Simple and Condensed β-Lactams. Part 11.[1] Reaction of some *p*-Nitrobenzyl (4-Oxoazetidin-1-yl) (triphenylphosphoranediyl)acetates and *p*-Nitrobenzyl (1-Oxoisoindolin-2-yl) (triphenylphosphoranediyl)acetate with Acetic Anhydride–Sulphoxide Reagents

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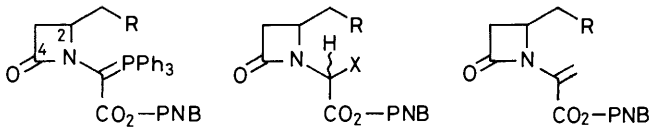
Reaction of the *p*-nitrobenzyl (4-oxoazetidin-1-yl)(triphenylphosphoranediyl)acetates (**1a** and **b**) with the acetic anhydride–DMSO reagent gave mixtures of the acetoxy (**2a** and **b**) and methylene derivatives (**5a** and **b**), the product ratio depending on the reaction temperature. *p*-Nitrobenzyl (1-oxoisoindolin-2-yl)(triphenylphosphoranediyl)acetate (**6**), on similar treatment, furnished the methylene derivative (**7**) exclusively while, with the acetic anhydride–diphenyl sulphoxide reagent, the acetoxy derivative (**8a**) was obtained. Type (**11**) pentacovalent phosphorus derivatives are thought to be the precursors of the acetoxy derivatives (**10**) [≡(**2**) or (**8a**)]. Although attempts at trapping the type (**13**) carbenes failed, some observations nevertheless suggest that these carbenes may be intermediates on the pathway leading from the pentacovalent phosphorus (**11**) to the acetoxy derivatives (**10**). The methylene derivatives (**26**) [≡(**5**) or (**7**)], on the other hand, are thought to arise *via* a Wittig-type reaction of the phosphoranes (**27**) [≡(**1**) or (**6**)].

The Woodward method[2] is one of the most widely used methods for the annulation of five- to seven-membered carbocyclic and heterocyclic rings to side *d* of azetidin-2-ones (Scheme 1). In some cases[2a–c, 3] the carbonyl group (Y = O) of

Scheme 1. A = carbon or hetero atom; Y = O, S; R = (substituted) alkyl or aryl, alkylthio, arylthio, *etc.*

the starting compound is generated *in situ* by Pitzer–Moffatt or related oxidations [dimethyl sulphoxide (DMSO)–dicyclohexylcarbodi-imide (DCC), DMSO–acetic anhydride, *etc.*][4] of a primary or secondary alcoholic function in the side chain. The yields reported for the latter variant are variable (28—85%)[2a–c,3] and this suggests that, in addition to oxidation of the alcoholic function, other competing reactions of the starting phosphonium ylides with the electrophilically activated DMSO might possibly take place.

In order to test the validity of this assumption, the β-lactam derivative (**1a**) which does not contain groups susceptible to oxidation by DMSO–acetic anhydride was allowed to react with this reagent. Two products were obtained, *viz.* the acetoxy



(**1**) (**2**) X = OAc (**5**)
(**3**) X = OH
(**4**) X = Cl

(1)—(5):† **a**; R = CO_2Me, **b**; R = CN

derivative (**2a**) as a mixture of diastereoisomers and the methylene derivative (**5a**), the ratio of these products depending on the reaction temperature: at lower temperatures compound (**2a**) was found to be the main product, while elevation of the temperature resulted in a shift of the product ratio in favour of the methylene compound (**5a**). (Thus, although esters are known to undergo, with phosphonium ylides, reactions leading to the formation of Wittig olefination products,[2e] no such reaction took place in the present case; at least a Wittig–Woodward-type ring closure was not the main course of the reaction.) The structures of the products were deduced from their i.r., ^1H n.m.r., and mass spectra, and corroborated by independent syntheses. Thus, compound (**2a**) was obtained by *O*-acetylation of the hydroxy derivative (**3a**) [which is an intermediate of the synthesis leading to compound (**1a**); see ref. 13], while compound (**5a**) was obtained by allowing compound (**1a**) to react with formaldehyde.

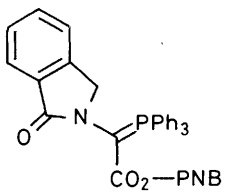
Similarly, the nitrile (**1b**) gave a mixture of compounds (**2b**) and (**5b**) when treated with DMSO–acetic anhydride.

[In this case the acetoxy derivative (**2b**) could not be obtained in sufficiently pure form to analyse correctly‡ but, as shown by their ^1H n.m.r. spectra, the samples of compound (**2b**) were only slightly contaminated.]

The exocyclic methylene groups of the products (**5**) obviously originate from methyl groups of DMSO. In agreement with this, compound (**5a**) was not formed when DMSO was replaced by diphenyl sulphoxide, the only product obtained from compound (**1a**) in this case being the acetoxy derivative (**2a**).

The isoindoline derivative (**6**), a γ-lactam, reacts similarly: with DMSO–acetic anhydride the methylene derivative (**7**) is formed [but, in contrast to the case of the β-lactam derivatives (**1a** and **b**), no acetoxy derivative (**8a**) is formed] while the

† All compounds described in the present communication are racemic. PNB = *p*-nitrobenzyl throughout this paper.
‡ *O*-Acetylation of the hydroxy derivative (**3b**) did not lead to an analytically pure sample of compound (**2b**), either.



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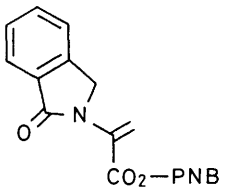

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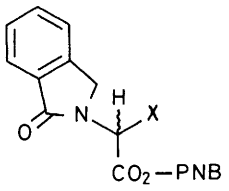


(8) a ; X = OAc
b ; X = OH
c ; X = Cl

acetoxy derivative (**8a**) results when DMSO is replaced by diphenyl sulphoxide.

