An MNDO Study of the Unimolecular Reactions of Methyl Acetate and its Sulphur Analogues

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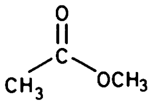
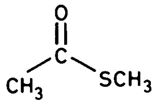
The unimolecular reactions of methyl acetate and its sulphur analogues, *S*-methyl and *O*-methyl monothioacetate and methyl dithioacetate, were investigated using the semi-empirical MNDO method with respect to ketene–thioketene formation and 1,3-methyl migration. For methyl acetate, 1,3-methyl migration of the methyl ester was calculated to be more favourable than ketene formation. *S*-Methyl monothioacetate undergoes ketene formation preferentially while *O*-methyl monothioacetate rearranges *via* 1,3-methyl migration to the more thermodynamically stable *S*-methyl isomer. Methyl dithioacetate also prefers methyl migration; however, unlike the other three compounds, the theoretical results condtradict earlier reported experimental results.

The unimolecular reactions of esters and their sulphur analogues are of general interest in organic chemistry. To this end, Carlsen *et al.* have recently published a series of articles dealing with the pyrolysis of methyl acetate (**1**),[1] methyl monothioacetates (**2**),(**3**),[2] and methyl dithioacetate (**4**).[3] The studies are of interest from several perspectives; not least is the comparative behaviour of oxygen and sulphur. The thermal stability of the esters was determined as were the aptitude to rearrangement *versus* ketene–thioketene formation, and enol–enethiol formation which, although commonly known with oxygen systems, are little studied with sulphur.[4]


(**1**)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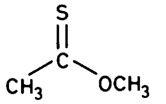
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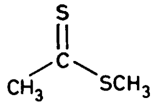

(**4**)

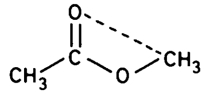
However, owing to the nature of the studies, the actual mechanism for ketene–thioketene formation could not be determined. Enethiol was observed for (**4**) and proposed for (**3**); however, whether its formation is in competition with or serves as an intermediate in the ketene–thioketene formation was not determined.[2,3] Furthermore, several anomalies were reported such as methyl migration for the methyl acetate (**1**) but not the dithio analogue (**4**) although S–C bonds are generally weaker and considered to be more 'flexible' than typical O–C bonds.[3,5] And contrary to earlier reports, no methyl migration was observed with (**3**) although it is unstable compared with the methyl-migration product (**2**).[6]

Theoretical calculations would complement the gas-phase results perfectly. The direct calculation of the reaction barriers and transition states should yield direct information on the different processes.

We report in this paper a semi-emperical MNDO study of the unimolecular reactions of compounds (**1**)—(**4**).

Methods

All calculations were performed with MNDO[7] and MNDOC[8] which are available through the MNDOC package. A general procedure of the calculation is exemplified by the methyl migration in methyl acetate (Scheme 1).


Scheme 1. Methyl migration in methyl acetate. Dashed line represents the reaction path co-ordinate

The oxygen and carbon atoms were brought together in increments of 0.2 Å starting from their equilibrium geometry of 3.0 Å. The energy increases gradually as the two atoms are brought together and decreases suddenly between 1.2 and 1.1 Å. At this point (1.2 Å) the geometry was entered in a transition state search calculation and the force constant matrix determined. The presence of one negative eigenvalue confirms the presence of the transition state.[9] In some cases more than one negative eigenvalue (sometimes two and rarely three) were obtained. However, these values were usually $<1\%$ of the value of the major eigenvalue and were often due to some minor dihedral angle twisting. Energy contribution due to the presence of the additional eigenvalues were usually not >0.5 kcal mol^{-1}.

