Novel syntheses of polynitroaromatic compounds by reversed-dipole ('umpolung') nitrations [1]

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Dedicated to Douglas Lloyd to mark the occasion of his 80th birthday

Abstract

Conventional nitrations use electrophilic reagents as the attacking species, and therefore electron-deficient substrates, such as certain nitrogen heterocycles and polynitroaromatics, react very slowly, giving low yields and extensive by-product formation. Because such substrates generally react readily with nucleophiles in high yield, reactions of heterocycles and polynitroaromatics with certain specific nucleophiles were therefore investigated with a view to generating intermediates containing 'masked' nitro groups, which could then be converted to nitrated products by simple oxidation procedures.

The method was applied to the nitration of several electron-deficient carbocyclic (i.e. benzenoid) or heterocyclic aromatic compounds, notably pyridines and diazines (pyrimidines and pyrazines). The methodology comprised:- i) reacting a haloaromatic with a diarylsulphilimine or its N- alkali metal salt, thereby generating an N-(hetero)aryl-S,S-diarylsulphilimine derivative, and ii) oxidising this intermediate under relatively mild conditions using a peroxycarboxylic acid such as *m*-chloroperbenzoic acid. Moderate to good yields of the corresponding nitro products, including some previously unreported compounds, were obtained. In certain cases the first step could be accomplished without the necessity of a halo precursor, i.e. by vicarious nucleophilic substitution. An attempted extension of the methodology to the aliphatic series, where phosphinimines were also employed as nucleophiles, was, however, largely unsuccessful.

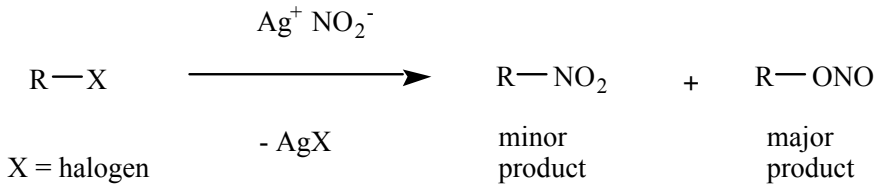
Keywords: Nitration, polynitroaromatics, reversed-dipole, umpolung

Introduction

Nitration reactions are employed to synthesise numerous energetic compounds,[2-4] for use in munitions, or nitrogen-containing intermediates for further elaboration into higher value products such as pharmaceuticals. In conventional nitration reactions, substrates are attacked by an

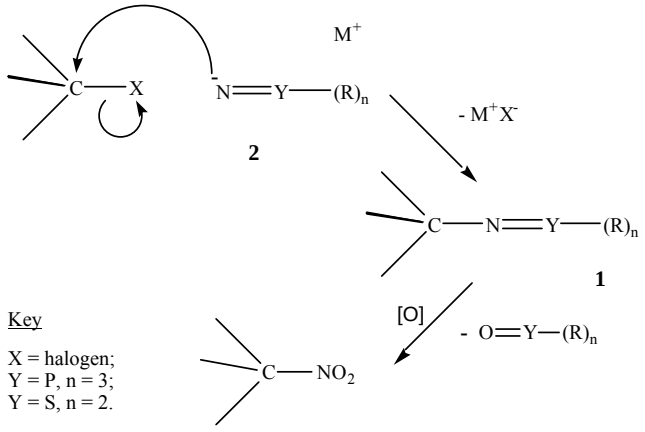
electrophile, usually the nitronium ion NO_2^+, resulting in the substitution, by nitro, of a leaving group, which is usually hydrogen (for C-nitration) although other leaving groups are possible (e.g. acyl moieties for N-nitration etc). The reactions are rapid and high-yielding when the substrate is electron-rich and numerous examples are known.[5-9] Conversely, electron-deficient substrates, for instance certain nitrogen heterocycles, react slowly and only under forcing conditions, giving low yields of the desired nitration products and extensive by-product formation, caused by reaction at alternative sites in the molecule (e.g. cleavage of rings, etc). For instance, the nitration of pyridine under electrophilic conditions (potassium nitrate/ oleum at 300 °C) yields only 4.5% of 3-nitropyridine.[10,11]

On the other hand, electron-deficient substrates generally react readily with nucleophiles in high yield. It is found that nitrite ion is not, however, a useful nucleophile to synthesize nitro derivatives, certainly in aromatic systems.[12] The reason is that the negative charge resides predominantly on the oxygen atoms and hence displacement of for instance halogen gives rise to nitrite esters rather than the desired nitro compounds (Scheme 1); the nitrite esters are hydrolytically unstable and the isolated products in the aromatic series are phenols.



Scheme 1. Nucleophilic displacement by nitrite.

Therefore a new approach was considered where reactions of heterocycles and polynitroaromatics with other nucleophiles would generate intermediates containing 'masked' nitro groups, which could then be converted to nitrated products by simple oxidation procedures. This novel methodology is outlined in Scheme 2.



Scheme 2. Principle of 'Umpolung' Nitration.

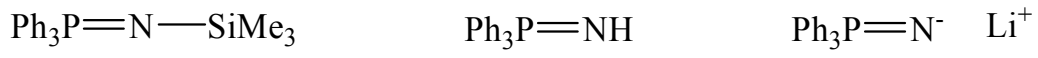
It was known from work in the 1980s that various imine derivatives of general structure **1** could be oxidised to nitro compounds, notably phosphinimines and sulphilimines.[13-17] More recent reports had indicated that the phosphinimine and sulphilimine precursors (general structure **2**) could act as nucleophiles and effect displacement of leaving groups such as halogen, particularly from heteroaromatic compounds.[18-19] It was considered that both steps could be combined into a single synthetic sequence wherein displacement of halide from readily accessible aromatic or heteroaromatic halo derivatives (or even displacement of hydrogen - see below) followed by oxidation would give rise to the nitro products directly, without the need for isolation and further elaboration of nitrogenous intermediates such as amines. Such a conversion would be termed an 'Umpolung' nitration because the polarity of the incoming group is reversed in the final product; 'Umpolung' (literally 'reversed dipole') conversions already exist for other functional groups, for instance nucleophilic carbonylation is achieved via dithioacetals,[20] and N-chloroamines can effect electrophilic amination,[21] reactions which normally occur by electrophilic and nucleophilic attack respectively.

