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The Mechanism of the *Mitsunobu* Azide Modification and the Effect of Additives on the Rate of Hydroxyl Group Activation.

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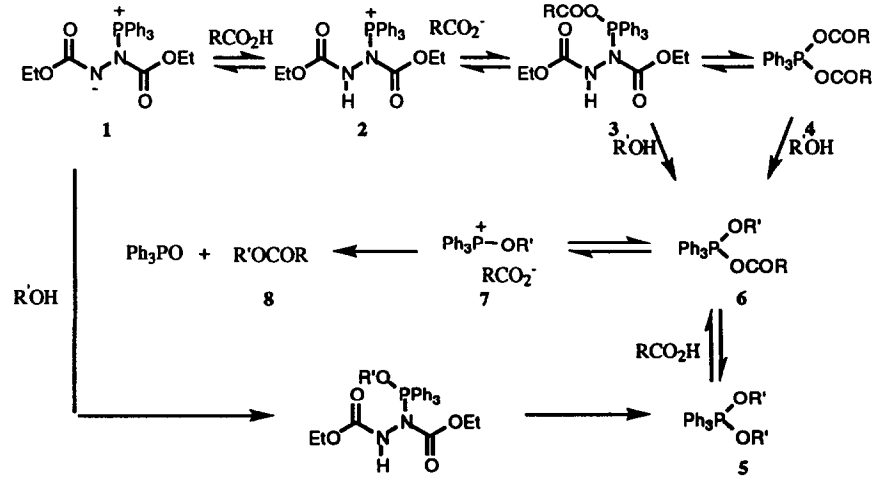
Abstract: The Mitsunobu azide modification has been studied by NMR using a hindered alcohol and the principle intermediates involved have been tentatively identified. The accelerated hydroxyl group activation in the presence of hydrazoic acid or of catalytic quantities of phenol gives us an insight into the reactivity of some of the intermediates involved in these reactions.

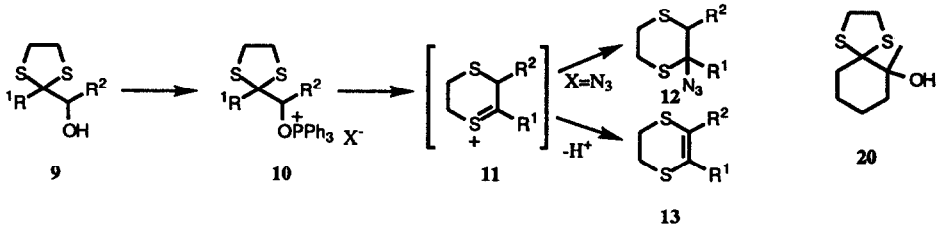
The mechanism of the *Mitsunobu* esterification[1] reaction has been the subject of numerous papers[2-4] over the last decade. New results[5,6] which clarify the system indicate that the mechanism is complex and many intermediates are involved. Some of these are probably transients which are of no consequence to the overall picture. The importance of this reaction in modern chemistry is high and justifies the interest shown. The ready and efficient inversion of stereochemistry at secondary hydroxyl groups is very important for the stereoselective syntheses of many important optically active hydroxylated compounds. At first it appears to be an unusual reaction and many of the intermediates represent an interrelation between the neutral five-coordinate phosphoranes and phosphonium salts. Scheme 1 outlines many of the possible intermediates generated during this reaction and the effects of adding acid or alcohol to the ylide first.



Scheme 1

Recent studies[5,6] on the *Mitsunobu* esterification reaction with triphenylphosphine indicate that alkoxyphosphonium **7** and probably (acyloxy) alkoxyphosphoranes **6** are involved although it is not known which species actually reacts to form the ester. Probably all of the intermediates indicated in scheme 1 exist at some stage and many are probably in equilibrium (**5**,**6**,**7**) at the time of the substitution reaction to form product **8**. In fact, many of the other intermediates have been observed (e.g. **2**) by NMR spectroscopy. The analogous reaction using tributylphosphine (TBP) does not appear to have the same stereoselectivity as that using triphenylphosphine (TPP) probably because activation of the carboxyl group and its subsequent reactivity competes successfully with the process of alcohol activation[7,8]. The TPP/DEAD ylide **1** reacts with benzoic acid to form benzoic anhydride slowly whereas with the TBP/DEAD ylide, the reaction to form the anhydride is much faster. Thus the positions of the equilibria appear to be different as are reactivities of the various systems. These differences have been attributed to the relative stabilities of the analogous phosphonium ions[7]. Overall these studies lend support to the original mechanism proposed by *Mitsunobu* in which the critical species is an alkoxyphosphonium salt (e.g. **7**).

