Reactions of Heterocycles with Thiophosgene. Part III.[1] 5-Isothiocyanatopenta-*trans*-2,*cis*-4-dienal, a Product obtained from Pyridine

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Pyridine undergoes ring scission when treated with thiophosgene and barium carbonate to give the products of both kinetic and thermodynamic control, *i.e.* the *trans,cis*- and *trans,trans*-5-isothiocyanatopenta-2,4-dienals, respectively. The reactions of the *trans,cis*-diene (1) with a wide variety of nucleophiles invariably give thioamides and anils. There was no evidence of any cyclisation to 1,2-dihydro-2-thioxopyridine-3-carbaldehyde (7).

In a previous report [2] we described the two isomeric dienes (1) and (2), which were prepared by the reaction of thiophosgene and alkali with pyridine. We have now examined this synthesis and the properties of the diene (1) in greater detail.

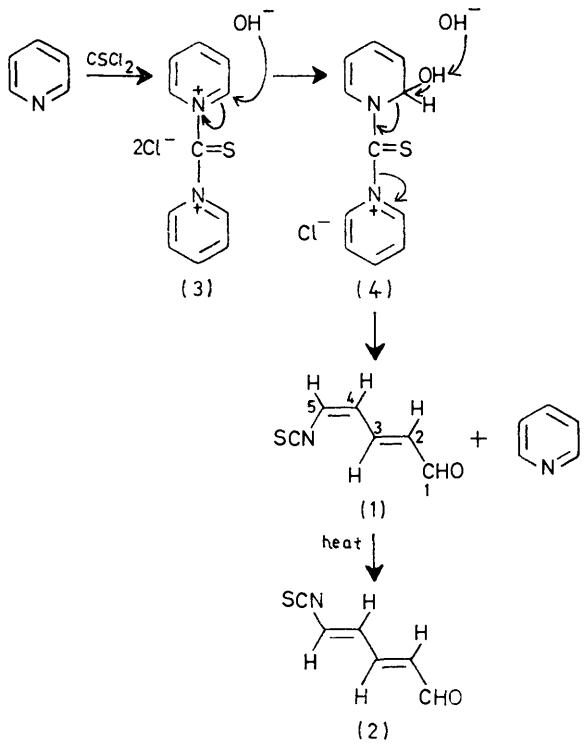
Pyridine reacted smoothly with thiophosgene and alkali in methylene chloride–water [3] at 15°. Extraction with ether yielded the *trans,cis*-diene (1), $\nu_{max.}$ 2096 (NCS), 1667 (conj. polyene CHO), 1610 and 1580 (C=C in a diene), and 980 cm^{-1} (*trans*-HC=CH). The n.m.r. spectrum showed considerable solvent dependence but in deuteriochloroform the formyl proton gave a sharp

[1] Part II, R. Hull, *J.C.S. Perkin I*, 1973, 2911.
[2] R. Hull, *J. Chem. Soc.* (*C*), 1968, 1777.
[3] F. D. Popp, W. Blount, and P. Melvin, *J. Org. Chem.*, 1961, **26**, 4930.

doublet at τ 0·32 (1H, *J* 7·8 Hz) due to coupling to H-2, which gave a four-line pattern centred at τ 3·79 (1H, *J* 7·8 and 15·4 Hz). The 3-proton gave a four-line pattern centred at τ 2·55 (1H, *J* 15·4 and 10·5 Hz) showing coupling with H-4, which also gave a four-line pattern, centred at τ 3·85 (1H, *J* 10·5 and 7·4 Hz). The 5-proton gave a doublet centred at τ 3·66 (1H, *J* 7·4 Hz). Considerable coincidence of peaks was evident and their assignment was based on double-resonance experiments. Irradiation at τ 0·32 changed the H-2 signal into a sharp doublet (*J* 15·4 Hz) centred at τ 3·79, and irradiation at τ 2·55 changed the H-2 and H-3 signals into doublets centred at τ 3·793 (*J* 7·8) and 3·85 (*J* 7·4 Hz), respectively. The latter coupling is characteristic of a cisoid arrangement of protons on a double bond.[4]

Recrystallisation (cyclohexane) of the crude reaction mixture gave the *trans,trans*-diene (2), $\nu_{max.}$ 2825, 2720 (CHO), 2065 (NCS), 1665 (conj. polyene CHO), 1608 and 1565 (C=C in a diene), and 980 cm^{-1} (*trans*-HC=CH). The n.m.r. spectrum also showed solvent dependence. In deuteriochloroform the formyl proton gave a sharp doublet at τ 0·43 (1H, *J* 7·8 Hz) due to coupling to H-2, which gave a four-line pattern centred at τ 3·77 (1H, *J* 7·8 and 15·5 Hz). Each line of this resonance was further split by virtual coupling * with H-4 and H-5. The 3-proton gave four-line pattern centred at τ 2·935 (1H, *J* 15·5 and 10·8 Hz) but the H-4 and H-5 signals overlapped, giving a complex multiplet between τ 3·2 and 3·76. In $(CD_3)_2SO$ however, although the formyl and H-2 signals remained unchanged the H-3, H-4, and H-5 resonances were shifted enough to destroy the virtual coupling effect and to give a spectrum suitable for first-order analysis. The 3-proton gave a four-line pattern centred at τ 2·75 (1H, *J* 15·4 and 10·8 Hz) showing coupling to H-4, which also gave a four-line pattern, centred at τ 3·43 (1H, *J* 10·8 and 13·3 Hz), and H-5 gave a doublet at τ 3·14 (1H, *J* 13·3 Hz).

