Magnesium methoxide complexation in the control of chemical reactions

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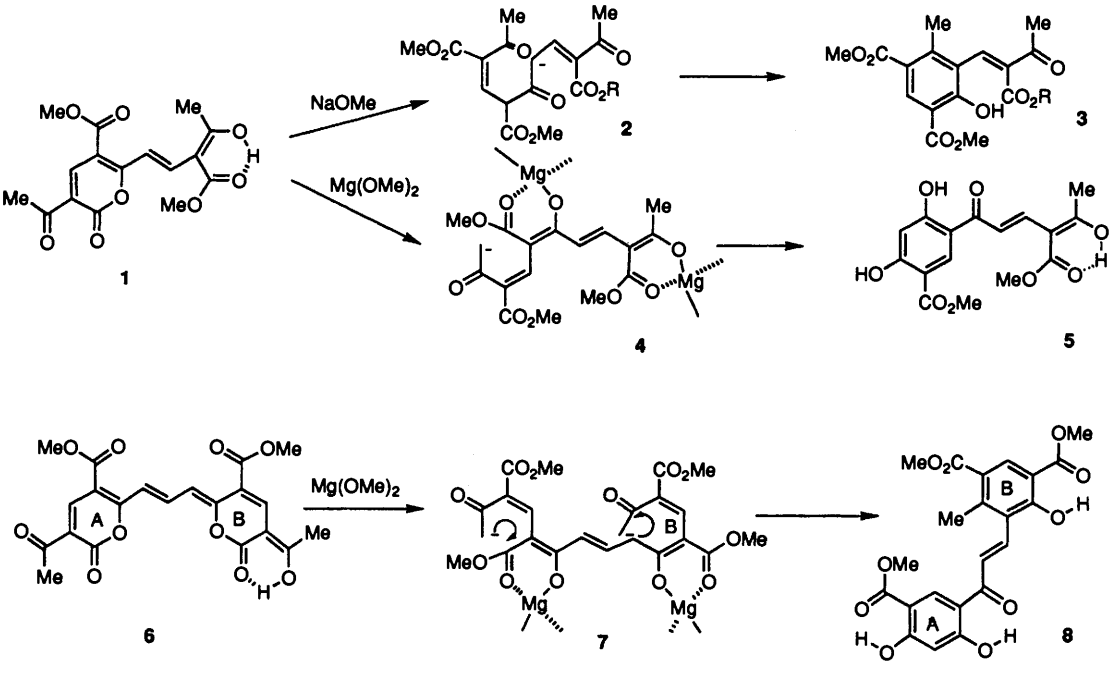
The insolubility of complex magnesium chelates makes experimentation difficult, so smaller complexes are used as models for NMR and deuteriation studies. Treatment of methyl cyanoacetate with magnesium methoxide however does not give a simple chelate but a novel kinetic Claisen condensation product, methyl 2,4-dicyano-3-hydroxybut-2-enoate, sequestrated as its magnesium-derivative. Replacement of magnesium methoxide by the non-chelating base sodium methoxide gives the known thermodynamic 1,2-addition product, dimethyl 3-amino-2-cyanopent-2-enedioate. A crossed Claisen product, dimethyl 2-cyano-3-hydroxybut-2-enedioate, has been obtained from diethyl oxalate and methyl cyanoacetate in the presence of magnesium methoxide. However, replacement of the oxalate by phenyl cyanomethyl sulfoxide gives a crossed 1,2-addition product, methyl 3-amino-2-cyano-4-phenylsulfinylbut-2-enoate.

Reactions between phenyl cyanomethyl sulfoxide or phenylsulfinylacetone and methyl 2-methoxymethyleneacetoacetate are carried out in the presence of varying amounts of sodium and magnesium methoxides. The products are pyrones, pyridones and aminobenzoates. When sodium methoxide is used in the phenylsulfinylacetone reaction the major product is a pyridine, but with magnesium methoxide it is a hydroxyaminobenzoate. This dichotomy may be explained as a consequence of magnesium complexation by the substrate.

During our earlier studies of electron deficient glutaconic and pyrone systems, some striking differences emerged between the products arising from treatment with the non-chelating base sodium methoxide, and those from the chelating base magnesium methoxide.[1,2] The molar ratio of magnesium methoxide to substrate can be very important. Examples from xanthyrone and glaucyrone chemistry are illustrative (Scheme 1). Dimethyl xanthophanic enol **1** on treatment with sodium methoxide in methanol gives, *via* aldol condensation substrate **2**, the isophthalate **3** or its coumarin, whilst with magnesium methoxide in excess (8 mol equiv.) it yields the resorcinol **5** (78% yield) (isolated as its magnesium chelate), a product of Claisen condensation involving the proposed magnesium chelate **4**.[3] In support of this interpretation, other explicable products are formed at lower magnesium methoxide ratios, where the substrate is partially, but not fully, complexed. Similarly, although treatment of dimethyl glaucophanic enol **6** with excess sodium methoxide gives ill-defined products, treatment with 12 mol equiv. magnesium methoxide gives **8** (74% yield) (isolated as its magnesium chelate), *via* a chelated species **7**, in a very clean reaction.[4]

Because of the difficulty in isolating and purifying such complex magnesium chelated intermediates, and their insolubility, there has been little direct evidence on their structures



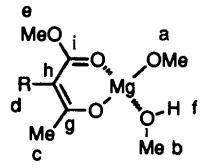
Scheme 1 Reactions of xanthophanic and glaucophanic enols with magnesium methoxide

Table 1 δ_H Values for magnesium mono-chelates and their precursors measured in $CDCl_3$

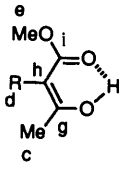
	Hydrogen atom					
	a	b	c	d	e	Other signals
Methyl acetoacetate						
9, Mg chelate	3.18	3.37	1.90	4.77	3.65	f, OH 4.70
9, Mg chelate (in C_6D_6)	3.69	3.26	1.98	5.34	3.77	
11, enol form	—	—	1.95	4.99	3.70	H-bonded OH 12.00
11, keto form			2.27	3.47	3.74	
Methyl α-methylacetoacetate						
10, Mg chelate	3.16	3.31	2.00	1.78	3.73	f, OH 6.20
12, keto form	—	—	2.22	1.32[a]	3.73	MeC*H*, 3.28, q, *J* 7 Hz
Acetylacetone						
13, Mg chelate	3.15	3.35	1.90	5.27	1.90	f, OH 4.46
13, Mg chelate (in C_6D_6)	3.01	3.38	1.62	5.07	1.62	
15, enol form	—	—	2.05	5.51	2.05	H-bonded OH 15.25
15, keto form	—	—	2.23	3.57	2.23	
α-Methylacetylacetone						
14, Mg chelate	3.12	3.31	2.04	1.83	2.04	f, OH 5.22
16, enol form	—	—	2.12	1.83	2.12	H-bonded OH, 15.77
16, keto form	—	—	2.20	1.32[a]	2.20	MeC*H*, 3.54, q, *J* 7 Hz
Dimethyl malonate						
17, Mg chelate	3.22	3.38	3.61	4.25	3.61	f, OH 4.90
19, keto form	—	—	3.66	3.40	3.66	
Dimethyl α-methylmalonate						
18, Mg chelate	3.21	3.31	3.73	1.71	3.73	f, OH 3.69
20, keto form	—	—	3.72	1.40[a]	3.72	MeC*H*, 3.43, q, *J* 7 Hz

[a] (CH_3, d, *J* 7 Hz).