The azide modification, where the carboxylic acid of the esterification reaction is replaced by hydrazoic acid, has also been much used for the substitution of a hydroxyl group by an azido group[1] which normally serves as a precursor for amino compounds. No study of the mechanism for this reaction has been forthcoming, perhaps because similar intermediates, to those of the esterification reaction, were assumed. It is also difficult to obtain hydrazoic acid solutions of sufficient purity for such a study. No anhydride is possible, however, so any intermediates derived from the reaction of the ylide with hydrazoic acid should be stable if no excess of phosphine is available. Our studies show that the mechanism is similar but that at least one more stable intermediate is involved.



9 **10** **11** **12** **13** **20**

Scheme 2

Our attention was drawn to the problem of the mechanism during a study of the 1,2-sulphur migration of 2-hydroxyalkyldithiolanes **9**. The hydroxyl group of **9** can be activated to leave by several reagents. The migration occurs immediately upon activation and no activated intermediate is observed[9]. The mechanism is thought to involve a stabilised carbocation **11** which we also hoped to trap. It has previously been possible to trap this carbocation, albeit in moderate yield, via intramolecular cyclisation but not by halide or pseudohalide ions such as chloride or azide. The TPP *Mitsunobu* ylide **1** is able to activate the hydroxyl group of **9** but only very slowly and, in the absence of a suitable nucleophile, the rearrangement proceeds with the formation of the dithiin **13** over several days. If benzoic acid is added no benzoate is formed even though the benzoate ester of compound **9** is perfectly stable. The rate limiting step is the reaction of the alcohol with a phosphorus species with formation of the activated intermediate. The relative rate of this reaction could be studied by observing the formation of the rearranged product by, for example, ^{1}H NMR. In the presence of hydrazoic acid, however, migration occurs and the intermediate carbocation is trapped as the azide **12**, a mixture of diastereoisomers[10].

Thus we had at hand an alcohol which reacted only very slowly with the *Mitsunobu* ylide and where the assumed intermediate **10** was not observed by ^{31}P NMR because it immediately underwent rearrangement.

When hydrazoic acid was included in the mixture, the formation of the products, a mixture of the normal unsaturated rearrangement product **13** (1-5%) and saturated azide **12** (52-60%)[11], was over within less than 3 minutes. This mixture results from incomplete reaction with azide and competing proton loss from the carbocation **11** to form the dithiin (scheme 2). Either the acid was catalysing the reaction by protonating and activating the ylide **1** or some other intermediate was being formed which was more reactive to the alcohol than is the ylide. The relatively unhindered 2-octanol reacts under these conditions almost instantly not allowing enough time to observe intermediates formed.

As has been adequately demonstrated by previous studies on the *Mitsunobu* reaction, ^{31}P NMR is a very powerful technique for observing the central phosphorus atom involved in this reaction. Strangely the solvent used has almost always been THF which has the possible distortive effect on the stability of ionic species because of its ligand properties. We observed that prolonged (>2h) contact between these phosphines and deuteriochloroform produced extra peaks in the NMR probably due to phosphonium salts resulting from the reaction of the two species. TBP reacted more rapidly with this solvent but still relatively slowly. A mixture of DEAD and TPP, in chloroform, produced a single peak at +44.9ppm (lit.[2] δ+44.8, $CDCl_3$), typical of a phosphonium species. On slowly adding a 1.4M solution of hydrazoic acid in benzene this signal was shifted to lower field and broadened (maximum downfield shift δ+52.3ppm). This we assume to be a result of the protonation of the ylide. This downfield shift has been observed by other groups on adding acids so we do not attribute this entirely to solvent effects. At the same time a peak appeared at δ-58.8ppm and after the addition of 2 equivalents of hydrazoic acid almost all of the protonated ylide had disappeared and the spectrum was again simple with a single peak at δ-53.5ppm.