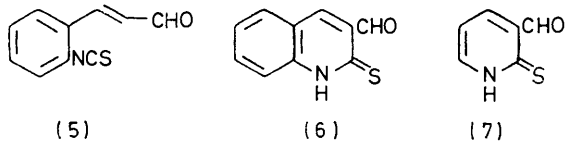
The reaction pathway (Scheme 1) probably proceeds *via* the bis-quaternary salt (3). Olofson and Zimmerman[6] have shown a related scission of pyridine from a bis-iminium cation formed from benzylidene bromide and pyridine. Attempts to isolate our intermediate from the reaction of thiophosgene with pyridine in anhydrous ether gave a yellow crystalline solid, but this was too hygroscopic to be characterised. The ring cleavage step (3) ⟶ (4) ⟶ (1) can be interpreted in terms of the hard/soft acid/base theory.[7] The bis-quaternary salt (3) would be expected to have a softer centre at the thiocarbonyl carbon atom than at C-2 (N^+ and S attached as opposed to N^+ only); consequently hard OH attack occurs at C-2 to give the anhydro-base (4), which after ring fission and isomerisation yields the *trans,cis*-aldehyde (1) together with pyridine. A further indication of the formation of the bis-quaternary salt (3) is the recovery of unchanged pyridine (30%) by extraction of the reaction mixture with acid during work-up.



SCHEME 1

To define the pK_a range over which this reaction would occur, substituted pyridines were selected with pK_a values from 0·7 to 6·0,[8] and treated with thiophosgene and alkali. The products provided an interesting stereochemical problem and i.r. and n.m.r. spectral analysis was used both for their identification and for a more detailed conformational study. The results of the latter investigation will be reported later.[4]

Although previous workers have reported on the reactivity of penta-2,4-dienals [9] no work appears to have been done on related dienes containing an isothiocyanato-group. We have shown previously [1] that the isothiocyanate (5) (a product obtained from quinoline) undergoes ring closure on treatment with bases to give the quinolinethione (6). The *trans,cis*-aldehyde (1) reacts (readily in most cases) with a variety of nucleophiles, *e.g.* diethyl malonate anion, hydroxide ion in ethanol,