Triphenylphosphine oxide was detected as the common co-product of all reactions studied. Diphenyl sulphide was detected as a further co-product of the reactions of compounds (**1a**) and (**6**) with diphenyl sulphoxide–acetic anhydride. Similarly, dimethyl sulphide is undoubtedly the co-product of the reaction of compounds (**1a** and **b**) with DMSO–acetic anhydride but no attempt was made towards its detection.

The sulphoxides and acetic anhydride are both essential for the reactions in question to take place: neither the acetoxy (**2a**), nor the methylene derivative (**5a**) were formed from the phosphonium ylide (**1a**) on treatment with DMSO–acetic acid, DMSO–acetic acid–sodium acetate, or acetic anhydride (in the absence of DMSO).

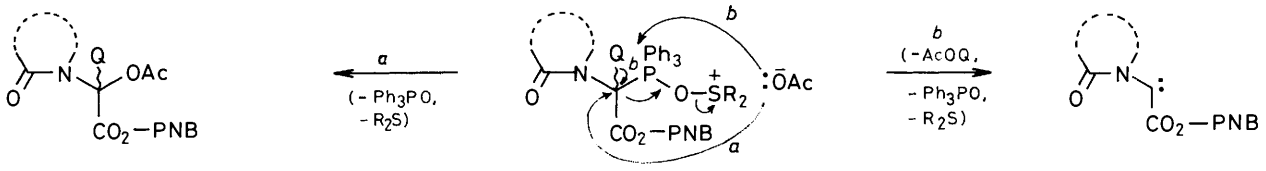
intermediates of the reactions. The assumption of such intermediates is in agreement with (i) the known formation of either α-acylated phosphonium ylides or α-acylated phosphonium salts from phosphonium ylides and acyclic anhydrides[2e,5] (depending on whether the starting phosphonium ylides contain α-hydrogen atoms or not)* and (ii) the ability of *O*-nucleophiles to convert phosphonium cations into pentacovalent phosphorus derivatives † which often immediately react further.[6]

$Ph_3P{=}CR{-}CO_2Me$ $AcCOCO_2{-}PNB$

(**14**) R = H (**16**)
(**15**) R = Ac

Attack of an acetate anion at the α-carbon atom should then lead, with elimination of Ph_3PO and R_2S, to the formation of the β-oxo esters (**9**). These would be cleaved, either in the reaction mixture or during work-up, to give the corresponding acetoxy derivatives (**10**) (Scheme 2, path *a*). In order to test this hypothesis, adduct (**18**) was prepared by allowing *p*-nitrobenzyl 2,3-dioxobutanoate (**16**)[7] to react with isoindolin-1-one (**17**)‡ and the product was *O*-acetylated to give compound (**19**). However, no *C*-deacetylation of the latter took place on treatment with DMSO–acetic anhydride and work-up of the resulting reaction mixture. Path *a* of Scheme 2 [with subsequent *C*-deacetylation of the resulting compounds (**9**)] is therefore ruled out as the mechanism of formation of the acetoxy derivatives (**10**). A further possibility would be formation of intermediates of type (**12**) rather than of type (**11**) (by reaction of the starting phosphonium ylides with the sulphoxides and acetic acid present in the anhydride, rather than with the anhydride itself). These would directly lead, *via* reaction *a*, to the acetoxy derivatives (**10**). This pathway is ruled out because treatment of phosphonium ylide (**1a**) with DMSO–acetic acid does not lead to the formation of the acetoxy derivative (**2a**).

Alternatively, attack of the acetate ion could take place at the carbonyl carbon atom of the Q = Ac group of compound (**11**) and result in elimination of acetic anhydride, triphenylphosphine oxide, and a sulphide, and formation of carbene (**13**) (Scheme 2, path *b*). The latter, by reaction with acetic acid (or even with



(**9**) Q = Ac
(**10**) Q = H [≡(**2**) or (**8a**)]

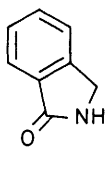
(**11**) Q = Ac
(**12**) Q = H

(**13**)

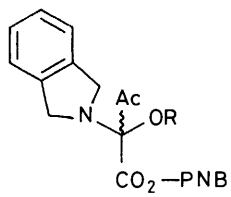
Scheme 2. R = Me, Ph

Speculations about the possible mechanisms of formation of the acetoxy derivatives (**2**) and (**8a**) led us to assume pentacovalent phosphorus derivatives of type (**11**) as the

acetic anhydride) and collapse of the resulting adduct (see Scheme 3) would lead to formation of the corresponding acetoxy derivative (**10**). Attack of the acetate anion at the



(**17**)

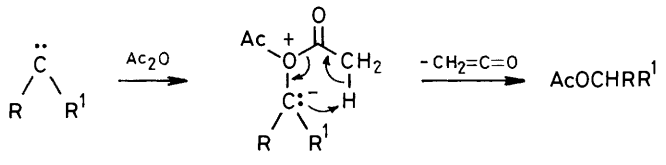


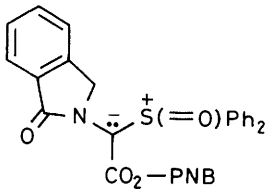
(**18**) R = H
(**19**) R = Ac

* Indeed, reaction of methyl triphenylphosphoranediylacetate (**14**) with acetic anhydride in DMSO afforded methyl 2-triphenylphosphoranediylacetoacetate (**15**) in good yield. (Heating of the latter with DMSO–acetic anhydride did not lead to the formation of methyl 2-acetoxy- or 2-methylene-acetoacetate.)

† We do not wish to speculate about the timing of formation of the α-C–Q and the P–O bonds during formation of the type (11) intermediates.

‡ The doubly activated carbonyl group of compound (**16**) reacted exclusively; for related reactions of compound (**16**)[7] with *N-un*protected α-lactams, see ref. 7.





