Oxidation of Benzylic Alcohols and Ethers to Carbonyl Derivatives by Nitric Acid in Dichloromethane

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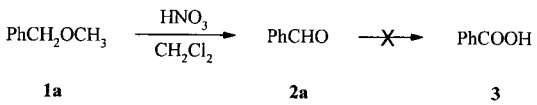
Keywords: Alcohols / Aldehydes / Ketones / Oxidations / Radical reactions

Nitric acid in dichloromethane may be successfully employed for the oxidation of benzylic alcohols and ethers to the corresponding carbonyl compounds. The proposed method proved to be of general applicability, affording very good yields of aldehydes and ketones and showing interesting chemoselectivity in many instances, allowing competitive aromatic nitration to be avoided, as well as – in the case of aldehydes – any further oxidation to carboxylic acids. The reaction probably proceeds by a radical mechanism, the active species in the oxidation process being NO_2. Competitive formation of nitro esters was observed in some cases, whereas poor results were obtained with allylic and non-benzylic substrates.

Introduction

In the course of our studies concerning the synthetic applications of the HNO_3/CH_2Cl_2 system, previously found to be very effective in *ortho*-oriented nitrations of some benzylic substrates (*chaperon* effect),[1] as well as a useful heterolytic (nitrolytic) reagent suitable for the deprotection of *N*-Boc derivatives,[2] *tert*-butyl and 1-adamantyl carboxylates,[3] we set out to explore the synthetic potential implicit in our initial observation[1] that methyl phenylmethyl ether (**1a**) underwent a rapid and quantitative transformation into benzaldehyde (**2a**), thus preventing any occurrence of ring nitration[4] and without undergoing further oxidation to benzoic acid (**3**, Scheme 1).[5] Such behaviour appeared particularly noteworthy in view of the fact that compound **1a** was reported to meet a completely different fate under classical nitration conditions.[6] Although a plethora of methods to achieve the oxidation of alcohols (and ethers as well) to the corresponding carbonyl compounds are described in the literature,[7] this investigation was deemed worthy of attention thanks to its straightforwardness of operation and the easy availability[8] and low cost of the chemicals to be employed.



Scheme 1

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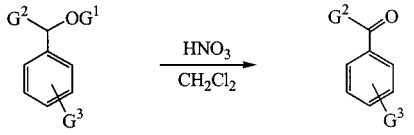
Results and Discussion

We first considered benzylic primary substrates (Scheme 2, compounds **1** and **4**, G^2 = H) on the basis of the well-known capability of HNO_3 to effect their oxidation to carbonyl compounds,[9] and taking account of the advantages of operating in an organic solvent.[10] Initially, we set out to establish reasonably good conditions for the oxidation of $PhCH_2OCH_3$ (**1a**) at room temperature, after initial mixing of the reagents at 0 °C. The results of different HNO_3/**1a** ratios at identical substrate concentration (see Exp. Sect.) are collected in Table 1, and show that a faster reaction can be achieved − without the occurrence of aromatic nitration − by increasing the ratio, a strategy useful to apply in the case of substrates sensitive in other locations to long exposures to this environment. We therefore decided to employ an excess of 3 mol of HNO_3 per mol of substrate to perform a number of experiments suitable to evaluate the applicability of the method, so as to obtain a comparative view of the behaviour of benzylic alcohols and ethers under these conditions. The obtained results are collected in Table 2.



1: G^1 = Alkyl
4: G^1 = H

2

Scheme 2

For most of the tested ethers that did not bear additional α-alkyl groups (**1**, G^2 = H), the conversion into the corres-

Table 1. Optimization of the HNO_3/**1a** ratio in the oxidation reaction to **2a** (Scheme 1)

Entry	**1a** [mol]	HNO_3 [mol]	Reaction time [h]	Conversion [%][a]
1	1.0	2.0	1	68
2	1.0	2.0	24	> 99
3	1.0	2.5	1	82
4	1.0	3.0	1	> 99

[a] Determined by ^{1}H NMR (see Exp. Sect.). Benzaldehyde (**2a**) was the sole product.

ponding aldehydes was quantitative within 1 h at room temperature (Table 2). We observed that the process is accelerated by relatively mild electron-releasing substituents, without suffering any significant activation towards competitive aromatic nitration, and slowed down by the presence of electron-withdrawing substituents. On the other hand, strongly electron-releasing substituents present in the benzene ring caused the unavoidable incursion of aromatic electrophilic substitution. Indeed, when 3-methoxy derivative **1p** was the substrate, concomitant ring nitration was evident (Scheme 3), resulting in the formation of a consistent amount (58%) of a mixture of isomeric nitro ethers (**5**). Interestingly enough, the observed complete absence of nitro aldehydes **6** in the reaction mixture was a good indication both of the deactivation of aromatic nitration exerted by the formyl substituent and of the inhibition of the oxidative process caused by the presence of the nitro function in derivatives **5**. When dibenzyl ether (**1z**) was the substrate and the amount of HNO_3 was adjusted appropriately, almost complete conversion into 2 mol of benzaldehyde (**2a**) was achieved, showing some remarkable improvement over a recently reported method.[11] In addition, benzyl ethers with an alkyl counterpart other than methyl (**1aa**−**dd**) behaved normally, affording PhCHO (**2a**) in almost quantitative yield (Table 2).

Benzylic alcohols with a variety of ring substituents were also tested and found to be more reactive than the corresponding ethers,[12] as confirmed by an appropriate competitive experiment involving $PhCH_2OH$ (**4a**) vs. $PhCH_2OCH_3$ (**1a**), in which a 1:1 mixture of the substrates was treated with an insufficient amount of HNO_3. Compound **1a** proved to be by and large preferentially oxidized to PhCHO (**2a**). Treatment of alcohols, however, although easier than treatment of ethers, may result in faster esterification by HNO_3, a competitive side process not eventually producing oxidation products under these conditions, as evidenced for **4m** and **4n**, to the point of becoming a convenient route to nitro esters in some cases.

Mechanistically, a nitric ester could be a candidate intermediate in our benzylic oxidations of alcohols (and possibly of ethers, following nitrolysis). When, though, benzyl nitrate (**7**) was treated with HNO_3 in CH_2Cl_2, only ring nitration to afford the three nitro derivatives **8**, **9**, and **10** was observed after 1 h at room temperature, with only traces of PhCHO (**2a**) being formed (Scheme 4). This result ruled out the occurrence of an E_{CO}-like, acid-catalysed elimination mechanism[13] as proposed in some instances, in which high temperatures were usually required.[14] This inference was confirmed when **7** was treated under otherwise identical conditions but with an equivalent amount of trifluoroacetic acid (TFA) in place of HNO_3. This produced a very sluggish reaction; no products were detectable after 1 h, and only 15% of **2a** was formed after 24 h (Scheme 4), thus indicating that an ionic pathway of elimination of HNO_2 is indeed possible, but slow (Scheme 5).

On the other hand, a long induction period associated with a slower reaction was observed for the isomeric nitro alcohols **4m** and **4n**, this behaviour having been taken as an indication of the involvement of a radical mechanism[15] with NO_2 acting as the active species,[16] whereas an ionic process[17] appears unlike under the current conditions. In fact, 4-nitrobenzyl nitrate (**10**) proved to be completely unreactive under these conditions, its reactivity being totally inhibited by the electron-withdrawing nitro groups, both towards oxidation and towards further aromatic nitration. In this context, the comparative behaviour of the 3-methoxy (**1p**, **4p**) and 3-phenoxy (**1q** and **4q**) derivatives under the usual reaction conditions is noteworthy (Table 2). 3-Methoxybenzyl alcohol (**4p**) gave a predominant oxidation pattern (66% 3-methoxybenzaldehyde, **2p**), whereas the corresponding methyl ether **1p**, less prone to oxidation, reacted competitively to give 42% aldehyde **2p** and 58% ring nitration products (Scheme 3). The electron-releasing action of the PhO group is much reduced, allowing the oxidation of 3-phenoxybenxyl alcohol (**4q**) to the corresponding aldehyde **2q** as the sole and quantitative process taking place, whereas methyl 3-phenoxybenzyl ether (**1q**), which would be expected to react more slowly in the oxidation process, indeed gave a final pattern similar to **1p**. In line with the above observations, (4-hydroxyphenyl)methanol (**15**) is believed[3b] to undergo faster aromatic nitration under the conditions employed for the oxidation. In fact, even the less activated 4-methoxy derivative **4r** gave only 44% of the corresponding benzaldehyde **2r**, undergoing prevalent competitive ring nitration. Nevertheless, when the phenolic function was selectively protected with the easily removable, but under these conditions quite stable,[3b] phenylmethoxycarbonyl group as in **4s**, the oxidation of the alcoholic function took place without any undesired ring nitration, affording the aldehyde **2s** in high yield, thus circumventing some previously reported drawbacks.[18]

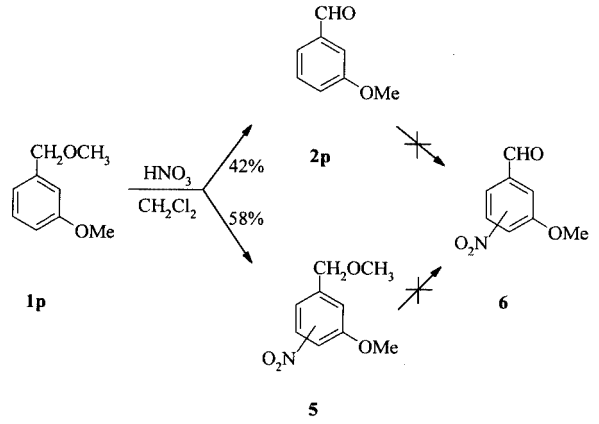
When an alcohol was the substrate, the product balance of the oxidation process had to be inorganic in nature, but in the case of ethers an organic counterpart was to be expected. In order to cast more light on the reaction mechanism, this point was carefully investigated. The substrate selected for the purpose was benzyl hexyl ether (**1aa**), which underwent smooth oxidation under our conditions to afford, besides the expected quantity of PhCHO (**2a**), a 70% yield of hexyl nitrite (**11**), accompanied by its likely products of hydrolysis[19] (hexanol, **12**, 6%) and oxidation[20] (hexanal, **13**, 18%), together with hexyl nitrate (**14**, 6%), the latter probably originating from direct esterification of **12**

Table 2. Oxidation of benzylic alcohols and ethers with HNO_3 in CH_2Cl_2 (Scheme 2)

