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LETTERS

Synthesis and structure of highly polarised double-bond compounds derived from *S*-proline

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Abstract

Reaction of the chiral iminium salt **3** with stabilised carbanions gives the compounds **4**–**9** containing a highly polarised double bond. The extent of this polarisation is determined by variable temperature ^{1}H NMR studies, comparison of ^{13}C NMR chemical shifts and an X-ray structure determination. © 2000 Elsevier Science Ltd. All rights reserved.

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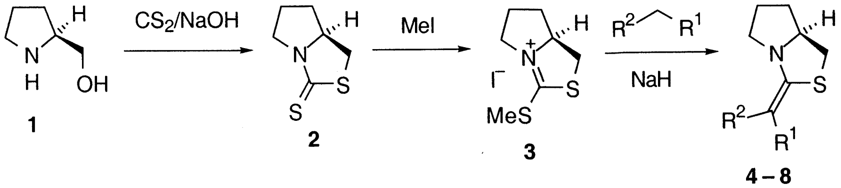
Some time ago we described the use of the chiral iminium salt **3** derived from (*S*)-proline for the kinetic resolution of secondary alcohols.[1] While this work was in progress, Yadav and co-workers briefly reported that the salt **3** reacted with the anions of dimethyl malonate and malononitrile to give **4** and the corresponding dinitrile[2], but the structure and reactivity of these products was not examined in detail. In view of the high degree of polarisation expected for the double bond of such compounds, their structure is of some interest and their chirality may potentially be exploited in developing new methods in asymmetric synthesis. We report here the synthesis of a wider range of such compounds, an examination of their structure using NMR methods and in one case an X-ray diffraction study, and a preliminary survey of their reactivity.



The salt **3** was readily prepared by treatment of (*S*)-prolinol **1** with CS_2 and aqueous sodium hydroxide to give the thiazolidinethione **2** followed by quaternisation with methyl iodide.

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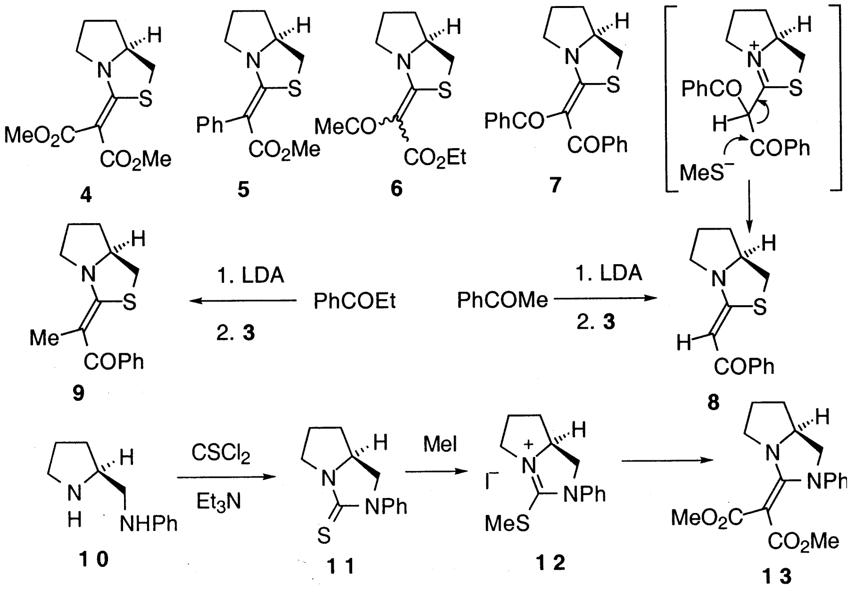
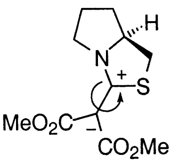
Addition of this to a THF solution of the appropriate acidic methylene compound and sodium hydride followed by aqueous work-up and chromatographic purification gave the desired compounds in moderate to good yield. Starting from dimethyl malonate, methyl phenylacetate and ethyl acetoacetate gave the products **4**, **5** and **6**, respectively.[3] The corresponding reaction of dibenzoylmethane proved to be more complex. Unexpectedly the products included 1,1-dibenzoylethane and 2,2-dibenzoylpropane presumably from methylation of the anion by **3**, and the desired product **7** was only formed in low yield and was accompanied by the monobenzoyl product **8**. As shown this probably results from attack of MeS^- on a benzoyl group in the intermediate rather than the deprotonation required to give **7**. Confirmation of the structure of **8** was obtained by its more rational synthesis by treatment of acetophenone with LDA followed by the salt **3**, and by starting from propiophenone the compound **9** was obtained similarly.