A further advantage of the 'Umpolung' nitration methodology was anticipated, namely, the introduction of nitro substituents into the aromatic ring results in an activating effect which makes the ring more labile to further substitution; thus potentially higher degrees of nitration are possible than under electrophilic conditions. The exact chemistry by which this novel nitration methodology was achieved will now be described.

Results and Discussion

Nucleophilic substitutions

Since electron-poor aromatics such as pyridines, pyrimidines and pyrazines, as well as polynitro-benzenes are not readily nitrated by conventional electrophilic nitrating agents, these appeared obvious substrates upon which to investigate the novel methodology (the attempted application to aliphatic systems is described later). In general, halo derivatives of these ring systems were also widely available, and chloro compounds were chosen as the best compromise between cost and reactivity. It was somewhat harder to predict the most suitable nucleophile, however, and some difficulties were encountered in early nucleophilic substitution reactions.

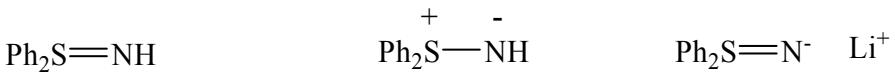


3 **4** **5**

The first nucleophile chosen was N-(trimethylsilyl)triphenylphosphine **3**, which had been efficacious in the nucleophilic substitution of heterocycles with labile chloride.[18] However, in our hands it was almost entirely inert (e.g. with 2-chloropyridine), so attention was turned to unsubstituted phosphinimine **4** or its salts, e.g. **5**. With these nucleophiles evidence was indeed

seen of halide displacement, but the heterocyclic phosphinimine products were, in general, too unstable to be isolated on account of their liability towards hydrolysis; often the only isolable products were triphenylphosphine oxide and an amino derivative of the starting heterocycle. Hence attention was turned away from phosphinimine nucleophiles in favor of their sulphur analogues, sulphilimines.

S,S-Diphenylsulphilimine **6** was known to react with various heteroaryl halides,[18] as well as polynitrochlorobenzenes,[22] in aromatic nucleophilic substitutions to give N-aryl-S,S-diphenylsulphilimine products ($Ph_2S{=}NAr$). The reactions with **6** (as the hydrate) were carried out in 100% molar excess (to remove hydrogen halide co-product), and were also found to be sensitive to choice of solvent, a significant improvement over literature yields being obtained when THF was used. The molecule is believed to react through an ylid form **7** which enhances the nucleophilicity.[23]



6 **7** **8**

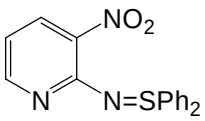
Table 1. Formation of sulphilimines from halo precursors

Substrate	Solvent	Conditions	Product (Yield)
2-Chloro-3-nitropyridine **9a**	EtOH	7hr/ reflux	**9b** (76%)
2-Chloro-5-nitropyridine **10a**	THF	4hr/ reflux	**10b** (81%)
2-Chloro-3,5-dinitropyridine **11a**	"	0.5hr/ reflux	**11b** (100%)
Pentachloropyridine **12a**	"	8hr/ reflux	**12b** (44%)*
2,6-Dichloropyrazine **13a**	"	18hr/ reflux	**13b** (95%)
2,4-Dichloropyrimidine **14a**	"	8hr/ reflux	**14b** (48%)
4,6-Dichloropyrimidine **15a**	"	8hr/ reflux	**15b** (72%)
2,4,6-Trichloropyrimidine **16a**	"	4 hr/reflux	**16b** (36%) & **17** (53%)
2,4,5,6-Tetrachloropyrimidine **18a**	"	4hr/ reflux	**18b** (55%)†
Pentafluoropyridine **19a**	"	6hr/ reflux	**19b** (84%)
2,3,5,6-Tetrafluoropyridine **20a**	"	4hr/ reflux	**20b** (95%)
2,4-Dichloro-6-(n-propoxy)-s-triazine **21a**	"	3 hr/ room temp.	**21b** (11%)

*2-isomer **12c** (4%) also formed; † 2-isomer **18c** (15%) also formed.

The sulphilimines which have been prepared in this way are shown in Table 1.24 The yields are in general good to excellent, with single products being formed cleanly in many cases. Disubstitution did not appear to occur without further activation of the aromatic nucleus (for example with nitro group(s)). Where by-products were formed, i.e. isomers from attack at a different position on the ring, these were easily separated by column chromatography.

In order to enhance the nucleophilicity of S,S-diphenylsulphilimine **6** and thereby extend the range of heterocyclic sulphilimines available, an investigation of the behavior of N-lithio-S,S-diphenylsulphilimine **8** was undertaken. **8** may be prepared either from **6** or from S,S-diphenylsulphonium chloride **22**, in each case by reaction



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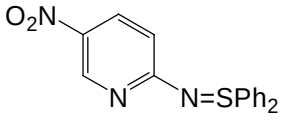

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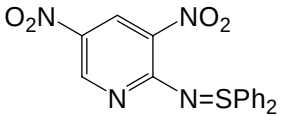

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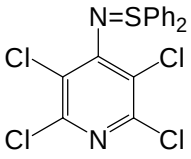

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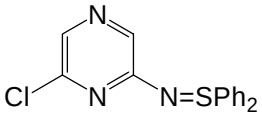

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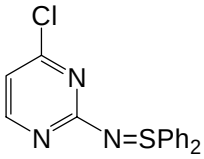

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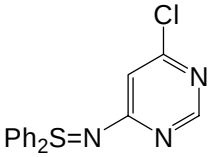

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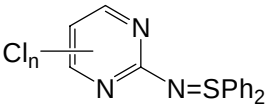
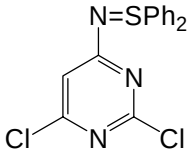


n = 2: **16b**
n = 3: **18b**



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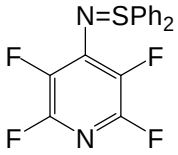

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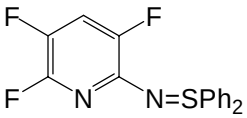

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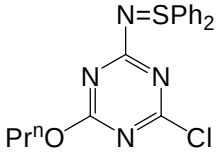
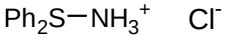


21b

with butyl lithium. The use of **8** did indeed enable some additional heterocyclic sulphilimines to be synthesised, for example pyrazine **23** was formed in 12% yield, but little advantage was found in other reactions with chloroheterocycles as substrates (notably, a di-(sulphilimino)heterocycle, **24**, was formed, albeit in meager (3%) yield).