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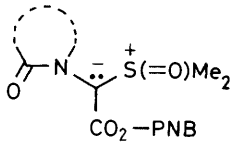

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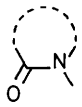
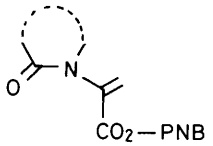
Scheme 3. R =  $R^1 = CO_2-PNB$

carbonyl carbon of the group Q = Ac of compound (**11**) should be favoured since this carbon atom is considerably less shielded against nucleophilic attack than the carbon atom α to the phosphorus atom. Moreover, the conversion of phosphine sulphides into phosphine oxides of opposite configuration by DMSO in strongly acidic solution [6a] (Scheme 4) appears to be quite analogous to reaction *b* of Scheme 2; in particular, the initially formed sulphur atom in Scheme 4 and the carbene (**13**)



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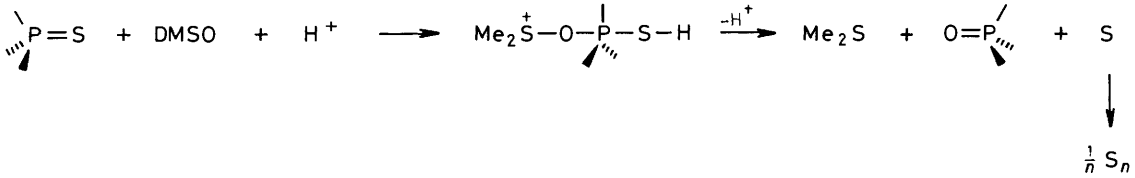


Scheme 4.

of Scheme 2 both have sextet electronic configurations. Support for the assumed subsequent conversion of the carbenes (**13**) into the corresponding acetoxy derivatives (**10**) *in the presence of sulphoxides* was nevertheless necessary since carbenes, *e.g.* (**20**), are known to react with sulphoxides to afford oxosulphonium ylides of type (**21**).[8]

:$C(CO_2R)_2$	$R_2\overset{+}{S}(O)\overset{-}{C}(CO_2R)_2$	$(EtO_2)_2CR'R''$
(**20**)	(**21**)	(**22**) R′ – R″ = N_2
a; R = Me	**a**; R = Et, R′ = Me	(**23**) R′ = OAc, R″ = H
b; R = Et		

The obvious precursors of carbenes of type (**13**), *viz.* the corresponding diazo compounds, being difficult to obtain, diethyl diazomalonate (**22**) was subjected to thermolysis in DMSO–acetic anhydride in the presence of copper(II) acetate. Diethyl acetoxymalonate (**23**) was obtained in good yield. The oxosulphonium ylide (**21**) [which was obtained by photolysis of compound (**22**) in DMSO[8]] is not an intermediate for the acetoxymalonate (**23**) since ylide (**21a**) is stable to heating with both acetic acid and acetic anhydride. When the above thermolysis experiment was carried out in the presence of added cyclohexene no product resulting from trapping of carbene (**20a**) by cyclohexene was detected.

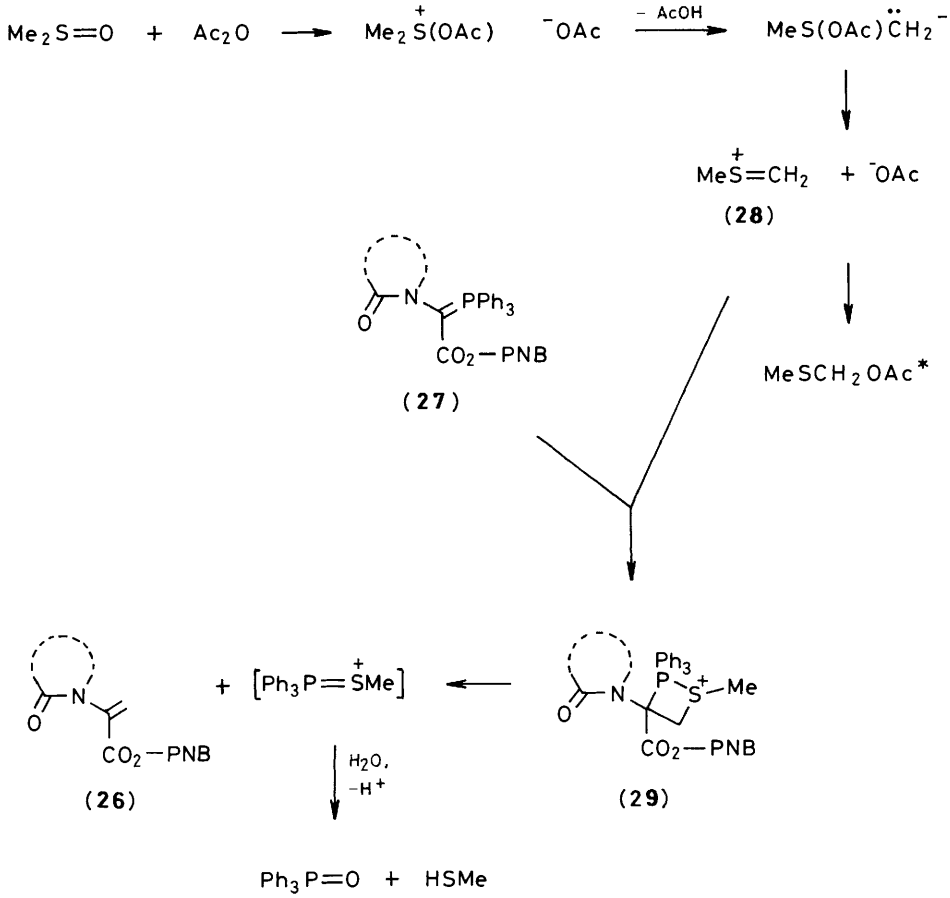
The above results demonstrate that formation of the acetoxy derivatives (**10**) [≡(**2**) or (**8a**)] from the corresponding phosphonium ylides (**1**) and (**6**) and DMSO or diphenyl sulphoxide–acetic anhydride *may* take place *via* carbenes of type (**13**), but *do not prove* the intermediacy of these carbenes. In order to prove this point, trapping of the suspected carbene intermediate of reaction (**6**) ⟶ (**8a**) was attempted. The most obvious trapping agent was the reagent diphenyl sulphoxide itself which, with the carbene, should afford the oxosulphonium ylide (**24**) but all our attempts to detect this product in the reaction mixture failed.* Our failure to trap the assumed type (**13**) carbene does not necessarily rule out the intermediacy of carbenes in the reactions in question since our failure might equally well be the result of the reactions (**13**) ⟶ (**10**) being of much higher rate than the attempted trapping reactions.