The imidazolidine-based salt **12** also reacted with the anion of dimethyl malonate to give the product **13**. Formation of salt **12** was achieved by treatment of the known diamine **10**[4] with thiophosgene and triethylamine to give **11** followed by quaternisation with methyl iodide.

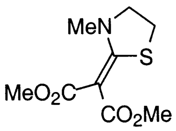
There has been considerable interest in compounds containing a double bond with electron donors on one end and acceptors on the other.[5] The bond may become so highly polarised that it is more accurately viewed in the fully charge-separated form with a single bond connecting delocalised anion and cation fragments. One consequence of this is that there is free rotation about the bond and this feature was immediately apparent in the spectra of **4**, **7** and **13**, which at room temperature showed only a single set of signals for the ester and ketone groups. In the cases of **4** and **13** this was quantified by means of a variable temperature ^{1}H NMR study, which gave coalescence temperatures and free energy barriers to rotation indicating a high contribution from the charge-separated forms **4a** and **13a** as shown. The values obtained for $\Delta G^{\#}$ are comparable to those reported for the model compounds **14**[6] and **15**.[7] It should be noted that all the compounds with $R^1 \neq R^2$ showed a single set of NMR signals at room temperature. In the case of **6** this probably also implies that there is essentially free rotation about the double bond, while for **5**, **8** and **9** with only a single strong electron withdrawing group present, the compounds exist as a single geometrical isomer, most likely the ones shown with the most powerful donor and acceptor groups *E* to one another as previously found.[5]



4a

T_C −50 °C

$\Delta G^{\#}$ 47.4 kJmol^{-1}



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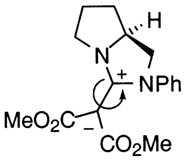
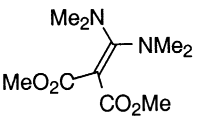
$\Delta G^{\#} < 39.5$ kJmol^{-1}



13a

T_C −27 °C

$\Delta G^{\#}$ 46.7 kJmol^{-1}



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$\Delta G^{\#} < 33.65$ kJmol^{-1}

A further measure of the extent of bond-polarisation in such compounds is the difference in chemical shift of the two carbons observed by ^{13}C NMR.[5] As shown in Table 1, the signal for the effectively cationic carbon adjacent to N comes in the range 160–170 ppm, while the effectively anionic carbon between the acceptor groups is greatly shielded and appears around 90–100 ppm or in the case of **13** at 75.5 ppm. Although there are few good models for compounds **4**–**9**, the value of $\Delta\delta$ for **13** may be compared with 85.3 for **16**.[8]

Table 1
Some properties of compounds **4**–**9** and **13**

Compound	Yield (%)	Mp (°C)	$[\alpha]_D$	δ_C (C=C)		$\Delta\delta$
4	81	79–80	−311.5	166.7	90.8	75.9
5	59	81–82	−147.5	161.9	98.2	63.7
6	56	(oil)	–	168.2	101.8	66.4
7	~10	–	–	168.8	108.9	59.9
8	78	122–124	−368.9	162.6	88.2	74.4
9	80	130–132	−217.2	166.6	101.7	64.9
13	84	135–137	−19.4	165.0	75.5	89.5