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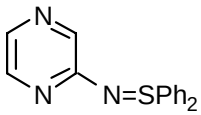

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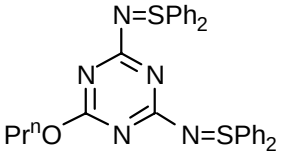


24

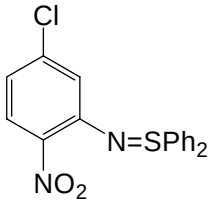
However, the greatest advantage in the use of the N-lithio salt, **8**, lay in its reactions with substrates containing nitro groups. In such compounds, for instance 2-chloro-3-nitropyridine, it was found that owing to the higher basicity of **8** compared to **6**, attack took place at the 4-position of the pyridine nucleus (in addition to the 2-position) with the occurrence of displacement of hydrogen. Such a displacement is termed a vicarious hydrogen substitution,[25] and the reaction was found to be general for several nitro-containing precursors (Table 2); carbocyclic aromatics (nitrobenzene derivatives) behaved similarly. This is the first reported instance of a vicarious substitution by a sulphur nucleophile of this type.[26]

Table 2. Formation of sulphilimines by vicarious nucleophilic substitution

Substrate	Conditions	Product (Yield)
1-Chloro-4-nitrobenzene **25a**	24 hr/ rt.	**25b** (19%)*
1,3-Dinitrobenzene **26a**	" " " "	**26b** (20%) & **27** (14%)
2-Chloro-3-nitropyridine **28a**	" " " "	**28b** (49%) & **9b** (34%)
2-Chloro-5-nitropyridine **29a**	" " " "	**29b** (4%)

* The yield was reduced (7%) upon prolonging the reaction time (72 hr).

Before turning to oxidations, the attempted extension of the methodologies described above to aliphatic systems should briefly be mentioned. The potential benefits of the "Umpolung' nitration methodology to aliphatics would be extensive, permitting a new entry into such compounds without resort to low-yielding 'dirty' reactions such as nitromercuration-demercuration or nitrite additions under Schechter-Kaplan conditions,[8] or alternatively gas phase nitrations,[29] which are the usual routes to nitroaliphatics.



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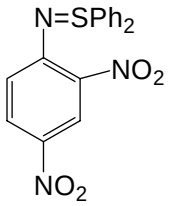

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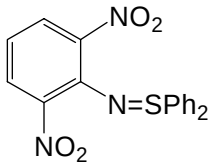

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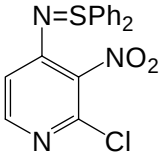

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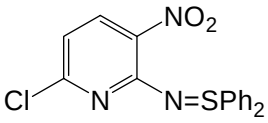
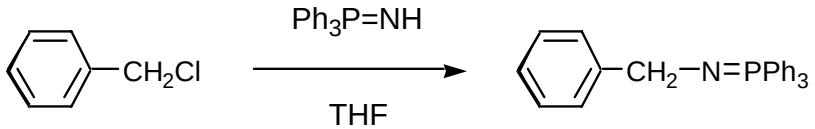


29b

The reactions of several alkyl chlorides, bromides and tosylates, particularly tertiary compounds such as *t*-butyl and adamantyl, were investigated using phosphinimine nucleophiles, but little evidence was obtained of nucleophilic substitution. It was presumed that the respective leaving groups were not sufficiently activated towards nucleophilic displacement. Ultimately, attention was turned to allylic systems, and although no phosphinimine could be obtained from allyl chloride or crotyl chloride, the desired reaction occurred with benzyl chloride (Scheme 3), and the phosphinimine **30** was obtained in 10% yield when triphenylphosphinimine ($Ph_3P=NH$) was used (generated *in situ* from aminotriphenylphosphine bromide). The subsequent reactions of **30** will be covered in the following section.



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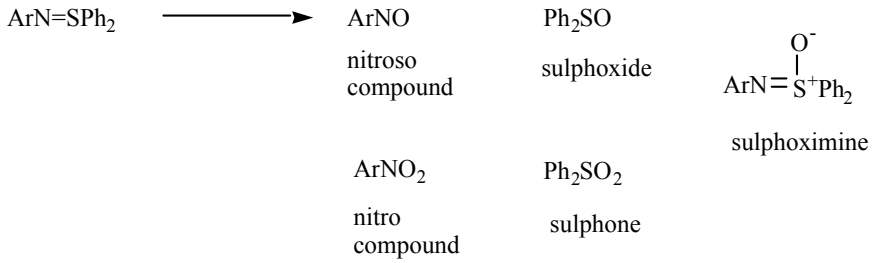
Scheme 3. Reaction of benzyl chloride with phosphinimine.

Oxidations

In early work[13,14] it was reported that ozone was effective as an oxidising agent in the conversion of phosphinimines to nitro compounds. However, in our hands it was found to be almost completely ineffective, and recourse was therefore made to other reported[15-17] oxidants, notably *m*-chloroperbenzoic acid (mCPBA). The novel clean oxidant dimethyldioxirane (DMD)[28,29] was also considered, although it was found to be of more limited utility than mCPBA.



Scheme 4. Sulphilimine oxidation products.

Because the conversion of sulphilimines and phosphinimines to nitro compounds depends on oxidation occurring at the nitrogen atom and not the hetero atom, choice of oxidising agent is crucial to the success of this step; the possible products and co-products which may be formed by this reaction are shown (Scheme 4). In practice, because the oxidizing agent is always in excess nitroso compounds are not isolated as products. However, a balance has to be struck between formation of nitro product (oxidation at N) and sulphoximine (oxidation at S), since under the conditions employed in this work further reaction of sulphoximine, to yield the nitro group, does not occur.[30] The sulphoxide and sulphone products are always formed, in variable amounts, as co-products from the N-S bond cleavage which yields the nitroso and nitro products already mentioned. Similar considerations apply to the oxidation of phosphinimines, although of course far fewer of these compounds were studied for the reasons given earlier (see "Nucleophilic Substitutions").