Several apparently reasonable pathways for the formation of the methylene derivatives (**26**) [≡(**5**) or (**7**)] necessitating the intermediacy of the same carbenes (**13**) may be formulated. Reaction of these carbenes with DMSO would yield the oxosulphonium ylides (**25**) from which several complex multistep pathways, involving rearrangements related to the thia-Stevens rearrangement,[9] could lead to the final products (**26**). In view of our findings mentioned above, *viz.* that (i) no oxosulphonium ylide (**24**) is formed from phosphonium ylide (**6**) on treatment with diphenyl sulphoxide–acetic anhydride and (ii) that oxosulphonium ylide (**21a**) is stable to heating with DMSO–acetic anhydride, the operation of these pathways appears, however, to be rather unlikely. We believe, therefore, that conversion of the phosphonium ylides (**27**) [≡(**1**) or (**6**)] into the methylene derivatives (**26**) [≡ (**5**) or (**7**)] involves reaction of the ylides with the cationic intermediates (**28**) of the Pummerer rearrangement of DMSO[10] to afford adducts (**29**) which subsequently collapse to give the methylene derivatives (**26**) (Scheme 5).

Experimental

M.p.s were determined in glass capillaries and are uncorrected. Unless otherwise stated, Kieselgel G and Kieselgel $PF_{254+366}$ were used as the adsorbents for medium-pressure column chromatography and t.l.c., respectively. The i.r. spectra were recorded with Spektromom 2000 (Hungarian Optical Works, Budapest) and Specord 75 (Zeiss, Jena, DGR) instruments. Unless otherwise stated, ^1H n.m.r. spectra at 100 MHz and ^{13}C n.m.r. spectra were obtained with a Varian XL-100 instrument at *ca.* 50 °C and room temperature, respectively, in $CDCl_3$ solution, using Me_4Si as the internal reference. 60 MHz ^1H n.m.r. spectra were recorded with a Perkin-Elmer R12

* Because of our failure to trap carbene (**20a**) with cyclohexene (see above) trapping of carbene (**13**) with the same reagent was not attempted.



Scheme 5. * Pummerer product

instrument. Electron ionization (EI) mass spectra and exact mass data were obtained at 70 eV with an AEI MS 902 instrument equipped with a direct insertion system. The chemical ionization (CI) mass spectrum was taken using an MM-12F1A mass spectrometer, and isobutane as the reagent gas.

Preparation of the Starting Phosphoranes (**1b**) *and* (**6**).—(*a*) Thionyl chloride (0.35 ml, 4.9 mmol) and a mixture of triethylamine (0.69 ml, 4.9 mmol) and tetrahydrofuran (THF) (5 ml) were successively added to a solution of (±)-*p*-nitrobenzyl 2-(2-cyanomethyl-4-oxoazetidin-1-yl)-2-hydroxyacetate (**3b**) (1.3 g, 4.1 mmol) (prepared by Mr E. Keskeny in this laboratory[11]) with continuous stirring and ice-salt cooling. The mixture was stirred for 45 min at 0 °C, diluted with cold CH_2Cl_2 (100 ml), washed successively with cold 0.1M aqueous HCl (50 ml) and cold brine (50 ml), dried ($MgSO_4$), and evaporated to dryness at room temperature. The resulting oily crude chloro derivative (**4b**) was taken up in dry THF (4 ml). Ph_3P (2.6 g, 10 mmol) was added and the mixture was stirred for 2 days at room temperature. CH_2Cl_2 was added, and the solution was washed with 10% aqueous Na_2CO_3 (2 × 30 ml), dried ($MgSO_4$), and evaporated to dryness. The residue was triturated with ether (50 ml) to give crystals (1.0 g, 43.5%, overall) of (±)-p-*nitrobenzyl* 2-(4-*cyanomethyl*-2-*oxoazetidin*-1-*yl*)-2-*triphenylphosphorane*-*diylacetate* (**1b**), m.p. 170—171 °C (from ethyl acetate); $\nu_{max.}$ 1 765—1 735 cm^{-1}; EI–MS (150 °C), *m/z* (rel. intensity, %) 563 (0.7; $M^{+\bullet}$; Found: M^+ 563.157. $C_{32}H_{26}N_3O_5P$ requires *M* 563.161), 496 (0.2, *M* − CH_2=$CHCH_2CN$), 477 (0.2), 411 (0.2, *M* − O–PNB), 360 [0.9, *M* − (CH_2=$CHCH_2CN$ + PNB)], 294 (8), 293 (11, *M* ± 270, 294 ± 1), 278 (52, $Ph_3PO^{+\bullet}$), 277 (93, 278 ± 1), 262 (100, $Ph_3P^{+\bullet}$), 261 (14, 262 ± 1), 217 (3), 215 (3), 201 (21, 278 − Ph), 199 [14, 277 ± (Ph + 1)], 185 (17, 262 − Ph), 184 [10, 262 ± (Ph + 1), 185 ± 1], 183 [50, 277 ± (Ph + 1), 184 ± 1, $C_{12}H_8P^+$], 153 (12, PNB–$OH^{+\bullet}$), 152 (10, PNB − O^+), 139 (7), 137 (8), 136 (9, $O_2NC_7H_6^+$), and 108 (22) (asterisks denote metastable transitions).