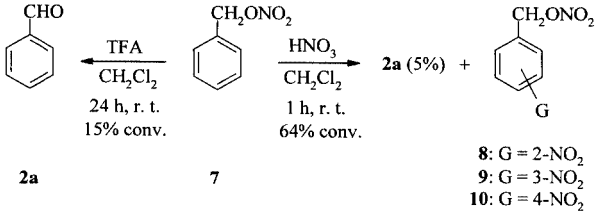
Entry	Substrate	G^1	G^2	G^3	Product[a]	Conversion [%][b]	Yield [%][c]
1	**1a**	CH_3	H	H	**2a**	> 99	83
2	**4a**	H	H	H	**2a**	> 99	91
3	**4b**	H	H	2-CH_3	**2b**	> 99	92
4	**1c**	CH_3	H	3-CH_3	**2c**	> 99	87
5	**1d**	CH_3	H	4-CH_3	**2d**	> 99	87
6	**4d**	H	H	4-CH_3	**2d**	> 99	90
7	**1e**	CH_3	H	4-$C(CH_3)_3$	**2e**	> 99	86
8	**1f**	CH_3	H	2-Cl	**2f**	> 99	82
9	**4f**	H	H	2-Cl	**2f**	> 99	85
10	**1g**	CH_3	H	3-Cl	**2g**	> 99	78
11	**1h**	CH_3	H	4-Cl	**2h**	> 99	86
12	**4h**	H	H	4-Cl	**2h**	> 99	91
13	**1j**	CH_3	H	2,4-Cl_2	**2j**	> 99[d]	81
14	**1k**	CH_3	H	2-NO_2	**2k**	59[e]	59[b]
15	**1m**	CH_3	H	3-NO_2	**2m**	95[f]	78
16	**4m**	H	H	3-NO_2	**2m**	> 99[g]	75[b]
17	**1n**	CH_3	H	4-NO_2	**2n**	69[h]	69[b]
18	**4n**	H	H	4-NO_2	**2n**	> 99[i]	76[b]
19	**1p**	CH_3	H	3-OCH_3	**2p**	> 99[j]	42[b]
20	**4p**	H	H	3-OCH_3	**2p**	> 99[k]	66[b]
21	**1q**	CH_3	H	3-OPh	**2q**	98[k]	56[b]
22	**4q**	H	H	3-OPh	**2q**	> 99	82
23	**4r**	H	H	4-OCH_3	**2r**	> 99[k]	44[b]
24	**4s**	H	H	4-$OCOOCH_2Ph$	**2s**	> 99	94
25	**4t**	H	H	4-CH_2OCH_3	**2t**	> 99[l]	79
26	**1u**	CH_3	H	4-COOH	**2u**	98	88
27	**1v**	CH_3	H	4-$COOCH_3$	**2v**	98[m]	86
28	**1w**	CH_3	H	4-$COOC(CH_3)_3$	**2w**	97[n]	0
29	**1x**	CH_3	H	4-CH_2Cl	**2x**	> 99	91
30	**1y**	CH_3	H	4-CH_2OOCCH_3	**2y**	98	80
31	**1z**	CH_2Ph	H	H	**2a**	> 99	184[o]
32	**1aa**	$(CH_2)_5CH_3$	H	H	**2a**	97[p]	81
33	**1bb**	CH_2CH_2Ph	H	H	**2a**	99[q]	57[b]
34	**1cc**	cyclopentyl	H	H	**2a**	> 99	83
35	**1dd**	$C(CH_3)_3$	H	H	**2a**	99[r]	88
36	**1ee**	CH_3	CH_3	H	**2ee**	> 99[s]	69
37	**4ee**	H	CH_3	H	**2ee**	> 99[t]	70[b]
38	**4ff**	H	CH_2Ph	H	**2ff**	> 99[u]	40[b]
39	**4gg**	H	COPh	H	**2gg**	43[v]	0
40	**1hh**	CH_3	Ph	H	**2hh**	> 99[w]	86
41	**4hh**	H	Ph	H	**2hh**	> 99[x]	85

[a] The reactions were carried out with 3.0 mol of HNO_3 per mol of substrate for 1 h at room temperature, and reaction products were isolated after distillation or crystallization from a suitable solvent. Unless otherwise indicated, the carbonyl compound **2** was the sole reaction product. [b] Determined by ^1H NMR (see Exp. Sect.). [c] Isolated product. [d] After 24 h; 76% after 1 h. [e] After 24 h; 2% after 1 h. [f] After 24 h; 34% after 1 h. [g] After 1 h the reaction mixture contained 55% of aldehyde **2m** and 45% of the nitro ester **9**; after 24 h, 75% of **2m** and 25% of **9**. [h] After 24 h; 3% after 1 h. [i] After 1 h, the reaction mixture contained 76% of aldehyde **2n** and 24% of the nitro ester **10**; no change after 24 h. [j] The reaction mixture contained 42% of aldehyde **2p** and 58% of a mixture of three isomeric products (in the ratio 58:32:10) generated by aromatic nitration of **1p**. [k] The reaction mixture consisted of the expected aldehyde, accompanied by various ring nitration products. [l] The reaction mixture contained some 8% of terephthalaldehyde (**27**). [m] After 24 h; 40% after 1 h. [n] The sole product formed was the acid **1u**, which was isolated in 91% yield. [o] 4.0 mol of HNO_3 was employed; 1.0 mol of substrate gave 2.0 mol of benzaldehyde (**2a**). [p] The reaction mixture contained, besides the expected amount of **2a** (^1H NMR analysis): hexyl nitrite (**11**, 70%), hexanol (**12**, 6%), hexanal (**13**, 18%) and hexyl nitrate (**14**, 6%). [q] The reaction mixture contained 2-phenylethyl nitrite (**23**, 33%) and phenylacetaldehyde (**24**, 10%). [r] The reaction mixture also contained 1,1-dimethylethyl nitrate (**25**) and 1,1-dimethylethyl nitrite (**26**) in a ratio of 59:41. [s] The reaction mixture contained **2ee** (85%), accompanied by some (15%) 1-phenylethyl nitrate (**17**). [t] After 1 h, the reaction mixture contained **2ee** (33%), accompanied by 67% of 1-phenylethyl nitrate (**17**); after 24 h, the ratio was 70:30. [u] The reaction mixture contained **2ff** (40%), accompanied by 60% of 1,2-diphenylethyl nitrate (**18**). After 24 h, the ratio was unchanged, whereas some aromatic nitration set in. [v] No oxidation took place: 2-oxo-1,2-diphenylethyl nitrate (**19**) was the only product formed (7% after 1 h; 43% after 24 h). [w] After 1 h, the degree of conversion was 83% and the reaction mixture contained 27% of **2hh**, accompanied by 56% of diphenylmethyl nitrate (**22**); after 24 h, the ketone **2hh** was the sole product present. [x] The reaction mixture contained 4% of **2hh**, accompanied by 96% of diphenylmethyl nitrate (**22**); after 24 h, the ketone **2hh** was the sole product present.

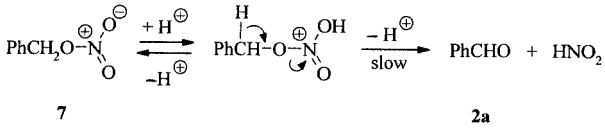
rather than metathetic exchange and/or direct oxidation[21] of **11** (vide infra). Such behaviour clearly points to the nitroso ester **11** as the likely cleavage partner in the oxidation. Nevertheless, some attack by HNO_3 might indeed occur on the alkyl side, being responsible for part of the formation of aldehyde **13**, but in this case and according to



Scheme 3



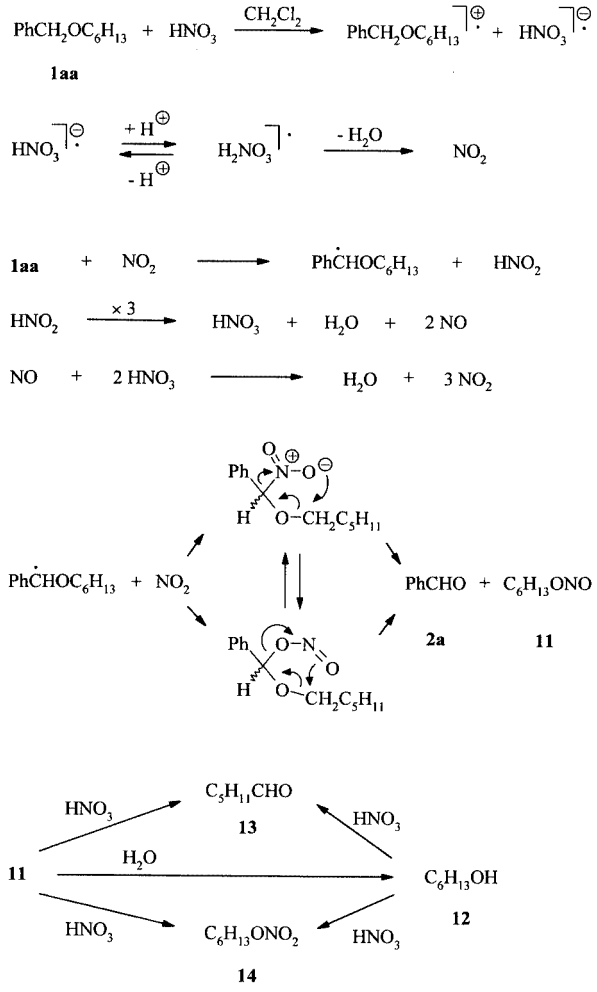
Scheme 4



Scheme 5

the above interpretation, phenylmethyl nitrite (**16**) should also be formed, and this, as we observed in an ad hoc experiment, goes on to produce **2a** quantitatively under these conditions.

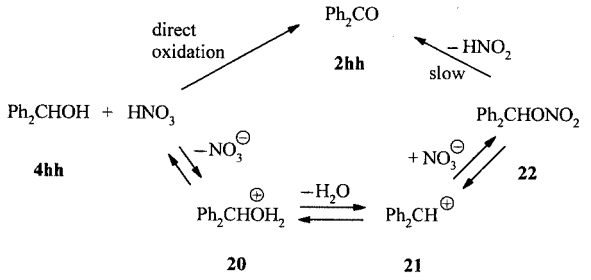
When carefully degassed HNO_3 was used, a definite induction time for the reactions was clearly observable in some experiments, made evident by subsequent sudden and rapid evolution of nitrous gas. Our working procedure ruled out the formation of significant amounts of NO_2 by the spontaneous decomposition of HNO_3[22] in CH_2Cl_2, the observed actual induction time being definitively shorter. This pattern may be viewed as an additional hint of a reaction mechanism radical in nature, although ruling out the initial operation of a single-electron-transfer reaction to form an unlikely NO_2^+ ion.[23] A possible alternative is outlined in Scheme 6, in which HNO_3 itself is proposed as the initiator of the oxidative process, in turn generating the active species NO_2 responsible for the rapid transformation of the substrates into the corresponding carbonyl compounds, in line with a number of previously reported observations.[24] Accordingly, the superior reactivity of alcohols relative to ethers in the oxidation reaction could probably be attributed to the higher basicity of the latter compounds, which are preferentially protonated in the reaction environment, making the homolytic abstraction of the α-hydrogen atom more difficult.