It is found that the oxidation pathway, and hence the nitro:sulphoximine ratio, depends strongly on the nature of the oxidising agent.[31] Thus with electrophilic oxidising agents such as peracids, nitroso/nitro product formation is favored, whilst with neutral or nucleophilic oxidants, such as DMD and peracid salts respectively, sulphoximines are the predominant products. The reason for this effect can best be understood if it is remembered that sulphilimines are effectively ylids, with contributions from dipolar forms (e.g. **7**: see "Nucleophilic Substitutions") which place a partial negative charge on the nitrogen atom; hence electrophilic oxidants, i.e. those where the oxygen bears a partial positive charge, will tend to react on the nitrogen atom. Conversely, nucleophilic oxidants, where the oxygen bears a partial negative charge, will tend to oxidise the sulphur atom. The results of several sulphilimine oxidations are shown in Table 3.

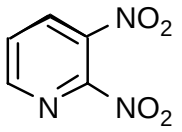
Table 3. mCPBA oxidations of sulphilimines

Substrate	Conditions*	Product (Yield)
2-(S,S-Diphenylsulphilimino)-3-nitropyridine **9b**	2 hr/ B	**31** (8%)
2-(S,S-Diphenylsulphilimino)-5-nitropyridine **10b**	0.5hr/B	(Ph_2SO_2 only)
2,3,5,6-Tetrachloro-4-(S,S-diphenylsulphilimino)pyridine **12b**	2 hr/ B	**32**(24%) & **33**(40%)
2-Chloro-6-(S,S-diphenylsulphilimino)-pyrazine **13b**	2 hr/ C	**34** (60%)
4-Chloro-6-(S,S-diphenylsulphilimino)-pyrimidine **15b**	2 hr/ B	**35** (4%)
2,3,5,6-Tetrafluoro-4-(S,S-diphenylsulphilimino)pyridine **19b**	18 hr/ A	**36**(21%) & **37**(16%)
2-(S,S-Diphenylsulphilimino)-3,5,6-trifluoropyridine**20b**	3 hr/ B	**38** (74%)
S,S-Diphenylsulphiliminopyrazine **23b**	2 hr/C	(Ph_2SO_2 only)
1-Chloro-3-(S,S-Diphenylsulphilimino)-4-nitrobenzene **25b**	2 hr/ C	**39**(32%) & **40**(26%)
2-Chloro-3-nitro-4-(S,S-diphenylsulphilimino)-pyridine **28b**	3 hr/ B	**41**(9%)
4-Chloro-6-(S,S-diphenylsulphilimino)-pyrimidine **15b**	3 hr/ B	**42**(12%) & **43**(19%)

* Sulphilimines were refluxed with excess mCPBA in 1,2-dichloroethane for the periods shown.

Workup is indicated by A through C as follows:

A. A: By flash chromatography
B. B: Product mixture chilled to –5 °C and m-chlorobenzoic acid removed by filtration.
C. C: Product mixture washed with aq. NaOH and water (to remove m-chloro-benzoic acid).



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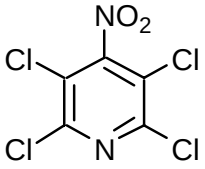

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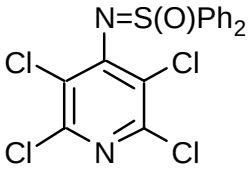

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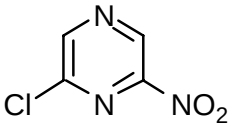

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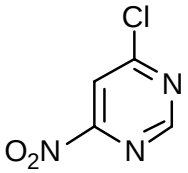

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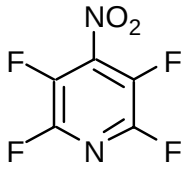

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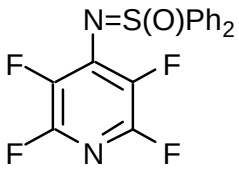

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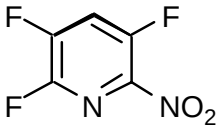

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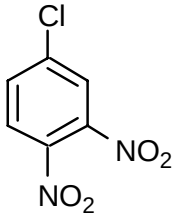

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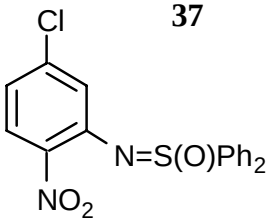

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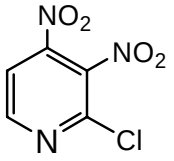

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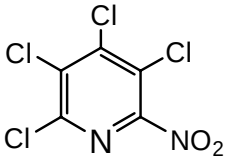

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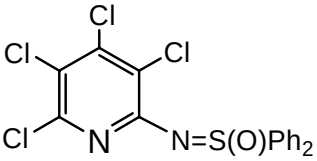
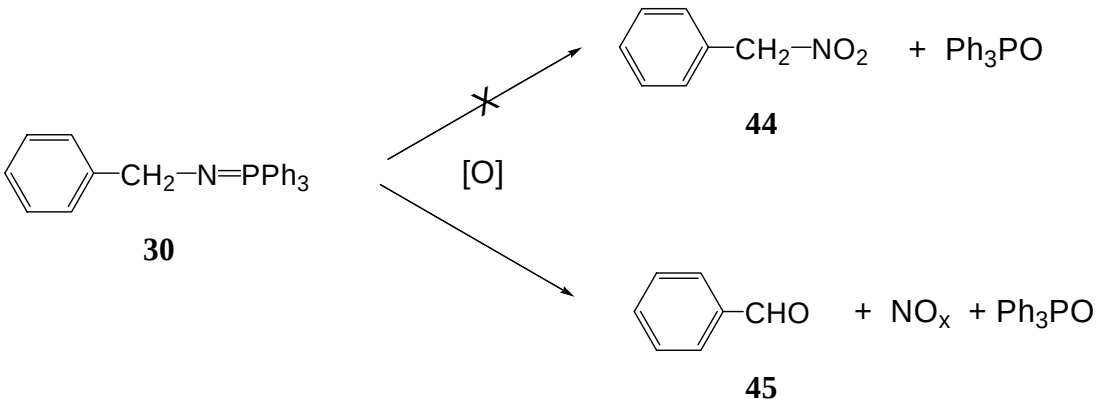


43

It is notable that the yield of nitro products is quite variable (4 to 74%) and in around half of the cases quoted, sulphoximines were obtained as major by-products. In two cases, no nitro products were isolated although clearly S-N bond cleavage had occurred as the formation of diphenylsulphoxide was detected. The behavior of the sulphilimines towards oxidation is therefore influenced not only by the oxidant used but also by the structure of the sulphilimine itself: hence in some cases (e.g. compounds **13b** and **20b**) it is a very good route to the nitro derivatives, whilst in others (e.g. **9b** and **15b**) it is not so efficient. Nevertheless, it should be remembered that, compared with yields in electrophilic nitrations of around 4% (see "Introduction"), yields in the 10 to 30 % category are a significant improvement.

