Imidoyl-substituted Oxosulphonium Ylides: Preparation and Reaction with Nitrile Oxides

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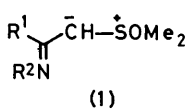
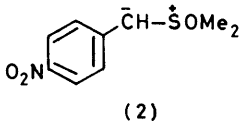
The *N*-arylbenzimidoyloxosulphonium ylides (3) have been isolated from the reaction of dimethyloxosulphonium methylide with *N*-arylbenzimidoyl chlorides. The crystalline oxosulphonium ylides (4) and (5) were similarly prepared from 2-chloropyrimidine and 3-chlorobenzisothiazole 1,1-dioxide, respectively. The ylides (3) reacted with nitrile oxides to give pyrazole 2-oxides (6). Dimethyloxosulphonium 4-nitrobenzylide (2) gave a 2 : 1 adduct (7) with benzonitrile oxide, but a 1 : 1 adduct (8) with benzonitrile *N*-phenylimide. The relevance of these observations to the mechanism of the reaction of sulphur ylides with nitrile oxides and nitrile imides is discussed.

SULPHONIUM and oxosulphonium ylides have become established as important synthetic intermediates.[1] We have investigated methods of preparing isolable oxosulphonium ylides (1) containing acyclic or cyclic imidoyl



(1)



(2)

groups conjugated to the carbanionic centre. Since such ylides have two nucleophilic centres, their reaction with electrophiles could provide a method of construction of heterocyclic systems.

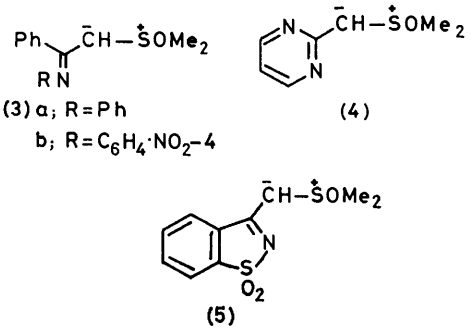
Oxosulphonium ylides are often considerably more stable than the corresponding sulphonium ylides, yet they may still retain a high degree of nucleophilic character. This is illustrated by the benzylides: dimethyloxosulphonium 4-nitrobenzylide (2) has been isolated as a crystalline solid but is still capable of reacting rapidly with nitrosobenzene and with benzylideneacetophenone,[2] whereas sulphonium benzylides are known only as transient intermediates. It seemed desirable in the present work to prepare isolable ylides in order to establish their structures unambiguously and to allow greater control over their subsequent reactions.

The imidoyl-substituted ylides (3) were prepared in

[1] B. M. Trost and L. S. Melvin, 'Sulfur Ylides,' Academic Press, New York, 1975.

[2] F. Dost and J. Gosselck, *Chem. Ber.*, 1972, **105**, 948.

high yield by the reactions of the appropriate imidoyl chlorides with 2 equiv. of dimethyloxosulphonium methylide in tetrahydrofuran. The crystalline ylides



(3) a; R = Ph
b; R = $C_6H_4 \cdot NO_2$-4

(4)

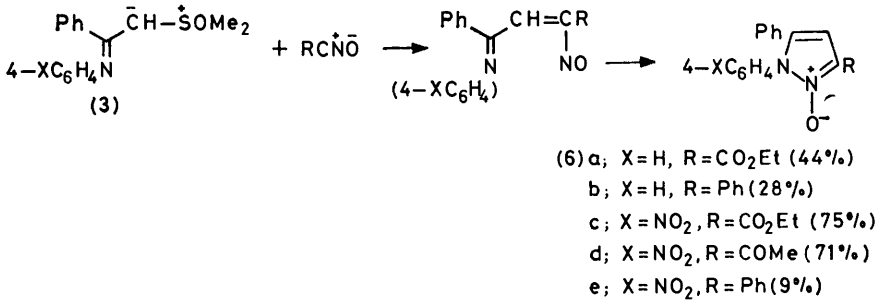
(5)

(4) and (5) were prepared in a similar way from 2-chloropyrimidine and 3-chlorobenzisothiazole 1,1-dioxide, respectively. The ylides are stable in air at room temperature but decompose above 100 °C. The ^1H n.m.r. spectra each show a singlet for the hydrogen atom attached to the carbanionic centre. The signals are at δ 3.87 for (3a), 4.14 for (3b), 4.37 for (4), and 5.35 for (5), the differences reflecting the varying degree of shielding by the imidoyl groups.