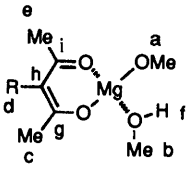
although they have been postulated as reaction intermediates in the literature,[5,6] so we have examined some relevant simpler complexes. This study supports our view, deduced from the stoichiometry of the reactions, that mono-chelates as shown are normally involved in the chemistry of the complex substrates when excess magnesium reagent is used. In addition, experiments with deuterium labelled alkoxide support our views on the reactivities of such chelates (suppression of aldol reaction as the electron acceptor partner but effectiveness as the donor, promotion of Claisen condensation *etc.*); we have lately used such effects to control the direction of cyclisation of unsymmetrically substituted γ-diketones.[7] Furthermore, a novel example of the capture of an unsuspected kinetic product through magnesium chelation is discussed and elaborated below. An example of magnesium chelation control in the formation of methyl 2-amino-4-hydroxy-5-phenylsulfinylbenzoate from phenylsulfinylacetone and methyl 2-methoxymethylenecyanoacetate is also given.



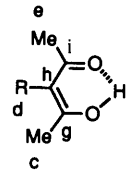
9, R = H
10, R = Me



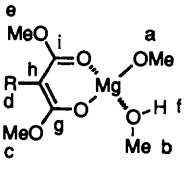
11, (enol) R = H
12, (enol) R = Me



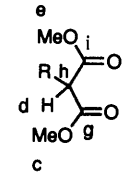
13, R = H
14, R = Me



15, (enol) R = H
16, (enol) R = Me



17, R = H
18, R = Me



19, (keto) R = H
20, (keto) R = Me

Magnesium mono-chelates of methyl acetoacetate, acetylacetone, dimethyl malonate and their α-methyl relatives

Although the magnesium acetylacetone bis-chelate **22** is comparatively well known as an isolated compound,[8,9] the mono-chelates **9**, **13** and **17** have seldom been isolated, and are normally employed in methanol solution. As there was little direct structural information, all three compounds were prepared by treatment with 1 mol equiv. (or excess) of magnesium methoxide in dry methanol and could be crystallised, *e.g.* from toluene. In addition, the corresponding magnesium mono-chelates from the *C*-methyl derivatives **10**, **14** and **18** were made: *C*-methylation of the unmagnesiated parent is known to reduce enolisation. The ^1H NMR characteristics for the six compounds are displayed in Table 1 along with comparative data for some of the metal-uncomplexed precursors. Table 2 supplies ^{13}C NMR data for **9**, **13** and **17**. It is clear that the magnesium chelates are all of the 1 : 1 type having methoxide and methanol ligands and that in the more complex cases (*e.g.* **4** and **7**) when an excess of magnesium methoxide is employed, each complexed site will be of a similar type. Indeed the bis-complexed sites would also be sterically hindered in large structures. The acetoacetate complexes **9** and **10** are not of a symmetrical type but the acetylacetones **13** and **14** and the dimethyl malonates **17** and **18** form magnesium chelates which can be represented as delocalised symmetrical forms *e.g.* **21**. Relative to the free enolates the compounds complexed with electropositive magnesium generally have corresponding protons displaced upfield in the ^1H NMR spectra and there are similar upfield shifts in the carbon spectra. The unusually high field resonance of the 'd' proton in the malonate complex **17** is worthy of note.

It seems likely that the magnesium mono-chelates are aggregated in solution through hydrogen bridges, but this aspect has not been studied in detail. However, it was noted that the ^1H

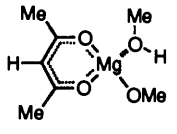
Table 2 δ_C Values for selected magnesium mono-chelates and precursors measured in $CDCl_3$[a]

	Carbon atom						
	a	b	c	e	g	h	i
Methyl acetoacetate							
9, Mg chelate	49.6	50.2	27.4	50.2	187.2	83.9	173.3
11, enol form	—	—	20.3	50.3	175.0	88.7	172.3
11, keto form	—	—	29.2	48.9	200.0	51.4	167.0
Acetylacetone							
13, Mg chelate	49.6	49.8	27.8	27.8	190.8	99.2	190.8
15, enol form	—	—	24.7	24.7	191.9	100.4	191.9
15, keto form	—	—	30.8	30.8	202.8	58.6	202.8
Dimethyl malonate							
17, Mg chelate	49.8	50.8	50.7	50.7	175.4	64.0	175.4
19, keto form	—	—	52.5	52.5	167.0	41.1	167.0

[a] Signal multiplicities (off resonance) as expected.

methoxide signal representing solvating methanol varied in line width from spectrum to spectrum. The spectrum (in $CDCl_3$) of a saturated solution of magnesium mono-methyl acetoacetate chelate was recorded, and then recorded again after two- and three-fold dilution. Initially the methanol signal at δ 3.37 was as high and sharp as the methoxide signal, but on dilution its signal height (though not the integral) declined relative to the other signals and became broadened. At three-fold dilution the relative height was about one half, with considerable broadening. The infrared spectra of all the magnesium chelates have the expected displaced carbonyls and olefinic stretching frequencies (see Experimental section).

The bis-acetylacetone magnesium complex **22** has been studied in some detail[9,12] and can be formed and isolated by using 0.5 mol equiv. magnesium methoxide: it crystallises from methanol, but such a bis-complex could not be isolated from dimethyl malonate or methyl acetoacetate in methanol. A bis-



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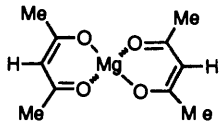
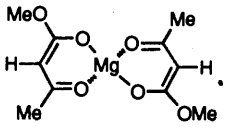


22



23

complex **23** has been reported from methyl acetoacetate in liquid ammonia[13] but not from methanol, possibly because methanol is a better second ligand than acetoacetate, or else for solubility reasons. Brittain[14,15] has found doubling of the methyl signals for the bis-acetylacetone complex in $CDCl_3$. In one form the oxygen atoms adopt a distorted tetrahedral configuration (D_{2d}) around the metal atom, and in the other a square planar configuration (D_{2h}) (solvent can occupy the remaining two coordination positions of the latter). Single crystal X-ray structures corresponding to both types of configuration are known. Chlorophyll is a well known planar type[16] with the magnesium held within a rigid environment: ethylmagnesium bromide tetraetherate is tetrahedral[17] and other cases of both types are known.[18,23] Semi-empirical MO calculations suggest that the D_{2d} type is more stable than the D_{2h} by ~10 kcal mol^{-1},†[14] The magnesium mono-complexes of major interest in our work would appear to be of the D_{2d} type as we have always represented them.

The possibility of magnesium exchange between the magnesium mono-chelate of dimethyl malonate and acetylacetone in $CDCl_3$ was examined by ^{1}H NMR spectroscopy. Addition of 0.25 mol of acetylacetone to the former magnesium chelate (1 mol) showed the emergence of the acetylacetone magnesium complex by exchange (acetyl methyl δ 1.90 and olefin signal of chelated acetylacetone 5.27) with a corresponding decrease of the magnesium dimethyl malonate complex signals. Further additions were made and at a 1 : 1 mixture 95% of the malonate had been freed from its magnesium complex. Above 100 mol% there was evidence of the formation of magnesium bis-acetylacetone complex. Release of a magnesium-chelated reaction product by competitive scavenging might therefore be a useful work-up technique in some circumstances. Addition of methyl acetoacetate to the magnesium derivative of dimethyl malonate also caused scavenging of magnesium by the former. The olefin signal of magnesium dimethyl malonate complex (δ 4.25) gradually disappears, until at 100 mol% of acetoacetate it is barely visible.