Turning to the behavior of the aliphatic phosphinimine **30** (see "Nucleophilic Substitutions"), a different behaviour was observed. Oxidation of **30** using either ozone or Oxone (DuPont) (Scheme 5) did not give rise to any nitro product **44**; instead, the only identifiable products were the aldehyde **45** and triphenylphosphine oxide. The reasons for this difference in chemistry from the aromatic systems probably lie in the stability of the carbonyl product **45** which drives the reaction along this pathway - one can only speculate as to which intermediates are involved.



Scheme 5. Oxidation of an aliphatic phosphinimine.

Conclusions

Therefore a new type of nitration methodology has been developed which facilitates the nitration of substrates deactivated towards electrophilic nitration methods, notably electron deficient heterocycles including pyridine and various diazines (pyrimidines, pyrazines) as well as polynitrated benzenes. The nitration, an 'Umpolung' methodology, relies on the introduction of the incipient or 'masked' nitro function as a nucleophile, most efficaciously a sulphilimine, which is converted to the desired nitro group in a separate oxidation step. Although overall yields as high as 60-70% have been obtained, in some cases yields fall below 10%; nevertheless, these lower figures are still an improvement on those obtained by conventional electrophilic nitration.

The methodology offers promise in the generation of novel energetic materials, or nitrogen-containing intermediates for further elaboration into higher value products such as pharmaceuticals

Experimental Section

General Procedures. ^{1}H and ^{13}C NMR spectra were measured in $CDCl_3$ (deuterated chloroform) using a Bruker AC 300 spectrometer. Multiplicities are described as singlet (s), doublet (d), triplet (t), quartet (q), doublet of doublets (dd), multiplet (m) and broad (br). Mass spectra were obtained using a Kratos Analytical Profile mass spectrometer under electron impact (EI) conditions; where GC-MS was required, a Shimadzu GC-14A gas chromatograph interface was used. Accurate masses were obtained by peak matching. The figures outside the brackets denote the molecular masses of the fragments seen and the contents of the bracket give the identity of the fragment and the intensity of its peak as a percentage. M denotes the molecular fragment. IR spectra where taken were consistent with the proposed structures. Microanalyses were carried out by Butterworth Labs. Ltd. of Teddington, Middx. U.K. Flash chromatography

columns were packed with Kieselgel 60 flash silica (Merck, particle size 0.040 - 0.063 mm) and retention factors are quoted for t.l.c. plates pre-coated with Kieselgel 60 F-254 (Merck). All starting materials were purchased from Aldrich Chemical Co. and their purity was checked by ^{1}H NMR. Diethyl ether, THF and petrol (bp 40–60 ^{o}C) were distilled over sodium, methanol was distilled over magnesium and dichloromethane was distilled over calcium hydride.

Typical nucleophilic substitution of a halogen precursor: preparation of 2-chloro-6-(S,S-diphenylsulphilimino)pyrazine (13b) from 2,6-dichloropyrazine (13a)

S,S-Diphenylsulphilimine monohydrate (0.540 g, 2.46 mmol, 2 equiv.) was weighed out into a 100 mL triple-necked round-bottomed flask. THF (distilled, 15 mL) was added, causing the sulphilimine to dissolve. 2,6-Dichloropyrazine (**13a**, 0.183 g, 1.23 mmol, 1 equiv., source: Aldrich chemical company, cat. no. 13,249-7) was added to the solution in the flask. The central neck of the flask was fitted with a Liebig condenser, a magnetic stirrer bar was placed in the flask and stoppers were placed in the remaining two necks of the flask. The contents of the flask were heated under reflux with stirring for 18 hours. During the first hour of reflux a white precipitate appeared. After the reflux period the flask was allowed to cool to room temperature, then the reaction mixture was filtered (fluted filter paper). The solid remaining on the filter paper was shown by $_1$H NMR spectroscopy and elemental analysis to be the salt diphenylaminosulphonium chloride, the by-product of N-aryl-S,S-diphenylsulphilimine formation. The THF was removed from the filtrate using a rotary evaporator. A yellow-brown oil remained, which was shown by $_1$H NMR to be a slightly impure form of the desired product, 2-chloro-6-(S,S-diphenylsulphilimino)pyrazine (**13b**, 0.366g, 95%). The impurity, unchanged starting material 2,6-dichloropyrazine (**13a**, 5%), was removed by flash column chromatography, using a column packed with 10 g of Merck Kieselgel 60 flash silica, eluted under pressure using small bellows with a 1:2 vol./vol. mixture of dichloromethane and 40-60^{o}C petrol followed by pure dichloromethane. The desired product had a retention factor of 0.16 eluted in dichloromethane, i.e. R_f = 0.16 (CH_2Cl_2). The impurity had a retention factor of 0.50 (CH_2Cl_2).

2-Chloro-6-(*S,S*-diphenylsulphilimino)pyrazine (13b). $_1$H NMR ($CDCl_3$, 300MHz): δ 7.60 (1H, s, Ar<u>H</u>) 7.42-7.78 (6H, m, Ar<u>H</u>) 7.71-7.79 (4H, m, Ar<u>H</u>) 8.10 (1H, s, Ar<u>H</u>). MS (EI): 313, 315 (M_+, 4%, 1%) 278 (M-Cl, 1) 204, 206 (M-SPh, 3, 1) 186 (SPh_2, 100) 109 (SPh, 17) 92 (M-Cl-SPh_2, 11) 83 (18), HRMS: $C_{16}H_{12}N_3SCl$ requires 313.044048. Found 313.04400, deviation 0.1 ppm.