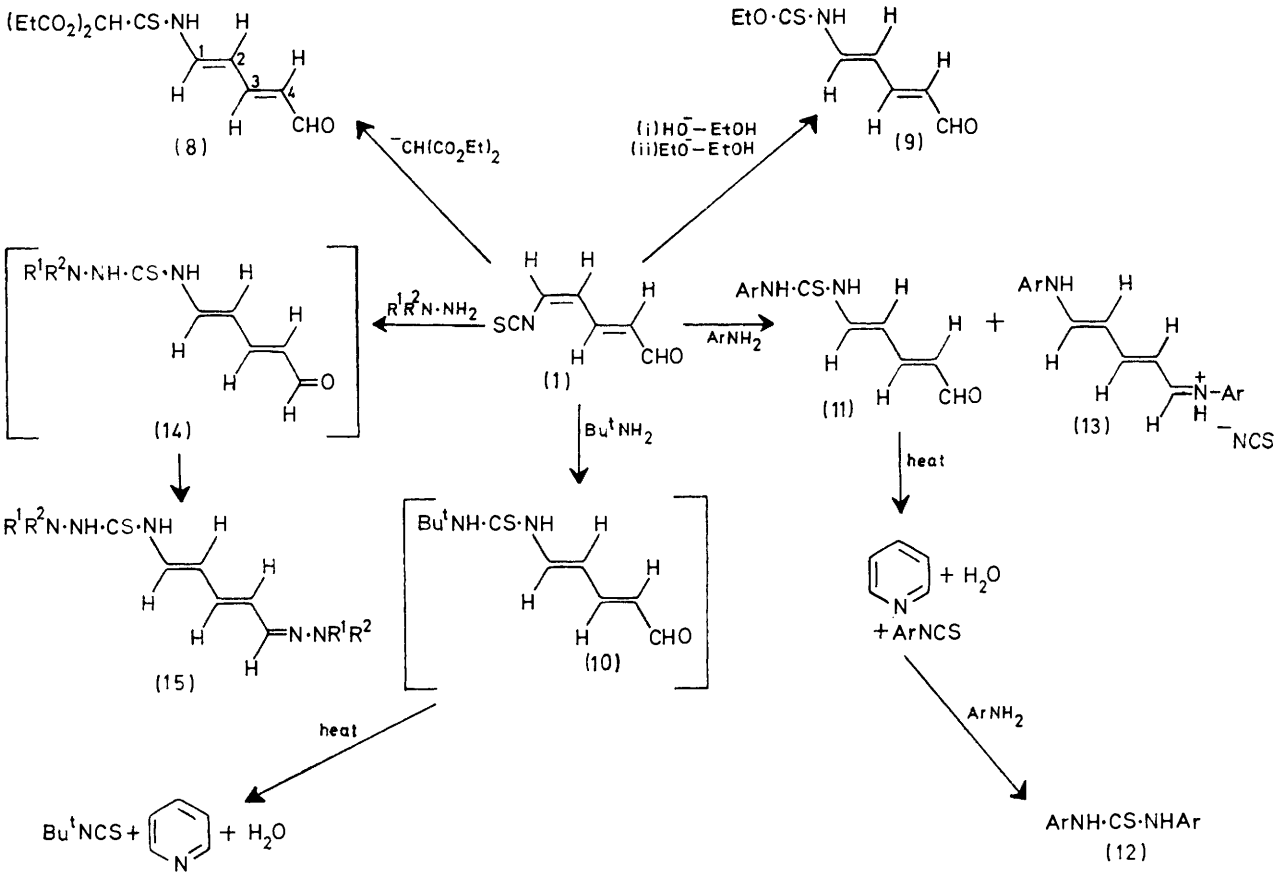


(5) (6) (7)

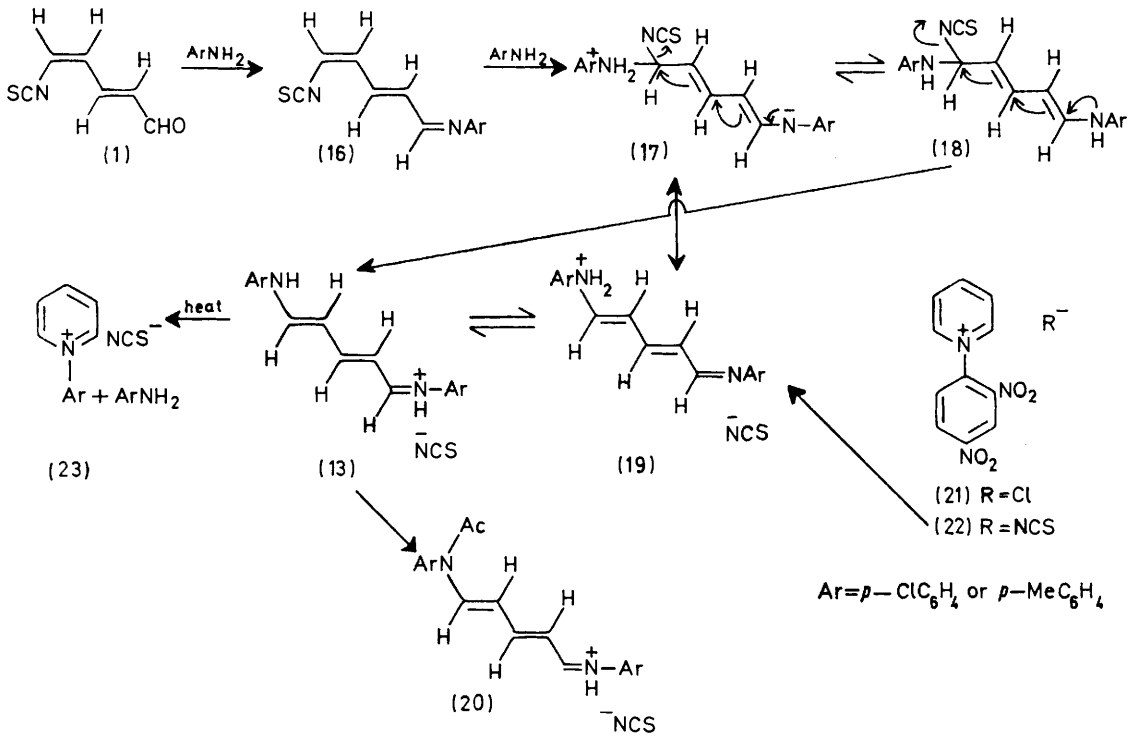
ethoxide in ethanol, and a range of nitrogen nucleophiles (primary alkyl- and aryl-amines, cycloalkylamines, and

* Although the coupling between H-3 and H-5 is effectively zero, the fact that H-3, H-4, and H-5 form a strongly coupled set of nuclei and that H-3 is chemically shifted from the other two (deshielded by C=O), results in a virtual coupling.[5]

[4] F. T. Boyle and R. Hull, unpublished data.
[5] J. I. Musher and E. J. Corey, *Tetrahedron*, 1962, **18**, 791.
[6] R. A. Olofson and D. M. Zimmerman, *J. Amer. Chem. Soc.*, 1967, **89**, 5057.
[7] R. G. Pearson, *Chem. in Brit.*, 1967, **3**, 103.
[8] K. Schofield, 'Hetero-Aromatic Nitrogen Compounds,' Butterworths, London, 1968, p. 146.
[9] G.P. 903,529; H. W. Whitlock and Y. N. Chuah, *J. Amer. Chem. Soc.*, 1965, **87**, 3605.