Scheme 6

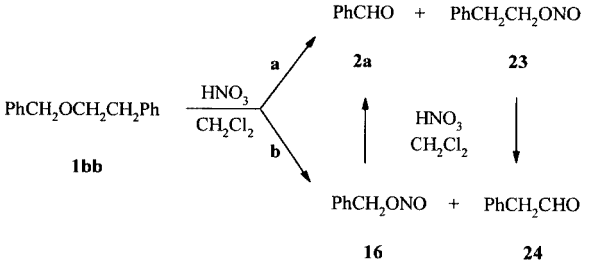
The presence of α-alkyl groups, facilitating the production of the intermediate cations, as in compounds **1ee**, **4ee**, and **4ff**, depressed the yields of carbonyl products owing to the competitive reaction affording nitric acid esters (**17** and **18**), which are stable products under the reaction conditions (Table 2).[25] In addition, when the formation of the nitrate ester **18** slowed down the oxidative process, as in the case of compound **4ff**, the deactivating effect on potential ring nitration was not equivalent, so that some occurrence of nitro derivatives was found to take place.[25] On the other hand, the presence of a carbonyl substituent (**4gg**), strong enough to prevent any ring nitration, suppressed the oxidation reaction completely and the nitrate ester **19** was the only product formed. When Ph_2CHOH (**4hh**) and the corresponding methyl ether (**1hh**) were the substrates, we observed that, although the overall conversion into Ph_2CO (**2hh**) was in both instances quantitative after 24 h, the reaction of the alcohol **4hh** was significantly faster (Scheme 7). Nevertheless, the protonated alcohol (**20**) gave rise to the rapid formation of the organic cation **21**, readily intercepted by NO_3^- to give the ester **22**, representing kinetic control

of the process; the irreversible oxidative route eventually leads to **2hh**.



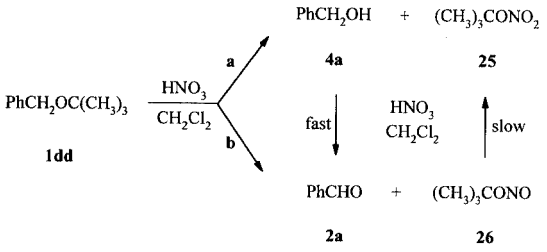
Scheme 7

The oxidation reaction was found to be highly chemoselective for the benzylic position and of higher velocity than a potential aromatic nitration, as shown by the behaviour of 2-phenylethyl phenylmethyl ether (**1bb**, Table 2) in which, in addition to ring nitration, a non-benzylic competitive reaction might be envisaged (Scheme 8). The system ran smoothly to give quantitative conversion into benzaldehyde (**2a**), accompanied by a close to stoichiometric amount of the expected 2-phenylethyl nitrite (**23**). Only minor amounts of phenylacetaldehyde (**24**) were detected, showing that the direct attack at the ether benzylic position (Scheme 8, path a) is largely prevalent, if not even exclusive. In fact, the alternative competitive reaction (Scheme 8, path b) would have yielded **24**, which, however, is also the product of decomposition of the nitrite **23** under acidic conditions. In any case, the absence of the implicit partner in path b, phenylmethyl nitrite (**16**), in the reaction mixture is due to its known prompt further reaction to afford **2a**.



Sdheme 8

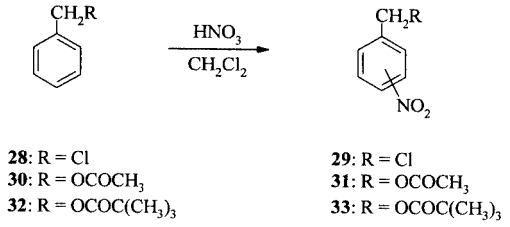
Comparison of the reactivities observed for the methyl (**1v**) and 1,1-dimethylethyl (**1w**) esters of 4-(methoxymethyl)-benzoic acid (**1u**) with the HNO_3/CH_2Cl_2 system under strictly comparable conditions is worth noting (Table 2). The former compound reacted more slowly, exclusively providing the expected aldehyde **2v**, whereas the acid-sensitive **1w** exclusively underwent nitrolysis[3a] to give 1,1-dimethylethyl nitrate (**25**) and the acid **1u**, thus indicating that the nitrolytic process was easier than the oxidative one. We therefore studied the reaction between 1,1-dimethylethyl phenylmethyl ether (**1dd**) and HNO_3 in order to evaluate the relative impact of the nitrolysis vs. direct benzylic oxidation (Scheme 9). The experiment was performed with the equivalents of HNO_3 usually employed in the oxidation of benzylic ethers, and resulted in quantitative conversion of **1dd** with production of **2a**, accompanied by the formation of 1,1-dimethylethyl nitrate (**25**) and 1,1-dimethylethyl nitrite (**26**) in a ratio of 59:41. The nitrolytic reaction therefore appears to be an intrinsically easier and fast process. In fact, although the aromatic product of the nitrolysis [phenylmethanol (**4a**)], which was not intercepted, would be bound to be rapidly oxidized to the corresponding aldehyde **2a**, the **25/26** ratio can be taken as a good representation of the outcome of the whole reaction, since we have shown that under the conditions employed, both the metathetic transformation and the oxidation of **26** to **25** are definitively much slower reactions.



Scheme 9

The simultaneous presence of both alcoholic and ether benzylic functions in the substrate, as in [4-(methoxymethyl)-phenyl]methanol (**4t**), allowed the chemoselectivity of the oxidation reaction to be better appreciated. Compound **4t** was attacked almost exclusively at the alcoholic site, with the formation of only a very minor amount of terephthalaldehyde (**27**), affording 4-(methoxymethyl)benzaldehyde (**2t**) in very good yield (Table 2). It was also of interest to observe the behaviour of other functions attached to a benzylic carbon atom when exposed to the oxidative conditions, with a view to obtaining simple polyfunctional chemicals by easy and inexpensive routes. It is known that HNO_3, at various concentrations and temperatures, rapidly converts phenylmethyl halides[26] and esters[27] into the corresponding carbonyl compounds in high yields, it being suggested that the intermediate in the oxidation process is the hydrolysis product, the corresponding phenylmethanol. When the substrate was phenylmethyl chloride (**28**, Scheme 10), our system was totally ineffective in performing this reaction, giving exclusive electrophilic ring substitution to afford the three nitro isomers **29**. When, though, 4-(methoxymethyl)benzyl chloride (**1x**) was subjected to identical conditions, it afforded 4-(chloromethyl)-benzaldehyde (**2x**) as the sole reaction product, in quantitative yield (Scheme 11). Carboxylic esters proved to be equally resistant towards nitric oxidation in CH_2Cl_2. In fact, benzyl acetate (**30**) was found to undergo only ring nitration, affording the isomeric mixture **31** (Scheme 10), as did the bulkier phenylmethyl 2,2-dimethylpropanoate (**32**), which underwent exclusive nitration to give **33** in a similar fashion, though in a slower reaction. Consistently, the bifunctional compound 4-(methoxymethyl)benzyl acetate (**1y**) underwent selective oxidation to 4-(acetoxymethyl)benzal-

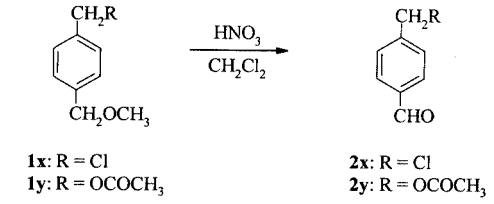
dehyde (**2y**) in quantitative yield under the usual conditions (Scheme 11).



28: R = Cl
30: R = $OCOCH_3$
32: R = $OCOC(CH_3)_3$

29: R = Cl
31: R = $OCOCH_3$
33: R = $OCOC(CH_3)_3$

Scheme 10



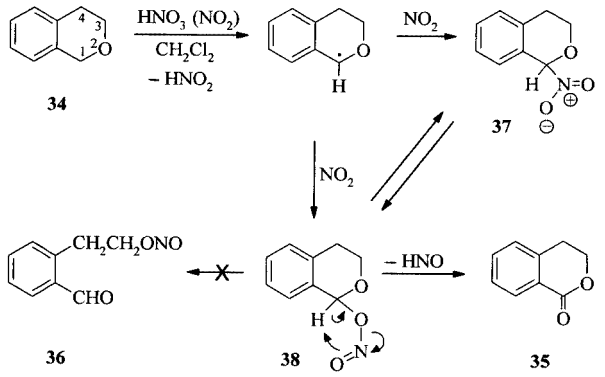
1x: R = Cl
1y: R = $OCOCH_3$

2x: R = Cl
2y: R = $OCOCH_3$

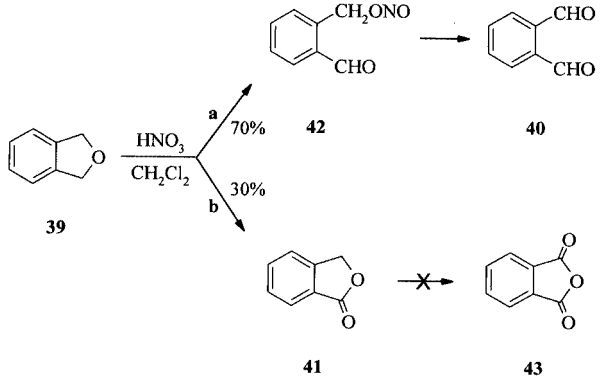
Scheme 11

3,4-Dihydro-1*H*-isochromene (**34**) is a benzylic substrate in which the ether function is part of a ring condensed to benzene. Our conditions resulted in exclusive α-oxidation to give the corresponding lactone **35**, any other product − particularly 2-(2-formylphenyl)ethyl nitrite (**36**) − being totally absent. This result contrasts with the behaviour of benzyl 2-phenylethyl ether (**1bb**), which, as discussed above, afforded benzaldehyde (**2a**) and 2-phenylethyl nitrite (**23**). Mechanistically, the divergent outcome of the two reactions may be explained as follows (Scheme 12). Formed NO_2, after abstracting a benzylic hydrogen atom from the ether substrate, reacts further to afford a covalent bond with either N and C (**37**) or O and C (**38**) to give species in equilibrium, an internal reaction by **38** eventually producing the lactone **35**. Such behaviour might find an explanation in a stereochemical consideration: the distance between C-3 and the NO oxygen atom in both the bicyclic intermediates **37** and **38** is too long to allow the reaction observed for **1bb**. This inference is supported by the reaction of 1,3-dihydro-2-benzofuran (**39**), which under identical conditions underwent the comparable transformations to the dialdehyde **40** and the lactone **41** (Scheme 13), the stereochemical problem inhibiting route a being at least partially removed. The intermediate nitroso ester **42**, which would be expected to undergo rapid and quantitative oxidation to give phthalaldehyde (**40**) by path a, was not detected in the reaction mixture; moreover, no further oxidation of lactone **41** to phthalic anhydride (**43**) occurred at all, pointing to the protecting effect on the benzylic position exerted by the ester function.