The preparations of other S,S-diphenylsulphilimino derivatives of aromatic compounds, synthesised by nucleophilic displacement of halogen, can be found in ref. 24.

Typical vicarious nucleophilic substitution (i.e. displacement of hydrogen *ortho* to nitro group): preparation of 1-chloro-3-(*S,S*-diphenylsulpilimino)-4-dinitrobenzene (25b) from 1-chloro-4-nitrobenzene (25a)

A 100 ml triple-necked round-bottomed flask containing a magnetic stirrer bar, a 20 ml syringe with Luer needle and a 5 ml syringe with Luer needle were dried in an oven for 24 hours at

150°C. The techniques described in this example are appropriate for the handling of pyrophoric materials, i.e. oxygen and water are excluded. The flask was removed from the oven, the central neck was fitted with a nitrogen bubbler and the remaining two necks were fitted with rubber septa. The flask was flushed with nitrogen. S,S-Diphenylsulphilimine monohydrate (1.097 g, 5 mmol, 1 equiv.) was added to the flask by briefly removing one of the rubber septa (without disrupting the flow of nitrogen). The 20 mL syringe was removed from the oven and used to add anhydrous THF (freshly distilled over calcium hydride, 15 mL) to the flask. The solution in the flask was degassed by attaching a long needle to a nitrogen supply and putting the needle through one of the septa so that the end of the needle was in the solution. Bubbles of nitrogen were allowed to pass through the solution in this way for 10 min. The long needle was then removed. The 5 mL syringe was removed from the oven and flushed with nitrogen for 5 minutes. It was then used to add n-butyllithium (4.0 mL of a 2.5 *M* solution in hexanes, 10 mmol, 2 equiv.; DANGER: pyrophoric compound!) dropwise to the stirred solution which immediately turned yellow, indicating the presence of N-lithio-S,S-diphenylsulphilimine. The empty 5 ml syringe was placed in a large beaker of butan-1-ol immediately after use. 1-Chloro-4-nitrobenzene **25a** (0.788 g, 5 mmol, 1 equiv.) was added to the yellow solution by briefly removing one of the septa, and the mixture was stirred under nitrogen at room temperature for 24 h. The mixture was then exposed to the air and the THF removed on a rotary evaporator. The crude product was purified by flash column chromatography (eluting solvent 1:2 vol./vol. CH_2Cl_2 : 40-60 °C petrol). 1-Chloro-3-S,S-diphenylsulphilimino-4-nitrobenzene (**25b**, 0.34 g) was obtained as a crystalline yellow solid in 19% yield; R_f=0.43 (CH_2Cl_2). Anal. $C_{18}H_{13}N_2ClO_2S$ required, C, 60.58, H, 3.67, N, 7.85%, found: C, 60.06, H, 3.57, N, 7.90,. ^{1}H NMR ($CDCl_3$, 300MHz) δ 6.56-6.60 (1H, dd, ArH) 6.94-6.95 (1H, d, ArH) 7.49-7.52 (6H, m, ArH) 7.69-7.73 (1H, d, ArH) 7.83-7.88 (4H, m, ArH) ppm. MS (EI) 356, 358 (M^+, 1%, 0.3%) 186 (SPh_2, 100): HRMS: $C_{18}H_{13}N_2SClO_2$ requires 356.038628, found 356.03771, dev. 2.5 ppm.

The preparations of other S,S-diphenylsulphilimino derivatives of aromatic compounds, synthesised by vicarious nucleophilic displacement of hydrogen, can be found in ref. 26.

Oxidation of S,S-diphenylsulphilimino derivatives of aromatic compounds (to nitro compounds)

Oxidation of 1-chloro-3-(S,S-diphenylsulphilimino)-4-nitrobenzene (25b). The oxidizing agent, 3-chloroperoxybenzoic acid (Aldrich, *ca*. 75% by wt., 0.320 g, 1.86 mmol, 6 equiv.), was weighed out into a 100 ml triple-necked round-bottomed flask. The three necks of the flask were fitted with a stopper, a water condenser and a thermometer respectively, and a magnetic stirrer bar was placed in the flask. HPLC grade 1,2-dichloroethane (20 mL) was added to the flask, and the flask and its contents were cooled to –5 °C using ice-salt mixture. 1-Chloro-3-(S,S-diphenylsulphilimino)-4-nitrobenzene (25b, 110 mg, 0.31 mmol, 1 equiv.) was added to the flask. The contents of the flask were stirred, the ice bath was removed, the flask was allowed to warm up to room temperature and it was then placed a paraffin oil bath. The reaction mixture was heated under reflux for 2 h and then allowed to cool. The mixture was washed with 0.5 *M*

aqueous sodium hydroxide (2 x 20 mL) followed by distilled water (2 x 20 mL). The reaction mixture was then dried over anhydrous magnesium sulphate, filtered, and 1,2-dichloroethane was removed from the filtrate on a rotary evaporator, leaving brown oil. The oil was purified by flash column chromatography in a similar manner to that described above (eluting solvent 1:3 vol./vol. CH_2Cl_2 : 40-60 ^oC petrol, gradient to 100% CH_2Cl_2). 1-Chloro-3,4-dinitrobenzene 39 was obtained as a yellow solid (20 mg) in 32% yield; R_f=0.79 (CH_2Cl_2). ^1H NMR ($CDCl_3$, 250 MHz) δ 7.69-8.18 (3H, 3m, ArH) (lit. [32] 7.70-8.10) ppm. MS (EI): m/z 202, 204 (M^+, 15%, 5%), 186, 188 (M-O, 8, 3), 172, 174 (M-NO, 4, 1), 156, 158 (M-NO_2, 38, 13), 139, 141 (42, 14), 128, 130 (8, 3). HRMS: $C_6H_3N_2ClO_4$ requires 201.97813; found 201.97703, dev. 5.4 ppm. Also obtained were: 1-chloro-3-(S,S-diphenylsulphoximino)-4-nitrobenzene 40, 30 mg (26%), mp 160–161 ^oC; R_f=0.62 (CH_2Cl_2), ^1H NMR ($CDCl_3$, 250 MHz) δ 6.86-6.91 (1H, dd, ArH), 7.37 (1H, d, ArH, *J* = 1.5 Hz), 7.49-7.59 (6H, m, ArH), 7.68-7.71 (1H, d, ArH, *J* = 7.5 Hz), 8.11-8.16 (4H, m, ArH); and a small amount of diphenylsulphone.