These reactions provide a very convenient method of alkylation of heterocyclic compounds such as 2-chloropyrimidine which are activated to nucleophilic displacement, since dimethyloxosulphonium methylide in tetrahydrofuran can be stored for several months with little decomposition. The major limitation of the method is the reactivity of the electrophilic substrate: thus, for example, 2-bromopyridine did not form an ylide. Taylor and his co-workers have recently described a similar method of alkylating some heterocyclic compounds by the use of diphenylsulphonium methylide and of triphenylphosphonium methylide as nucleophiles,[3] so that a range of ylides of different types is now available.

The ability of the nitrogen atoms in the ylides (3)—(5) to act as internal nucleophiles was explored by investigating their reaction with nitrile oxides. Reaction of the *N*-arylimidoyl ylides (3) with nitrile oxides gave 1 : 1 adducts in variable yields. Compounds (6a and b) were identified as pyrazole 2-oxides by deoxygenation and comparison of the products with independently prepared specimens of the corresponding pyrazoles. The reaction thus follows the sequence shown in Scheme 1, nitrosoalkenes being implicated as intermediates.

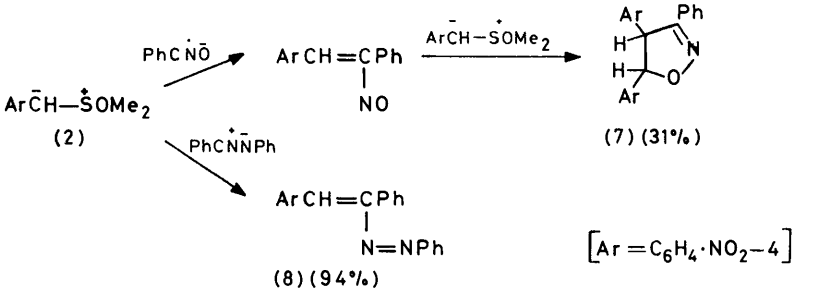
Our attempts to extend these reactions to the ylides (4) and (5) have so far been unsuccessful: mixtures containing a large number of components are obtained.



(6) a; X = H, R = CO_2Et (44%)
b; X = H, R = Ph (28%)
c; X = NO_2, R = CO_2Et (75%)
d; X = NO_2, R = COMe (71%)
e; X = NO_2, R = Ph (9%)

SCHEME 1

The reaction of the benzylide (2) with benzonitrile oxide gave a 2 : 1 adduct, which was assigned the isoxazoline structure (7); in contrast, the ylide (2) gave with benzonitrile *N*-phenylimide a red crystalline 1 : 1 adduct to which the azoalkene structure (8) was assigned. These results are summarized in Scheme 2.



(7) (31%)

(8) (94%)

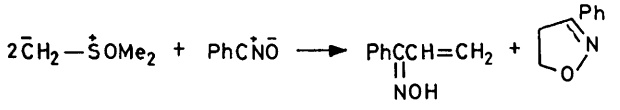
[Ar = $C_6H_4 \cdot NO_2$-4]

SCHEME 2

The nitroso-alkene intermediate which is formed from (2) and benzonitrile oxide is likely to be very susceptible

[3] E. C. Taylor and S. F. Martin, *J. Amer. Chem. Soc.*, 1972, **94**, 2874; *ibid.*, 1974, **96**, 8095; E. C. Taylor, M. L. Chittenden, and S. F. Martin, unpublished results quoted in ref. 1, pp. 201—208.

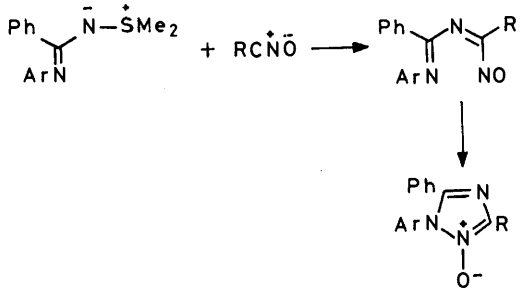
to nucleophilic attack,[4] and its reaction with a second molecule of the ylide clearly takes precedence over any cyclization on to the 4-nitrophenyl substituent. Indeed, previously studied reactions of sulphur ylides with nitrile oxides have all resulted in 2 : 1 adducts; [5,6] for example, dimethyloxosulphonium methylide and benzonitrile oxide gave acrylophenone oxime and 3-phenylisoxazoline as major products (Scheme 3).[5] The reaction