SCHEME 2 Square brackets denote species too unstable for isolation but observed by n.m.r.



SCHEME 3

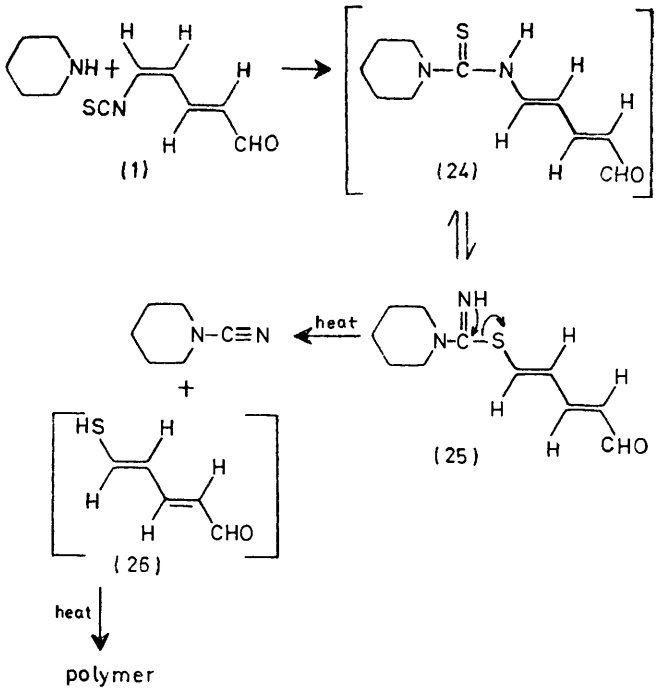
hydrazines). The results are summarised in Scheme 2. In no case did we observe any evidence for formation of the pyridinethione (7).

The isothiocyanato-group generally reacted to form thioamide derivatives [*e.g.* (9)]. In some cases these compounds were too unstable to be isolated and were rapidly converted into other products. Their formation was indicated by n.m.r. and u.v. spectral determinations. Thus diethyl malonate anion and ethoxides reacted typically at the NCS group [10] to give the thioamides (8) and (9), respectively. The products, which generally showed $\nu_{max.}$ *ca.* 1670 cm^{-1} (conj. CHO), were shown to have the stereochemistry indicated by the n.m.r. spectra: ^3J_t 15·5 and 13·5 Hz, respectively; τ *ca.* 0·4 (d, J 7·8 Hz, CHO) and *ca.* 3·87 (q, J 7·8 and 15·5 Hz, H-2). t-Butylamine did not yield the expected product (10); after work-up a 50 : 50 mixture of t-butyl isothiocyante and pyridine was obtained. Proof of the formation of the intermediate (10) was obtained from an experiment in which stoicheiometric amounts of the reactants were mixed in deuteriochloroform at −10° and the n.m.r. spectral changes were observed. However primary arylamines (Ar = *p*-ClC_6H_4 or *p*-MeC_6H_4) did yield the expected thioamides (11), but these were thermally unstable. For example, recrystallisation from chloroform gave a mixture of the aryl isothiocyanate and pyridine. Similar cyclisation reactions have been reported by Olofson and Zimmerman.[6] A closer examination of the original reaction mixture revealed two other products: thiocarbanilide (12), formed from the aryl isothiocyanate and the excess of arylamine,[11] and the iminium isothiocyanate (13).

Presumably in this case initial attack by the arylamine occurs at the aldehyde group to form the Schiff's base (16), with subsequent displacement of the isothiocyanate group by a second molecule of the arylamine [(17) ⇌ (18) ⟶ (19) ⇌ (13)]. The structure of compound (13) was confirmed by comparison of its physical characteristics with those of an authentic sample prepared *via* the Zincke salts (21) and (22).[12] The dianil (13) can be readily *N*-acylated with boiling acetic acid to give the product (20). Compound (13) readily undergoes cyclisation to give equivalent amounts of the *N*-arylpyridinium salt (23) and the arylamine.

Piperidine reacted with the *trans,cis*-aldehyde (1) *via* the thiourea (24) (identified by n.m.r. analysis) to give *N*-cyanopiperidine.[13] It is not clear how this product is formed but one possibility is outlined in Scheme 4. N ⟶ S Migration [(24) ⟶ (25)] of the pentadienal group gives the imine (25), which on heating decomposes to *N*-cyanopiperidine and a 5-mercaptopentadienal (26). The extensive polymerisation which occurred during work-up probably indicates the ultimate fate of such an intermediate.

Phenylhydrazine and *N*-aminopiperidine [14] reacted in like manner with the *trans,cis*-aldehyde (1) to give the thiosemicarbazide hydrazones (15) *via* the thiosemicarbazide pentadienals (14).



