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ADDITION OF *N*-METHYLTRIAZOLINEDIONE TO BIADAMANTYLIDENE

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The addition of *N*-methyltriazolinedione (M) to biadamantylidene (A) gives the [2 + 2) adduct P, but clearly does not proceed in one step beause an aminoaziridinium intermediate (I) can be observed to build up during the reaction. The overall rate of P formation correlates with the amount of I that builds up, but not with any solvent polarity parameter, despite the fact that charge-separated intermediates are involved. NMR experiments established that the equilibrium constant for I formation is $>1000\ M^{-1}$ in $CDCl_3$, $\geq 500\ M^{-1}$ in CD_2Cl_2 and in the range *ca* 2–15 M^{-1} for C_6D_6 and C_6D_5Br. It is very unlikely that I is directly on the reaction pathway between M + A and P, and it is proposed that the zwitterionic intermediate with one CN bond, X, is the probable precursor of both I and P, although X does not build up in concentration enough to be observed. CH hydrogen bonding stabilizing both X and I in chloroform is suggested as a possible rationalization for the correlation between overall rate of P formation and stability of I relative to the starting materials. Formation of P in benzene is catalyzed by Meldrum's acid. M unfortunately reacts too rapidly with compounds containing OH bonds to study formation of P in the presence of strong hydrogen bonding reagents. © 1997 by John Wiley & Sons, Ltd.

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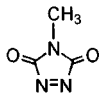
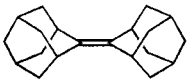
INTRODUCTION

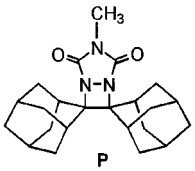
The [2 + 2] cycloaddition of triazolinediones such as the *N*-methyl derivative **M** to biadamantylidene (**A**) to give the diazetidene **P** was reported by Seymour and Greene.[1]



M

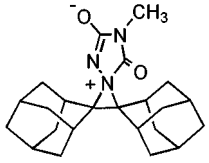


A



P

The x-ray structure of **P** and rate constants for addition of *N*-phenyltriazolinedione to **A** in several solvents using optical spectrometry to determine the rate of triazolinedione disappearance have also been reported.[2] Relative addition rates in benzene acetone, acetonitrile and methylene chloride were 1·0:1·1:9·5:99. Although the reaction rate is sensitive to solvent, the rate constants clearly do not follow the order of solvent polarity. Nelsen and Kapp[3] found that an intermediate builds up during the reaction of **A** and **M** in chloroform, and identified it by NMR and IR spectroscopy as the aziridinium imide **I**. The only other aziridinium imide intermediate which has been directly observed is in the ene reaction of *trans*-cycloheptene with **M**, where an intermediate assigned as the aziridinium imide derived from *cis*-cycloheptene builds up at low temperature.[4]



I

RESULTS AND DISCUSSION

Kinetics of *N*-methyltriazolinedione addition to biadamantylidene

The **A** + **M** addition reaction was studied in other solvents in addition to chloroform. Attempts to measure the equilibrium

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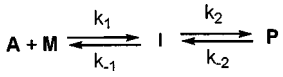


Scheme 1

constant for **I** formation directly, using long equilibration times at low enough temperatures such that **I** does not rearrange to **P**, were frustrated by solubility problems at the low temperatures required, as well as other decomposition reactions of **M** occurring during the long times required for equilibration, and were abandoned. Kinetic studies near room temperature were carried out at concentrations where both the build-up and decrease of **I** could be followed. Four 2 s scans were averaged in determining the spectra. Concentrations of **M**, **A**, **I** and **P** as a function of time were determined by NMR integration in $CDCl_3$ and CD_2Cl_2 using CH_2Cl_2 as an integration standard. The concentration versus time plots were fit to simulations using program GIT.[5] The data were adequately simulated using a 'linear' kinetic scheme (Scheme 1). For a sample of the fit obtained, see Figure 1.