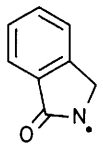
(*b*) Finely pulverized tin (10 g, 84 mmol) was added portionwise to a refluxing mixture of phthalimide (5.0 g, 34 mmol), ethanol (90 ml), and conc. hydrochloric acid (20 ml) with continuous stirring during 2 h. The mixture was kept overnight, and conc. hydrochloric acid and, under the same conditions as above, a further portion of pulverized tin (10 g, 84 mmol) were added. The mixture was filtered through a Seitz plate, concentrated to *ca.* 40 ml, and made alkaline (pH 10) by addition of Na_2CO_3 with cooling. The resulting heterogeneous mixture was extracted by being stirred for a few minutes with ether (5 × 100 ml). The ethereal layers were combined, dried ($MgSO_4$), and evaporated to dryness. Recrystallization of the residue from benzene gave isoindolin-1-one (**17**) (2.35 g 52%), m.p. 153—156 °C (lit.[12] 150—151 °C); $\nu_{max.}$ 1 675 cm^{-1}; δ_H (60 MHz) 4.4 (s, CH_2), 7.3—7.6 (m, 3 × ArH), 7.9 (dd, 7-H), and 8.6 (br, NH).

A mixture of compound (**17**) (2.66 g, 20 mmol), *p*-nitrobenzyl glyoxylate monohydrate (4.54 g, 20 mmol), and dry benzene (60 ml) was refluxed for 3 h, the water formed being continuously removed with the aid of a water separator tube. The hot solution was treated with Norite and allowed to cool to give crystals (5.4 g, 79%) of (±)-p-*nitrobenzyl* 2-*hydroxy*-2-(1-*oxoisoindolin*-2-*yl*)*acetate* (**8b**), m.p. 137 °C (Found: C, 59.45; H, 4.3; N, 8.3, $C_{17}H_{14}N_2O_6$ requires C, 59.65; H, 4.12; N, 8.19%); $\nu_{max.}$(KBr)

* Two diastereoisomers.

3 250br, 1 755, 1 670, 1 520, and 1 350 cm^{-1}; δ_H 4.36 + 4.56 (AB, J_{gem} 16.4 Hz, NCH_2), 4.66 (d, J 6.0 Hz, OH), 5.36 (s OCH_2Ar), 6.12 (d, J 6.0 Hz, NC*H*OH), 7.3—7.9 (m, 4 × ArH), and 7.50 + 8.16 (AA'BB', J 8.8 Hz, PNB group); δ_C 46.62 (NCH_2), 66.34 (OCH_2), 73.42 (NCHOH), 123.11, 124.12, 128.30, 132.53, 131.05, 141.74 (condensed benzene ring), 123.85, 128.64, 141.91, 147.90 (C-3 + -5, C-2 + -6, C-1, and C-4, respectively, of PNB group), and 169.10 and 169.24 (lactam and ester carbonyls).

A solution of triethylamine (1.68 ml, 12 mmol) in THF (4 ml) was added (within 5 min) dropwise to a precooled mixture of compound (**8b**) (3.4 g, 10 mmol), anhydrous THF (50 ml), and thionyl chloride (0.87 ml, 12 mmol) with continuous stirring at −10 °C. The mixture was stirred for 30 min at 0 °C, diluted with cold CH_2Cl_2 (300 ml), washed successively with cold 0.1 M hydrochloric acid (100 ml) and cold brine (100 ml), dried ($MgSO_4$), and evaporated to dryness. The resulting crude chloro derivative (**8c**) was stirred for 40 h with a mixture of Ph_3P (5.25 g, 20 mmol) and anhydrous THF (10 ml) under argon. The mixture was diluted with CH_2Cl_2 (200 ml), washed with 10% aqueous Na_2CO_3, dried ($MgSO_4$), and evaporated to dryness. The residue was taken up in ether and purified by column chromatography (200 kPa) to give p-*nitrobenzyl* 2-(1-*oxoisoindolin*-2-*yl*)-2-(*triphenylphosphoranediyl*)*acetate* (**6**) (2.44 g, 42% overall), m.p. 194 °C (from EtOH); $\nu_{max.}$(KBr) 1 690, 1 620, 1 510, and 1 340 cm^{-1}; δ_H 3.82 + 4.67 (AX, J_{gem} 16.5 Hz, NCH_2), 5.13 + 5.18 (AB, J_{gem} 13 Hz, OCH_2Ar), and 6.75—8.2 (m, 23 × ArH); EI-MS (150 °C), *m/z* (rel. intensity, %) 586 (19, $M^{+\bullet}$; Found: M^+, 586.161. $C_{35}H_{27}N_2O_5P$ requires M, 586.166), 479 (1, M − 107), 454 (0.6, M − **a**), 407 (1.4), 406 (1, M − CO_2–PNB), 401 (2, M ± Ph_2P), 301 (0.7, M − 285), 288 (2, 454 ± 166) 278 (6, $Ph_3PO^{+\bullet}$), 277 (10, 278 ± 1), 263 (21), 262 (100, $Ph_3P^{+\bullet}$), 261 (14, 262 ± 1), 201 (3), 185 (8, 262 − Ph), 184 [8, 262 ± (Ph + H), 185 ± 1], 183 [40, 261 ± (Ph + H), 184 ± 1], 133 (10), and 108 (21).



(**a**)

Preparation of Authentic Samples of Acetates (**2a**) *and* (**8a**).—(*a*) A mixture of compound (**3a**)[13] (0.35 g, 1.0 mmol), CH_2Cl_2 (10 ml), and acetic anhydride (1 ml) was refluxed for 3 h and evaporated to dryness. The residue was worked up by preparative t.l.c. (ether) to give authentic (±)-p-*nitrobenzyl* 2-*acetoxy*-2-(2-*methoxycarbonylmethyl*-4-*oxoazetidin*-1-*yl*)*acetate* (**2a**) (0.27 g, 70%) as an oily mixture of diastereoisomers (Found: C, 57.65; H, 4.35; N, 6.95. $C_{17}H_{18}N_2O_9$ requires C, 57.78; H, 4.60; N, 7.10%); $\nu_{max.}$(film); 1 770—1 720 br, with several local maxima, 1 520 and 1 350 cm^{-1}; δ_H 2.14 and 2.13 (2 × s, Ac*), 2.55 + 2.71 (ABX, J_{gem} 16.7, J_{vic} 6.8 and 6.7 Hz, respectively, 2-CH_2CO_2Me), 2.80 + 3.22 (ABX, J_{gem} 15.5, J_{vic} 3.0 and 5.6 Hz, respectively, 3-H_2), 3.66 and 3.68 (2 s, CO_2Me*), 4.22 (tdd, J *ca.* 6.8, 3.0, and 5.6 Hz, 2-H), 5.30 and 5.32 (2 s, OCH_2Ar*), 6.24 and 6.44 (2 s, CHOAc*), and 7.55 + 8.25 (AA'BB', J 8.6 Hz, ArH). According to its ^1H n.m.r. spectrum, compound (**2a**) proved to be a *ca.* 85:15 mixture of epimers.