A further insight into the structure of these compounds was provided by a single-crystal X-ray diffraction study of **5** (Fig. 1).[9] This showed two inequivalent, but closely similar, molecules to be present in the unit cell. Besides confirming the relative *E* configuration of the nitrogen and ester groups about the double bond, this allowed assessment of the extent of polarisation of the double bond. The length of 1.37 Å for the C(1)–C(7) bond is indicative of about 80% double bond character and may be compared to the values shown for the model compounds **17**–**19**.[10] As expected there is also significant shortening of the C(1)–S(1) (1.778 Å) and C(1)–N(1) (1.346 Å) bonds, but there is no evidence for pyramidalisation at either C(1) or C(7).

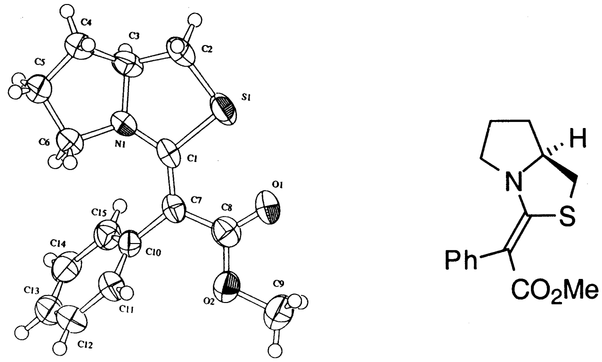
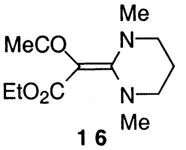


Figure 1. X-Ray structure of **5**. Selected bond lengths; C(1)–S(1) 1.778(4), C(2)–S(1) 1.803(5), C(1)–N(1) 1.346(5), C(1)–C(7) 1.370(6), C(7)–C(10) 1.497(6), C(7)–C(8) 1.445(6), C(8)–O(1) 1.217(5), C(8)–O(2) 1.351(6) Å; dihedral angles S(1)–C(1)–C(7)–C(8) 5.8(8), S(1)–C(1)–C(7)–C(10) 167.5(4), C(1)–C(7)–C(8)–O(1) 7.5(10), C(1)–C(7)–C(8)–O(2) 173.3(5)°; angle sum at C(1) 360.0, C(7) 359.6°

A preliminary study of the reactivity of **4** with nucleophiles and electrophiles showed it to be quite unreactive. Treatment with methyl iodide gave no reaction, while with methyl triflate the only process observed was protonation by adventitious triflic acid. Compound **4** was also inert to butyllithium and ethylmagnesium bromide. It appears that the charge in **4** is too delocalised to permit reaction with either nucleophiles or electrophiles, but compounds such as **5**, **8** and **9** where the extent of anion delocalisation is less may show useful reactivity and this is currently being examined.



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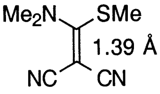

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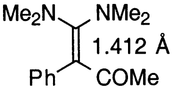

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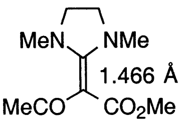

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9. Crystal data for **5**: $C_{15}H_{17}NO_2S$, $M=275.36$, colourless plate, crystal dimensions 0.50×0.40×0.20 mm, monoclinic, space group $P2_1$ (#4), $a=8.555(3)$, $b=15.555(3)$, $c=10.663(2)$ Å, $\beta=91.23(2)°$, $V=1418.7(5)$ Å^3, $Z=4$, $D_{calcd}=1.289$ Mg m^{-3}, $T=293$ K, $R=0.037$, $R_w=0.030$ for 1930 reflections with $I>3\sigma(I)$ and 342 variables. Data were collected on a Rigaku AFC7S diffractometer with graphite-monochromated Mo Kα radiation ($\lambda=0.71069$ Å). The structure was solved by direct methods (SIR92) and refined using full-matrix least-squares methods. CCDC 146743.
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