Deuteriation studies of magnesium mono-chelates

In order to learn more about the reactivity of the different elements of a magnesium chelate structure, a series of deuterium exchanges were monitored by ^{1}H NMR spectroscopy. Measured aliquots of fully deuteriated methanol (CD_3OD) were added to known amounts of magnesium mono-acetylacetone complex **13** in deuteriated benzene (C_6D_6) and in deuteriochloroform ($CDCl_3$), the proton spectra being recorded at 5 min after each addition, and at further intervals as necessary. Initially, exchange of the solvating methanol was observed and further additions of CD_3OD resulted in reduction of the methoxy ligand signal height. This was more rapid in $CDCl_3$ (16 mol equiv. of CD_3OD giving 50% reduction after 20 min) than in C_6D_6 (50 mol equiv. giving the same reduction after 30 min). The olefinic proton was also exchanged, though less rapidly than the methoxy ligand. In $CDCl_3$ both of these were completely exchanged on addition of 200 mol equiv. of CD_3OD (35 min after the addition). In C_6D_6 800 mol equiv. of CD_3OD gave complete exchange of the methoxy ligand (75 min) but the olefinic proton was not totally exchanged until the solution had been left overnight. Deuteriation of the acetyl methyl protons was not observed to an appreciable extent—this would require base beyond that available in the ligands.

The sequence of deuteriation reflects the loosely bonded alcohol ligand, the more strongly σ-bonded methoxy ligand and the still less easily exchanged olefinic hydrogen. A possible mechanism for the latter is shown in **24**. Although the chelate ring has been depicted in covalent form, the magnesium complex can alternatively be viewed as an ion-pair. Deuteriation of the acetylacetone at C-3, followed by enolisation with proton

† 1 cal = 4.184 J.

Table 3 δ_H Values for cyano derivatives produced by $Mg(OMe)_2$ promoted condensation

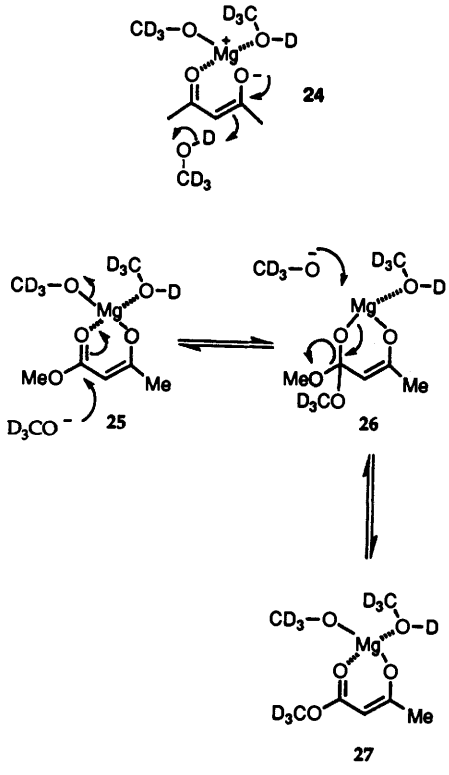
	Hydrogen atoms			
	a	h	i	Other signals
Methyl 2,4-dicyano-3-hydroxybut-2-enoate **30**	3.97	3.81	3.81	chelated OH 13.0
Methyl 2,4-dicyano-3-hydroxypent-2-enoate **34**	3.98	1.70[a]	4.08[b]	chelated OH 13.3
Methyl 2,4-dicyano-3-hydroxy-4-methylpent-2-enoate **33**	3.95	1.86	1.86	chelated OH 14.5
Dimethyl 2-cyano-3-hydroxybut-2-enedioate **35**	4.00[c]	—	—	chelated OH 12.80

[a] d, *J* 8 Hz. [b] q, *J* 8 Hz. [c] and g.

Table 4 δ_C Values for cyano derivatives produced by $Mg(OMe)_2$ promoted condensation

	Carbon atom								
	a	b	c	d	e	f	g	h	i
Methyl 2,4-dicyano-3-hydroxybut-2-enoate **30**	53.9	169.5	83.3	112.7	177.8	23.9	118.8[a]	—	—
Methyl 2,4-dicyano-3-hydroxypent-2-enoate **34**	53.9	169.8	82.0	112.6	182.3	30.9	115.9	16.8	—
Methyl 2,4-dicyano-3-hydroxy-4-methylpent-2-enoate **33**	54.0	171.4	80.5	112.6	186.3	39.0	119.2	25.0	25.0

[a] Shows slight triplet splitting in off-resonance spectrum: all multiplicities as expected.



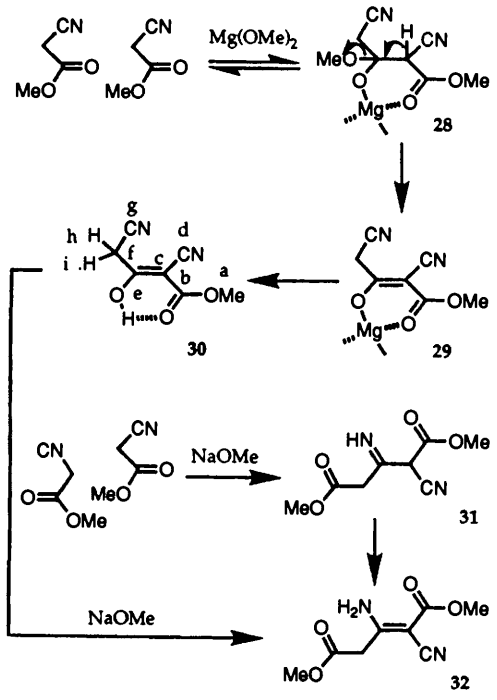
loss, would then give exchange of the olefinic hydrogen. The process would be expected to be of higher energy than that involving exchange of the methoxy ligand (above). Electrophilic attack at C-3 is well known in the context of alkylation at this centre.

The study was now continued using 1 mol of the magnesium mono-chelate of methyl acetoacetate **9** in the presence of 1 mol of magnesium methoxide in C_6D_6 with CD_3OD additions as required, ^1H NMR spectra being monitored at 5 min intervals. This provides a good model for the more complex β-keto ester systems involved in xanthyrone[24] and glaucyrone[4] chemistry in which excess magnesium methoxide is employed. Initially, exchange of the solvating ligand was observed, followed by exchange of the methoxy ligand, and then the olefinic proton, as before. Partial exchange of the acetyl methyl and ester methoxy protons occurred after 45 min with 100 mol CD_3OD. Allowing the solution to stand overnight with 200 mol CD_3OD gave 60% exchange, the exchange continuing to progress with time. These results can be explained as follows. Addition of excess CD_3OD to a solution containing magnesium methoxide forms deuteriated methoxide ions and nucleophilic attack of these at the ester carbonyl activated by the electropositive magnesium results in ester exchange **25** ⟶ **26** ⟶ **27**. This models the Claisen condensation which is so characteristic of these magnesium chelates. Exchange of the acetyl methyl protons occurs *via* a carbanion stabilised by delocalisation into the adjacent chelate ring. In chemistry involving magnesium chelates this models the mode of action as the nucleophilic partner in aldol condensations. The chelate itself is screened from attack as an acceptor in the reversible aldol reaction, and does not lead to product.