(*b*) A mixture of compound (**8b**) (0.34 g, 1 mmol), acetic anhydride (0.2 ml, 2 mmol), and benzene (10 ml) was refluxed for 8 h and evaporated to dryness. The residue was triturated with ether to give crystals of (±)-p-*nitrobenzyl* 2-*acetoxy*-2-(1-*oxoisoindolin*-2-*yl*)*acetate* (**8a**) (0.35 g, 91%), m.p. 86—88 °C (from MeOH) (Found: C, 59.15; H, 4.45; N, 7.05. $C_{19}H_{16}N_2O_7$ requires C, 59.39; H, 4.20; N, 7.29%); $\nu_{max.}$(KBr) 1 750, 1 570, 1 520, and 1 350 cm^{-1}; δ_H 2.15 (s, Ac), 4.43 + 4.59 (AB, J_{gem} 16.0 Hz, NCH_2), 5.36 (s, OCH_2Ar), 7.02 (s, NCHOAc), 7.4—8.0 (m, 4 ArH, condensed benzene ring), and 7.53 + 8.21 (AA'BB', J 8.8 Hz, PNB group).

Preparation of an Authentic Sample of the Methylene Compound (**5a**).—A mixture of the phosphorane (**1a**)[13] (100 mg, 0.17 mmol), paraformaldehyde (10 mg, 0.34 mmol), and dry ether (20 ml) was stirred for 50 h at room temperature and evaporated to dryness. The residue was worked up by t.l.c. (benzene–acetone, 10:1) to give (±)-p-*nitrobenzyl* 2-(2-*methoxycarbonylmethyl*-4-*oxoazetidin*-1-*yl*)*acrylate* (**5a**) (55 mg, 93%) as an oil which gradually solidified, m.p. 92 °C (Found: C, 55.4; H, 4.35; N, 7.95. $C_{16}H_{16}N_2O_7$ requires C, 55.17; H, 4.63; N, 8.04%); $\nu_{max.}$ 1 760—1 720br, 1 530, 1 360, and 880 cm^{-1}; δ_H 2.61 + 2.84 (ABX, J_{gem} 15.8, J_{vic} 7.6 and 5.0 Hz, respectively, 2-CH_2CO_2Me), 2.84 + 3.26 (ABX, J_{gem} 15.5, J_{vic} 2.7 and 5.4 Hz, respectively, 3-H_2), 3.66 (s, CO_2Me), 4.58 (dddd, J 7.6, 5.0, 2.7, and 5.4 Hz, 2–H), 5.32 (s, OCH_2Ar), 5.99 + 6.07 (AB, J_{gem} 0.6 Hz, C=CH_2), and 7.57 + 8.25 (AA'BB', J 9.0 Hz, ArH); δ_C($CDCl_3$ + [$^2H_6$]DMSO) 37.90 (CH_2CO_2Me), 43.39 (C-3), 50.31 (C-2), 51.67 (CO_2Me), 65.69 (OCH_2Ar), 114.63 (C=CH_2), 123.72 (C-3′ + -5′), 128.63 (C-2′ + -6′), 131.24 (*C*=CH_2), 142.61 (C-1′), 147.75 (C-4′), 161.92 (CO_2PNB), 165.09 (C-4), and 170.32 (CO_2Me). Further elution gave Ph_3PO (33 mg, 70%), identified by its i.r. spectrum.

Reactions of Phosphoranes (**1a**), (**1b**), *and* (**6**) *with Sulphoxide–Acetic Anhydride Mixtures.*—(*a*) Mixtures of the phosphorane (**1a**) (1.0 g, 1.7 mmol), DMSO (25 ml), and acetic anhydride (25 ml) were stirred (i) for 100 h at 45–50 °C or (ii) for 50 h at 65–70 °C and evaporated to dryness (26 Pa, < 100 °C). The residues were worked up by column chromatography (200 kPa; ether) to give (i) 44% of compound (**2a**) and 18% of compound (**5a**), and (ii) traces of compound (**2a**) and 43% of compound (**5a**). While the former is an oil, the latter is a crystalline product, m.p. 92 °C. Both proved identical (i.r., ^1H n.m.r., R_F) with the respective authentic samples (see above). In addition, some of the co-product Ph_3PO was isolated as the last fraction in both cases and identified by its i.r. spectrum.

Compound (**2a**) showed MS (150 °C), *m/z* (rel. intensity, %) 351 (0.2, M − Ac), 335 (0.6, M − CO_2Me), 321 (6, M − CH_2CO_2Me), 308 (1), 293 (1), 277 (7), 256 (1), 248 (1), 247 (1), 214.071 1 (40, $C_9H_{12}NO_5$. Calc. 214.071 5, M − $CO_2CH_2C_6H_4NO_2$), 172 (100, 214 ± CH_2CO), 153 (6, $O_2NC_7H_6OH^{+\bullet}$), 151 (10), 137 (20), 136 (40, $C_7H_6NO_2^+$), 130 (10, 172 − CH_2CO), 127 (100, 172 ± 45), 106 (20, 136 ± NO), 102 (10), 100 (30), 95 (10), 90 (20, 136 − NO_2), and 89 (25); CI-MS (150 °C), *m/z* (rel. intensity, %) 395 (31, M + H) and 335 (100, M − 59).

(*b*) A mixture of compound (**1b**) (160 mg, 0.28 mmol), DMSO (4ml), and acetic anhydride (4 ml) was stirred at 45—50 °C until compound (**1b**) was consumed (*ca.* 80 h), and evaporated to dryness. The residue was worked up by t.l.c. (CH_2Cl_2–acetone, 10:1) to give not completely pure acetate (**2b**) (17 mg, 17%) as an oily mixture of diastereoisomers, compound (**5b**) (42 mg, 47%), m.p. 105 °C, and Ph_3PO (78 mg, 100%) (identified by t.l.c. and its i.r. spectrum).