The dialkoxytriphenylphosphoranes have ^{31}P chemical shifts in this region (δ-45- -65ppm)[2,5] and we are of the opinion that the signal at δ-53.5ppm represents the diazide **16** and that the signal at δ-58.8ppm is due to a phosphorane with one azido group and one DEAD ligand **15**. We suspect that the chemical shift dependence upon the quantity of hydrazoic acid added could be due to an equilibrium between monoazide **15** and diazide **16**, although because we were adding benzene, some solvent effects cannot be ruled out. The addition of the alcohol **9** to this mixture resulted in the disappearance of this species and the formation of triphenylphosphine oxide. Probably one or both of the azido groups are replaced by the alkoxide and the reaction proceeds rapidly to form the observed products.

Parallel studies using ^{1}H and ^{13}C NMR indicate that in the ylide two distinct ethyl groups exist (only one amide carbonyl was observed in the ^{13}C spectrum because the other is enolised) and that on adding hydrazoic acid (2 equivalents) these collapsed to form equivalent ethyl ester groups. ThisOn adding the alcohol **9** the formation of the expected products **12** and **13** could be clearly seen[12] (see also experimental part). No further changes in the signals due to DEAD were observed justifying the assignment of structure **15** to the intermediate. Similar results were obtained in the ^{1}H NMR when ylide was treated with phenol to form **17** (R=R'=Ph)

This assumed diazido intermediate **16** is much more reactive than the ylide **1.** Although it could be argued that this species is in equilibrium with the protonated ylide we believe that the former is the case since two equivalents of hydrazoic acid were necessary to complete the conversion to the intermediate observed. With more reactive alcohols the order of addition may have some effect upon the intermediates present. The

dialkoxide could be directly attacked to form products or some other intermediate could intervene. In order to study this aspect the ylide was reacted, in $CDCl_3$, with phenol to form the diphenoxide **17** (R=Ph) which was observed by ^{31}P NMR at -64.5ppm (lit.[2] δ-65.5 in THF). This diphenoxide is not readily attacked, at the activated ring carbon atom, by nucleophilic species such as azide. On adding hydrazoic acid a new peak at δ+66.1ppm was observed indicative of a phosphonium ion[5,6]. The addition of phenol to the diazide **16** produced the same species which we assume to be **19** (R=Ph). An analogous moiety was not observed with the alcohol **9** probably because, as is usual, the activated hydroxyl is immediately displaced by intramolecular or intermolecular nucleophiles. These results are analogous to those obtained for the esterification reaction using alcohols of low reactivity at the substitution step. Tertiary alcohol **20**[13] was unreactive to the ylide **1** or diazide **16**.

To further test the reactivity of phosphorane intermediates we reacted diphenoxytriphenylphosphorane **17** (R=Ph) with the hindered alcohol **9**[14]. The formation of rearrangment product **13** was greatly accelerated indicating again a greater reactivity for this species, which could also have been in equilibrium with the phenoxytriphenylphosphonium phenoxide. As little as 4mol% of phenol caused a large increase in the rate of formation of the product **13**. After 2h, the reaction without phenol had advanced only 10% whereas over the same period that with phenol (4mol%) was 70% complete. Ligand exchange seems to be more rapid than reaction of the ylide with the hindered alcohol which has to approach a hindered phosphonium ion having the bulky DEAD ligand attached. The species which undergoes this exchange is not known and could be a phosphorane or an oxyphosphonium salt. The presence of relatively stable anionic counterions would be expected to increase the concentration of the important oxyphosphonium which then reacts to form products.

Additon of benzoic acid to a mixture of the ylide **1** and alcohol **9** caused the reaction to stop altogether. Ligation of the phosphorus atom by benzoic acid or further stabilisation of the protonated ylide impedes attack by the alcohol and the reagents are consumed by the formation of benzoic anhydride.