SCHEME 3

of the ylide (2) with benzonitrile *N*-phenylimide proceeds in an analogous manner, but in this case the azoalkene (8) is stable enough to permit its isolation. This is the first example of the isolation of a 1 : 1 adduct from a reaction of a sulphur ylide with a nitrile imide; 2 : 1 adducts and more complex products have been isolated previously.[6,7]

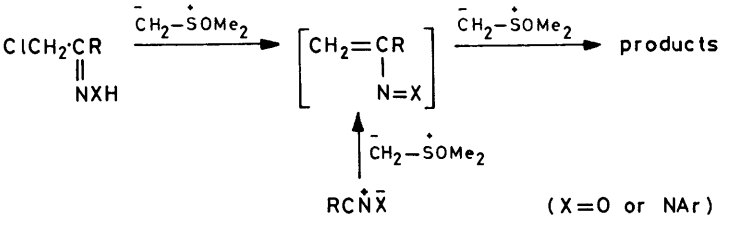
Nitroso- and azo-alkenes have previously been considered as likely intermediates in reactions of this type,



SCHEME 5

the main evidence being that oximes and arylhydrazones derived from α-chloro-ketones react with an excess of dimethyloxosulphonium methylide to give the same products as are obtained from the reaction of the ylide with nitrile oxides and nitrile imides (Scheme 4).[8] The present work is also clearly in accord with this general mechanism. Further support for the intermediacy of azoalkenes in the formation of 2 : 1 adducts is provided by the work of Overend and his co-workers, who have found that certain azoalkenes will react further with dimethyloxosulphonium methylide to give pyrazolines.[9] The mechanism of the reaction of sulphur ylides with other 1,3-dipoles, such as azides, remains to be established, but a similar nucleophilic addition–elimination mechanism might also operate in these systems.

In earlier investigations of the reactions of dipolar sulphur–nitrogen species with nitrile oxides, it has been shown that dipoles of this type which are substituted at nitrogen with imidoyl, pyridyl, pyrimidyl, and aryl groups are all capable of forming cyclic adducts; [10] for example, the imidoyl compounds give 1,2,4-triazole 2-oxides (Scheme 5). Nitroso-imine intermediates are



SCHEME 4

implicated in these reactions. The reactions of the corresponding oxosulphonium ylides are thus very similar in type, but the intermediate nitroso-alkenes can undergo further nucleophilic attack in competition with cyclisation.

EXPERIMENTAL

Dimethyloxosulphonium methylide was prepared as a solution in tetrahydrofuran by the reaction of trimethyloxosulphonium chloride with sodium hydride,[11] and the solution was standardized by titration with hydrochloric acid. Dimethyloxosulphonium 4-nitrobenzylide (2) was prepared by the literature procedure.[2] All operations were carried out in an atmosphere of dry nitrogen.

Dimethyloxosulphonium 2-Phenyl-2-phenyliminoethylide (3a).—*N*-Phenylbenzimidoyl chloride (1.1 g, 5 mmol) in dry tetrahydrofuran (50 cm³) was added dropwise during 1 h to a stirred solution of dimethyloxosulphonium methylide (10 mmol) in tetrahydrofuran (35 cm³) at 20 °C. After a further 1 h the mixture was filtered and the filtrate was evaporated. The residue was purified by precipitation from dichloromethane solution by addition of hexane, followed by cry-

[4] *Cf.* M. Ohno, N. Naruse, S. Torimitsu, and M. Okamoto, *Bull. Chem. Soc. Japan*, 1966, **39**, 1119.
[5] P. Bravo, G. Gaudiano, and A. Umani-Ronchi, *Gazzetta*, 1967, **97**, 1664.
[6] Y. Hayashi, T. Watanabe, and R. Oda, *Tetrahedron Letters*, 1970, 605.
[7] G. Gaudiano, A. Umani-Ronchi, P. Bravo, and M. Acampora, *Tetrahedron Letters*, 1967, 107; Y. Hayashi and R. Oda, *ibid.*, 1969, 853; G. Gaudiano, P. P. Ponti, and A. Umani-Ronchi, *Gazzetta*, 1968, **98**, 48.
[8] P. Bravo, G. Gaudiano, C. Ticozzi, and A. Umani-Ronchi, *Chem. Comm.*, 1968, 1311; *Gazzetta*, 1969, **99**, 549; P. Bravo, G. Gaudiano, P. P. Ponti, and C. Ticozzi, *Tetrahedron*, 1972, **28**, 3845.
[9] P. M. Collins, D. Gardiner, S. Kumar, and W. G. Overend, *J.C.S. Perkin I*, 1972, 2611.
[10] T. L. Gilchrist, C. J. Harris, and C. W. Rees, *J.C.S. Chem. Comm.*, 1974, 485; T. L. Gilchrist, C. J. Harris, C. J. Moody, and C. W. Rees, *ibid.*, p. 487; T. L. Gilchrist, M. E. Peek, and C. W. Rees, *ibid.*, 1975, 913.
[11] E. J. Corey and M. Chaykovsky, *J. Amer. Chem. Soc.*, 1965, **87**, 1353.