An attempt was made to extend the application of the oxidation procedure to allylic and to non-benzylic, fully aliphatic substrates, but the obtained results proved quite unsatisfactory. With non-benzylic substrates, the oxidation reaction employing HNO_3 in CH_2Cl_2, though very rapid even after the excess of acid is reduced (2.0 mol of HNO_3 per



Scheme 12



Scheme 13

mol of substrate), appears difficult to control and marred by considerable amounts of side products, in part a consequence of the presence of enolizable α-hydrogen atoms.[28] Indeed, when the reaction was performed on 2,2-dimethylpropanol (**44**), the corresponding aldehyde **45** was formed in 66% yield, accompanied by minor amounts of 2,2-dimethylpropyl nitrite (**46**, 9%), 2,2-dimethylpropyl nitrate (**47**, 10%) and 2,2-dimethylpropanoic acid (**48**, 15%).[29] This behaviour highlights the important role played by conjugation with the benzene ring in stabilizing the aldehyde towards further oxidation to the corresponding carboxylic acid.[5] Such a stabilizing effect had previously been attributed to the formation of a stable adduct between HNO_3 and the carbonyl compound,[30] though this was never observed in our reaction mixtures. The presence of an electron-withdrawing α-Cl atom in the substrate, as in 2-chloro-2-methylpropanol (**49**), still allowed the formation of the corresponding aldehyde (**50**, 9%) but slowed down the whole process (79% conv. after 1 h, > 99% after 24 h), thus favouring the competitive and predominant formation of large amounts of nitroso (**51**, 30%) and nitro (**52**, 40%) esters of **49**, together with some 2-chloro-2-methylpropanoic acid (**53**, 21%). The presence of additional α-positioned Cl substituents, as in 2,2-dichloropropanol (**54**) and 2,2,2-trichloroethanol (**55**), completely inhibited the oxidation, causing the exclusive formation of the corresponding nitro

esters **56** and **57** in a slow reaction (82 and 72% conv. after 24 h at room temperature, respectively).

In conclusion, the oxidation of benzylic alcohols and ethers to the corresponding carbonyl compounds may be easily achieved by the use of HNO_3 in CH_2Cl_2, avoiding further oxidation, aromatic nitration and formation of unwanted side products, with some limitations. The reaction, most probably proceeding by a radical mechanism, failed in the case of allylic substrates and gave coherent but poor results with non-benzylic ones. The proposed method is simple, environmentally friendly and economically convenient, offering interesting chemoselectivity in many instances and thus representing a valuable alternative to the existing approaches, on both the laboratory and the industrial scale. In addition, owing to its operation in organic solvent, with alcoholic substrates particularly resistant to oxidation it may represent a convenient, straightforward and simple alternative route to the corresponding nitro esters.

Experimental Section

General Remarks: Unless otherwise specified, reagents and solvents were commercially available (Aldrich Italia, Milano, Italy) and used as received. Commercial 100% HNO_3 (d = 1.51)[24] was purchased from Hydro Chemicals France (Nanterre, France) and kept at 4 °C in the dark to avoid decomposition; the acid was freshly distilled and its titre, averaging ca. 24 M, alkalimetrically checked prior to use. TLC analyses and column chromatography were performed on silica gel 60 from Merck (Darmstadt, Germany). The courses of all the described reactions were monitored by TLC when suitable, and by a parallel accurate ^{1}H NMR quantitative evaluation. Analyses were performed after simple dilution of the reaction mixture (0.2 mL) with $CDCl_3$ (0.3 mL); in addition, 0.2 mL of the same mixture was admixed with $CDCl_3$ (0.5 mL), washed with 10% aqueous Na_2SO_4, dried with anhydrous Na_2SO_4, filtered, suitably concentrated, and subjected to ^{1}H NMR analysis. Melting points were determined in open-ended capillary tubes with a Mettler FP 61 automatic apparatus and are uncorrected. Elemental analyses were obtained by use of a Carlo Erba CHN/OS 1106 analyser and found to be satisfactory. IR spectra were recorded with a Nicolet FTIR Magna 550 spectrophotometer by the KBr technique. Unless otherwise indicated, ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ with a Bruker AC 200 spectrometer at 200 and 50 MHz, respectively (s: singlet, d: doublet, t: triplet, q: quadruplet, m: multiplet, br: broad, sym: symmetrical). The proton chemical shifts are reported in ppm on the δ scale relative to TMS as an internal reference (δ = 0.00 ppm); the carbon chemical shifts are reported in ppm relative to the centre line of the $CDCl_3$ triplet (δ = 77.00 ppm) or, when $[D_6]Me_2SO$ was the solvent, the centre line of the corresponding septuplet (δ = 39.50 ppm). The coupling constants are given in Hz. MS measurements were carried out with a Fisons TRIO-2000 apparatus, working in the positive-ion electron impact mode (70 eV), by direct introduction of the sample into the ion source and heating from 50 up to 300 °C. The five most intense peaks and the molecular peak for each individual compound are reported, with intensity values in parentheses.

Synthesis of Intermediates and Substrates: Phenylmethyl 2,2-dimethylpropanoate (**32**) was prepared by a reported method.[31] 2-Chloro-2-methylpropanol (**49**)[32] and 2,2-dichloropropanol (**53**)[33] were prepared by $NaBH_4$ reduction of the corresponding aldehydes (**50** and **58**)[34] in 82% (6.65 g) and 61% (7.85 g) yields, respectively, by a described procedure.[35] 1,2-Diphenylethanol (**4ff**, 5.23 g, 88%)[36] was obtained from deoxybenzoin (**2ff**) in a similar way.[37] 1-(Iodomethyl)-2-nitrobenzene (**59**),[38] 1-(iodomethyl)-3-nitrobenzene (**60**),[39] and 1-(iodomethyl)-4-nitrobenzene (**61**)[40] were prepared in 88% (5.79 g), 77% (5.06 g), and 78% (5.13 g) isolated yields, respectively, by simply mixing of solutions of the corresponding chlorides in acetone (18.0 mmol in 4.0 mL) and NaI in the same solvent (18.0 mmol in 15.0 mL), by a described procedure.[41] The following alkyl and arylalkyl nitrites were prepared by a known general method:[20] hexyl nitrite (**11**, 3.93 g, 60%),[42] phenylmethyl nitrite (**16**, 4.93 g, 72%).[43]

2,2-Dimethylpropyl Nitrite (46): Yield: 3.50 g (48%); pale yellow liquid, b.p. 32 °C/17332 Pa. ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C): δ = 0.96 (s, 9 H, CH_3), 4.47 (s, 2 H, CH_2) ppm. ^{13}C NMR (50 MHz, $CDCl_3$, 25 °C): δ = 26.46 (CH_3), 31.91(CMe_3), 78.18 (CH_2). IR (film): $\tilde{\nu}_{max}$ = 2963 s, 1653 s, 1609 w, 1370 s, 1018 w, 978 m, 922 m, 796 s, 749 w, 643 m cm^{-1}. MS (EI): *m*/*z* (%) = 71 (66), 57 (100), 41 (97), 39 (50), 30 (63). $C_5H_{11}NO_2$ (117.15): calcd. C 51.26, H 9.47, N 11.96; found C 51.18, H 9.49, N 11.95.

2-Chloro-2-methylpropyl Nitrite (51): Because of the poor stability of the alcohol **49**[32a] the nitroso ester **51** was not prepared, but its presence in the oxidation reaction mixture was inferred by the observation in the ^{1}H NMR spectrum of a signal [δ = 4.90 ppm (s)] attributable to $-CH_2ONO$.

2-Phenylethyl Nitrite (23): Yield: 2.95 g (65%); pale yellow liquid, b.p. 73 °C/1600 Pa. ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C): δ = 2.99 (t, J = 7.1 Hz, 2 H, $PhCH_2$), 4.87 (t, J = 7.1 Hz, 2 H, $ONOCH_2$), 7.13−7.36 (m, 5 H, Ar-H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$, 25 °C): δ = 35.53 ($PhCH_2$), 68.71 ($ONOCH_2$), 126.70, 128.56, 128.90, 137.19 ppm. IR (film): $\tilde{\nu}_{max}$ = 3439 w, 3026 w, 2943 w, 1650 m, 1610 w, 1385 s, 1217 m, 1039 w, 759 s, 700 w cm^{-1}. MS (EI): *m*/*z* (%) = 151 (< 1) [M$^+$], 122 (9), 105 (7), 92 (25), 91 (100), 65 (5). $C_8H_9NO_2$ (151.17): calcd. C 63.57, H 6.00, N 9.27; found C 63.45, H 6.02, N 9.25.