Another unreactive alcohol, which has also been used in previous studies, is neopentyl alcohol. It has been observed that this alcohol reacts rapidly with TPP ylides to form a stable dialkoxyphosphorane which is of relatively low reactivity to nucleophiles. In this case the activated hydroxyl is still not very reactive and only intermolecular processes are possible. In chloroform, at room temperature, neopentyl alcohol reacted only slowly with the TPP/DEAD ylide (δ44.6ppm) to form only the dialkoxyphosphorane **5** (R'=neopentyl) which gave a signal in the ^{31}P NMR at δ-57.8ppm. This reaction was not complete (80%) after 1.5h at room temperature. This result highlights a problem which has to be addressed which is the effect of solvents on reaction rates and their effect upon the stability of the intermediates involved in these reactions. To this mixture was added hydrazoic acid (1eq) and within 4 min. all of the dialkoxyphosphorane and ylide was consumed and a single peak was formed at +62.2ppm (^{31}P NMR) indicative of an alkoxytriphenylphosponium azide. By mixing TPP/DEAD ylide with hydrazoic acid a solution of the species showing a single peak at -57.6ppm in the ^{31}P NMR. Neopentyl alcohol (1eq.) was added and the ^{31}P NMR again measured. A single peak was recorded at +62.6ppm corresponding to the species produced in the previous experiment. It appears therefore that in the presence of the azide ion, alkoxyphosponium species are stable in solution with respect to any other possible phosphoranes.

Finally we studied the effect of using the ylide derived from tributylphosphine (TBP) instead of TPP. Using this ylide, alcohol **9** was converted to dithiin **13** in 65% isolated yield, in 2h. This indicates that the TBP ylide is much more reactive although considering stability factors the opposite should be the case[15]. We assign

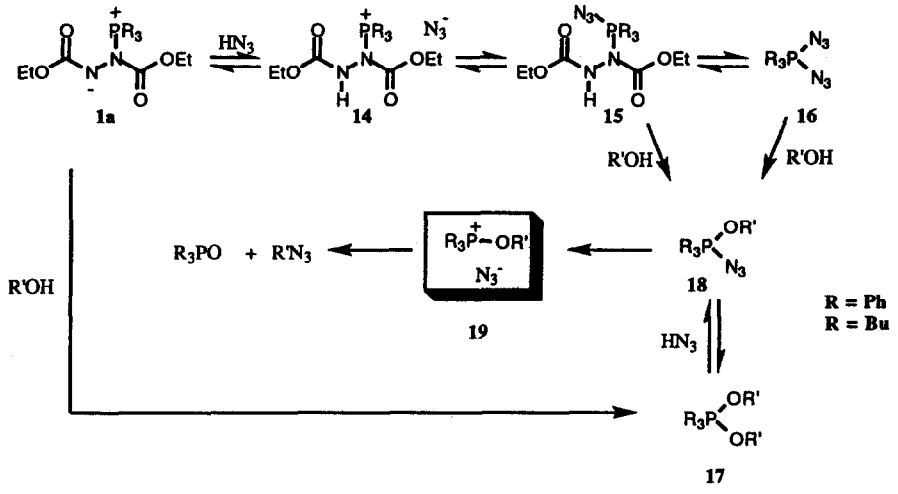
this greater reactivity to the lower steric hindrance experienced by the attacking alcohol when approaching the ylide. The activation of the acid moiety in some Mitsunobu esterifications using TBP may also be due to steric effects.

A study of the intermediates involved in this reaction by ^{31}P NMR indicate a very different picture to that painted by the analogous study with TPP. On mixing DEAD and TBP at 0°C in chloroform only the expected ylide (**1a**, R=Bu) (δ+67.3ppm, lit.[7] +66.8 in THF using diisopropyl azodicarboxylate) and a small amount of tributylphoshine oxide (TBPO) δ +49.4 (lit.[7] +46.9 in $CDCl_3$ at 25 °C; +43.9 in THF at 0°C) was formed as was observed by Jenkins et al[7]. On adding hydrazoic acid (2eq.) all of the ylide peak disappeared, no high field signals were observed and only two peaks were evident at δ+78.2ppm and δ+60.2ppm. The addition of phenol (1eq.) to this mixture afforded only one species which shows a resonance at δ +104.7ppm. When phenol (2 eq.) was added to a solution of the ylide, no signals in the phosphorane region were observed only a broad peak at δ+95.3ppm and another sharper signal at δ+68.4ppm which appears to be a shifted ylide signal. On adding hydrazoic acid (1eq.) the spectrum simplified to the signal at δ +104.3ppm which we assign to the phenoxytributylphosphonium azide (**19**, R=Bu, R'=Ph). Alkoxytributylphosphonium species show signals at much lower field in the ^{31}P NMR compared to their alkoxytriphenylphosphonium counterparts.