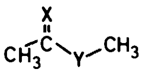
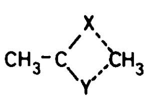
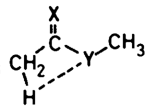
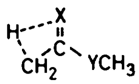
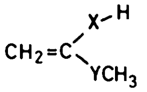
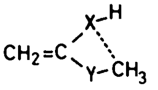
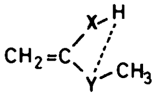
The use of MNDO in the calculation of sulphur-containing compounds is not without controversy. MNDO is not parametrized for *d*-orbitals which are found to be important in some types of sulphur compounds.[10]

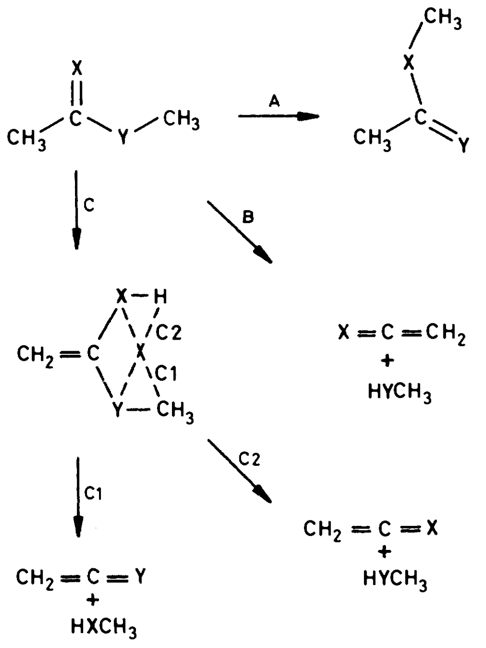
In Dewar's evaluation of the performance of MNDO with sulphur compounds, they report that for organic monosulphides of varying geometries and stoicheiometry, the mean absolute error in the heats of formation was only 6.5 kcal mol^{-1}.[10] And reassuringly, in the calculation of rotational barriers of some disulphides, good agreement was found between calculated and experimentally obtained values despite the total range of <10 kcal mol^{-1}.

Numerous other MNDO studies of sulphur have been performed with at least qualitative agreement with experimental results.[11,12] With respect to the current system, Schweig and his co-workers report an experimental study of the thermal fragmentation of 1,3-dithiol-2-one and its derivatives.[12] They find excellent agreement between experimental observation and trends predicted by MNDO calculations.

The calculations of transition states and reaction barriers using MNDOC represent another major controversy. However, a recent paper by Thiel and Schröder, which compares semi-empirical- and *ab initio*-calculated transition states, show satisfactory agreement between MNDO and MNDOC and the highest-level *ab initio* calculations.[13]

Table. Stationary points in selected unimolecular reactions of methyl acetate and its sulphur analogues. All energies are expressed in kcal mol^{-1}. All relative heats of formation are with respect to the starting esters. The numbers in parentheses are relative heats of formation calculated with some type of CI treatment, *i.e.* BWEN for methyl acetate and 2 × CI for methyl dithioacetate

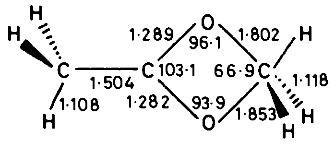
X,Y		Starting Ester	T.S. A	T.S. B	T.S. C	Int. for C	T.S. C1	T.S. C2
								
O O	ΔH_f	−93.8	−5.9	2.5	4.4	−78.1	28.2	3.8
	$\Delta\Delta H_f$		87.9	96.3	98.2		122.0	97.6
			(83.0)	(93.3)	(93.1)		(124.8)	(100.0)
O S	ΔH_f	−51.9	33.0	29.8	48.0	36.6	55.1	52.5
	$\Delta\Delta H_f$		85.0	81.7	99.9		107.0	104.4
S O	ΔH_f	−37.7	32.3	62.4	36.5	−23.9	73.9	35.1
	$\Delta\Delta H_f$		69.8	100.0	74.2		111.5	72.8
S S	ΔH_f	3.7	63.2	88.8	77.2	11.0	88.1	73.5
	$\Delta\Delta H_f$		59.5	84.5	73.5		84.4	69.8
			(59.5)	(85.2)	(71.9)		(84.5)	(69.7)



Scheme 2. The reaction paths calculated for the unimolecular reactions of methyl acetate and its sulphur analogues. Path A represents the 1,3-methyl shift, B direct ketene formation *via* 1,2-elimination, and C *via* enol formation. X = O,S; Y = O,S

Results and Discussion

We investigated the unimolecular reactions of methyl acetate, methyl monothioacetates, and methyl dithioacetate in terms of their relationship to ketene and thioketene formation in the gas phase (Scheme 2). These reactions include methyl migration *via* a 1,3-sigmatropic methyl shift (path A), loss of methanol or the corresponding methanethiol *via* a direct 1,3-elimination (path B), and a 1,3-sigmatropic hydrogen shift to form the corresponding enol and enethiol (path C). From the enol–enethiol, two additional reaction paths were calculated (paths C1 and C2) leading to the corresponding ketenes and thioketenes. All the reaction paths shown with the exception of C2 have been previously proposed. Path C1 has been proposed to account for the ketene formation after enolization.[2,3] However, reaction path C2 may actually be faster due to the size and the spherical symmetry of hydrogen atom compared with the methyl group.