SCHEME 4

EXPERIMENTAL

Elemental analyses were carried out with a Technicon automatic C, H, and N analyser. All purified products gave single spots on t.l.c. (Kieselgel GF_{254}; 7 : 3 benzene–ethyl acetate). I.r. spectra were measured with a Perkin-Elmer 21 or 137 spectrometer, u.v. spectra with a Perkin-Elmer 137 spectrometer (methanol as solvent unless otherwise stated), and n.m.r. spectra with a Varian A-60 (60 MHz) or HA-100 (100 MHz) spectrometer. M.p.s were measured on a Kofler hot-stage microscope and are corrected.

5-*Isothiocyanatopenta*-trans-2,cis-4-*dienal* (1).—Thiophosgene (15·3 ml) in methylene chloride (60 ml) was added dropwise during 30 min to a vigorously agitated suspension of barium carbonate (40 g) in water (200 ml) and pyridine (15·8 ml) in methylene chloride (140 ml) between 5 and 10°. The brown mixture was agitated for a further 30 min, kept at 15° for 1·5 h and then filtered through a thin layer of Supercel. The residue was washed with methylene chloride (300 ml) and then water (500 ml). The methylene chloride layer was separated from the filtrate and washed successively with water (200 ml), 2N-hydrochloric acid (4 × 100 ml), and water (200 ml), then dried ($CaCl_2$) overnight at −4°. Concentration of the dried extract under reduced pressure (water bath at 20°) gave a light brown crystalline residue (2·4 g, 9%), m.p. 48—53°. Extraction with cold ether gave the trans,cis-*aldehyde* (2·2 g, 8%) as yellow leaflets, m.p. 59—61° (Found: C, 51·8; H, 3·8; N, 9·8. C_6H_5NOS requires C, 51·8; H, 3·6; N, 10·1%).

5-*Isothiocyanato*-trans-2,trans-4-*dienal* (2).—Recrystallis-

[10] N. Kharasch, 'Organic Sulfur Compounds,' Pergamon, Oxford, 1961, vol. 1, p. 326.
[11] N. P. Buu-Hoï, N. D. Xuong, and V. T. Suu, *J. Chem. Soc.*, 1958, 2815.
[12] Th. Zincke, G. Heuser, and W. Möller, *Annalen*, 1904, **333**, 296.
[13] W. L. Garbrecht and R. M. Herbst, *J. Org. Chem.*, 1953, **18**, 1003.
[14] L. Knorr, *Annalen*, 1883, **221**, 297.

ation of the light brown product (2·4 g; m.p. 48—53°) from a similar reaction from cyclohexane (25 ml) gave the trans,-trans-*aldehyde* as reddish-brown plates (1·6 g, 6%), m.p. 84—85° (Found: C, 51·7; H, 3·7; N, 10·0. C_6H_5NOS requires C, 51·8; H, 3·6; N, 10·1%).

O-*Ethyl* N-(4-*Formylbuta*-trans-1,trans-3-*dienyl*)*thiocarbonate* (9).—(*a*) Sodium hydroxide (0·4 g) in water (5 ml) was added in one portion to a stirred solution of the *trans,-cis*-aldehyde (1·39 g) in ethanol (50 ml) and then stirred for 2 min. The red solution was acidified (pH 2·5) with 5N-sulphuric acid, filtered to remove sodium sulphate, and then concentrated to 20 ml. A pink solid formed which crystallised from benzene to give the *carbamate* (0·6 g, 30%), as prismatic needles, m.p. 139—141° (Found: C, 51·9; H, 6·0; N, 7·7. $C_8H_{11}NO_2S$ requires C, 51·85; H, 5·95; N, 7·55%).

(*b*) Ethanolic sodium ethoxide (11·6 ml) [from sodium (0·058 g)] was added in portions to a stirred solution of the *trans,cis*-aldehyde (0·35 g) in absolute ethanol (30 ml). 5N-Acetic acid (0·5 ml) was added and after stirring for 85 min the excess of solvent was removed under reduced pressure. Water (20 ml) and methylene chloride were added to the residue and the organic layer was separated, washed with water (3 × 25 ml), dried ($CaCl_2$), and concentrated to give the carbamate as a buff-coloured solid (0·35 g, 75%), identical (i.r.) with the product from (*a*).

Reaction of the trans,cis-*Dienal* (1) *with Sodium Hydroxide in Acetone*.—2N-Sodium hydroxide (1·25 ml) was added in one portion to a solution of the *trans,cis*-aldehyde (0·35 g) in acetone (50 ml) and the mixture was stirred for 45 h at 20°. The yellow solution was neutralised with 10N-hydrochloric acid (pH 7) and then extracted with methylene chloride (3 × 25 ml). The extract was washed with water, (3 × 25 ml), dried ($CaCl_2$) and concentrated under reduced pressure to give the unchanged aldehyde (0·34 g, 97%).