1,1-Dimethylethyl nitrate (**47**) has been reported in a previous paper.[44] Alkyl and arylalkyl nitrates were prepared by known general methods.[45] Hexyl nitrate (**14**, 2.44 g, 83%),[46] phenylmethyl nitrate (**7**, 2.33 g, 76%),[47] (2-nitrophenyl)methyl nitrate (**8**, 3.13 g, 79%),[48] (4-nitrophenyl)methyl nitrate (**10**, 3.13 g, 79%),[48] and diphenylmethyl nitrate (**22**, 3.85 g, 84%),[47] were prepared by treatment of CH_3CN solutions of the appropriate halides (chloride in the case of **22**, bromide for **7**, iodide for **14**, **8**, **9**, and **10**; 20.0 mmol in 5.0 mL) with a solution of $AgNO_3$ in the same solvent (25.0 mmol in 5.0 mL), by a known procedure (Method A).[49]

(3-Nitrophenyl)methyl Nitrate (9): Yield: 2.97 g (75%, Method A); yellowish solid, m.p. 44 °C. ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C): δ = 5.56 (s, 2 H, CH_2), 7.57−7.71 (m, 1 H, Ar-H), 7.73−7.85 (m, 1 H, Ar-H), 8.21−8.33 (m, 2 H, Ar-H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$, 25 °C): δ = 72.83 (CH_2), 123.53, 124.13, 129.96, 134.41, 134.57, 148.28 ppm. IR (KBr): $\tilde{\nu}_{max}$ = 3090 w, 2893 w, 1695 s, 1535 s, 1087 s, 987 s, 892 m, 749 w, 714 m, 670 w cm^{-1}. MS (EI): *m*/*z* (%) = 198 (7) [M$^+$], 151 (100), 150 (78), 136 (65), 94 (68), 77 (55). $C_7H_6N_2O_5$ (198.13): calcd. C 42.43, H 3.05, N 14.14; found C 42.36, H 3.05, N 14.11.

2,2-Dimethylpropyl nitrate (**25**, 9.71 g, 73%),[50] 2-chloro-2-methylpropyl nitrate (**52**, 6.42 g, 38%),[51] 1-phenylethyl nitrate (**17**, 11.36 g, 68%),[52] 1,2-diphenylethyl nitrate (**18**, 10.2 g, 42%),[37] and 2-(nitrooxy)-1,2-diphenylethanone (**19**, 16.45 g, 64%)[53] were prepared by treatment of CH_2Cl_2 solutions of the corresponding alco-

hols (100.0 mmol in 5.0 mL) with a mixture of HNO_3 (200.0 mmol) and H_2SO_4 (100.0 mmol), by a reported procedure (Method B).[54]

2,2-Dichloropropyl Nitrate (56): Yield: 11.00 g (63%, Method B); colourless liquid, b.p. 63 °C/3333 Pa. ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C): δ = 2.17 (s, 3 H, CH_3), 4.86 (s, 2 H, CH_2) ppm. ^{13}C NMR (50 MHz, $CDCl_3$, 25 °C): δ = 33.75 (CH_3), 78.13 (CH_2), 82.98 (CCl_2) ppm. IR (film): $\tilde{\nu}_{max}$ = 2925 m, 1800 m, 1743 w, 1646 s, 1376 s, 1284 m, 1126 w, 856 s, 744 s, 581 w cm^{-1}. MS (EI): *m*/*z* (%) = 101 (12), 99 (65), 97 (100), 63 (15), 61 (41). $C_3H_5Cl_2NO_3$ (173.98): calcd. C 20.71, H 2.90, Cl 40.76, N 8.05; found C 20.67, H 2.91, Cl 40.87, N 8.03.

2,2,2-Trichloroethyl Nitrate (57): Yield: 13.77 g (71%, Method B); colourless liquid, b.p. 80 °C/6666 Pa. ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C): δ = 5.15 (s, 2 H, CH_2) ppm. ^{13}C NMR (50 MHz, $CDCl_3$, 25 °C): δ = 79.31 (CH_2), 93.10 (CCl_3) ppm. IR (film): $\tilde{\nu}_{max}$ = 3437 w, 2934 w, 1668 s, 1385 s, 1282 m, 1218 w, 1060 w, 828 m, 759 s, 613 w cm^{-1}. MS (EI): *m*/*z* (%) = 121 (30), 119 (100), 117 (97), 76 (42), 46 (26). $C_2H_2Cl_3NO_3$ (194.40): calcd. C 12.36, H 1.04, Cl 54.71, N 7.21; found C 12.32, H 1.04, Cl 54.78, N 7.20.

Benzyl methyl ethers were almost exclusively prepared by the classical Williamson synthesis, by treatment of an MeOH solution of the appropriate halide (100.0 mmol in 100 mL) with MeONa in MeOH (200 mmol in 100 mL), by a described procedure (Method A).[55] 1-(Methoxymethyl)-3-methylbenzene (**1c**, 11.02 g, 81% from the chloride),[56] 1-(1,1-dimethylethyl)-4-(methoxymethyl)benzene (**1e**, 14.60 g, 82% from the bromide),[57] 1-chloro-2-(methoxymethyl)benzene (**1f**, 11.70 g, 75% from the chloride),[58] 1-chloro-3-(methoxymethyl)benzene (**1g**, 12.48 g, 80% from the chloride),[58] 1-chloro-4-(methoxymethyl)benzene (**1h**, 12.17 g, 78% from the chloride),[59] 1,3-dichloro-4-(methoxymethyl)benzene (**1j**, 17.57 g, 92% from the chloride),[60] 1-(methoxymethyl)-2-nitrobenzene (**1k**, 12.53 g, 75% from the iodide),[61] 1-(methoxymethyl)-3-nitrobenzene (**1m**, 13.03 g, 78% from the iodide),[62] 1-(methoxymethyl)-4-nitrobenzene (**1n**, 12.69 g, 76% from the iodide),[62] and diphenylmethyl methyl ether (**1hh**, 17.62 g, 89% from the chloride)[63] were prepared by Method A. [(1,1-Dimethylethoxy)methyl]benzene[64] (**1dd**, 7.22 g, 44%) was prepared in a similar way, from benzyl bromide and potassium *tert*-butoxide. The remaining ethers were prepared by alkylation of the corresponding alcohols by a known procedure,[65] with minor modifications (Method B, see below).

General Procedure for the Synthesis of Some Ethers (Method B): A solution of the selected alcohol in diglyme (100.0 mmol in 15.0 mL) was added dropwise, over 15 min and underan inert gas, to a previously heated (55 °C) stirred suspension of NaH (125.0 mmol, 60% dispersion in mineral oil) in diglyme (70 mL). After the addition was complete, the obtained mixture was stirred for an additional 30 min at 55 °C. Subsequently, the temperature was raised to 90 °C and a solution of the appropriate amount (135.0 mmol) of the alkylating agent in diglyme (15.0 mL) was introduced dropwise. Stirring was continued at 90 °C for 2 h, and the reaction mixture was then allowed to cool to room temperature, poured into H_2O (250 mL) and extracted with Et_2O (3 × 100 mL). The combined organic phases were dried with anhydrous Na_2SO_4 and filtered, and the solvent was evaporated off. The obtained residue was fractionally distilled and the desired product was purified as convenient. The following ethers were prepared by Method B: 1-(methoxymethyl)-4-methylbenzene (**1d**, 10.88 g, 80% from the corresponding alcohol and Me_2SO_4),[59] 1-methoxy-3-(methoxymethyl)benzene (**1p**, 12.77 g, 84% from the corresponding alcohol and Me_2SO_4),[66] (hexyloxymethyl)benzene (**1aa**, 10.56 g, 55% from hexanol and phenylmethyl bromide),[67] [(cyclopentyloxy)methyl]benzene (**1cc**, 15.14 g, 86% from cyclopentanol and phenylmethyl bromide),[68] and (1-methoxyethyl)benzene (**1ee**, 12.92 g, 95% from 1-phenylethanol and Me_2SO_4).[69]

1-(Methoxymethyl)-3-phenoxybenzene (1q): Yield: 19.69 g (92%, Method B, from the corresponding alcohol and Me_2SO_4); colourless liquid, b.p. 104 °C/8 Pa. ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C): δ = 3.36 (s, 3 H, OCH_3), 4.41 (s, 2 H, $ArCH_2$), 6.87−7.13 (m, 6 H, Ar-H), 7.23−7.38 (m, 3 H, Ar-H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$, 25 °C): δ = 58.09 (OCH_3), 74.15 (OCH_2), 117.86, 117.92, 118.84, 122.29, 123.17, 129.62, 129.66, 140.25, 157.07, 157.32 ppm. IR (film): $\tilde{\nu}_{max}$ = 3441 w, 2928 w, 2359 m, 1587 w, 1383 s, 1254 w, 1216 m, 1101 w, 760 s, 682 w cm^{-1}. MS (EI): *m*/*z* (%) = 214 (100) [M^+], 213 (15), 184 (51), 183 (38), 181 (24). $C_{14}H_{14}O_2$ (214.26): calcd. C 78.48, H 6.59; found C 78.31, H 6.62.

[(2-Phenylethoxy)methyl]benzene (1bb): Yield: 18.23 g (86%, Method B, from 2-phenylethanol and phenylmethyl bromide); colourless liquid, b.p. 96 °C/13 Pa. ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C): δ = 2.91 (t, *J* = 7.2 Hz, 2 H, $PhCH_2$), 3.66 (t, *J* = 7.2 Hz, 2 H, OCH_2), 4.49 (s, 2 H, $PhCH_2O$), 7.16−7.32 (m, 10 H, Ar-H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$, 25 °C): δ = 36.27 ($PhCH_2$), 71.12 (OCH_2), 72.81 ($PhCH_2O$), 126.06, 127.39, 127.45, 128.21 (two overlapped signals), 128.81, 138.32, 138.86 ppm. IR (film): $\tilde{\nu}_{max}$ = 3440 w, 3024 w, 2861 w, 2399 w, 2359 w, 1483 w, 1382 s, 1215 m, 1104 m, 760 s cm^{-1}. MS (EI): *m*/*z* (%) = 212 (51) [M^+], 182 (14), 106 (12), 92 (16), 91 (100). $C_{15}H_{16}O$ (212.29): calcd. C 84.87, H 7.60; found C 84.65, H 7.61.