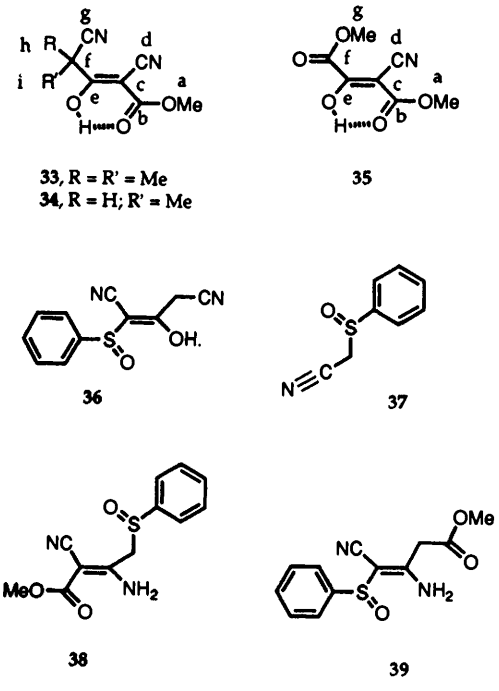
Reaction between methyl cyanoacetate and magnesium methoxide

Since some of the xanthyrones made by us possess cyano ester termini,[25] methyl cyanoacetate was added to the list of simple examples studied, and the work had an interesting and unexpected outcome. When allowed to react in methanol at 20 °C, using a 1:1 mol ratio of reactants, a stable colourless complex precipitated which on decomposition with aqueous acid gave a new compound in 78% yield, as crystals from methanol, mp 92–93 °C, $C_7H_6O_3N_2$. The compound gave a red ferric chloride reaction and ^1H and ^{13}C spectra (Tables 3 and 4) define its structure as methyl 2,4-dicyano-3-hydroxybut-2-enoate **30**: it apparently exists almost entirely in the chelated enolic form (ester carbonyl ν_{max} 1660 cm^{-1}). On the other hand if methyl cyanoacetate is refluxed with the non-chelating base sodium methoxide in methanol, the product is the known crystalline dimer (*Z*)-dimethyl 3-amino-2-cyanopent-2-enedioate **32**,[26–28] a useful intermediate in heterocyclic synthesis.[29,30] If the new compound **30** is refluxed with sodium methoxide it is converted into the latter dimer but if the latter dimer **32** is treated with magnesium methoxide it remains unchanged (Scheme 2).[31]

It is clear that **30**, the kinetic product from the 1,2-addition–Claisen competition, is intercepted and captured from solution as the magnesium complex **28**, the precursor to **29** in a reaction that in the presence of a non-chelating methoxide normally leads to the thermodynamic product **32** *via* **31**. The magnesium chelate can be monomethylated **34** and dimethylated **33** at C-4, but released from its chelate the compound itself becomes labile towards methoxide ions. Attempts were made to design a magnesium methoxide-catalysed crossed condensative version of the Claisen reaction and succeeded with methyl cyanoacetate and diethyl oxalate as components in a refluxing solution. Interestingly the reaction gave no precipitate but on acid work-up dimethyl 2-cyano-3-hydroxybut-2-enedioate **35**, mp 108–



Scheme 2 The kinetic and thermodynamic products from treatment of methyl cyanoacetate with methoxide ion

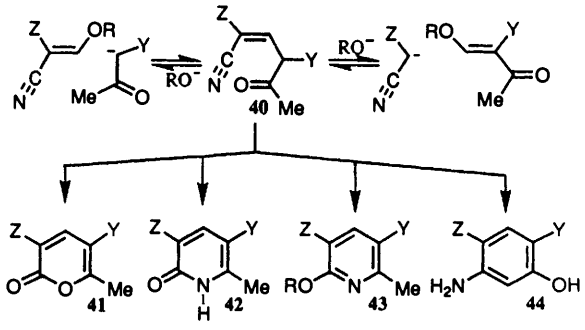


109 °C was obtained in 85% yield. However, attempted crossed condensations using methyl cyanoacetate with methyl acetate, formate, *p*-nitrobenzoate or benzoate in the presence of magnesium methoxide failed, though the product **30** from self-condensation of the cyanoacetate could be isolated as the magnesium complex.

The reaction between methyl cyanoacetate and phenyl cyanomethyl sulfoxide **37** was also studied in the presence of magnesium methoxide in refluxing methanol, but the product formed as the magnesium complex was not the Claisen structure **36** but the mixed 1,2-addition product $C_{12}H_{12}O_3N_2S$, methyl 3-amino-2-cyano-4-phenylsulfinylbut-2-enoate **38** (47% yield), mp 191–192 °C as shown by ^1H and ^{13}C NMR and other data (see Experimental section). At room temperature the same product was formed, but in much lower yield. An X-ray structure determination has been carried out by the late Dr M. J. Begley in our laboratory and confirms the structure and shows that it is the less congested (*Z*)-isomer which also has hydrogen bonding between the ester carbonyl and the amino group. The second possible type of 1,2-addition product **39**, derived from initial ionisation of phenyl cyanomethyl sulfoxide, was not isolated. Since neither **36** nor **39** was obtained, initial ionisation of phenyl cyanomethyl sulfoxide is not a favoured process and preferential ionisation of methyl cyanoacetate leads to **38** only.

Condensation of nitriles and alkoxymethylenes catalysed by chelating and non-chelating base

Our earlier studies have shown that the condensation of nitriles with alkoxymethylene-substituted 1,3-dicarbonyls and related systems can lead *via* **40** to 2-pyrones **41**, 2-pyridones **42**, 2-alkoxypyridines **43** or *m*-hydroxyanilines **44** as summarised in Scheme 3 where Z and Y are electron withdrawing groups.[32] The product type is dependent on the nature of the substituent groups (only dinitriles have been found to give alkoxypyridines) and the character (chelating or non-chelating), and initial molarity, of the base employed. Owing to the prototropic mobility of the propene group flanked by electron withdrawing substituents in **40**, the synthesis can be approached from either side of Scheme 3.



Scheme 3 Formation of 2-pyrones, 2-pyridones, 2-alkoxypyridines and *m*-hydroxyanilines from condensations involving alkoxymethylenes

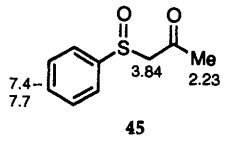
In our previous work Z and Y were chosen to be alkoxycarbonyl, acetyl or nitrile, but for reasons of chemical and pharmacological interest in the products, the present work was undertaken to determine the suitability of the system to synthesise phenylsulfinyl-substituted heterocyclic and aromatic compounds, and to monitor the effect of base type and initial molarity on product formation. Two condensations were selected for more detailed consideration. These were the reaction of phenyl cyanomethyl sulfoxide **37** with methyl 2-methoxymethyleneacetoacetate (which proceeds *via* the propene **47**) and phenylsulfinylacetone **45** with methyl 2-methoxymethylenecyanoacetate (which proceeds *via* the propene **48**). Phenyl cyanomethyl sulfoxide **37** was made (42%) by treating thiophenol with bromoacetonitrile in the presence of sodium methoxide, followed by controlled oxidation with hydrogen peroxide and titanium trichloride at 0 °C using the method of Watanabe *et al.*[33] This gave phenyl cyanomethyl sulfoxide in 88% yield. Phenylsulfinylacetone **45** was synthesised by the method of Iriuchijima and Tsuchihashi[34] using the irradiation of thiophenol and methacrylonitrile in the presence of oxygen for 6 h. Dehydrocyanation of the crude product with 0.1 M aqueous sodium hydroxide gave the required β-keto sulfoxide in 76% yield.

As a preliminary, attention was focussed on the ability of phenylsulfinylacetone **45** to form a complex with the chelating base magnesium methoxide **46**. Sulfinyl esters and amides are chelated by the magnesium from *tert*-butylmagnesium bromide and chelated structures of this kind have been proposed as

Table 5 Reaction between phenyl cyanomethyl sulfoxide **37** (1 mol) and methyl 2-methoxymethyleneacetoacetate (1 mol) catalysed by sodium methoxide in methanol

Amount of NaOMe/mol	Reflux time/h	Yield of pyridone **49** (%)	Yield of pyrone **50** (%)	Yield of benzoate **51** (%)
0.05	12	trace	0	0
0.15	12	3[a]	6[a]	0[a]
0.5	12	6	14	0
1.0	12	43	18	0
2.0	12	26[a]	21[a]	11[a]
4.0	12	12	29	14
8.0	12	3	24	25

[a] Yields determined by ^{1}H NMR analysis (all others by chromatographic isolation).