Diethyl 4-*Formylbuta*-trans-1,trans-3-*dienylthiocarbamoylmalonate* (8).—The *trans,cis*-aldehyde (0·7 g) in AnalaR benzene (35 ml) was added dropwise during 5 min to a stirred suspension of sodium hydride (50% dispersion; 0·24 g) and diethyl malonate (0·8 g) in AnalaR benzene (15 ml) at *ca.* 30°. The resulting suspension was stirred for 20 min. 5N-Acetic acid (1 ml) was added and when effervescence ceased the organic layer was separated and dried ($MgSO_4$) for 2 h. The dried extract was concentrated to dryness under reduced pressure giving a reddish-brown oil (1·4 g). I.r. analysis indicated that unchanged *trans,cis*-aldehyde was still present. The oil was therefore redissolved in AnalaR benzene (50 ml) and added to a suspension of sodium hydride (50% dispersion; 0·24 g) and diethyl malonate (0·8 g) in AnalaR benzene (15 ml), and the mixture was stirred for a further 20 min. 5N-Acetic acid (1 ml) was added and the mixture was stirred for 20 min. The organic layer was filtered and concentrated under reduced pressure to give a reddish-brown oil contaminated with liquid paraffin (1·3 g). Trituration with light petroleum (b.p. 40—60°) (150 ml) gave the *trans,trans*-pentadienal as a brown oil (1·1 g), $\nu_{max.}$ ($CHCl_3$ solution) 1735 (C=O), 1670 (αβ-unsat. C=O), 1625 and 1615 (C=C in a diene), and 977 cm^{-1} (*trans*-C=C); τ ($CDCl_3$) 0·26 (1H, d, NH), 0·47 (1H, d, CHO), 2·07 (1H, q, H-1), 2·80 (1H, q, H-3), 3·58 (1H, q, H-1), 3·87 (1H, q, H-4), 6·63 [1H, s $(EtO)_2CH$], 5·77 (4H, q, 2 × OCH_2), and 8·7 (6H, t, 2 × Me).

Reaction of the trans,cis-*Diene* (1) *with* p-*Chloroaniline*.—*p*-Chloroaniline (1·66 g) in dry AnalaR benzene (15 ml) was added dropwise during 6 min to a stirred solution of the *trans,cis*-aldehyde (0·9 g) in dry AnalaR benzene (35 ml) at 25°. The initially formed red solution precipitated a buff-coloured solid after 1 min. The mixture was stirred for 55 min and filtered, and the residue was washed with dry AnalaR benzene (20 ml) to give a crude yellow amorphous solid (0·8 g, 47%), m.p. 114—116°. Crystallisation from chloroform gave 5-(N′-p-*chlorophenylthioureido*)*penta*-trans-2,trans-4-*dienal* (11; Ar = *p*-ClC_6H_4) as yellow needles (0·06 g), m.p. 122° (Found: C, 54·1; H, 4·3; N, 9·7. $C_{12}H_{11}ClNO_2S$ requires C, 54·1; H, 4·1; N, 10·05%); $\nu_{max.}$ (Nujol) 3280 and 3180 (NH), 1655 (αβ-unsat. C=O), 1625 (C=C in a diene), 980 (*trans*-C=C), and 820 cm^{-1} (*para*-substituted aromatic); τ [$(CD_3)_2SO$–$CDCl_3$] −0·14 (1H, d, NH), 0·16 (1H, s, NH), 0·56 (1H, d, CHO), 1·96 (1H, q, H-5), 2·63 (4H, s, Ph), 2·81 (1H, q, H-3), 4·02 (1H, q, H-4), and 4·66 (1H, q, H-2). Concentration of the chloroform filtrate under reduced pressure gave a brown oil (0·75 g) which was identified by t.l.c. and superimposition of i.r. spectra as a mixture of *p*-chlorophenyl isothiocyanate and pyridine. Concentration of the original benzene mother liquors after 4 days at ambient temperature gave a mixture of sticky violet crystals and light brown prisms (1·25 g). A sample of the brown prisms was recrystallised from aqueous dioxan to give NN′-*bis*-p-*chlorophenylthiourea* as light brown needles, m.p. 171—172° (Found: C, 52·4; H, 3·6; N, 9·4; S, 10·7. $C_{13}H_{10}Cl_2N_2S$ requires C, 52·6; H, 3·4; N, 9·4; S, 10·7%). The remainder of the residue was recrystallised from glacial acetic acid to give the iminium isothiocyanate (13; Ar = *p*-ClC_6H_4) as purple feather-like crystals, m.p. 136—137°, and its acetyl derivative (20; Ar = *p*-ClC_6H_4) as deep maroon prisms, m.p. 137—138°, identical with the samples described later.