stallisation to give the *ylide* (3a) (1.15 g, 83%), m.p. 155—158 °C (from benzene) (Found: C, 70.6; H, 6.2; N, 5.0. $C_{16}H_{17}NOS$ requires C, 70.8; H, 6.3; N, 5.2%); $\lambda_{max.}$ (EtOH) 290 nm (ε 14 500); δ ($CDCl_3$) 3.42 (6 H), 3.87 (1 H), and 6.58—7.30 (10 H, m); *m/e* 271 (M^+) and 193 (M^+ — Me_2SO) (base).

Dimethyloxosulphonium 2-(4-*Nitrophenylimino*)-2-*phenylethylide* (3b).—*N*-(4-Nitrophenyl)benzimidoyl chloride (4.12 g, 15.8 mmol) in dry tetrahydrofuran (80 cm³) was added dropwise during 1.5 h to dimethyloxosulphonium methylide (31.6 mmol) in tetrahydrofuran (40 cm³). After a further 1 h the mixture was filtered and the filtrate was evaporated. The solid orange residue was dissolved in dichloromethane and the solution was washed with water. Addition of hexane to the solution gave the *ylide* (4.7 g, 94%), m.p. 163—164 °C (from benzene) (Found: C, 60.95; H, 5.1; N, 8.6. $C_{16}H_{16}N_2O_3S$ requires C, 60.75; H, 5.1; N, 8.9%); $\lambda_{max.}$ 412 nm (ε 11 400); δ ($CDCl_3$) 3.54 (6 H), 4.14 (1 H), 6.55 (2 H, d, *J* 8.5 Hz), 7.22 (5 H), and 7.88 (2 H, d, *J* 8.5 Hz); *m/e* 316 (M^+), 238 (M^+ — Me_2SO), and 225 (base).

Dimethyloxosulphonium Pyrimidin-2-*ylmethylide* (4).—To a stirred solution of 2-chloropyrimidine (0.251 g, 2.2 mmol) in tetrahydrofuran (70 cm³) was added dimethyloxosulphonium methylide (5.4 mmol) in tetrahydrofuran (10 cm³). After 20 h the precipitate was removed by filtration and the filtrate was evaporated. The residue was dissolved in dichloromethane and the solution was washed with water and dried; after evaporation the crude ylide (0.288 g) remained as an oily solid. Crystallisation gave the *ylide* (4) (0.193 g, 52%), m.p. 113—116 °C (from benzene–hexane) (Found: C, 49.6; H, 5.8; N, 16.5. $C_7H_{10}N_2OS$ requires C, 49.4; H, 5.9; N, 16.5%); $\lambda_{max.}$ (EtOH) 289 nm (ε 19 000); δ ($CDCl_3$) 3.47 (6 H), 4.37br (1 H), 6.44 (1 H, t, *J* 5 Hz), and 8.26 (2 H, d, *J* 5 Hz); *m/e* 170 (M^+, base) and 107.

Dimethyloxosulphonium (1,1-*Dioxobenzisothiazol*-3-*yl*)-*methylide* (5).—Dimethyloxosulphonium methylide (1 mmol) in tetrahydrofuran (1.8 cm³) was added to 3-chlorobenzisothiazole 1,1-dioxide (0.10 g, 0.5 mmol) in tetrahydrofuran (25 cm³). After 2 h the precipitate was removed by filtration, the filtrate was evaporated, and the residue was shaken with chloroform and water. The organic phase was dried and evaporated to leave the crude ylide (0.131 g). This was washed with dichloromethane and crystallised to give the *ylide* (5) (0.065 g, 51%), m.p. 220 °C (decomp.) (from ether–acetonitrile) (Found: C, 46.7; H, 4.4; N, 5.15. $C_{10}H_{11}NO_3S_2$ requires C, 46.65; H, 4.3; N, 5.4%); δ (CD_3CN) 3.61 (6 H), 5.35 (1 H), and 7.62—7.88 (4 H, m); *m/e* 257 (M^+) and 194 (base).