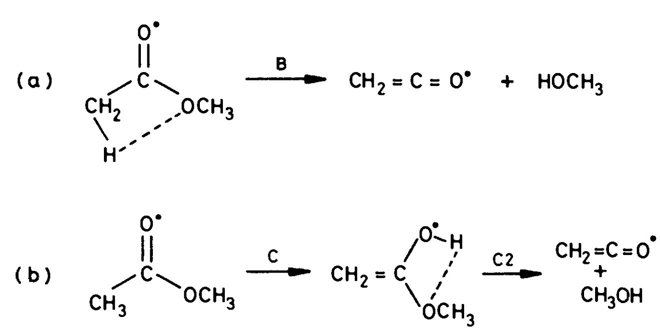
Scheme 3. The transition state structure of methyl migration in methyl acetate (**1**). The transition state is planar with a dihedral angle of 0.0° about the four reaction centres. All bond angles are in degrees

The calculated barriers for all the reactions are in the Table. The term 'activation barrier' or simply 'barrier' will be loosely used throughout the text to refer to the difference in the relative heats of formations between the transition states and the lowest-energy conformation of the starting ester. In all cases, the lowest conformation is the *cis* form (*cis* about the C–Y bond) which is found to be lower than the next stable conformation, the *trans*, by an average of 4 kcal mol^{-1}. Varying the dihedral angle about the X–C–Y–C atoms of the input geometry always yielded either the *cis* or *trans* depending on which is closer to the input geometry. Each compound will be discussed separately in detail.

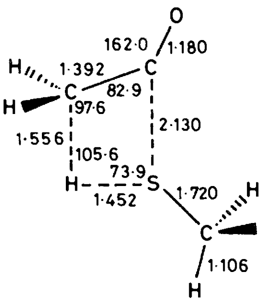
(A) *Methyl Acetate* (**1**).—The 1,3-methyl shift of the methoxy methyl to the carbonyl oxygen atom is calculated to be the most favourable of the three major pathways. The rearrangement proceeds with a barrier of 87.9 kcal mol^{-1} corresponding quite well to the reaction observed experimentally at 1 400 K.[1]

The transition state of this 1,3-shift is quite symmetrical with a bond-breaking and -forming O–C distance of 1.853 and 1.803 Å, respectively (Scheme 3). The small difference of 0.05 Å may be attributed to the presence of a second and third negative eigenvalue, as mentioned earlier, in the force constant matrix. These additional eigenvalues are $<2\%$ of the largest negative eigenvalue. Numerous efforts to suppress the two smaller negative eigenvalues were unsuccessful. However, in other systems where suppression of these eigenvalues was possible, a change of usually no more than 0.5 kcal mol^{-1} was obtained. The length of the migrating carbon to the oxygen, at the transition state, is significantly longer than the calculated equilibrium value of 1.404 Å (C–O single bond of the ester). However, the C–O distance of the stationary carbon to both oxygen atoms is nearly equivalent (1.289 and 1.282 Å, respectively) to the C–O double bond (1.228 Å) of the starting ester.

Formation of the ketene favours the direct 1,3-elimination (path B) over the enol formation by only 1.9 kcal mol^{-1}. Hence, the two pathways may actually be in direct competition (96.3



Scheme 4. The most favourable reaction pathways for ketene formation from methyl acetate (**1**). (a) Direct ketene formation *via* 1,2-elimination (Path B), and (b) *via* enol formation (Path C)