Reaction of the trans,cis-*Diene* (1) *with* p-*Toluidine*.—*p*-Toluidine (1·1 g) in dry AnalaR benzene (20 ml) was added dropwise during 10 min to a solution of the *trans,cis*-aldehyde (0·7 g) in dry AnalaR benzene (30 ml) with stirring. The initially formed red solution deposited an orange solid after 7 min. After stirring for 30 min the product was filtered off and washed with dry AnalaR benzene; yield 0·9 g (77%), m.p. 96—97°. Crystallisation from chloroform gave 5-(N′-p-*tolylthioureido*)*penta*-trans-2,trans-4-*dienal* (11; Ar = *p*-MeC_6H_4) as yellow needles (0·20 g), m.p. 145—146° (Found: C, 62·9; H, 5·8; N, 11·2. $C_{13}H_{14}N_2OS$ requires C, 63·4; H, 5·8; N, 11·4%); $\nu_{max.}$ (Nujol) 3280 and 3150 (NH), 1640 (αβ-unsat. C=O), 1625 (C=C in a butadiene), and 975 cm^{-1} (*trans*-C=C); τ [$(CD_3)_2SO$–$CDCl_3$] −0·02 (1H, s, NH), 0·59 (1H, d, CHO), 2·02 (1H, d, NH), 2·75 (4H, m, Ph), 3·91 (1H, q, H-4), 4·07 (1H, q, H-2), and 7·75 (3H, s, Me). Concentration of the chloroform filtrate under reduced pressure gave a red oil (0·7 g) which was identified by t.l.c. and comparison of i.r. spectra as a mixture of *p*-tolyl isothiocyanate and pyridine.

1-(2,4-*Dinitrophenyl*)*pyridinium Isothiocyanate* (22).—(*a*) 1-Chloro-2,4-dinitrobenzene (10 g) was heated on a steam-bath with dry pyridine (30 ml) for 10 min and then cooled in ice. The mixture was filtered and the residue was washed with light petroleum (50 ml). The Zincke salt (21) (21 g, 67%) was not further purified.

(*b*) Sodium thiocyanate (2·25 g) in water (10 ml) was added to a solution of the Zincke salt (21) (5·0 g) in water (40 ml) to give a yellow oil. After 2 days at 25° the oil crystallised to give the *pyridinium salt* (3·4 g, 60%) as yellow rectangular prisms, m.p. 124—125° (Found: C, 47·7; H, 2·9; N, 18·4. $C_{12}H_8N_4O_4S$ requires C, 47·4; H, 2·6; N, 18·4%).

N-(5-p-*Chloroanilinopenta*-trans-2,trans-4-*dienylidene*)-*anilinium Isothiocyanate* (13; Ar = *p*-ClC_6H_4).—A mixture of *p*-chloroaniline (1·7 g) and the pyridinium isothiocyanate (22) (2·0 g) in methanol (40 ml) was maintained at reflux for 6 min. On cooling the *iminium isothiocyanate* crystallised as dark red needles (0·65 g, 26%), m.p. 137—139° (Found: C, 57·1; H, 4·2; N, 10·6. $C_{18}H_{15}Cl_2N_3S$ requires C, 57·4; H, 4·0; N, 11·1%); $\nu_{max.}$ (Nujol) 2040 cm^{-1} (NCS^-); τ [$(CD_3)_2SO$] 1·46 (2H, d, H-1 and -5), 2·19 (1H, t, H-3), 2·59 (4H, s, aromatic), 3·74 (2H, t, H-2 and -4), and 6·3—6·9 (2H, s, NH and NH^+). Attempted recrystallisation from boiling glacial acetic acid gave a deep red solution from which precipitated the hydrated N-*acetyl derivative* (20; Ar = *p*-ClC_6H_4) (0·5 g, 75%) as deep violet prisms, m.p. 129—131° (Found: C, 55·4; H, 4·3; N, 9·3. $C_{20}H_{17}Cl_2N_3OS,H_2O$ requires C, 55·6; H, 4·4; N, 9·7%); $\nu_{max.}$ (Nujol) 2060 (NCS^-) and 1715 cm^{-1} (C=O).

Reaction of the trans,cis-*Diene* (1) *with t-Butylamine.*—t-Butylamine (0·29 ml) was added to a stirred solution of the *trans,cis*-aldehyde (0·35 g) in chloroform (25 ml) at −75°. A yellow precipitate was initially formed which redissolved as the mixture was allowed to warm up to 20°. The red solution was concentrated to dryness under reduced pressure to give a brown oil (0·4 g), which was identified by t.l.c. and superimposition of i.r. spectra as a mixture of t-butyl isothiocyanate and pyridine.

N.m.r. investigation. t-Butylamine (0·01 g) in deuteriochloroform (0·5 ml) cooled to −70° was added to the *trans,-cis*-aldehyde (0·018 g) in deuteriochloroform (0·75 ml) containing tetramethylsilane (3 drops) at −70° in an n.m.r. tube. The tube was sealed and placed in the HA-100 n.m.r. probe under thermostat control at −10°. Changes in the spectrum due to the formation of 5-(*N'*-t-butylureido)penta-*trans*-2,*trans*-4-dienal (10) were recorded: τ ($CDCl_3$) −0·14 (1H, d, NH), 0·66 (1H, d, CHO), 1·86 (1H, s, NH), 2·73 (2H, m, H-3 and -5), 4·095 (1H, q, H-2), 4·17 (1H, q, H-4), and 8·52 (9H, s, Bu^t).