2,3-Dinitropyridine (31) from sulphilimine **9b**. Yellow oil (9% yield), R_f=0.58 (CH_2Cl_2); ^1H NMR ($CDCl_3$, 300 MHz) δ 7.80-7.85 (1H, m, ArH) 8.51-8.54 (1H, m, ArH) 8.77-8.79 (1H, m, ArH) ppm (lit.[33]); (D_6-acetone) δ 8.16, 8.87, 8.92 ppm; MS: (EI) 169 (M_+, 100) 147 (4) 105 (10) 99 (33) 77 (M-2NO_2, 13); HRMS: $C_5H_3N_3O_2$ requires 169.012350, found 169.01169, dev. 3.9 ppm. The oxidation co-product diphenylsulphone was also obtained.

4-Nitro-2,3,5,6-tetrachloropyridine (32) from sulphilimine **12b**. Yellow oil (24% yield); R_f=0.82 (CH_2Cl_2); IR ν_{max} ($CHCl_3$)/cm^{-1}: 1337 (s, NO_2) 1563 (s, NO_2); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 121.4 (C3 and C5) 147.81 (C2 and C6) 155.1 (C4); MS (*m/z*) (EI) 260, 262 (M_+, 9%, 12%) 230, 232 (M-NO, 20, 24) 214, 216 (M-NO_2, 20, 24) 179, 181 (M-Cl-NO_2, 5, 7) 139 (100); HRMS: $C_5N_2Cl_4O_2$ requires 259.871388, found 259.87189, dev. 1.9 ppm. 4-(S,S-Diphenylsulphoximino)-2,3,5,6-tetrachloropyridine (40%) was also obtained as a by-product; mp 158-159 ^oC; R_f=0.63 (CH_2Cl_2); Anal: found, C, 47.36, H, 1.87, N, 6.30, $C_{17}H_{10}N_2Cl_4OS$ required, C, 47.24, H, 2.33, N, 6.48%. ^1H NMR ($CDCl_3$, 300MHz) δ 7.45-7.60 (6H, m, ArH) 8.00-8.11 (4H, m, ArH); MS (*m/z*) (EI) 430, 432 (M_+, 12%, 16%) 397 (M-Cl, 2) 305, 307 (M-SOPh, 2, 2) 270, 272 (7, 7) 218 (Ph_2SON, 13) 202 (12) 186 (SPh_2, 13) 154 (20) 125 (SOPh, 100) 109 (SPh, 34) 77 (Ph, 58); HRMS: $C_{17}H_{10}N_2SCl_4O$ requires 429.926797, found 429.92741, dev.1.4 ppm.

2-Nitro-3,4,5,6-tetrachloropyridine (42) from sulphilimine **12c**. Yellow oil with a caramel odour (63% yield); R_f= 0.79 (CH_2Cl_2); MS (*m/z*) (EI) 262,260 (M_+, 13%, 12%) 230, 232 (M-NO, 61, 49) 214, 216 (M-NO_2, 94,75) 181, 179 (M-Cl-NO_2, 47); HRMS: $C_5N_2Cl_4O_2$ requires 259.871388, found 259.87094, dev. 1.7 ppm. 2-(S,S-Diphenylsulphoximino)-3,4,5,6-tetrachloropyridine (19%) was obtained as a by-product; R_f=0.68 (CH_2Cl_2); ^1H NMR ($CDCl_3$, 300 MHz) δ 7.48-7.59 (6H, m, ArH) 8.05-8.11 (4H, m, ArH); MS (*m/z*) (EI) 430, 432 (M_+, 1%) 353, 355 (M-Ph, 4, 5) 305, 307 (M-SOPh, 2, 1) 202 (Ph_2SO, 2) 125 (PhSO, 12) 109 (SPh, 16) 77 (Ph, 20): HRMS: $C_{17}H_{10}N_2SCl_4O$ requires 429.926797, found 429.92741, dev. 1.4 ppm.

4-Chloro-6-nitropyrimidine (35) from sulphilimine **15b**. Oil (4%), co-elutes with diphenylsulphone; R_f= 0.42 (CH_2Cl_2); ^1H NMR ($CDCl_3$, 300 MHz) δ 8.17 (1H, s, ArH) 9.19

(1H, s, ArH) ppm. GC-MS (EI): m/z 159, 161 (M^+, 3%, 1%), 129 131 (M-NO, 5, 2), 112, 114 (100, 35), 86 (30); HRMS: $C_4H_2N_3ClO_2$ requires 158.983554, found 158.98303, dev. 3.3 ppm.

4-Nitro-2,3,5,6-tetrafluoropyridine (36) from sulphilimine **19b**. Yellow oil with a caramel odour (21% yield); R_f= 0.88 (CH_2Cl_2); IR ν_{max} ($CHCl_3$)/cm^{-1}: 1581 (s, NO_2) 1370 (s, NO_2); ^{19}F NMR ($CDCl_3$, 376.4 MHz) δ 22.40 (F3 & F5), 76.40 (F2 & F6); MS (*m/z*) (EI) 177 (M-F, 3%) 158 (M-F_2, 31), 166 (M-NO, 2), 150 (M-NO_2, 6) 139 (M-3F, 100). 4-(S,S-Diphenylsulphoximino)-2,3,5,6-tetrafluoropyridine (16%) was also obtained as a by-product; R_f=0.61 (CH_2Cl_2); ^{19}F NMR ($CDCl_3$, 376.4 MHz) δ 13.08 (F3 & F5), 70.76 (F2 & F6); MS (*m/z*) (EI) 366 (M^+, 24%) 347 (M-F, 1) 241 (M-SOPh, 9) 222 (M-F-SOPh, 4) 202 (5) 154 (Ph_2, 20) 125 (SOPh, 97) 109 (SPh, 39) 77 (Ph, 100).