Ethyl 1,5-*Diphenylpyrazole*-3-*carboxylate* 2-*Oxide* (6a).—Ethyl α-chloroglyoxylate oxime [12] (0.076 g, 0.5 mmol) in dichloromethane (15 cm³) was added dropwise during 2 h to a stirred solution of the ylide (3a) (0.271 g, 1 mmol) in dichloromethane (10 cm³). After a further 1 h the solvent was removed and the oily residue was subjected to layer chromatography (silica; ethyl acetate–chloroform, 1 : 3). This gave the *pyrazole* 2-*oxide* (6a) (0.067 g, 44%), m.p. 158—159 °C (from dichloromethane–hexane) (Found: C, 69.8; H, 5.2; N, 9.1. $C_{18}H_{16}N_2O_3$ requires C, 70.1; H, 5.2; N, 9.1%); $\nu_{max.}$ (Nujol) 1 695 cm⁻¹ (C=O); δ ($CDCl_3$) 1.40 (3 H, t, *J* 7 Hz), 4.42 (2 H, q, *J* 7 Hz), 6.83 (1 H), and 7.10—7.60 (10 H, m).

1,3,5-*Triphenylpyrazole* 2-*Oxide* (6b).—Benzohydroximoyl chloride (0.078 g, 0.5 mmol) in dichloromethane (15 cm³) was added dropwise during 1.5 h to a stirred solution of the ylide (3a) (0.271 g, 1 mmol) in dichloromethane (10 cm³). After 18 h the solvent was removed and the residue, after washing with water, was subjected to layer chromatography (silica; ethyl acetate–chloroform 1 : 5). This gave the *pyrazole* 2-*oxide* (6b) (0.044 g, 28%), m.p. 214—215 °C (from ethanol) (Found: N, 9.1. $C_{21}H_{16}N_2O$ requires N, 9.0%); δ ($CDCl_3$) 6.77 (1 H), 7.20—7.70 (13 H, m), and 8.20—8.45 (2 H, m); *m/e* 312 (M^+) and 296.

Ethyl 1-(4-*Nitrophenyl*)-5-*phenylpyrazole*-3-*carboxylate* 2-*Oxide* (6c).—Ethyl chloroglyoxylate oxime (0.076 g, 0.5 mmol) in dichloromethane (15 cm³) was added during 2 h to a stirred solution of the ylide (3b) (0.316 g, 1 mmol) in dichloromethane (10 cm³). After 16 h the product was isolated by layer chromatography (silica; ethyl acetate–chloroform 1 : 3); this gave the *pyrazole* 2-*oxide* (6c) (0.133 g, 75%) as orange crystals, m.p. 205—209 °C (from ethyl acetate) (Found: C, 60.9; H, 4.4; N, 11.9. $C_{18}H_{15}N_3O_5$ requires C, 61.2; H, 4.3; N, 11.9%); $\nu_{max.}$ (Nujol) 1 720 cm⁻¹ (C=O); δ ($CDCl_3$) 1.44 (3 H, t, *J* 7 Hz), 4.46 (2 H, q, *J* 7 Hz), 6.84 (1 H), 7.08—7.40 (5 H, m), 7.56 (2 H, d, *J* 9 Hz), and 8.32 (2 H, d, *J* 9 Hz); *m/e* 353 (M^+) and 337.

3-*Acetyl*-1-(4-*nitrophenyl*)-5-*phenylpyrazole* 2-*Oxide* (6d).—1-Chloropyruvaldehyde oxime [13] (0.061 g, 0.5 mmol) in dichloromethane (15 cm³) was added dropwise during 2 h to a solution of the ylide (3b) (0.316 g, 1 mmol) in dichloromethane (10 cm³). After 19 h the solvent was removed and the residue was partitioned between water and dichloromethane. The organic solution was evaporated and the residue was triturated with acetone to give the *pyrazole* 2-*oxide* (6d) (0.114 g, 70%), m.p. 239—246 °C (decomp.) (from ethyl acetate) (Found: C, 63.1; H, 4.1; N, 13.3. $C_{17}H_{13}N_3O_4$ requires C, 63.1; H, 4.1; N, 13.0%); $\nu_{max.}$ (Nujol) 1 665 cm⁻¹ (C=O); δ ($CDCl_3$) 2.79 (3 H), 6.86 (1 H), 7.04—7.40 (5 H, m), 7.55 (2 H, d, *J* 9 Hz), and 8.33 (2 H, d, *J* 9 Hz); *m/e* 323 (M^+) and 307.