In both chloroform and methylene chloride, k_{-1} proved too small to measure; fits with the same standard deviation could be obtained when k_{-1} was set equal to zero as when it was optimized and the deviations from the experimental points only became detectably larger when k_1/k_{-1} was set to be smaller than about 1000 in $CDCl_3$ and 500 in CD_2Cl_2. Despite our best efforts, there is considerable experimental error in the rate constants obtained, probably largely because of inaccuracy in the NMR integrations, especially in the rapid rise region, where points had to be taken rapidly, and concentration variations over the 8 s data acquisition time are significant. The data are summarized in Table 1. We were not able to demonstrate conclusively from these kinetic runs that the addition actually is reversible in these solvents because product formation from **I** is significantly faster than reversal. The temperature study in $CDCl_3$ gives for k_1 $\Delta G^{\ddagger}(25\ ^{\circ}C) = 17{\cdot}9 \pm 0{\cdot}13$ kcal mol^{-1} (1 kcal = 4·184 kJ), $\Delta H^{\ddagger} = 6{\cdot}0 \pm 1{\cdot}3$ kcal mol^{-1} and $\Delta S^{\ddagger} = -40 \pm 5$ cal mol^{-1} K^{-1}; a small activation energy but very negative enthalpy, as might be expected, for the formation of **I**. The corresponding values for k_2 are $\Delta G^{\ddagger}(25\ ^{\circ}C)$-$20{\cdot}5 \pm 0{\cdot}08$ kcal mol^{-1}; $\Delta H^{\ddagger} = 16{\cdot}4 \pm 0{\cdot}8$ kcal mol^{-1} and $\Delta S^{\ddagger} = -14 \pm 3$ cal mol^{-1} K^{-1}. These numbers are probably not mechanistically significant, because **P** is unlikely to arise directly from **I** (see below).

We also examined the reaction in aromatic solvents. **M**, **I** and **P** could be integrated successfully in C_6D_5Br, but only **I** and **P** were sufficiently resolved from other peaks to be integrated in C_6D_6. In the aromatic solvents $K_{eq} = k_1/k_{-1}$ is significantly smaller, as is shown qualitatively by the smaller maximum fraction of **A** converted to **I** (see Table 2). Partitioning back to **A** + **M** from **I** is more favorable, and the simulations proved to be sensitive to k_{-1}. The reproducibility for obtaining the rate constants was not very good, as can be seen from the data in Tables 1 and 2.

Although Scheme 1 fits the experimental data satisfactorily, it is not expected actually to represent the mechanism of the reaction. It is very unlikely that both C—N bonds of **I** form simultaneously: [2 + 2] cycloaddition is 'forbidden' to be concerted unless the addition were to opposite sides of the double bond of **A**, which is geometrically infeasible. In agreement with this, including a direct **A** + **M** → **P** pathway in addition to Scheme 1 did not improve fit to the experimental data. Furthermore, **I** cannot reasonably be converted to **P** without breaking a C—N bond, because this conversion requires a nearly 90° twist of the triazolinedione unit relative to the biadamantylidene unit. The 'T-shaped' Scheme 2, proceeding through the single N—C bonded

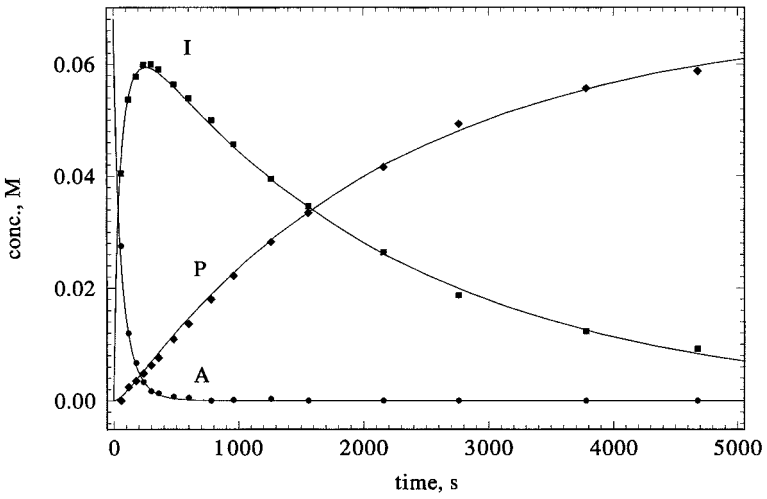


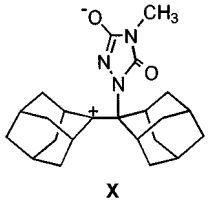
Figure 1. Plot of fit to Scheme 1 for File 148, $CDCl_3$ at 273 K, $[\mathbf{M}]_0 = 0{\cdot}115$, $[\mathbf{A}]_0 = 0{\cdot}068$ M, using $k_1 = 0{\cdot}18_4$ M^{-1}, s^{-1}, $k_{-1} = 3{\cdot}4 \times 10^{-4}$ s^{-1}, $k_2 = 4{\cdot}5_9 \times 10^{-4}$ s^{-1}

Table 1. Variation of rate constants for reaction of **A** with **M**, analyzed using Scheme 1