4-(Hydroxymethyl)phenyl Phenylmethyl Carbonate (4s): Benzyl chloroformate (6.0 mL, 40.0 mmol) was added dropwise, at 0 °C and with vigorous stirring, to a solution of (4-hydroxyphenyl)methanol (4.96 g, 40.0 mmol) in NaOH (4 M, 10.0 mL, 40.0 mmol), while the pH was kept between 9 and 11 by careful addition of NaOH (4 M). After the addition was complete, the reaction mixture was allowed to reach room temperature, kept overnight whilst stirring, diluted with H_2O (100 mL) and extracted with Et_2O (3 × 50 mL), and the combined organic phases were washed with 10% aqueous Na_2SO_4 (2 × 50 mL), filtered, and concentrated to dryness. The obtained oily residue was purified by column chromatography (SiO_2), affording compound **4s**. Yield: 4.33 g (42%); pale yellow solid, m.p. 56 °C. ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C): δ = 2.35 (t, *J* = 4.5 Hz, 1 H, OH), 4.57 (d, *J* = 4.5 Hz, 2 H, $ArCH_2O$), 5.24 (s, 2 H, $PhCH_2O$), 7.08−7.16 (m, 2 H, Ar-H), 7.26−7.46 (m, 7 H, Ar-H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$, 25 °C): δ = 64.31 ($HOCH_2$), 70.28 (OCH_2), 120.95, 127.92, 128.43, 128.60, 128.68, 134.63, 138.75, 150.29, 153.62 (OCOO) ppm. IR (KBr): $\tilde{\nu}_{max}$ = 3310 s (br), 2926 w, 1753 s, 1382 m, 1272 s, 1242 s, 1214 m, 913 w, 698 m, 526 w cm^{-1}. MS (EI): *m*/*z* (%) = 258 (< 1) [M^+], 214 (4), 92 (9), 91 (100), 77 (4), 65 (8). $C_{15}H_{14}O_4$ (258.27): calcd. C 69.76, H 5.46; found C 69.68, H 5.47.

4-(Methoxymethyl)benzoic acid (**1u**)[70] was prepared by a reported method.[71] The corresponding methyl ester (**1v**) was obtained by careful treatment (−30 °C) of MeOH (100 mL) with $SOCl_2$ (40.0 g, 336.0 mmol), followed by addition at room temperature of acid **1u** (8.3 g, 50.0 mmol), stirring for 4 h at room temperature, solvent evaporation and distillation of the residue.

Methyl 4-(Methoxymethyl)benzoate (1v): Yield: 7.83 g (87%); colourless oil, b.p. 109 °C/133 Pa. ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C): δ = 3.40 (s, 3 H, OCH_3), 3.90 (s, 3 H, $COOCH_3$), 4.49 (s, 2 H, OCH_2), 7.35−7.43 (m, 2 H, Ar-H), 7.97−8.06 (m, 2 H, Ar-H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$, 25 °C): δ = 51.86 (ester CH_3), 58.21 (OCH_3), 73.84 (OCH_2), 127.00, 129.20, 129.53, 143.41,

166.73 (C=O) ppm. IR (film): $\tilde{\nu}_{max}$ = 2952 m, 1723 s, 1610 w, 1434 m, 1416 w, 1382 s, 1278 s, 1108 s, 966 w, 757 m cm^{-1}. MS (EI): *m*/*z* (%) = 180 (19) [M^+], 165 (91), 149 (88), 133 (75), 121 (100), 89 (44). $C_{10}H_{12}O_3$ (180.20): calcd. C 66.65, H 6.71; found C 66.60, H 6.71.

The 1,1-dimethylethyl ester **1w** was obtained by treatment of a solution of the corresponding acid **1u** in CH_2Cl_2 (1.66 g, 10.0 mmol in 25 mL) with an excess of liquid 2-methylpropene (ca. 20 mL), followed by addition of a catalytic amount of H_2SO_4 (0.3 mL) and stirring of the mixture at room temperature for 24 h. After evaporation of the solvent, dissolution of the residue in Et_2O (50 mL), washing with 5% aqueous $NaHCO_3$ (20.0 mL), drying with Na_2SO_4, filtration and concentration to dryness, the oily residue was chromatographed on SiO_2 to afford pure **1w**.

1,1-Dimethylethyl 4-(Methoxymethyl)benzoate (1w): Yield: 1.58 g (71%); colourless oil, b.p. 65 °C/106 Pa (extensive decomposition). ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C): δ = 1.59 [s, 9 H, $C(CH_3)_3$], 3.39 (s, 3 H, OCH_3), 4.50 (s, 2 H, OCH_2), 7.33−7.41 (m, 2 H, Ar-H), 7.93−8.01 (m, 2 H, Ar-H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$, 25 °C): δ = 28.10 (ester CH_3), 58.17 (OCH_3), 73.97 (OCH_2), 80.81 (CMe_3), 126.95, 129.43, 131.17, 142.85, 165.51 (C=O) ppm. IR (film): $\tilde{\nu}_{max}$ = 2979 s, 1711 s, 1616 w, 1460 w, 1293 s, 1165 m, 1112 s, 1020 w, 851 m, 760 m cm^{-1}. MS (EI): *m*/*z* (%) = 222 (2) [M^+], 167 (100), 149 (88), 133 (39), 121 (38), 57 (32). $C_{13}H_{18}O_3$ (222.28): calcd. C 70.25, H 8.16; found C 70.41, H 8.18.

[4-(Methoxymethyl)phenyl]methanol[72] (**4t**, 5.72 g, 94%) was prepared by reduction of methyl ester **1v** (40.0 mmol) with $LiAlH_4$ (40 mmol) in Et_2O (80.0 mL). 1-(Chloromethyl)-4-(methoxymethyl)-benzene[73] (**1x**, 1.51 g, 89%) was prepared by treatment of the alcohol **4t** (10.0 mmol) with $SOCl_2$ (11 mmol) in CH_2Cl_2 (10.0 mL). 4-(Methoxymethyl)benzyl acetate[72] (**1y**, 1.63 g, 84%) was obtained by direct acetylation of alcohol **4t** (10.0 mmol) with excess Ac_2O (106 mmol).

General Procedure for the Oxidation of Benzylic Alcohols and Ethers to the Corresponding Carbonyl Compounds: A solution of HNO_3 (*d* = 1.51, 4.73 g, 75.0 mmol) in CH_2Cl_2 (5.0 mL) was added dropwise, at 0 °C and with stirring, to a solution of the selected substrate (25.0 mmol) in CH_2Cl_2 (5.0 mL). After the addition was complete, the homogeneous reaction mixture was allowed to reach room temperature and stirring was continued for 1 h or, when necessary, prolonged to 24 h. Evolution of brown fumes of nitrogen oxides was observed in association with the beginning of the oxidation reaction, after variable induction times: in some cases efficient chilling of the mixture was required to control the reaction. In order to monitor the composition of reaction mixtures, aliquots (0.2 mL) were withdrawn at suitable times, diluted with $CDCl_3$ (0.3 mL) and subjected to ^{1}H and ^{13}C NMR analysis. The analyses were also repeated after the sample solution had been washed with aqueous Na_2SO_4 (10%, 0.5 mL) and dried with Na_2SO_4, the solvent had been carefully evaporated, and the residue had been taken up in $CDCl_3$. After the completion of the oxidation, the reaction mixture was diluted with CH_2Cl_2 (50.0 mL), washed with 10% aqueous Na_2SO_4 (2 × 30.0 mL), dried with Na_2SO_4, filtered, and concentrated to dryness. When suitable, the obtained reaction products were conveniently isolated by standard techniques (Table 2): 4-(methoxymethyl)benzaldehyde (**2t**, 2.96 g, 79%),[74] methyl 4-formylbenzoate (**2v**, 3.53 g, 86%),[75] 4-(chloromethyl)benzaldehyde (**2x**, 3.50 g, 91%),[76] and 4-[(acetyloxy)methyl)]benzaldehyde (**2y**, 3.56 g, 80%).[77]

4-Formylphenyl Phenylmethyl Carbonate (2s): Yield: 6.02 g (94%); yellow solid, m.p. 54 °C. ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C): δ = 5.28 (s, 2 H, $PhCH_2O$), 7.31−7.48 (m, 7 H, Ar-H), 7.86−7.94 (m, 2 H, Ar-H), 9.97 (s, 1 H, CHO) ppm. ^{13}C NMR (50 MHz, $CDCl_3$, 25 °C): δ = 70.67 ($PhCH_2O$), 121.62, 128.53, 128.69, 128.87, 131.17, 134.04, 134.34, 152.69, 155.42 (OCOO), 190.68 (CHO) ppm. IR (KBr): $\tilde{\nu}_{max}$ = 3066 w, 2855 w, 1754 s, 1700 m, 1272 s, 1218 s, 962 w, 860 m, 739 m, 700 w cm^{-1}. MS (EI): *m*/*z* (%) = 256 (< 1) [M^+], 92 (10), 91 (100), 89 (2), 77 (3), 65 (6). $C_{15}H_{14}O_4$ (256.26): calcd. C 70.31, H 4.72; found C 70.11, H 4.74.

Reaction between 3,4-Dihydro-1*H*-isochromene (34) and HNO_3 in CH_2Cl_2: A solution of 3,4-dihydro-1*H*-isochromene (**34**, 3.35 g, 25.0 mmol) in CH_2Cl_2 (5.0 mL) was treated as described in the general oxidation procedure (> 99% conv. after 1 h), affording 3,4-dihydro-1*H*-isochromen-1-one (**35**)[78] in 81% (3.00 g) isolated yield.

Reaction between 1,3-Dihydro-2-benzofuran (39) and HNO_3 in CH_2Cl_2: A solution of 1,3-dihydro-2-benzofuran (**39**, 3.00 g, 25.0 mmol) in CH_2Cl_2 (5.0 mL) was treated as described in the general oxidation procedure. After 1 h at room temperature, a quantitative conversion was observed and the reaction mixture was found to contain (^{1}H NMR analysis) phthalaldehyde (**40**, 61%) and 2-benzofuran-1(3*H*)-one (**41**, 39%).

Competitive Oxidation of Phenylmethanol (4a) and (Methoxymethyl)benzene (1a): A solution of HNO_3 (*d* = 1.51, 4.73 g, 75.0 mmol) in CH_2Cl_2 (5.0 mL) was added dropwise, at 0 °C and with stirring, to a solution of phenylmethanol (**4a**, 2.70 g, 25.0 mmol) and (methoxymethyl)benzene (**1a**, 3.05 g, 25.0 mmol) in CH_2Cl_2 (5.0 mL). After the addition was complete, the homogeneous reaction mixture was allowed to reach room temperature and stirring was continued for 1 h. After this time, the reaction mixture (0.2 mL) was diluted with $CDCl_3$ (0.3 mL), washed with 10% aqueous Na_2SO_4 (0.5 mL), dried with Na_2SO_4, and concentrated to dryness, and the residue was dissolved in $CDCl_3$ and subjected to ^{1}H and ^{13}C NMR analysis. Complete conversion of the alcohol **4a** into the corresponding aldehyde **2a** was observed, whereas the ether **1a** was found essentially unchanged in the reaction mixture.