Compound (**2b**).† $\nu_{max.}$(film) 2 330w, 1 760—1 740br, 1 520, and 1 350 cm^{-1}; δ_H 2.17 (s, Ac), 2.80 + 2.86 (ABX, J_{gem} 18, J_{vic} 4.5 and 5.0 Hz, CH_2CN), 3.02 + 3.28 (ABX, J_{gem} 15.5, J_{vic} 3.3 and 5.5 Hz, 3-H_2), 4.14 (dddd, J 4.5, 5.0, 5.5, and 3.3 Hz; 2-H), 5.32 + 5.38 (AB, J_{gem} 13 Hz, OCH_2Ar), 6.28 (s, NCHOAc), and 7.55 + 8.25 (AA'BB', J 8.8 Hz, PNB group).

Compound (**5b**) (Found: C, 57.25; H, 4.3; N, 13.15. $C_{15}H_{13}N_3O_5$ requires C, 57.14; H, 4.15; N, 13.33%); $\nu_{max.}$(KBr)

† Main component of the mixture.

Table. Thermolysis of diethyl diazomalonate (**22**)

Reactants								
(**22**)	Ac_2O	AcOH	DMSO	Ph_2SO	$Cu(OAc)_2$ (Catalyst)	Reaction time (h)	Temperature (°C)	(**23**) [a] Yield (%)
2.4 g	24 ml		2.4 ml		0.15 g	5	100—110	50 [b]
2.4 g	24 ml			2.85 g	0.15 g	5	120	25
2.4 g		25 ml	2.4 ml			5	120	43
2.4 g		25 ml				10	120	

[a] Identical with an authentic sample prepared as described in the literature.[16] [b] Addition of cyclohexene did not cause any change in the product composition. In particular, no product resulting from trapping of the intermediate carbene was formed.

2 300 w, 1 760—1 715br, 1 520, 1 350, and 870 cm^{-1}; δ_H 2.87 (d, *J* 5.0 Hz, CH_2CN), 2.97 + 3.33 (ABX, J_{gem} 15.5, J_{vic} 2.8 and 5.6 Hz, 3-H_2), 4.60 (tdd, *J* 5.0, 5.6, and 2.8 Hz, 2-H), 5.35 (s, OCH_2Ar), 6.09 + 6.28 (J_{gem} 0.7 Hz, $C{=}CH_2$), and 7.55 + 8.26 (AA′BB′, *J* 9.0 Hz, PNB group).

(*c*) A mixture of compound (**1a**) (86 mg, 0.14 mmol), diphenyl sulphoxide (1.0 g, 0.72 mmol), and acetic anhydride (2.5 ml) was stirred at 80 °C until compound (**1a**) was consumed (*ca.* 70 h; no reaction took place when the mixture was stirred for 70 h at 45 °C), and evaporated to dryness at reduced pressure. The residue was worked up by column chromatography (ether–hexane, 7:2) to give compound (**2a**) (36 mg, 63%) as a 60:40 (^1H n.m.r.) oily mixture of two diastereoisomers; in addition, diphenyl sulphide and Ph_3PO were identified (i.r., t.l.c.) as the co-products.

Compound (**2a**) had $\nu_{max.}$(film) 1 760—1 740br, 1 520, and 1 350 cm^{-1}; δ_H 2.14 and 2.13 (2 s, Ac*), 2.55 + 2.73 and 2.70 + 2.85 (2 ABX, J_{gem} 16.7, J_{vic} 6.8 and 6.7 Hz, CH_2CO_2Me*), 2.80 + 3.23 (ABX, J_{gem} 15.5, J_{vic} 3.0 and 5.6 Hz, 3-H_2), 3.66 and 3.68 (2 s, CO_2Me*), 4.24 and 4.16 (2 tdd, *J ca.* 6.8, 3.0, and 5.6 Hz, 2-H*), 5.30 and 5.33 (2 s, OCH_2Ar*), 6.24 and 6.44 (2 s, NC*H*OAc*), and 7.55 + 8.25 (AA′BB′, *J* 8.8 Hz, PNB group).

(*d*) A mixture of compound (**6**) (0.30 g, 0.51 mmol), DMSO (4 ml), and acetic anhydride (4 ml) was stirred at 45 °C until compound (**6**) was consumed (150 h), and evaporated to dryness. The residue was worked up by column chromatography (200 kPa; CH_2Cl_2–ether, 10:1) to give compound (**7**) (0.14g, 82%), m.p. 155 °C, and Ph_3PO (0.14, 98%) (identified by i.r. and t.l.c.). Acetate (**8a**) could not be detected in the reaction mixture.

Compound (**7**) (Found: C, 64.1; H, 4.3; N, 8.35. $C_{18}H_{14}N_2O_5$ requires C, 63.90; H, 4.17; N, 8.28%); δ_H 4.73 (s, NCH_2), 5.39 (s, OCH_2Ar), 5.81 + 6.14 (J_{gem} 1 Hz, $C{=}CH_2$), 7.4—8.0 (m, 4 × ArH, condensed benzene ring), and 7.57 + 8.23 (AA′BB′, *J* 8.6 Hz, PNB group).

(*e*) A mixture of compound (**6**) (0.24 g, 0.41 mmol), diphenyl sulphoxide (0.24 g, 1.2 mmol), and acetic anhydride (5 ml) was stirred at 95 °C until compound (**6**) was consumed (76 h), and evaporated to dryness at reduced pressure. The residue was worked up by column chromatography (200 kPa; ether–hexane, 7:2) to give Ph_2S (75 mg, *ca.* 100%), identified by i.r. and t.l.c., compound (**8a**) (40 mg, 26%), identical (i.r., t.l.c.) with an authentic sample (see above), and *p*-nitrobenzyl acetate (20 mg, 25%). In addition, Ph_3PO was detected by t.l.c. in the reaction mixture. According to their i.r. spectra, none of the more polar fractions of the reaction mixture was identical with (or contained) the sulphonium ylide (**24**).