In a previous ^{31}P NMR study using THF as solvent dialkoxytributylphosphoranes had been observed to form rapidly when the ylide was reacted with an unreactive alcohol such as neopentyl alcohol. We repeated this experiment in chloroform (1eq. of neopentyl alcohol) and found that reaction was not very rapid (after 30min. at 0°C and 10min. at room temperature no significant changes in the spectrum were evident), no observable quantities of dineopentoxytributylphosphorane or alkoxytributylphosphonium was formed. Immediately on adding 1 equivalent of hydrazoic acid, however, a single peak was produced at δ+98.3ppm which we assign to neopentoxytributylphosphonium azide. The addition of another equivalent of hydrazoic acid did not alter the spectrum. The formation of neopentyl azide from this species was slow since the relative intensities of this signal to that of TBPO did not change significantly.

Finally some experiments were carried out using the alcohol **9**. We knew that this alcohol reacted with the DEAD/TBP ylide and we did not carry out the direct reaction between the two in an NMR experiment. Surprisingly our experiments had shown that alcohol **9** reacted much more rapidly with the DEAD/TBP ylide than neopentyl alcohol. For the DEAD/TPP system the opposite reactivity was observed. These results are difficult to explain but were totally repeatable. Although the reactions of the phosphonium species from alcohol **9** and neopentyl alcohol with azide cannot be compared mechanistically, we considered it interesting to observe the disappearance of the intermediates involved when azide was present. Addition of 1 equivalent of alcohol **9** to the reagent formed by reacting the ylide with 2 equivalents of hydrazoic acid, at 0°C, resulted in the immediate formation of more TBPO and the appearance of a peak at δ+98.0ppm. The reaction to form products was relatively slow at this temperature and considerable quantities of what we believe to be the alkoxyphosphonium azide (+98.0ppm) persisted during 20min. We then warmed the reaction to RT and the reaction was complete within a further 15min. We next reacted a solution of phenoxytributylphosphonium azide (1eq. of phenol: 2eq. hydrazoic acid) with 1 equivalent of the alcohol **9** to see if similar intermediates were observed. Immediately upon addition of **9** the TBPO peak, observed at δ+51.7ppm due to solvent induced shifts, increased slightly in intensity and the signal due to the phenoxyphosphonium azide at δ+104.5ppm (**19**, R=Bu, R'=Ph) was accompanied by a smaller peak at δ +97.8 ppm which corresponded to the signal at δ+98.0ppm observed in the previous experiment. The ratio of phenoxide to alkoxide remained essentially constant (5-6:1 respectively). In

these latter two experiments it appeared that we had increased the rate of formation of the alkoxyphosphonium azide to such an extent that the rate determining step had become the rearrangement to form the ring expanded stabilised carbonium ion **11**. Under these conditions the alkoxyphosphonium from DEAD/TPP/9/HN_3 was never observed.



Scheme 3

Scheme 3 shows the probable course of the azide modification as indicated by our study. This is analogous to the mechanism for the Mitsunobu esterification reaction. A key step is the reaction of the alcohol with the ylide or other activated phosphorus species. The TPP ylide appears to be a bulky electrophile and many reactions may fail due to its low reactivity. A possible way round this problem would be the substitution of the diazodicarboxylate ligand with smaller but weakly nucleophilic ligands such as phenoxidewhich are then exchanged by the alcohol more readily. TBP ylides are more reactive than TPP ylides and in some cases represent a useful alternative to TPP ylides. In chloroform the corresponding tributylphosphoranes are not observable and perhaps are only transitory intermediates on the way to the tributylphosphonium species which appear to be more stable than triphenylphosphonium species. One disadvantage in the use of the TBP ylide in the esterification reaction is that the formation of anhydrides is also accelerated and may result in esterification with retention. This may also be the result of the rapid formation of the highly reactive tributylphosphonium intermediate.With reactive alcohols use of the correct sequence for adding the reagents, adding the acid last, could reduce or eliminate this problem.