Reaction between Phenylmethyl Nitrate (7) and HNO_3 in CH_2Cl_2: A solution of HNO_3 (*d* = 1.51, 4.73 g, 75.0 mmol) in CH_2Cl_2 (5.0 mL) was added dropwise, at 0 °C and with stirring, to a solution of phenylmethyl nitrate (**7**, 3.83 g, 25.0 mmol) in CH_2Cl_2 (5.0 mL) and the resulted homogeneous reaction mixture was stirred at room temperature and analysed by NMR in the usual way. After 1 h, the observed degree of conversion was 64% and the reaction mixture consisted of an isomeric mixture of (nitrophenyl)methyl nitrates (**8**, **9**, and **10**, 59%), accompanied by traces (5%) of benzaldehyde (**2a**). The experiment was repeated with an equivalent amount of TFA in place of HNO_3; no reaction was evident after 1 h at room temperature; after 24 h, only 15% conversion into **2a** was observed.

Reaction between (4-Nitrophenyl)methyl Nitrate (10) and HNO_3 in CH_2Cl_2: The title compound was recovered unchanged after 24 h of treatment with HNO_3 under the usual conditions.

Reaction between Phenylmethyl Nitrite (16) and HNO_3 in CH_2Cl_2: The title compound was quantitatively converted into aldehyde **2a** (NMR analysis) after 1 h of treatment with HNO_3 under the usual conditions.

Reaction between 1,1-Dimethylethyl Nitrite (26) and HNO_3 in CH_2Cl_2: Compound **26** (0.515 g, 5.0 mmol), when exposed to the oxidative treatment according to the general procedure, underwent

only 33% conversion into the corresponding nitrate ester **25** after 1 h at room temperature (NMR analysis).

Reaction between Phenylmethyl Chloride (28) and HNO_3 in CH_2Cl_2: A solution of HNO_3 (d = 1.51, 4.73 g, 75.0 mmol) in CH_2Cl_2 (5.0 mL) was added dropwise, at 0 °C and with stirring, to a solution of phenylmethyl chloride (**28**, 3.17 g, 25.0 mmol) in CH_2Cl_2 (5.0 mL) and the resulted homogeneous reaction mixture was stirred at room temperature and analysed by NMR in the usual way. After 1 h, the observed degree of conversion was 92% and the only products detected in the reaction mixture were an isomeric mixture of (nitrophenyl)methyl chlorides (**29**); no trace of aldehyde **2a** was present.

Reaction between Phenylmethyl Acetate (30) and HNO_3 in CH_2Cl_2: A solution of HNO_3 (d = 1.51, 4.73 g, 75.0 mmol) in CH_2Cl_2 (5.0 mL) was added dropwise, at 0 °C and with stirring, to a solution of phenylmethyl acetate (**31**, 3.75 g, 25.0 mmol) in CH_2Cl_2 (5.0 mL) and the resulted homogeneous reaction mixture was stirred at room temperature and analysed by NMR in the usual way. After 1 h, the observed degree of conversion was 26%, exclusively affording an isomeric mixture of (nitrophenyl)methyl acetates (**31**); no oxidation took place.

Reaction between Phenylmethyl 2,2-Dimethylpropanoate (32) and HNO_3 in CH_2Cl_2: Ester **32** (4.80 g, 25.0 mmol) was treated as above, undergoing exclusive ring nitration to give the three isomers **33** (12% conv. after 1 h, 33% conv. after 24 h); no oxidation was observed.

General Procedure for the Oxidation of Non-Benzylic Alcohols and Ethers: A solution of HNO_3 (d = 1.51, 3.15 g, 50.0 mmol) in CH_2Cl_2 (5.0 mL) was added dropwise, at 0 °C and with stirring, to a solution of the selected substrate (25.0 mmol) in CH_2Cl_2 (5.0 mL). After the addition was complete, the homogeneous reaction mixture was allowed to reach room temperature and stirring was continued for 1 h or, when necessary, prolonged for 24 h. In order to monitor the composition of reaction mixtures, aliquots (0.2 mL) were withdrawn at suitable times, diluted with $CDCl_3$ (0.3 mL) and subjected to ^1H and ^{13}C NMR analysis. The analyses were also repeated after the diluted sample solution had been washed with 10% aqueous Na_2SO_4 (0.5 mL) and dried with Na_2SO_4, the solvent had been evaporated and the residue had been taken up in $CDCl_3$. After the completion of the reaction, the resulting mixture was diluted with CH_2Cl_2 (50.0 mL), washed with 10% aqueous Na_2SO_4 (2 × 30.0 mL), dried with Na_2SO_4, filtered, and concentrated to dryness. When suitable, the obtained reaction products were conveniently isolated by fractional distillation.

Acknowledgments

This work was supported in part by research grants to P. S. from the University of Udine (FURD, 1999−2000), Udine, Italy. We are indebted to Prof. G. Verardo for MS data collection and to Dr. P. Martinuzzi for recording the NMR spectra.

[1] P. Strazzolini, A. G. Giumanini, A. Runcio, M. Scuccato, *J. Org. Chem.* **1998**, *63*, 952−958.
[2] P. Strazzolini, T. Melloni, A. G. Giumanini, *Tetrahedron* **2001**, *57*, 9033−9043.
[3] [3a] P. Strazzolini, M. G. Dall'Arche, A. G. Giumanini, *Tetrahedron Lett.* **1998**, *39*, 9255−9258. [3b] P. Strazzolini, M. Scuccato, A. G. Giumanini, *Tetrahedron* **2000**, *56*, 3625−3633.
[4] D. G. Markees, *Helv. Chim. Acta* **1973**, *56*, 1382−1384.
[5] O. Buddenberg, *Methoden der Organischen Chemie (Houben-Weyl)*, 4th ed., G. Thieme Verlag, Stuttgart, **1981**, vol. IV/1a, (Oxidation), pp. 703−704.
[6] S. R. Hartshorn, R. B. Moodie, K. Schofield, *J. Chem. Soc. B* **1971**, 2454−2461 and references cited therein.
[7] [7a] O. Bayer, *Methoden der Organischen Chemie (Houben-Weyl)*, 4th ed., G. Thieme Verlag, Stuttgart, **1954**, vol. VII/1 (Aldehyde), pp. 159−193. [7b] K.-D. Bode, D. Dieterich, B. Eistert, R. Gipp, H. Henecka, H. Herlinger, R. Jira, D. Kramer, H.-J. Kabbe, A. Lüttringhaus, M. Regitz, C.-W. Schellhammer, H. Söll, H. Stetter, H. Wilms, F. Wingler, *Methoden der Organischen Chemie (Houben-Weyl)*, 4th ed., G. Thieme Verlag, Stuttgart, **1973**, vol. VII/2a (Ketone), pp. 699−777. [7c] J. Bracht, W. Friedrichsen, K. Krohn, H. Kropf, M. Maher-Detweiler, P. Margaretha, P. Messinger, G. Ohloff, E. Schaumann, *Methoden der Organischen Chemie (Houben-Weyl)*, 4rth ed., G. Thieme Verlag, Stuttgart, **1984**, vol. VI/1b (Alkohole III), pp. 878−896. [7d] A. H. Haines, *Best Synthetic Methods. Methods for the Oxidation of Organic Compounds (Alcohols, Alcohols Derivatives)*, Academic Press, London, UK, **1988**, pp. 5−238. [7e] M. Hudlicky, *Oxidations in Organic Chemistry*, ACS Monograph 186, American Chemical Society, Washington, DC, USA, **1990**, pp. 114−150. [7f] M. B. Smith, J. March, *March's Advanced Organic Chemistry. Reactions, Mechanisms and Structure*, 5th ed., John Wiley & Sons, Inc., Chichester, UK, **2001**, pp. 1514−1517. [7g] R. C. Larock, *Comprehensive Organic Transformations. A Guide to Functional Group Preparation*, 2nd ed., Wiley-VCH, Chichester, UK, **1999**, pp. 1230−1250.
[8] P. Strazzolini, A. G. Giumanini, A. Runcio, *Tetrahedron Lett.* **2001**, *42*, 1387−1389.
[9] O. Buddenberg, *Methoden der Organischen Chemie (Houben-Weyl)*, 4th ed., G. Thieme Verlag, Stuttgart, **1981**, vol. IV/1a (Oxidation), pp. 678−680.
[10] [10a] O. Bayer, *Methoden der Organischen Chemie (Houben-Weyl)*, 4th ed., G. Thieme Verlag, Stuttgart, **1954**, vol. VII/1 (Aldehyde), pp. 181−182. [10b] O. Buddenberg, *Methoden der Organischen Chemie (Houben-Weyl)*, 4th ed., G. Thieme Verlag, Stuttgart, **1981**, vol. IV/1a (Oxidation), p. 652.
[11] S. R. Joshi, S. B. Sawant, J. B. Joshi, *Org. Process Res. Dev.* **2001**, *5*, 152−157.
[12] A. H. Haines, *Best Synthetic Methods. Methods for the Oxidation of Organic Compounds (Alcohols, Alcohols Derivatives)*, Academic Press, London, UK, **1988**, p. 184.
[13] J. W. Baker, A. J. Neale, *J. Chem. Soc.* **1955**, 608−615.
[14] S. D. Ross, E. R. Coburn, M. Finkelstein, *J. Org. Chem.* **1968**, *33*, 585−587.
[15] J. W. Baker, T. G. Heggs, *J. Chem. Soc.* **1955**, 616−630.
[16] [16a] P. Gray, A. D. Yoffe, *Chem. Rev.* **1955**, *55*, 1069−1154. [16b] P. Gray, A. D. Yoffe, *Quart. Rev. (London)* **1955**, *9*, 362−390. [16c] O. Buddenberg, *Methoden der Organischen Chemie (Houben-Weyl)*, 4th ed., G. Thieme Verlag, Stuttgart, **1981**, vol. IV/1a (Oxidation), p. 651.
[17] H. Suzuki, T. Takeuchi, T. Mori, *Bull. Chem. Soc. Jpn.* **1997**, *70*, 3111−3115.
[18] A. McKillop, M. E. Ford, *Synth. Commun.* **1972**, *2*, 307−313.
[19] E. Iglesias, L. Garcia-Rio, J. R. Leis, M. E. Pena, D. L. H. Williams, *J. Chem. Soc., Perkin Trans. 2* **1992**, 1673−1679.
[20] W. A. Noyes, in: *Organic Syntheses, Collective Vol. 2*, John Wiley & Sons, Inc., New York, **1943**, pp. 108−109.
[21] I. Sakai, N. Kawabe, M. Ohno, *Bull. Chem. Soc. Jpn.* **1979**, *52*, 3381−3383.
[22] S. A. Stern, J. T. Mullhaupt, W. B. Kay, *Chem. Rev.* **1960**, *60*, 185−207.
[23] L. Eberson, *Electron Transfer Reactions in Organic Chemistry*, Springer-Verlag, Heidelberg, **1987**, p. 91.
[24] [24a] Y. Ogata, Y. Sawaki, *J. Am. Chem. Soc.* **1966**, *88*, 5832−5837. [24b] T. Nishiguchi, F. Asano, *J. Org. Chem.* **1989**, *54*, 1531−1535. [24c] T. Nishiguchi, M. Bougauchi, *J. Org. Chem.* **1990**, *55*, 5606−5609. [24d] T. Nishiguchi, H. Okamoto, *J. Chem. Soc., Chem. Commun.* **1990**, 1607−1608.
[25] K.-D. Bode D. Dieterich, B. Eistert, R. Gipp, H. Henecka, H.