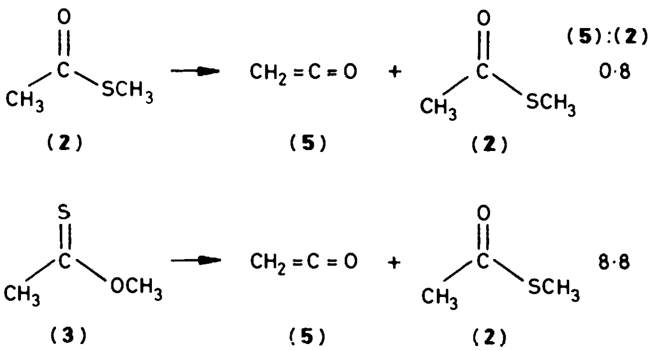
Scheme 5. The transition state for direct 1,2-elimination of CH_3SH from *S*-methyl monothioacetate (**2**). The structure is nearly planar with a dihedral angle of 1.1°

versus 98.2 kcal mol^{-1}, respectively). In which case, ketene formation from the enol may also be important (*i.e. via* paths C1 and C2). Our calculation show that ketene–methanol formation involving the movement of hydrogen atom and the methoxy group (C2) is much more favourable than the corresponding methyl and hydroxy motion (C1) by 24.4 kcal mol^{-1} (97.6 and 122.0 kcal mol^{-1}, respectively). Interestingly, the product of this reaction, if one O were labelled, would be identical with the product from the direct 1,3-elimination (Scheme 4).

Treatment of all the transition states by a perturbational CI treatment (BWEN) has only minor effects on the relative heights of the barrier (Table). The largest absolute effect seems to be on the enol formation which is lowered by 5.1 kcal mol^{-1}. With the inclusion of the CI treatment, this pathway becomes as favourable for ketene formation as the direct 1,3-elimination. The absence of drastic energy lowering also indicates the absence of orbital degeneracy near the HOMO of the transition state.

(B) S-*Methyl Monothioacetate* (**2**).—For the *S*-methyl monothioacetate (**2**), the endothermicity of the methyl shift from sulphur to oxygen (ΔH_R 14.3 kcal mol^{-1}) makes path A unfavourable compared with the single-step loss of methanethiol to form the ketene (85.0 *versus* 81.7 kcal mol^{-1}, respectively). The transition state for ketene formation is late with a long breaking C–H bond (1.556 Å), a short forming S–H bond (1.452 Å), and a long breaking C–S bond (2.130 Å). The ketene is almost totally formed with a O–C–C bond angle of 162°. The four reaction centres lie in a near perfect plane with a dihedral angle of only 1.1° (Scheme 5).

The gas-phase thermolysis results for (**2**) are in good agreement with our calculations. The pyrolysis of this monothioacetate gives predominantly methanethiol and ketene at 1 043 K.[2] Formation of the enol is calculated to be 18.2 kcal mol^{-1} less favourable than 1,2-elimination. The height of the barrier towards enol formation is nearly identical to the analogous process for methyl acetate (99.9 *versus* 98.2 kcal mol^{-1}, respectively) indicating the small effects of the methoxy and thiolo groups.

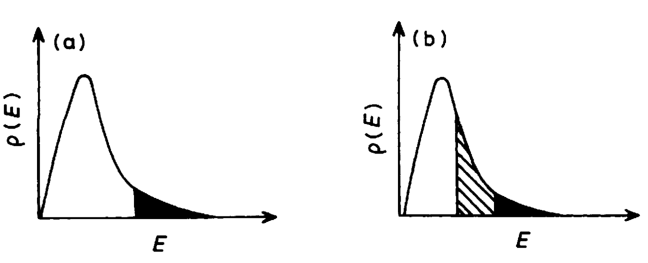


Scheme 6. Results of pyrolysis studies by Carlsen and Egsgaard[2] with the relative ratio of ketene (**5**) formed to *S*-methyl monothioacetate (**2**) either formed through rearrangement from (**3**) or recovered as starting material from (**2**)