Experimental Section

Reagent quality solvents were distilled prior to use. Diethyl azodicarboxylate (DEAD) and deuterochloroform were dried by standing over molecular sieves. Tributylphosphine was distilled under argon prior to use. Triphenylphosphine was recrystallized successively from a solution of ethanol and petroleum ether 40/60. Anhydrous dichloromethane was prepared by distillation from phosphorus pentoxide under argon. Benzene was dried by standing over sodium wire. Anhydrous diethyl ether was prepared by distillation from sodium/benzophenone ketyl under argon. Column chromatography was performed using Silica gel Merck 60 H (Art. 7736) and for analytical TLC aluminum-backed silica gel Merck 60 F_{254} plates . Mass spectra (MS) and exact masses (HRMS) were obtained using a Kratos MS 25 RF and AEI/VG MS 9 mass spectrometers. Infra-

red spectra (IR) were recorded on a Buck Scientific Mod. 500 infra-red spectrophotometer. ^{1}H, ^{13}C and ^{31}P NMR were recorded on a Bruker CXP300 spectrometer. Chemical shifts are reported as δ values relative to tetramethylsilane ($\delta_H = 0$ ppm), $CDCl_3$ ($\delta_C = 77.0$) or external 85% phosphoric acid ($\delta_P = 0$). HPLC analyses were performed using the following Merck/Hitachi components: L-600 A, L-4250, T-6300, D-6000 with a Lichrocart® 250-4, 5μm, Si 60 column at 30°C and UV detector at λ 223 nm. Literature procedures were used for the preparation of reported compound[9].

Preparation of 2,3-dimethyl-5,6-dihydro-1,4-dithiin 13 (R^1=R^2=Me) using DEAD/TPP and catalytic phenol. Diethyl azodicarboxylate (0.10ml, 0.64mmol) was added dropwise (2min.) to a stirred solution of dithiolane **9** (R^1=R^2=Me) (0.095g, 0.58mmol), triphenylphosphine (0.167g, 0.64mmol) and phenol (2mg, 0.02mmol, 4 mol%) in anhydrous benzene (2.9ml) under argon at room temperature. After 2h analysis by GC indicated about 70% reaction. After 3h the solvent was partially evaporated and the crude product was chromatographed on a silica gel column (eluent: pet. ether 40/60 : diethyl ether from 1:0 to 8:2) to afford, in order of elution dithiin **13** (0.057g, 67%) as a clear colourless oil with spectral data identical to that reported[9] and recovered dithiolane **9** (0.015g, 16%).

Preparation of 2,3-dimethyl-5,6-dihydro-1,4-dithiin 13 (R^1=R^2=Me) using DEAD/TBP. Diethyl azodicarboxylate (0.11ml, 0.68mmol) was added dropwise (2 min.) to a stirred solution of dithiolane **9** (R^1=R^2=Me) (0.101g, 0.62mmol) and tributylphosphine (0.17ml, 0.68mmol) in anhydrous benzene (3ml) at room temperature under argon. After 4h. the solvent was partially evaporated and the crude product was chromatographed on silica gel (eluent: pet. ether 40/60 : diethyl ether from 1:0 to 8:2) to afford compound **13** (R^1=R^2=Me) (0.057g, 64%) and starting dithiolane **9** (0.016g, 16%).

Preparation of 2-Azido-2,3-dimethyl-1,4-dithiane 12 (R^1=R^2=Me) using DEAD/TPP/HN_3[17] Diethyl azodicarboxylate (0.53 ml, 3.35 mmol) was added dropwise (5 min) to a stirred solution of **9** (0.500 g, 3.04 mmol), triphenylphosphine (0.878 g, 3.35 mmol) in anhydrous benzene (15ml) and hydrazoic acid[16] (2.4 ml of 1.4 M solution in benzene, 3.35mmol) under argon at room temperature (water bath), and stirring was continued for 3 days. The reaction mixture was evaporated and the crude product was chromatographed on a silica gel column (eluents: petroleum ether 40/60 : ethyl acetate from 1:0. to 8:2) to afford in order of elution **13** (0.004 g, 1%), as a clear colourless oil; spectral data identical to those reported[9]; **12** (0.346g, 60%) as a clear colourless oil; b.p. 100°C/0.9mm Hg (kugelrohr) two diastereoisomers in the ratio 6.0:1 as determined by HPLC using hexane at a flow rate of 1ml/min.; ν_{max} (film) 2980, 2920, 2110 (N_3), 1450, 1415, 1380, 1295, 1255, 1110, 1080, 860, 835 cm^{-1}; ^{1}H δ(300 MHz, $CDCl_3$) (major isomer[18]) 1.52 (3H, d J=7.1, Me-3), 1.60 (3H, s, Me-2), 2.64-2.71 (1H, m), 2.80-2.87 (1H, m), 2.82 (1H, s if irradiated at1.52ppm, H-3), 2.97 (1H, ddd J 15.8,10.4, 2.7), 3.16 (1H, ddd J 15.8, 10.4, 2.9) (minor isomer) 1.20 (3H,d J 7.2, Me-3), 1.64 (3H, s, Me-2), 2.84 (1H, s if irradiated at 1.20ppm); ^{13}C δ(75.47 MHz, $CDCl_3$) (major isomer) 17.3 (Me-3), 24.2 (C-5 or C-6), 24.9 (C-5 or C-6), 29.5 (Me-2), 43.3 (C-3), 69.4 (C-2), (minor isomer) 16.4 (Me-3), 24.2 (C-5 or C-6), 29.1 (C-5 or C-6), 31.2 (Me-2), 46.8 (C-3); m/z (EI^+) 189 (M^+), 161 (M^+-CH_2=CH_2), 146 (M^+-HN_3), 120, 118, 105, 92; HRMS calcd for $C_6H_{11}N_3S_2$: 189.0394, found: 189.0401; and recovered **9** (0.159g, 32%).