Herlinger, R. Jira, D. Kramer, H.-J. Kabbe, A. Lüttringhaus, M. Regitz, C.-W. Schellhammer, H. Söll, H. Stetter, H. Wilms, F. Wingler, *Methoden der Organischen Chemie (Houben-Weyl)*, 4th ed., G. Thieme Verlag, Stuttgart, **1973**, vol. VII/2a (Ketone), p. 765.
[26] [26a] O. Bayer, *Methoden der Organischen Chemie (Houben-Weyl)*, 4th ed., G. Thieme Verlag, Stuttgart, **1954**, vol. VII/1 (Aldehyde), p. 194. [26b] O. Buddenberg, *Methoden der Organischen Chemie (Houben-Weyl)*, 4th ed., G. Thieme Verlag, Stuttgart, **1981**, vol. IV/1a (Oxidation), pp. 672−673.
[27] O. Bayer, *Methoden der Organischen Chemie (Houben-Weyl)*, 4th ed., G. Thieme Verlag, Stuttgart, **1954**, vol. VII/1 (Aldehyde), p. 181.
[28] K.-D. Bode, D. Dieterich, B. Eistert, R. Gipp, H. Henecka, H. Herlinger, R. Jira, D. Kramer, H.-J. Kabbe, A. Lüttringhaus, M. Regitz, C.-W. Schellhammer, H. Söll, H. Stetter, H. Wilms, F. Wingler, *Methoden der Organischen Chemie (Houben-Weyl)*, 4th ed., G. Thieme Verlag, Stuttgart, **1973**, vol. VII/2a (Ketone), p. 763.
[29] D. G. Kundiger, G. F. Morris, *J. Am. Chem. Soc.* **1958**, *80*, 5988−5990.
[30] O. Bayer, *Methoden der Organischen Chemie (Houben-Weyl)*, 4th ed., G. Thieme Verlag, Stuttgart, **1954**, vol. VII/1 (Aldehyde), p. 180.
[31] J. W. Hilborn, E. MacKnight, J. A. Pincock, P. J. Wedge, *J. Am. Chem. Soc.* **1994**, *116*, 3337−3346.
[32] [32a] E. L. Eliel, C. Herrmann, J. T. Traxler, *J. Am. Chem. Soc.* **1956**, *78*, 1193−1198. [32b] E. L. Eliel, T. J. Prosser, *J. Am. Chem. Soc.* **1956**, *78*, 4045−4049.
[33] C. R. Dick, *J. Org. Chem.* **1962**, *27*, 272−274.
[34] F. Bellesia, L. De Buyck, F. Ghelfi, E. Libertini, U. M. Pagnoni, F. Roncaglia, *Tetrahedron* **2000**, *56*, 7507−7511.
[35] A. Salgado, T. Huybrechts, L. De Buyck, J. Czombos, A. Tkachev, N. De Kimpe, *Synth. Commun.* **1999**, *29*, 57−63.
[36] K. Itami, T. Kamei, J. Yoshida, *J. Am. Chem. Soc.* **2001**, *123*, 8773−8779.
[37] C. J. Easton, A. J. Ivory, C. A. Smith, *J. Chem. Soc., Perkin Trans. 2* **1997**, 503−507.
[38] M. A. Smith, B. Weinstein, F. D. Greene, *J. Org. Chem.* **1980**, *45*, 4597−4602.
[39] J. M. Aizpurua, B. Lecea, C. Palomo, *Can. J. Chem.* **1986**, *64*, 2342−2347.
[40] T. Imamoto, T. Matsumoto, T. Kusumoto, M. Yokoyama, *Synthesis* **1983**, 460−461.
[41] J. H. Clark, J. M. Miller, K.-H. So, *J. Chem. Soc., Perkin Trans. 1* **1978**, 941−946.
[42] S. Oae, Y. H. Kim, D. Fukushima, K. Shinhama, *J. Chem. Soc., Perkin Trans. 1* **1978**, 913−917.
[43] R. G. Gillis, *J. Org. Chem.* **1956**, *21*, 805−808.
[44] P. Strazzolini, M. G. Dall'Arche, A. G. Giumanini, *Tetrahedron Lett.* **1998**, *39*, 9255−9258.
[45] R. Boschan, R. T. Merrow, R. W. Van Dolah, *Chem. Rev.* **1955**, *55*, 485−510.
[46] G. A. Olah, Q. Wang, X. Li, G. K. Surya Prakash, *Synthesis* **1993**, 207−208.
[47] P. Frøyen, *Phosphorus, Sulfur, Silicon Relat. Elem.* **1997**, *129*, 89−97.
[48] H. Suzuki, T. Murashima, I. Kozai, T. Mori, *J. Chem. Soc., Perkin Trans. 1* **1993**, 1591−1597.
[49] A. F. Ferris, K. W. McLean, I. G. Marks, W. D. Emmons, *J. Am. Chem. Soc.* **1953**, *75*, 4078.
[50] G. B. Bachman, N. W. Connon, *J. Org. Chem.* **1969**, *34*, 4121−4125.
[51] L. Henry, *C. R. Acad. Sci.* **1906**, *142*, 493−497.
[52] R. J. Lewis, R. B. Moodie, *J. Chem. Soc., Perkin Trans. 2* **1997**, 563−567.
[53] A. McKillop, B. P. Swann, M. E. Ford, E. C. Taylor, *J. Am. Chem. Soc.* **1973**, *95*, 3641−3645.
[54] S. M. Tsang, A. P. Paul, M. P. DiGiaimo, *J. Org. Chem.* **1964**, *29*, 3387−3390.
[55] N. C. Deno, N. H. Potter, *J. Am. Chem. Soc.* **1967**, *89*, 3550−3554.
[56] B. Ortiz, F. Walls, F. Yuste, H. Barrios, R. Sanchez-Obregon, L. Pinelo, *Synth. Commun.* **1993**, *23*, 749−756.
[57] S. Torii, T. Inokuchi, S. Takagishi, H. Horike, H. Kuroda, K. Uneyama, *Bull. Chem. Soc. Jpn.* **1987**, *60*, 2173−2188.
[58] B. Halton, C. J. Randall, G. J. Gainsford, W. T. Robinson, *Aust. J. Chem.* **1987**, *40*, 475−489.
[59] C. Imrie, T. A. Modro, E. R. Rohwer, C. C. P. Wagener, *J. Org. Chem.* **1993**, *58*, 5643−5649.
[60] D. V. Carter, P. T. Charlton, A. H. Fenton, J. R. Housley, B. Lessel, *J. Pharm. Pharmacol.* **1958**, *10*, suppl. 149T−159T.
[61] B. Wladislaw, A. Giora, *J. Chem. Soc.* **1964**, 1037−1040.
[62] P. Wan, S. Muralidharan, I. McAuley, C. A. Babbage, *Can. J. Chem.* **1987**, *65*, 1775−1783.
[63] [63a] H. Ishikawa, T. Mukaiyama, S. Ikeda, *Bull. Chem. Soc. Jpn.* **1981**, *54*, 776−780. [63b] R. Popielarz, D. R. Arnold, *J. Am. Chem. Soc.* **1990**, *112*, 3068−3082.
[64] N. Hartz, G. K. Surya Prakash, G. A. Olah, *Synlett* **1992**, 569−572.
[65] K. Horita, T. Yoshioka, T. Tanaka, Y. Oikawa, O. Yonemitsu, *Tetrahedron* **1986**, *42*, 3021−3028.
[66] H. Tomioka, K. Tabayashi, Y. Ozaki, Y. Izawa, *Tetrahedron* **1985**, *41*, 1435−1440.
[67] B. H. Lipshutz, D. Parker, J. A. Kozlowski, *J. Org. Chem.* **1983**, *48*, 3334−3336.
[68] M. Ochiai, T. Ito, H. Takahashi, A. Nakanishi, M. Toyonari, T. Sueda, S. Goto, M. Shiro, *J. Am. Chem. Soc.* **1996**, *118*, 7716−7730.
[69] E. C. Brown, J. T. Kurek, M.-H. Rei, K. L. Thompson, *J. Org. Chem.* **1984**, *49*, 2551−2557.
[70] T.-X. Xiang, B. D. Anderson, *J. Pharm. Sci.* **1994**, *83*, 1511−1518.
[71] O. Exner, J. Jonas, *Collect. Czech. Chem. Commun.* **1962**, *27*, 2296−2306.
[72] T.-A. Kobayashi, M. Tanaka, *J. Mol. Catal.* **1988**, *47*, 41−49.
[73] T.-A. Kobayashi, F. Abe, M. Tanaka, *J. Mol. Catal.* **1988**, *45*, 91−109.
[74] M. Eikawa, S. Sakaguchi, Y. Ishii, *J. Org. Chem.* **1999**, *64*, 4676−4679.
[75] S. K. Sharma, M. Tandon, J. W. Lown, *Eur. J. Org. Chem.* **2000**, 2095−2103.
[76] M. E. Pierce, G. D. Harris, Q. Islam, L. A. Radesca, L. Storace, R. E. Waltermire, E. Wat, P. K. Jadhav, G. C. Emmet, *J. Org. Chem.* **1996**, *61*, 444−450.
[77] C. Gennari, S. Ceccarelli, U. Piarulli, K. Aboutayab, M. Donghi, I. Paterson, *Tetrahedron* **1998**, *54*, 14999−15016.
[78] N. A. Noureldin, D. Zhao, D. G. Lee, *J. Org. Chem.* **1997**, *62*, 8767−8772.

Received July 26, 2002
[O02428]