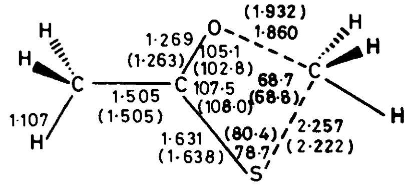
(C) O-*Methyl Monothioacetate* (**3**).—The relative instability of (**3**), compared with the *S*-methyl isomer is reflected in a smaller activation barrier for the 1,3-methyl shift transforming (**3**) to (**2**) (69.8 kcal mol^{-1}) compared with the barrier for both the 1,2-elimination (100.3 kcal mol^{-1}) and the enol formation (74.2 kcal mol^{-1}). Thus, rearrangement (**3**) ⟶ (**2**) is expected to precede ketene formation. These results, however, appear to show a serious disagreement between MNDO predictions and the experimental results reported by Carlsen and Egsgaard.[2] From their study they concluded no methyl migration, favouring instead enethiol formation followed by elimination of CH_3SH *via* path C1 to produce ketene. For the last step we calculate a barrier of 111.5 kcal mol^{-1}. Their analysis is based on the ratio of ketene (**5**) produced to the *S*-methyl monothioacetate (**2**) recovered, the latter either being formed as a rearrangement product of (**3**) or isolated as starting material as in the case of (**2**) (Scheme 6). For (**3**) the ketene *versus* *S*-methyl monothioacetate value [(**5**):(**2**)] after pyrolysis was found to be 8.8. For (**2**), the analogous value was only 0.8. Hence, they inferred that the amount of ketene from (**3**) due to the rearrangement to (**2**) could only be 0.8 of 8.8, or 9%. The remaining 91% of the ketene (**5**), they assumed, must be formed *via* enolization followed by elimination of CH_3SH.

The (**5**):(**2**) ratio for (**2**) represents the ratio of ketene formed to unchanged starting esters. The shaded region of Scheme 7A illustrates a hypothetical fraction of molecules (**2**) with sufficient energy to undergo ketene formation. The (**5**):(**2**) ratio for this compound is therefore the ratio of the shaded to non-shaded area. The analogous ratio for (**3**) is a little more ambiguous. If we initially assume that ketene formation proceeds only through the rearrangement of (**3**) to (**2**), then we have the condition illustrated in Scheme 7B. The entire shaded area (light and dark shaded) represents a hypothetical fraction of molecules (**3**) with enough energy to rearrange to (**2**). Of this fraction, a further fraction has enough energy to form the ketene (dark shaded area). The (**5**):(**2**) ratio for (**3**) therefore represents the ratio of ketene formed to the rearranged ester (**2**) or the ratio of dark shaded area to light shaded area. Since the rate-determining step for both (**2**) and (**3**) is identical, *i.e.* 1,2-elimination from (**2**), then the areas of the dark-shaded portions should be similar so that the (**5**):(**2**) ratio for (**3**) should yield a higher value than that for (**2**), as is indeed observed experimentally.

The likeliest reaction for (**3**) must therefore proceed through



Scheme 7. Hypothetical Boltzmann distributions of two methyl monothioacetates: (a) (**2**) and (b) (**3**). (a) Dark shaded area represents fraction of (**2**) with sufficient energy to undergo ketene formation. The (**5**):(**2**) ratio is the ratio of shaded are to non-shaded area. (b) Total shaded area (light and dark shaded) represents the fraction of (**3**) with sufficient energy to undergo rearrangement to (**2**). Dark shaded area represents the fraction of (**3**) with sufficient energy to undergo ketene formation. The (**5**):(**2**) ratio for this system is the ratio between the dark shaded and the light shaded area only



Scheme 8. Comparison of the transition states for 1,3-methyl migration in methyl monothioacetate from (**2**) to (**3**) and (**3**) to (**2**) (in parentheses). Both structures are nearly planar about the four reaction centres (dihedral angle 0.0° and 3.1°, respectively)

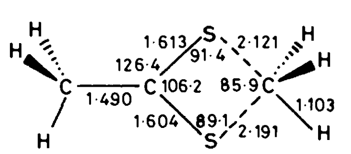
the 1,3-methyl shift to form (**2**). This would also explain why (**2**) and (**3**) produce identical products during pyrolysis.[2]

The reaction pathway for the 1,3-methyl shift for (**3**) must be identical to but the reverse of that for (**2**). The two transition states which have been independently calculated must therefore be identical, and this provides a good test for the consistency of the MNDO method (Scheme 8).