General Procedure for ^{13}C and ^{31}P NMR Experiments. Diethyl azodicarboxylate (31 μl, 0.198 mmol) was added dropwise to a solution of triphenylphosphine (52.0 mg, 0.198 mmol) in $CDCl_3$ (2 ml) under argon at room temperature in a 10mm NMR tube with rubber seal. The mixture was shaken and after 4 min the

^{31}P NMR spectrum was recorded. Hydrazoic acid[16] (283 µl of 1.4 M solution in benzene, 0.396 mmol) was added dropwise. The mixture was shaken and after 4 min the ^{31}P NMR spectrum was recorded again. The alcohol **9** (27 µl, 0.198 mmol) was added dropwise and the mixture was shaken. After 4 min the ^{31}P NMR spectrum was recorded again.

For the tributylphosphine experiments the phosphine (49 µl, 0.198 mmol) was added dropwise to a solution of diethyl azodicarboxylate (31 µl, 0.198 mmol) in $CDCl_3$ (2 ml) under argon at 0°C. The NMR spectra were recorded as for the triphenylphosphine experiments above but at 0°C.

For ^1H NMR experiments the above procedure was followed using solutions of triphenylphosphine (14.0 mg, 0.053 mmol) in $CDCl_3$ (0.5 ml) under argon in a 5-mm NMR tube with rubber seal. The stoichiometric quantities of reagent were added as for the ^{31}P studies.

Acknowledgments.

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11. Some starting material is also recovered even though all the phosphine has been converted to oxide. The experimental conditions described here were not optimised.
12. ^1H and ^{13}C NMR data: **TPP+DEAD** (ratio of areas for the two ethyl species 1:1) ^1H δ ($CDCl_3$, 300MHz) 0.942 (t, J 7.2Hz), 1.205 (t, J 7.2Hz), 3.735 (q, J 7.2Hz), 4.172 (q, J 7.2Hz). ^{13}C ($CDCl_3$) 166.15, 122.41, 121.05, 63.44, 59.48, 15.15, 14.16. **TPP+DEAD+HN_3** (1eq.) (ratio of areas for the two types of ethyl 2.6:1) ^{13}C ($CDCl_3$) 121.51, 120.16, 64.03, 61.81, 60.11, 14.80, 14.01. **TPP+DEAD+HN_3** (3eq.) ^1H δ ($CDCl_3$, 300MHz) 2.407 (t), 1.418 (t), 4.339 (q), 4.342 (q). **TPP+DEAD+HN_3** (3eq.)+9 ^1H δ ($CDCl_3$, 300MHz) 1.410 (t, J 7.1Hz), 4.339 (q, J 7.1Hz).
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15. For a discussion of effect of ligands on the relative stabilities of phosphoranes and phosphoniums see reference 7.
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17. This reaction when carried out on optically active (e.e. >97%) alcohol (+)-9 to give a mixture of diastereoisomers with $[\alpha]_D^{20}$=+163 (c 1.4, chloroform).
18. The major diastereoisomer is the *cis*-isomer with respect to the two methyl groups as shown by ^1H and ^{13}C and based upon analogous results for a similar compound (2-azido-3-methyl-2-phenyl-1,4-dithiane) for which we have an x-ray crystal structure[10].

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