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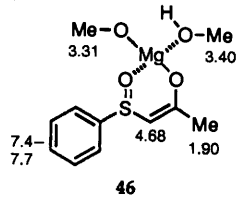

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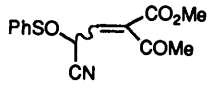

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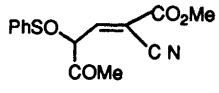

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models for transition states in asymmetric syntheses involving magnesium.[35,36] Refluxing magnesium methoxide in methanol (1 mol) with phenylsulfinylacetone gave a yellow crystalline solid, the ^{1}H NMR ($CDCl_3$) signals for which corresponded with a chelated structure analogous to those described for methyl acetoacetate and acetylacetone (see Table 1). For example in compounds **45** and **46**, the acetyl methyl has moved upfield of the ketonic precursor (from δ 2.23 to 1.90), as is found with other magnesium chelates, and the expected signals for the olefinic hydrogen and the methoxide and solvating methanol are present. There are also signals of relatively low intensity at δ 2.23 and 3.84 ascribed to unchelated phenylsulfinylacetone. In view of the analogous situation of chelation involving a proton, where sufoxides are known to be stronger hydrogen bonding agents than ketones,[37] the formation of such magnesium chelates is hardly surprising.

As Table 5 shows, three products were identified from the sodium methoxide catalysed reactions between phenyl cyanomethyl sulfoxide and methyl 2-methoxymethyleneacetoacetate in refluxing methanol. These proved to be 5-methoxycarbonyl-6-methyl-3-phenylsulfinyl-2-pyridone **49**, $C_{14}H_{13}NO_4S$, mp 249–251 °C; 5-methoxycarbonyl-6-methyl-3-phenylsulfinyl-2-pyrone **50**, $C_{14}H_{12}O_5S$, mp 94–95 °C; and methyl 4-amino-2-hydroxy-5-phenylsulfinylbenzoate **51**, $C_{14}H_{13}NO_4S$, mp 160–165 °C, all derived *via* **47** and separated chromatographically. Their structures accord with ^{1}H NMR and infrared spectra as indicated in the Experimental section. When catalysed by 1 mol equiv. of sodium methoxide none of the benzoate **51** was formed but the pyridone **49** was obtained in 43% yield and the pyrone **50** in 18% yield (Table 5). On increasing the methoxide to 8 mol equiv. however, 26% of benzoate **51** was now obtained along with 24% of pyrone **50** and 3% of pyridone **49**. The mechanism of similar responses to the molarity of base has been discussed in our earlier paper[32] and the requirement for excess base in order to form the carbocylic aromatic is in agreement with that work.

Table 6 Reaction between phenylsulfinylacetone **45** (1 mol) and methyl 2-methoxymethylenecyanoacetate (1 mol) catalysed by sodium methoxide in methanol

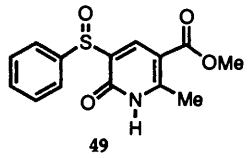
Amount of NaOMe/mol	Reflux time/h	Yield of pyridone **52** (%)
0.05	12	3[a]
0.125	12	3[a]
0.5	12	8
1.0	12	33
2.0	12	15[a]
4.0	12	14[a]
8.0	12	13[a]

[a] Yields determined by ^{1}H NMR analysis (all others by isolation).

Table 7 Reaction between phenylsulfinylacetone **45** (1 mol) and methyl 2-methoxymethylenecyanoacetate (1 mol) catalysed by magnesium methoxide in methanol at 20 °C

Amount of $Mg(OMe)_2$/mol	Reaction time/h	Yield of pyridone **52** (%)	Yield of benzoate **54** (%)
0.125	24	0	0
0.5	24	1	0
1.0	24	30	0
2.0	24	13	35
4.0	24	6[a]	36[a]

[a] Yields determined by isolation (all others by ^{1}H NMR analysis).



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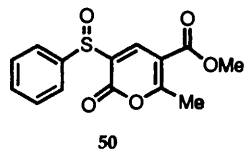

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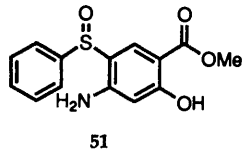

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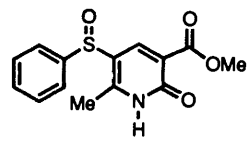

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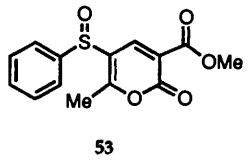

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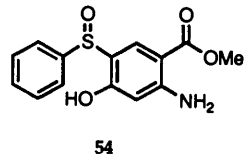

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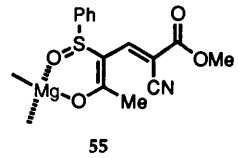

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The condensation of phenylsulfinylacetone with methyl 2-methoxymethylenecyanoacetate in refluxing methanol containing 1 mol equiv. sodium methoxide gave 3-methoxycarbonyl-6-methyl-5-phenylsulfinyl-2-pyridone **52** (33%) but only a little 3-methoxycarbonyl-6-methyl-5-phenylsulfinyl-2-pyrone **53** was detected (and this spectroscopically). No methyl 2-amino-4-hydroxy-5-phenylsulfinylbenzoate **54** was obtained even after 8 mol equiv. of sodium methoxide was employed (Table 6). Replacement of the sodium methoxide by 1 mol equiv. of magnesium methoxide at 20 °C again gave the pyridone **52** (30%),

but with little sign of the benzoate **54** or pyrone **53**. However the benzoate **54** could be obtained in 36% yield [along with a little pyridone **52** (6%), but no pyrone **53**], when excess (4 mol equiv.) magnesium methoxide was employed (Table 7). This provides another example of the considerable effects that substitution of a chelating base for a non-chelating base can have. It would appear that in the reactions with excess magnesium methoxide much or all the substrate is in magnesium-complexed form **55**, with further base available, as discussed above. This complex is suitably oriented for carbocyclisation by formation of the carbon anion next to the magnesium chelate ring, followed by addition across the nitrile, and tautomeric change, leading irreversibly to the aminobenzoate **54**. Although yields of substituted benzoates and pyridines in the present phenylsulfinyl examples are modest, the products are easily obtained and in our earlier paper[32] examples reach 74% (pyridone) and 87% (substituted benzoate).

Experimental

Melting points are uncorrected and were determined using a hot stage microscope. Infrared spectra were recorded on a Pye Unicam SP-200 spectrophotometer as either a liquid film, a solution in chloroform, or a KBr disc. Routine ^{1}H NMR spectra were determined on a Perkin-Elmer R32 machine at 90 MHz, others being obtained on Bruker instruments at 80, 250 and 400 MHz, all in $CDCl_3$ unless stated otherwise. ^{13}C Spectra were measured using a Bruker FT instrument at 63.1 MHz. Gas chromatography was carried out using either a capillary Carbowax 20M column (25 m) or a capillary OV 17 column (25 m). Mass spectra were obtained using an upgraded V.G. Micromass 7070E mass spectrometer. Methanol was dried by the magnesium methoxide method.