2-Nitro-3,5,6-trifluoropyridine (38) from sulphilimine **20b**. Yellow oil (74% yield); R_f= 0.65 (CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.65-7.76 (1H, dd, ArH) ppm; ^{19}F NMR ($CDCl_3$, 376.4 MHz) δ 42.13, 45.67 (F3 & F5), 79.47 (F6); MS (EI): 178 (M_+, 5%) 159 (M-F, 3) 148 (M-NO, 2) 139 (M-F_2, 100) 132 (M-NO_2, 7) 111 (58); HRMS: $C_5HN_2F_3O_2$ requires 177.999012, found 177.99954, dev. 2.9 ppm. No sulphoximine by-product was observed.

2-Chloro-3,4-dinitropyridine (41) from sulphilimine **28**. Yellow oil (9% yield); R_f=0.54 (CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 300MHz) δ 8.02-8.08 (1H, d, ArH, *J* = 12 Hz) 8.83-8.87 (1H, d, ArH, *J* = 12 Hz); GC- mass spectrum (EI) 203,205 (M_+, 39%,12%) 84 (100), $^{12}C_5{}^1H_2{}^{14}N_3{}^{35}Cl{}^{16}O_4$ requires 202.973383, found 202.97373, dev. 1.7 ppm. No sulphoximine by-product was observed.

The following nitro derivative was also prepared (by oxidation of sulphilimine **13b**) but was isolated in an impure state (owing to inadvertent contamination with vacuum oil) and could not be completely characterised:

2-Chloro-6-nitropyrazine (34). Yellow oil (60%) R_f= 0.59 (CH_2Cl_2), ^{1}H NMR ($CDCl_3$, 300 MHz) δ 9.21 (2H, m, ArH). The oxidation co-product, diphenylsulphone, was also obtained (69%).

The following sulphilimines were oxidised by mCPBA by the general method given above, but no nitro products could be isolated (presumed to have decomposed on chromatography): (S,S-Diphenylsulphilimino)pyrazine, **23**; 2-(S,S-diphenylsulphilimino)-5-nitropyridine, **10**; 2-chloro-4-(S,S-diphenylsulphilimino)pyrimidine, **17**; 2-chloro-(S,S-diphenylsulphilimino)-6-(*n*-propoxy)-1,3,5-triazine, **21**, 2,5,6-trichloro-4-(S,S-diphenylsulphilimino)pyrimidine, **18**. In the cases of the last two compounds, the corresponding sulphoximines were isolated (10% and trace yields resp.); with the others, diphenylsulphone was the only identifiable product.

Preparation (attempted) of an aliphatic nitro compound via a phosphinimine intermediate:

***N*-benzyl triphenylphosphinimine (30).** To a jacketed vessel (50 mL) fitted with a thermometer, serum cap and magnetic follower, aminotriphenyl phosphine bromide (1.99 g, 5.54 mmol) was added and THF (50 mL) added by syringe. The resultant suspension was cooled to –10 ºC by an external water/glycerol circulator. N-Butyl lithium (2.50 mL, 2.5 *M* soln. in n-hexane, 6.25 mmol) was added dropwise by syringe over 30 min. The resultant solution was stirred for 20 min and the suspension cleared. Benzyl chloride (0.71 g, 5.61 mmol) in THF

(10 mL) was added by syringe over 30 min. Stirring was continued for 14 hr and the reaction allowed to warm to room temperature. The solvent was removed *in vacuo* to afford a yellow liquid that crystallised on standing. This was extracted with n-hexane (2 x 20 mL). The hexane layer was reduced in volume and washed with a mixture of ethyl acetate and methanol (10 mL, 5:1 vol./vol.) and a solid formed, this was filtered off and corresponded to triphenylphosphine oxide. The filtrate was reduced in volume to afford a pale yellow oil which solidified on standing, mp 199-200 ºC; this corresponded to N-benzyl-triphenylphosphinimine (0.212 g, 10% yield). ^{1}H NMR ($CDCl_3$, TMS, 60 MHz) δ 4.0 d (1H, N-C$\underline{H}_a$CH_b-Ar), 4.3 d (1H, N-CH_aC$\underline{H}_b$-Ar), 7.1 s (5H, Ar), 7.4-8.0 m (15H, Ar). MS (EI): 366 (M^+-1), 290, 276, 262, 182, 108, 91.

The following aliphatic halides were investigated under similar reaction conditions outlined above but none of the reactions yielded the corresponding aliphatic phosphine imines: 1-Iodoadamantane, 2-iodo-2-methyl-propane, iodo-cyclohexane, 1-chloro-2-butene.

Oxidation of *N*-benzyl triphenylphosphinimine (30)

Using Oxone (potassium peroxymonosulphate, DuPont Inc.): To a round bottom flask (500 mL) fitted with a pressure equalising funnel, thermometer and magnetic follower, acetone (200 mL), water (60 mL) and N-benzyl triphenylphosphinimine **30** (0.36 g, 0.1 mmol) were added. The resultant mixture was stirred and cooled to 0 ºC. To the dropping funnel oxone (17.56 g) and water (100 mL) were added and the mixture agitated to ensure mixing. The suspension was added over 3 h at 0 ºC and then allowed to warm to room temperature overnight.

The reaction mixture was filtered and the filtrate was washed with diethyl ether (3 x 100 mL) and the organic extracts were combined and washed with saturated sodium chloride solution. The organic layer was separated off, reduced to half its original volume and dried over magnesium sulfate. The sample was filtered and the solvent removed to afford yellow viscous oil. HPLC analysis of the sample using a reversed phase column (RP-18, Merck) with a mobile phase of acetonitrile:water (1:1 vol./vol.) showed the presence of two materials, which were identified as triphenylphosphine oxide and benzaldehyde **45** by comparison against authentic materials.

Using ozone: To a three neck round bottom flask fitted with a serum cap, thermometer and a dry column freshly distilled dichloromethane (100 mL) was added and cooled to –78 ^{o}C. Dry ozone was bubbled through the solvent for 30 min. and the solution turned blue in colour. N-benzyl triphenylphosphinimine **30** (0.26 g, 0.74 mol) in dichloromethane (5 mL) was added dropwise by syringe to the ozone solution. Stirring was continued for 10 min. and then nitrogen was bubbled through the solution and the reaction mixture allowed to warm to room temperature. The solvent was removed *in vacuo* to afford pale yellow viscous oil (0.321 g). HPLC analysis of the sample using a reversed phase column (details as above) showed the presence of two materials, which were identified as triphenylphosphine oxide and benzaldehyde by comparison against authentic materials.

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References and Notes

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