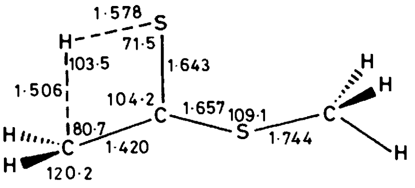
The heats of formation of the transition-state structures from either (**2**) or (**3**) vary by 0.8 kcal mol^{-1}. The bond lengths are essentially identical, with the largest discrepancy for the C$_{\text{methyl}}$–O bond which is longer for the one starting from (**3**) than for that starting from (**2**) by 0.072 Å (1.932 *versus* 1.860 Å, respectively). This slight difference is, again, due to the number of eigenvalues in the force constant matrix.

(D) *Methyl Dithioacetate* (**4**).—For (**4**), the most favourable reaction pathway calculated corresponds to 1,3-methyl migration. This reaction proceeds over a barrier of 59.5 kcal mol^{-1} being lower than that for the analogous methyl acetate process by 28.4 kcal mol^{-1}. This result is in perfect agreement with an unoptimized MNDO value reported also by Carlsen and Egsgaard[14] of 20 kcal mol^{-1}. Several factors contribute to the facility of this reaction including (1) the weakness of C–S bonds compared with corresponding C–O bonds,[5] (2) the longer bond length of C–S single bonds as observed in our own calculation, and (3) the lower force constants of bond bending in sulphur compounds.[3] Throughout the study, we generally observed more favourable reaction barriers for reactions involving S than for O centres.

The transition state for this transformation, as expected, is perfectly symmetrical, having long C–S bonds (2.121 and 2.191 Å, respectively) and a nearly planar structure about the four reaction centres (4.7°; Scheme 9). The C–S bonds from the stationary carbon are longer (1.737 and 1.628 Å) than the C=S bonds (1.513 Å) unlike the transition-state structure for the analogous oxygen reaction.



Scheme 9. Transition-state structure for methyl migration in methyl dithioacetate (**4**)



Scheme 10. Transition state for the enethiol formation from methyl dithioacetate (**4**)

Surprisingly, Carlsen and Egsgaard report no intramolecular exchange for this compound.[3] They reasoned that formation of the enethiol, *via* path C (Scheme 10), prevented such migration. However, formation of the enethiol proceeds through a barrier 14 kcal mol^{-1} higher than that of the methyl migration. The large enethiol barrier (73.5 kcal mol^{-1}) is in good agreement with *ab initio* studies on the thioketone.[4] The STO-3G study of Bruno *et al.*[4] shows a reaction barrier of *ca.* 85 kcal mol^{-1} for an unoptimized transition state. Optimization and the use of higher-level basis sets should decrease their calculated barrier even further. As with the normal ketone, methoxy and thioxy exert similar effects on the activation barrier to the enethiol. For the normal ketone the reaction barrier varied by 1.8 kcal mol^{-1} while with the thioketone the analgous barrier varied by only 0.7 kcal mol^{-1}.

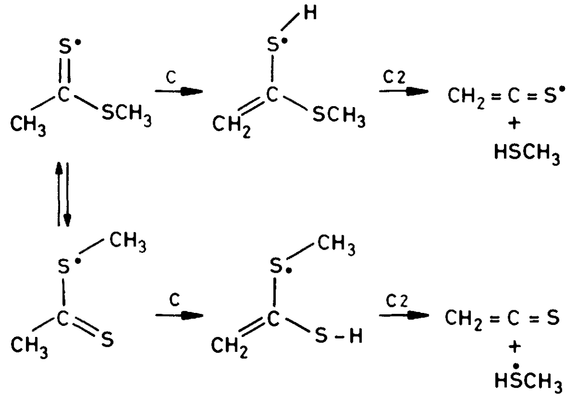
The transition-state structure of the enthiol formation shows a fairly long C–H bond (1.506 Å) and a forming S–H bond of 1.578 Å. The four reaction centres are slightly non-planar with a twist angle of 7.0°. The carbon of origin of the migrating hydrogen atom is nearly fully *sp*^{2} hybridized with a C–C–H bond angle of 120° and a shortened C–H bond length of 1.098 Å (Scheme 10).

Formation of the thioketene by direct 1,2-elimination must overcome a significantly higher barrier of 84.5 kcal mol^{-1}. Thioketene formation *via* the enethiol route, and subsequent loss of methanethiol through the C2 path, proceeds through an overall barrier of 73.5 kcal mol^{-1} above the starting ester. This barrier, belonging to the enethiol formation, lies 11.0 kcal mol^{-1} below the direct 1,2-elimination. The second step, *via* C2, requires less with 69.8 kcal mol^{-1} of energy. This path is lower in energy than the alternative path, C1 (84.4 kcal mol^{-1}, Scheme 11).