Preparation of magnesium mono-chelates

The appropriate ligand (20.6 mmol) was added slowly to a solution of magnesium methoxide [from magnesium (0.5 g, 20.6 mmol) and dry methanol (50 cm^3)] and refluxed for 1 h. After cooling, the precipitated chelate was filtered off, washed with anhydrous diethyl ether and dried. It was then purified by recrystallisation under dry nitrogen. ^{1}H NMR data are given in Table 1 and ^{13}C NMR data in Table 2.

Magnesium mono-chelate of acetylacetone 13. This chelate was made from dry acetylacetone (2.06 g, 20.6 mmol), and formed colourless needles (3.64 g, 95%) from dry methanol, mp 300 °C (decomp.); ν_{max}(KBr)/cm^{-1} 3400 (OH), 1605 (chelated carbonyl), 1515 (C=C).

Magnesium mono-chelate of methyl acetoacetate 9. This chelate was made from methyl acetoacetate (2.39 g, 20.6 mmol), and formed needles (4.04 g, 97%) from dry toluene, mp 289 °C (decomp.); ν_{max}(KBr)/cm^{-1} 3290 (OH), 1640 (chelated ester carbonyl), 1515 (C=C). Preparations using 0.5, 1.0 or 6 mol of magnesium methoxide gave the same product.

Magnesium mono-chelate of dimethyl malonate 17. This chelate was prepared from dimethyl malonate (2.64 g, 20 mmol) and formed both needle-shaped and cubic crystals [mp ~300 °C (decomp.)] when recrystallised from methanol in a dry box. The two forms had closely similar spectra: ν_{max}(KBr)/cm^{-1} 2950 (OH), 1660 (chelated esters).

***C*-Methyl complexes 10, 14 and 18.** This series of complexes was similarly prepared to those above and details of the ^{1}H NMR spectra are reported in Table 1.

Magnesium mono-chelate of phenylsulfinylacetone 46. Phenylsulfinylacetone (0.455 g, 2.5 mmol) in a little dry methanol was added dropwise to magnesium methoxide in methanol [from magnesium (0.068 g, 2.5 mmol) in dry methanol (12 cm^3)]. The mixture was refluxed for 1 h and stirred at room temperature for 14 h after which the solvent was distilled off and the residue was dried under vacuum. Attempts to purify it by recrystallisation were not successful and the ^{1}H NMR spectrum showed contamination with some uncomplexed phenylsulfinylacetone. δ_H 1.90 (3 H, s, Me), 3.31 (3 H, s, MgOMe), 3.40 (s, *Me*OH), 4.68 (1 H, s, CH=), 7.40–7.77 (m, ArH).

Magnesium bis-chelate of acetylacetone 22. Following the general method this was synthesised from acetylacetone (4.12 g, 41.2 mmol) and magnesium methoxide [from magnesium (0.5 g, 20.6 mmol) in dry methanol (50 cm^3)]. When recrystallised from methanol it formed colourless needles (4.4 g, 98%) mp 265–267 °C (lit.,[12] 265–267 °C); ν_{max}(KBr)/cm^{-1} 1610 (keto carbonyl), 1515, (C=C).

Investigation of proton–deuterium exchange between the magnesium mono-chelate of acetylacetone 13 and deuteriated methanol in $CDCl_3$

Magnesium mono-chelate of acetylacetone (12 mg, 0.064 mmol) was dissolved in $CDCl_3$ (0.5 cm^3) and measured aliquots of CD_3OD corresponding to 4, 5, 12, 16, 30, 50 and 100 mol equiv. relative to the chelate were added. After shaking and standing for 5 min, the ^{1}H NMR spectrum (80 MHz) of the solution was recorded in each case.

Investigation of proton–deuterium exchange between the magnesium mono-chelate of acetylacetone 13 and deuteriated methanol in C_6D_6

Magnesium mono-chelate of acetylacetone (12 mg, 0.064 mmol) was dissolved in deuteriated benzene (0.5 cm^3) and measured aliquots of CD_3OD corresponding to 25, 50, 100, 200 and 800 mol equiv. relative to the chelate were added. After shaking and standing for 15 min, the ^{1}H NMR spectrum (80 MHz) of the solution was recorded in each case. With 800 mol equiv. of CD_3OD the solution was also allowed to stand for 24 h and the proton spectrum was re-recorded.

Investigation of proton–deuterium exchange between the magnesium mono-chelate of methyl acetoacetate 9 and deuteriated methanol in the presence of magnesium methoxide (1.0 mol equiv.)

Magnesium mono-chelate of methyl acetoacetate (12 mg, 0.064 mmol) and magnesium methoxide (5.5 mg, 0.064 mmol) were dissolved in C_6D_6 (0.5 cm^3) and the ^{1}H NMR spectrum was recorded. Measured aliquots of CD_3OD corresponding to 10, 50, 100 and 200 mol equiv. relative to the chelate were added. The procedure of the preceding experiment was then followed.

Methyl 2,4-dicyano-3-hydroxybut-2-enoate 30

Methyl cyanoacetate (8.0 g, 0.08 mol) was added to stirred magnesium methoxide solution [from magnesium (1.0 g, 0.042 mol) in anhydrous methanol (100 cm^3)] and stirred under nitrogen at room temperature for 24 h. The solvent was evaporated and the residue was washed with dry diethyl ether (20 cm^3). Hydrochloric acid (4 M; 50 cm^3) and ice were added and the solution was extracted with chloroform (3 × 20 cm^3). The combined organic extracts were washed with water, dried and evaporated to give a yellow solid which when recrystallised from cyclohexane or isopropyl alcohol gave *methyl 2,4-dicyano-3-hydroxybut-2-enoate* **30** (7.3 g, 55%), mp 93 °C (Found: C, 50.85; H, 3.75; N, 16.6%; M$^+$, 166.038. $C_7H_6N_2O_3$ requires C, 50.6; H, 3.65; N, 16.85%; *M*, 166.038); λ_{max}(EtOH)/nm 262 (ε/dm^3 mol^{-1} cm^{-1} 16050) shifting to λ_{max} 255 (13100) in 0.01 M ethanolic HCl, and 267 (18400) in 0.01 M ethanolic KOH; ν_{max}(KBr)/cm^{-1} 3250–3600 (chelated OH), 2270 (CN), 2230 (CN conjugated), 1660 (chelated ester carbonyl), 1590 (C=C). The best yield attained was 78%.

Methyl 2,4-dicyano-3-hydroxypent-2-enoate 34

Methyl cyanoacetate (0.98 g, 10 mmol) was added to a stirred solution of magnesium methoxide [from magnesium (0.5 g, 20.6 mmol) and anhydrous methanol (50 cm^3)] and stirring under nitrogen was continued at room temperature for 18 h. Methyl

iodide (0.71 g, 5 mmol) was added and the mixture was stirred for a further 4 h. The solvent was evaporated and the residue was taken up in 2 M hydrochloric acid and the resulting solution was extracted with chloroform. Washing with water, drying ($MgSO_4$) and evaporation, followed by crystallisation from hexane gave *methyl* 2,4-*dicyano*-3-*hydroxypent*-2-*enoate* **34** (0.42 g, 47%) as plate-like crystals, mp 77–79 °C (Found: C, 52.95; H, 4.45; N, 15.35%; M^+, 180.054. $C_8H_8N_2O_3$ requires C, 53.35; H, 4.45; N, 15.55%; *M*, 180.053); $\nu_{max}(CHCl_3)/cm^{-1}$ 3600–3650 (OH), 2240 (CN), 1670 (chelated ester carbonyl), 1600 (C=C).