1-(4-*Nitrophenyl*)-3,5-*diphenylpyrazole* 2-*Oxide* (6e).—Benzohydroximoyl chloride (0.050 g, 0.32 mmol) in dichloromethane (15 cm³) was added dropwise during 1.2 h to a stirred solution of the ylide (3b) (0.20 g, 0.63 mmol) in dichloromethane (10 cm³). After 20 h the product was isolated by layer chromatography (silica; ethyl acetate–chloroform, 1 : 5) which gave the *pyrazole* 2-*oxide* (6e) (0.01 g, 9%), m.p. 220—228 °C (from ethanol) (Found: C, 70.6; H, 4.3; N, 11.7. $C_{21}H_{15}N_3O_3$ requires C, 70.6; H, 4.2; N, 11.8%); δ ($CDCl_3$) 6.73 (1 H), 7.10—7.50 (8 H, m), 7.58 (2 H, d, *J* 9 Hz), and 8.32 (2 H, d, *J* 9 Hz, with 2 H, m, superimposed); *m/e* 357 (M^+) and 341.

Deoxygenation of the N-*Oxides* (6a *and* b).—(*a*) The *N*-oxide (6a) (0.029 g) and phosphorus trichloride (0.02 cm³) in ethanol-free chloroform (10 cm³) were heated under reflux for 0.5 h to give ethyl 1,5-diphenylpyrazole-3-carboxylate (0.026 g, 94%), m.p. 88—89 °C (lit.,[14] 87.5—88.5 °C), which was identical [i.r. spectrum and mixed m.p. (85—88.5 °C)] with a specimen prepared by the literature method.

(*b*) The *N*-oxide (6b) (0.03 g) and phosphorus trichloride (0.01 cm³) were heated in chloroform for 0.5 h to give 1,3,5-triphenylpyrazole (0.016 g, 57%), m.p. 140—141.5 °C (lit.,[15] 139 °C), which was identical [i.r. spectrum and mixed m.p.

[12] G. S. Skinner, *J. Amer. Chem. Soc.*, 1924, **46**, 731.
[13] G. Hesse and G. Krehbiel, *Chem. Ber.*, 1955, **88**, 130.
[14] R. Huisgen, K. Adelsberger, F. Aufderhaar, H. Knupfer, and G. Wallbillich, *Monatsh.*, 1967, **98**, 1618.
[15] I. I. Grandberg and A. N. Kost, *Zhur. obshchei Khim.*, 1959, **29**, 658.

(138—140.5 °C)] with a specimen prepared by the literature method.

4,5-Dihydro-4,5-bis-(4-nitrophenyl)-3-phenylisoxazole (7).—Benzohydroximoyl chloride (0.073 g, 0.47 mmol) in dichloromethane (15 cm^3) was added during 2 h to a stirred solution of the ylide (2) (0.20 g, 0.94 mmol) in dichloromethane (20 cm^3) at −20 °C. After the mixture had been stirred at −20 °C for 1 h and at room temperature for 1 h the volume was reduced to 5 cm^3. The precipitate was filtered off and was washed with water. Crystallisation of the residue gave the *isoxazoline* (7) (0.056 g, 31%), m.p. 170—176 °C (from acetone) (Found: C, 64.6; H, 4.3; N, 10.9. $C_{21}H_{15}N_3O_5$ requires C, 64.8; H, 3.9; N, 10.8%); *m/e* 389 (M^+) and 387 ($M^+ - 2$ H).

2-(4-Nitrophenyl)-1-phenyl-1-(phenylazo)ethene (8).—α-Chlorobenzaldehyde phenylhydrazone [16] (0.108 g, 0.47 mmol) in dichloromethane (15 cm^3) was added during 0.5 h to a stirred solution of the ylide (2) (0.20 g, 0.94 mmol) in dichloromethane (20 cm^3) at −20 °C. After the mixture had been stirred at −20 °C for 0.5 h and at room temperature for 4 h it was subjected to layer chromatography (silica; chloroform). This gave the *azoalkene* (8) as a red solid (0.144 g, 94%), m.p. 150—151 °C (from ethanol) (Found: C, 72.6; H, 4.4; N, 12.7. $C_{20}H_{15}N_3O_2$ requires C, 72.9; H, 4.6; N, 12.8%); $\lambda_{max.}$ (EtOH) 368 (ε 33 000) and 291 nm (30 000); *m/e* 329 (M^+).

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[16] H. von Pechmann and L. Seeberger, *Ber.*. 1894. **27**, 2121.