Attempted Reactions of Phosphorane (**1a**) *with DMSO–Acetic Acid and DMSO–Acetic Acid–Sodium Acetate Mixtures, and with Acetic Anhydride.*—(*a*) A mixture of the phosphorane (**1a**) (0.35 g), DMSO (2 ml), and acetic acid (5 ml) was heated for 24 h at 45—50 °C. Neither of the compounds (**2a**) and (**5a**) was formed.

(*b*) A mixture of the phosphorane (**1a**) (0.18 g), DMSO (5 ml), acetic acid (0.02 ml), and sodium acetate (5 mg) was heated for 100 h at 45 °C. Again neither (**2a**) nor (**5a**) was formed.

(*c*) Heating of the phosphorane (**1a**) with acetic anhydride for 80 h at 60—70 °C did not lead to the formation of either of the compounds (**2a**) and (**5a**).

Reaction of Methyl (Triphenylphosphoranediyl)acetate (**14**) *with DMSO–Acetic Anhydride.*—A mixture of compound (**14**)[14] (3.34 g, 10 mmol), DMSO (15 ml) and acetic anhydride (15 ml) was stirred for 2 h at 45 °C [most of compound (**14**) was consumed within a few minutes], and evaporated to dryness. The residue was triturated with water and neutralized by addition of a small volume of 10% aqueous NaOH to give a crude product (3.5 g, 93%) which proved identical (m.p., i.r.,[15] ^1H n.m.r.) with compound (**15**).[15] In the absence of DMSO, acetylation of compound (**14**) with acetic anhydride requires more vigorous conditions.

Compound (**15**): δ_H (60 MHz) 2.43 and 3.15 (3 H, each s) and 7.2–7.8 (m, 15 H); m.p. 150—153 °C.

When heated with a mixture of DMSO and acetic anhydride at 100 °C, compound (**15**) was consumed within *ca.* 10 h, but neither methyl 2-acetoxy-, nor methyl 2-methylene-acetoacetate could be detected among the products.

(±)-p-*Nitrobenzyl 2-Acetoxy-2-(1-oxoisoindolin-2-yl)acetoacetate* (**19**).—A mixture of *p*-nitrobenzyl 2,3-dioxobutanoate (**16**)[7] (1.3 g, 5.2 mmol), isoindolin-1-one (**17**) (0.7 g, 5.2 mmol), and dry benzene (20 ml) was refluxed for 4 h [according to t.l.c., both the isoindolinone (**17**) and its adduct (**18**) were present at this point in the solution, possibly in form of an equilibrium mixture]. Acetic anhydride (3.0 ml, 32 mmol) was added, and the mixture was refluxed for 10 h, and evaporated to dryness. The residue which, according to t.l.c., proved to be a mixture of both starting compounds and two products, was worked up by chromatography (200 kPa; CH_2Cl_2–ether, 7:1) to give the desired title compound (**19**) (0.34 g, 17%) [no attempts were made to optimize the yield of this compound], m.p. 209 °C, and a small amount of the *N*-acetyl derivative[12] of compound (**17**).

Compound (**19**) (Found: C, 59.35; H, 4.2; N, 6.3. $C_{21}H_{18}N_2O_8$ requires C, 59.15; H, 4.25; N, 6.57%); $\nu_{max.}$(KBr) 1 775, 1 765, 1 750, 1 690, 1 510, and 1 340 cm^{-1}; δ_H ($CDCl_3$ + [$^2H_6$]DMSO; 80 °C) 2.16 (s, OAc), 2.45 (s, C-Ac), 4.83 + 5.05 (AB, J_{gem} 17.0 Hz, NCH_2), 5.41 (s OCH_2Ar), 7.4—7.8 (m, 4 × ArH, condensed benzene ring), and 7.62 + 8.23(AA′BB′, *J* 8.8 Hz, PNB group).

N-Acetyl-(**17**), $\nu_{max.}$(KBr) 1 710 and 1 675 cm^{-1}; δ_H (60 MHz) 2.62 (s, Ac), 4.71 (s, CH_2), 7.25–7.6 (m, 3 × ArH), and 7.8 (dd, 7-H).

Attempted C-*Deacetylation of Compound* (**19**).—Mixtures of compound (**19**) (20 mg, 52 mmol), DMSO (1 ml), and acetic

* Two diastereoisomers.

anhydride (0.2 ml) were kept for 12 h at room temperature or heated for 12 h at 50 °C, and worked up as described for the reaction mixture obtained by treating the phosphorane (**6**) with DMSO–acetic anhydride mixtures. Deacetylation to give compound (**8a**) did not take place. No deacetylation took place, either, when the experiment at 50 °C was carried out in the presence of an equimolecular amount of added Ph_3PO.

Thermolysis of Diethyl Diazomalonate (**22**).—Mixtures of compound (**22**) and the compounds listed in the Table were heated for 5—10 h at 100—120 °C, and distilled under reduced pressure (2.0—2.6 kPa). The fractions distilling between 80 and 150 °C were worked up by column chromatography (CH_2Cl_2) to give diethyl acetoxymalonate (**23**)[16] in the yields indicated.

In none of the experiments was the sulphonium ylide (**21**)[17] [prepared, *inter alia*, by irradiation of compound (**22**) in DMSO[17]] obtained.

Dimethyloxosulphonium-bis(ethoxycarbonyl)methanide (**21a**). —This was obtained as described in the literature,[17] m.p. 115 °C (from EtOH) (lit.,[17] 105—106 °C); i.r. and n.m.r. spectra were identical with those published in the literature.[17]

Attempted Conversion of Oxosulphonium Ylide (**21a**) *into Diethyl Acetoxymalonate* (**23**).—Ylide (**21a**) proved stable to treatment with acetic acid at room temperature (15 h) or at 100—110 °C (3 h), and with acetic anhydride at room temperature (15 h) or at 100—110 °C (10 h) both in the absence and presence of copper(II) acetate.

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