Methyl 2,4-dicyano-3-hydroxy-4-methylpent-2-enoate 33

The magnesio-derivative **29** was prepared as above and treated with methyl iodide (2.83 g, 20 mmol) as above. Work up as before gave *methyl* 2,4-*dicyano*-3-*hydroxy*-4-*methylpent*-2-*enoate* **33** (0.58 g, 30%) as needles from hexane, mp 117–119 °C (Found: C, 55.7; H, 5.25; N, 14.5%; M^+, 194.069. $C_9H_{10}N_2O_3$ requires C, 55.65; H, 5.15; N, 14.45%; *M*, 194.069); $\nu_{max}(CHCl_3)/cm^{-1}$ 3600–3500 (OH), 2240 (CN), 1665 (ester carbonyl), 1590 (C=C).

Dimethyl 2-cyano-3-hydroxybut-2-enedioate 35

Diethyl oxalate (3.65 g, 0.025 mol) was added dropwise to a stirred and refluxing solution of magnesium methoxide in methanol [from magnesium (0.6 g, 0.025 mol) and anhydrous methanol (25 cm^3)]. Methyl cyanoacetate (1.24 g, 0.012 mol) was added, and the solution was refluxed for 12 h, after which the solvent was evaporated under reduced pressure and the residue was washed with dry diethyl ether. Hydrochloric acid (4 M; 25 cm^3) was added and the resulting solution was extracted with chloroform (3 × 30 cm^3). The combined organic extracts were washed with water, dried and evaporated. Recrystallisation of the product from ethyl acetate–hexane gave *dimethyl* 2-*cyano*-3-*hydroxybut*-2-*enedioate* **35** (2.7 g, 58%) as needles, mp 108–109 °C (Found: C, 45.6; H, 4.05; N, 7.4%; M^+, 185.032. $C_7H_7NO_5$ requires C, 45.4; H, 3.8; N, 7.55%; *M*, 185.032); λ_{max}(EtOH)/nm 267; $\nu_{max}(KBr)/cm^{-1}$ 2235 (CN), 1745 (unchelated ester carbonyl), 1665 (chelated ester carbonyl), 1605 (C=C). In another experiment the yield was 85%.

(*Z*)-Methyl 3-amino-2-cyano-4-phenylsulfinylbut-2-enoate 38

Phenyl cyanomethyl sulfoxide **37** (0.495 g, 3 mmol) was added to a stirred solution of magnesium methoxide [from magnesium (0.072 g, 3 mmol) and anhydrous methanol (12 cm^3)]. Methyl cyanoacetate (0.297 g, 3 mmol) was then added and the solution was refluxed for 20 h. The solvent was evaporated and the residue was washed with diethyl ether. Hydrochloric acid (4 M; 10 cm^3) was added and the solution was extracted with chloroform (3 × 10 cm^3). The combined organic extracts were washed with water, dried and evaporated. Recrystallisation of the resulting white solid from methanol gave (Z)-*methyl* 3-*amino*-2-*cyano*-4-*phenylsulfinylbut*-2-*enoate* **38** (0.37 g, 47%) as colourless crystals mp 191–192 °C (Found: C, 54.3; H, 4.7; N, 10.9%; M^+, 264.056. $C_{12}H_{12}N_2O_3S$ requires C, 54.55; H, 4.6; N, 10.6%; *M*, 264.057); $\nu_{max}(KBr)/cm^{-1}$ 3220, 3280, 3310 (NH), 3380 (NH), 2220 (CN), 1680 (ester carbonyl), 1625 (C=C), 1040 (S=O); λ_{max}(EtOH)/nm 205 infl. ($\varepsilon/dm^3\ mol^{-1}\ cm^{-1}$ 19 300), 259 infl. (5300), 291 (13 300); δ_H(400 MHz) 3.70 (3 H, s, CO_2Me), 3.80 (1 H, d, *J* 10, H_aCS=O), 3.97 (1 H, d, *J* 10, H_bCS=O), 7.1 (1 H, br s, NH), 7.55–7.68 (5 H, m, ArH), 8.98 (1 H, br s, NH chelated); δ_C(100.5 MHz) 51.97 (OMe), 57.07 (CH_2), 117.74 (CN), 124.10, 129.82 and 132.38 (ArCH), 140.00, 162.88, 167.47.

Phenylthioacetonitrile

Freshly distilled thiophenol (55 g, 0.5 mol) was added under nitrogen to sodium (11.5 g, 0.5 mol) dissolved in dry methanol (150 cm^3), followed by bromoacetonitrile (60 g, 0.5 mol) added dropwise. The product was allowed to stand at 20 °C for 2 h and then at 50 °C for 5 h. The methanol was removed under reduced pressure and water (150 cm^3) was added. The product was isolated by extraction with chloroform and purified by column chromatography on silica eluting with 20% diethyl ether in hexane. Phenylthioacetonitrile was obtained as a colourless oil (31.3 g, 42%) (lit.,[38] bp 154–157 °C) (Found: M^+, 149.027. C_8H_7NS requires *M*, 149.030); ν_{max}(film)/cm^{-1} 2260 (CN); $\delta_H(CDCl_3)$ 3.56 (2 H, s, CH_2), 7.3–7.6 (5 H, m, ArH).

Phenyl cyanomethyl sulfoxide 37

Phenylthioacetonitrile (14.9 g, 0.1 mol) and titanium trichloride (30.8 g, 0.2 mol) in methanol (200 cm^3) and water (50 cm^3) were treated at 0 °C with hydrogen peroxide (0.7 mol, 79.5 cm^3; 30% aqueous) in methanol (200 cm^3). The progress of the reaction was monitored by TLC (silica plates, eluting with chloroform and ethyl acetate 91 : 1). After 30 min water (200 cm^3) was added and the product was extracted with chloroform (4 × 100 cm^3). Evaporation and chromatography on dry silica (eluting with 5% ethyl acetate in chloroform) gave phenyl cyanomethyl sulfoxide **37** (14.52 g, 88%), mp 63.5–64.5 °C (lit.,[33] 64–65 °C) (Found: M^+, 165.023. C_8H_7NOS requires *M*, 165.025); ν_{max}(KBr)/cm^{-1} 2275 (CN), 1060 (S=O); $\delta_H(CDCl_3)$ 3.65 (1 H, d, *J* 18), 3.96 (1 H, d, *J* 18), 7.58–7.95 (5 H, m, ArH).

Methyl 4-amino-2-hydroxy-5-phenylsulfinylbenzoate 51 5-methoxycarbonyl-6-methyl-3-phenylsulfinyl-2-pyrone 50 and 5-methoxycarbonyl-6-methyl-3-phenylsulfinyl-2-pyridone 49

Phenyl cyanomethyl sulfoxide **37** (0.5 g, 3.0 mmol) was refluxed for 12 h with methyl 2-methoxymethyleneacetoacetate (0.5 g, 3.2 mmol) and sodium methoxide solution [from sodium 0.276 g, 12 mmol) and dry methanol (12 cm^3)]. Work-up and column chromatography on silica gel HF 254 (eluent 10% ethyl acetate in hexane) gave *methyl* 4-*amino*-2-*hydroxy*-5-*phenylsulfinyl*-*benzoate* **51** (0.12 g, 14%), mp 160–160.5 °C from isopropyl alcohol (Found: C, 57.8; H, 4.75; N, 4.6%; M^+, 291.054. $C_{14}H_{13}NO_4S$ requires C, 57.7; H, 4.5; N, 4.8%; *M*, 291.056); $\nu_{max}(KBr)/cm^{-1}$ 3405 (NH), 3310 (NH), 3205 (OH), 1665 (ester carbonyl), 1565, 1495 (Ar), 1040 (S=O); $\delta_H(CDCl_3)$ 3.92 (3 H, s, CO_2Me), 5.45 (2 H, br s, NH_2), 6.05 [1 H, s, ArH (benzoate)], 7.4–7.7 [5 H, m, ArH(phenyl)], 8.00 [1 H, s, ArH(benzoate)], 11.08 (1 H, s, OH); $\delta_C(CDCl_3)$ 52.07 (Me), 102.61 (C-6), 102.72, 115.57, 124.84, 128.92, 130.33 (Ar-C), 132.24 (C-3), 143.11, 153.86, 165.46, 169.71.

