (c) W. Ando, *Sulfur Rep.* **1**, 143 (1981); (d) C. S. Foote, in *Singlet Oxygen*, edited by H. H. Wasserman and R. W. Murray, p. 139. Academic Press, New York (1979); (e) F. Jensen, in *Advances in Oxygenated Processes*, edited by A. L. Baumstark, Vol. **4**, p. 49. JAI Press, Greenwich, CT (1995); (f) G. O. Schenk and C. H. Krauch, *Angew. Chem.* **74**, 510 (1962).
2. F. Jensen, A. Greer and E. L. Clennan, *J. Am. Chem. Soc.* **120**, 4439 (1998).
3. M. L. McKee, *J. Am. Chem. Soc.* **120**, 3963 (1998).
4. T. Takata, K. Hoshino, E. Takeuchi, Y. Tamura and W. Ando, *Tetrahedron Lett.* **25**, 4767 (1984); T. Takata, K. Ishibashi and W. Ando, *Tetrahedron Lett.* **26**, 4609 (1985).
5. E. J. Corey and C. Ouannès, *Tetrahedron Lett.* 4263 (1976).
6. W. Ando, T. Nagashima, K. Saito and S. Kohmoto, *J. Chem. Soc., Chem. Commun.* 154 (1979); T. Akasaka, A. Sakurai and W. Ando, *J. Am. Chem. Soc.* **113**, 2696 (1991).
7. S. M. Bonesi, M. Mella, N. d'Alessandro, G. G. Aloisi, M. Vanossi and A. Albini, *J. Org. Chem.* **63**, 9946 (1998).
8. K. Ishiguro, M. Hayashi and Y. Sawaki, *J. Am. Chem. Soc.* **118**, 7265 (1996).
9. F. Jensen and C. S. Foote, *J. Am. Chem. Soc.* **109**, 1478 (1987); F. Jensen, *J. Org. Chem.* **57**, 6478 (1992).
10. P. C. Hiberty, *Isr. J. Chem.* **23**, 10 (1983).
11. T. Takata, K. Ishibashi and W. Ando, *Tetrahedron Lett.* **26**, 4609 (1985).
12. G. Modena, *Gazz. Chim. Ital.* **89**, 834 (1960).
13. W. E. Bacon and W. M. LeSuer, *J. Am. Chem. Soc.* **76**, 670 (1954).
14. M. Dagonneau and J. Vialle, *Bull. Soc. Chim. Fr.* 2072 (1972).
15. A. Cerniani, G. Modena and P. E. Todesco, *Gazz. Chim. Ital.* **90**, 3 (1960).
16. Y. Kodama, S. Zuschi, K. Nishihata, M. Nishio and J. Uzawa, *J. Chem. Soc., Perkin Trans. 2* 1307 (1980).
17. S. Becher, Y. Fort and P. Caubère, *J. Org. Chem.* **55**, 6194 (1990).
18. J. Buechi, M. Prost, H. Eichenberger and R. Lieberherr, *Helv. Chim. Acta* **35**, 1527 (1952).
19. J. Drabowicz and M. Mikolajczyk, *Org. Prep. Proced. Int.* **14**, 45 (1982).
20. J. J. P. Stewart, *J. Comput. Chem.* **10**, 209 (1989).