Reaction of the trans,cis-*Diene with Piperidine.*—The *trans,cis*-aldehyde (0·7 g) in dry AnalaR benzene (30 ml) was added dropwise during 3 min to a stirred solution of piperidine (0·86 g) in dry AnalaR benzene (25 ml) at 25°. The solution was stirred for 3 h and then kept for 2 days. The excess of benzene was removed under reduced pressure and the resultant oil redissolved in methylene chloride (70 ml). The solution was then washed successively with water (100 ml), 2N-hydrochloric acid (3 × 50 ml), and water (100 ml), dried ($CaCl_2$), and concentrated to dryness under reduced pressure. The i.r. spectrum (liquid film) of the resultant oil showed a C=N stretching vibration at 2200 cm^{-1}. Vacuum sublimation (0·075 mmHg) of a sample of the oil (0·3 g) at 40° gave *N*-cyanopiperidine (0·1 g) as an oil, b.p. 88—90° at 10 mmHg (lit.,[13] 107—110° at 17 mmHg), identical (comparison of the g.l.c. retention times and i.r. spectra) with an authentic sample.[13]

N.m.r. investigation. Piperidine (0·7 ml) was added dropwise to a stirred solution of the *trans,cis*-aldehyde (0·35 g) in methylene chloride (20 ml) at −77°. The solution was concentrated to dryness (bath temperature less than 30°) and the resulting oil was stored at −77°. A sample (20 mg) was immediately dissolved in deuteriochloroform (1 ml) and the n.m.r. spectrum was recorded. The 5-(piperidinothiocarbonylamino)penta-*trans*-2,*trans*-4-dienal (24) had τ 0·58 (1H, d, CHO), 0·81 (1H, d, NH), 1·79 (1H, q, H-5), 2·81 (1H, q, H-3), 3·77 (1H, q, H-4), 4·06 (1H, q, H-2), 6·11br (4H, s, $N[CH_2]_2$), and 8·35br (6H, s, $[CH_2]_3$).

Reaction of the trans,cis-*Diene* (1) *with Phenylhydrazine.*—Phenylhydrazine (0·78 g) was added [during 1 min] to a stirred solution of the *trans,cis*-aldehyde (0·5 g) in dry AnalaR benzene (50 ml) at 28°. A yellow precipitate was formed immediately. Stirring was continued for 83 min, the mixture was filtered, and the yellow solid was collected (0·85 g, 70%); m.p. 134—135°. Recrystallisation from AnalaR methanol (20 ml) gave the 5-(*phenylhydrazinothiocarbonylamino*)*penta*-2,4-*dienal phenylhydrazone* (15; R^1 = Ph, R^2 = H) as yellow needles (0·5 g, 41%), m.p. 144° (Found: C, 64·0; H, 5·6; N, 21·0. $C_{18}H_{19}N_5S$ requires C, 64·2; H, 5·6; N, 20·8%); the stereochemistry of the product was not investigated.

Reaction of the trans,cis-*Diene with N-Aminopiperidine.*[14]—The *trans,cis*-aldehyde (0·35 g) in dry AnalaR benzene (30 ml) was added during 22 min to a stirred solution of *N-aminopiperidine* (0·5 g) in dry AnalaR benzene (20 ml) at 25°. The solution was stirred for 30 min and kept at −20° for 24 h. On warming to 25° a yellow amorphous solid formed which was recrystallised from methanol to give 1-[5-(*N'-piperidinothioureido*)*penta*-trans-2,trans-4-*dienylideneamino*]*piperidine* (15; R^1R^2 = $[CH_2]_5$) as yellow plates (0·1 g, 12·5%), m.p. 150—152° (Found: C, 59·9; H, 8·3; N, 21·7. $C_{16}H_{27}N_5S$ requires C, 59·8; H, 8·3; N, 21·8%); τ ($CDCl_3$) 0·99 (1H, d, NH), 2·53 (1H, q, H-5), 2·66 (1H, s, NH), 2·74 (1H, d, H-1), 3·67—3·79 (2H, m, H-2 and -3), 4·11 (1H, q, H-4), 7·0 (4H, m, $N[CH_2]_2$), 7·6 (4H, m, $N[CH_2]_2$), and 8·33 (12H, m, 2 × $[CH_2]_3$).

N.m.r. investigation. *N*-Aminopiperidine (25 mg) in deuteriochloroform (0·5 ml) was added to a solution of the *trans,cis*-aldehyde (35 mg) in deuteriochloroform (1 ml) containing trimethylsilane (3 drops) in an n.m.r. tube. The tube was sealed and placed in the HA-100 probe, and the spectrum was recorded. The 5-(*N'*-piperidinothioureido)-penta-*trans*-2,*trans*-4-dienal (14; R^1R^2 = $[CH_2]_5$) had τ 0·51 (1H, d, CHO), 0·56 (1H, d, NH), 2·05 (1H, q, H-5), 2·83 (1H, q, H-3), 3·93 (1H, q, H-4), 3·98 (1H, q, H-2), 6·25 (1H, s, NH), 7·27 (2H, m, NCH_2), 7·65 (2H, m, NCH_2), and 8·35 (6H, m, $[CH_2]_3$).

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