Also eluted from the column was 5-*methoxycarbonyl*-6-*methyl*-3-*phenylsulfinyl*-2-*pyrone* **50** (0.249 g, 29%), which gave needles from ethyl acetate–hexane, mp 94–95 °C (Found: C, 57.3; H, 4.15%; M^+, 292.041. $C_{14}H_{12}O_5S$ requires C, 57.55; H, 4.15%; *M*, 292.040); $\nu_{max}(KBr)/cm^{-1}$ 3200–3260 (enolic OH), 1745 (pyrone carbonyl), 1720 (ester carbonyl), 1620, 1550 (Ar), 1060 (S=O); δ_H(400 MHz, $CDCl_3$) 2.70 (3 H, s, CMe), 3.93 (3 H, s, CO_2Me), 7.45–7.70 (3 H, m, ArH), 7.66–8.05 (2 H, m, ArH), 8.57 (1 H, s, pyrone CH); δ_C(100.5 MHz, $CDCl_3$) 20.19 (Me), 52.97 (Me), 109.85, 125.32, 129.31, 129.77, 131.95 (ArC), 140.19 (pyrone CH), 142.25, 156.27, 163.48, 172.78.

A third compound eluted from the column proved to be 5-*methoxycarbonyl*-6-*methyl*-3-*phenylsulfinyl*-2-*pyridone* **49** (0.104 g, 12%), which gave crystals from methanol, mp 249–251 °C (Found: C, 57.1; H, 5.1; N, 4.5%; M^+, 291.055. $C_{14}H_{13}NO_4S$ requires C, 57.7; H, 4.5; N, 4.8%; *M*, 291.056); $\nu_{max}(KBr)/cm^{-1}$ 3480 (NH), 1720 (ester carbonyl), 1650 (pyridone carbonyl), 1045 (S=O); $\delta_H(CDCl_3)$ 2.72 (3 H, s, Me), 3.92 (3 H, s, CO_2Me), 7.4–7.57 (3 H, m, ArH), 7.78–7.94 (2 H, m, ArH), 8.73 (1 H, s, pyridone CH), 13.10 (1 H, br s, NH); δ_C(20.1 MHz) 19.3 (Me), 52.1 (OMe), 101.9, 109.8, 125.5, 129.05, 131.59 (Ar-C), 138.87 (pyridone CH), 143.48, 155.19, 160.60, 164.51. See also Table 5.

Phenylsulfinylacetone 45

Freshly distilled thiophenol (17 g, 0.156 mol) and methacrylonitrile (15 g, 0.173 mol) were dissolved in hexane (2 dm^3) in a photochemical cell. Oxygen was bubbled through the solution

which was irradiated with a 450 W medium pressure ultraviolet lamp for 6 h. The reaction was monitored by GLC using a Carbowax 20M column at 180 °C. Evaporation gave crude phenyl 2-cyano-2-hydroxypropyl sulfoxide (29 g) which was dissolved in benzene (800 cm^3) and stirred at 45 °C with 0.1 M aqueous sodium hydroxide (600 cm^3) for 3 h. The organic phase was separated and the aqueous liquors re-extracted with benzene. The combined organic extracts were washed with water, dried (Na_2SO_4) and evaporated to give a white solid which was chromatographed on silica gel 60 H eluting with 15% ethyl acetate in chloroform. Phenylsulfinylacetone **45** (21 g, 76%) was obtained as colourless crystals from ethyl acetate–hexane, mp 78–79 °C (lit.,[34] 76–77 °C) (Found: M^+, 182.039. Calc. for $C_9H_{10}O_2S$: *M*, 182.040); ν_{max}(KBr)/cm^{-1} 1708 (C=O); δ_H(80 MHz, $CDCl_3$) 2.22 (3 H, s, Me), 3.88 (2 H, s, CH_2), 7.4–7.9 (5 H, m, ArH).

Reaction between phenylsulfinylacetone 45 and methyl 2-methoxymethylenecyanoacetate catalysed by sodium methoxide (1 mol equiv.)

Phenylsulfinylacetone (0.445 g, 2.5 mmol) and 2-methoxymethylenecyanoacetate (0.38 g, 2.7 mmol) were added to sodium methoxide solution [from sodium (0.058 g, 2.5 mmol) and dry methanol (12 cm^3)] and refluxed for 12 h. The product was neutralised with 2 M hydrochloric acid and extracted with chloroform. The combined chloroform extracts were washed with water, dried (Na_2SO_4) and evaporated to give a solid (0.789 g). Crystallisation from methanol gave *3-methoxycarbonyl-6-methyl-5-phenylsulfinyl-2-pyridone* **52** (0.237 g, 33%), mp 233–244 °C (Found: C, 58.05; H, 4.75; N, 4.5%; M^+, 291.059. $C_{14}H_{13}NO_4S$ requires C, 57.7; H, 4.5; N, 4.8%; *M*, 291.056); ν_{max}(KBr)/cm^{-1} 3440 (NH), 1755 (ester carbonyl), 1670 (pyridone carbonyl), 1050 (S=O); δ_H(80 MHz, $CDCl_3$) 2.63 (3 H, s, Me), 3.88 (3 H, s, CO_2Me), 7.4–7.64 (5 H, m, ArH), 8.48 (1 H, s, pyridone CH), 12.64 (1 H, br s, NH). See also Table 6.

Reaction between phenylsulfinylacetone 45 and methyl 2-methoxymethylenecyanoacetate catalysed by magnesium methoxide (4 mol equiv.)

Phenylsulfinylacetone **45** (0.455 g, 2.5 mmol) and methyl 2-methoxymethylenecyanoacetate (0.38 g, 2.7 mmol) were added to magnesium methoxide solution [from magnesium (0.243 g, 10 mmol) and dry methanol (12 cm^3)] and stirred under nitrogen at 20 °C for 24 h. Chloroform (10 cm^3) was added and the solution was neutralised (2 M HCl). Extraction with chloroform gave a solid (0.6 g) which was chromatographed on silica gel HF 254, eluting with ethyl acetate–hexane (1 : 1) to give *methyl 2-amino-4-hydroxy-5-phenylsulfinylbenzoate* **54** (0.262 g, 36%), as needles from isopropyl alcohol, mp 169–170 °C (Found: C, 57.8; H, 4.65; N, 4.95%; M^+, 291.056. $C_{14}H_{13}NO_4S$ requires C, 57.7; H, 4.5; N, 4.8%; *M*, 291.056); ν_{max}(KBr)/cm^{-1} 3530 (NH), 3400 (NH), 3260 (OH), 1690 (ester carbonyl), 1620, 1520 (aromatic ring), 1045 (S=O); δ_H(80 MHz, $CDCl_3$) 3.85 (3 H, s, CO_2Me), 6.05 (2 H, br s, NH_2), 7.26 (1 H, s, HOC=C*H*CNH_2), 7.47–7.95 (5 H, m, ArH), 7.87 (1 H, s, OSC=CHCCO_2), 10.00 (1 H, s, OH).

3-Methoxycarbonyl-6-methyl-5-phenylsulfinyl-2-pyridone **52** (0.044 g, 6%), identical with the specimen above, was also isolated from the column. See also Table 7.

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