As with oxygen, a CI treatment (here only 2 × 2 was used since MNDOC which contains BWEN is not parametrized for sulphur) seems to have little or no effect on the height of the barriers. The largest change appears to be the lowering of the barrier to the enethiol formation by 1.6 kcal mol^{-1}.

The discrepency between calculated and experimental results is disturbing. The huge difference of 14 kcal mol^{-1} between the methyl migration and enol formation seems too large even for MNDO.

There are of course at least two possibilities to consider. The first is that MNDO calculates the barrier to enethiol formation too high and/or the methyl migration too low due to the lack of *d* orbitals. The other possibility could be a problem in the experimental interpretation. However, with the two methyl



Scheme 11. Most probable pathway calculated by MNDO for the thioketene formation from methyl dithioacetate (**4**)

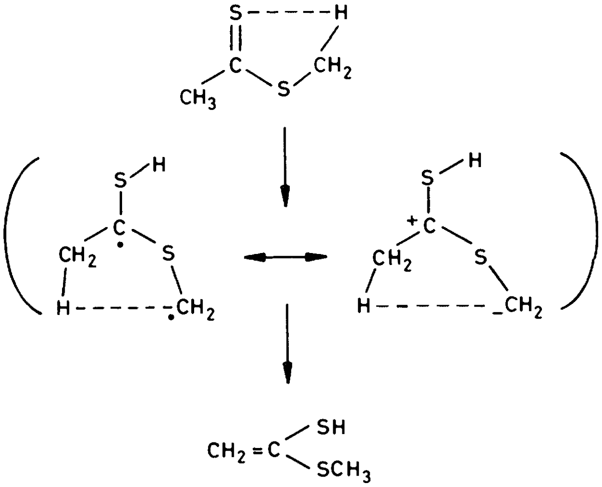
monothioacetates (**2**) and (**3**), reasonable agreement is obtained between MNDO and the experimental results so that the MNDO predictions may actually be correct. The most obvious solution would be to recalculate the two transition states using *ab initio* with high-level basis sets and *d* orbitals on sulphur. This should finally determine which of the two pathways is the most favourable in the unimolecular reaction of methyl dithioacetate. Also, a re-investigation of the pyrolysis behaviour of (**4**) is also highly suggested.

Finally, for the sake of completeness, 1,4-hydrogen migration was calculated with the hydrogen atom originating from the *S*-methyl group. There should be no reason for this process to be more favourable than the simple 1,3-methyl migration since the intermediate formed would be somewhere in between a diradicaloid or some dipolar species (Scheme 12). Indeed the calculation of this hydrogen migration yields a barrier 12.0 kcal mol^{-1} (75.2 kcal mol^{-1}) higher than the methyl migration.

Surprisingly, MNDO predicts this process to be as energetically favourable or even slightly more so (by 2.0 kcal mol^{-1}) than the normal enethiol formation. However, caution should be taken when calculating such compounds since MNDO was not parametrized with these type of compounds in mind and hence may pose a problem for the method.

Conclusions.—The most facile reaction for all but the *S*-methyl monothioacetate is 1,3-methyl migration. For methyl acetate, ketene formation proceeds through two competing pathways which produce identical products. Methyl dithioacetate prefers to proceed *via* enol formation followed by H and SCH_3 motion to produce the thioketene. Both monothioacetates proceed through the same reaction path for ketene formation, *i.e.* direct 1,2-elimination from (**2**). Methyl thionoacetate (**3**) first rearranges to the thermodynamically more stable ester (**2**).

MNDO predictions are in agreement with the experimental results of Larsen and Egsgaard with respect to all the compounds studied except the methyl dithioacetate. For this compound MNDO predicts that the degenerate 1,3-methyl rearrangement should precede thioketene formation in contrast to experimental findings. MNDO results are, however, more in line with common expectation for the reactivity of methyl dithioacetate.



Scheme 12. Alternative mechanism for enethiol formation from methyl dithioacetate *via* consecutive 1,4-hydrogen shifts

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