File	Solvent[a]	T (K)	k_1 (M^{-1}) s^{-1}	k_{-1} (s^{-1})	K_{eq} (M^{-1})	k''[c]	
94	Chl	253	$7{\cdot}1\times10^{-2}$	—[b]	$4{\cdot}0\times10^{-5}$	≥1000	>0·026
96	Chl	253	$5{\cdot}1\times10^{-2}$	—[b]	$3{\cdot}0\times10^{-5}$	≥1000	>0·030
148	Chl	273	$1{\cdot}8\times10^{-1}$	—[b]	$4{\cdot}6\times10^{-4}$	≥1000	>0·013
150	Chl	273	$1{\cdot}5\times10^{-1}$	—[b]	$4{\cdot}5\times10^{-4}$	≥1000	>0·011
68	Chl	283	$3{\cdot}0\times10^{-1}$	—[b]	$1{\cdot}1_6\times10^{-3}$	≥1000	>0·024
72	Chl	283	$3{\cdot}1\times10^{-1}$	—[b]	$1{\cdot}1_5\times10^{-3}$	≥1000	>0·025
74	Chl	293	$3{\cdot}6\times10^{-1}$	—[b]	$3{\cdot}4\times10^{-3}$	≥1000	>0·032
78	Chl	293	$2{\cdot}9\times10^{-1}$	—[b]	$3{\cdot}4\times10^{-3}$	≥1000	>0·027
82	Chl	293	$3{\cdot}8\times10^{-1}$	—[b]	$3{\cdot}9\times10^{-3}$	≥1000	>0·034
142	MC	273	$6{\cdot}6\times10^{-2}$	—[b]	$5{\cdot}4\times10^{-4}$	≥500	>0·053
144	MC	273	$6{\cdot}4\times10^{-2}$	—[b]	$4{\cdot}8\times10^{-4}$	≥500	>0·051
146	MC	273	$8{\cdot}1\times10^{-2}$	—[b]	$5{\cdot}3\times10^{-4}$	≥500	>0·062
46	PhBr	298	$5{\cdot}5\times10^{-2}$	$3{\cdot}6\times10^{-3}$	$1{\cdot}4\times10^{-3}$	15	0·015
48	PhBr	298	$2{\cdot}6\times10^{-2}$	$2{\cdot}6\times10^{-3}$	$1{\cdot}7\times10^{-3}$	10	0·010
38	PhD	293	$3{\cdot}1\times10^{-2}$	$4{\cdot}2\times10^{-3}$	$6{\cdot}9\times10^{-3}$	7	0·019
40	PhD	293	$9{\cdot}2\times10^{-3}$	$4{\cdot}5\times10^{-3}$	$1{\cdot}0\times10^{-3}$	2	0·002
76	PhD	293	$1{\cdot}5\times10^{-2}$	$3{\cdot}9\times10^{-3}$	$7{\cdot}6\times10^{-3}$	4	0·010

[a] Chl = $CDCl_3$, MC = CD_2Cl_2, PhBr = C_6D_5Br, PhD = C_6D_6.
[b] Too small to measure (see text).
[c] $k' = k_2k_1/(k_2+k_{-1})$.

intermediate **X**, is much more likely. We expect the **M** unit to be twisted about 90° with respect to the central CC bond of the **A** unit in intermediate **X** for steric reasons. We therefore believe that closure of **X** to **I** will be much faster than the closure to **P**, which requires a sterically hindered rotation of the **M** unit with respect to the **A** unit. The experimental NMR data could be fit using the more complicated Scheme 2 as well as using Scheme 1, although obtaining such fits proved tedious because of interaction between the rate constant values employed. We do not provide here any of the rate constants thus obtained, because they give no additional mechanistic information. Because **X** does not build up to detectable levels, **I** is presumably more stable than **X**. The rate at which **I** is observed to be converted to **P** (k_2 in Scheme 1) cannot be interpreted mechanistically using Scheme 2 because the **X**–**I** energy difference is unknown. The k_3 obtained from a fit to Scheme 2 depends upon the free energy gap between **X** and **I**, i.e. upon k'_2/k'_{-2}, which is unknown in the absence of observing **X**. For the chloroform and methylene chloride data, where reversal to starting materials is slow, k_2 (Scheme 1) = $k_3k'_{-2}/k'_2$ (Scheme 2), but the rate constants cannot be separated from the data available.



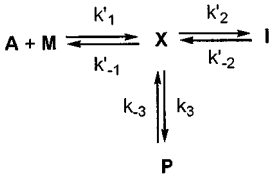
X

The reaction is significantly slower in bromobenzene and benzene than in chloroform and methylene chloride, as indicated by the $k'' = k_1k_2/(k_2+k_{-1})$ values (last column in Table 1). The equilibrium constant for the formation of intermediate **I** from **A** and **M** is also significantly smaller in

Table 2. Summary of initial concentrations of **A** and **M** and the maximum fraction of **I** for kinetic runs near room temperature

File	Solvent[a]	T (K)	$[\mathbf{A}]_0$	$[\mathbf{M}]_0$	fr$(\mathbf{I})_{max}$[b]
148	Chl	273	0·068	0·115	0·87
150	Chl	273	0·053	0·110	0·85
142	MC	273	0·014	0·085	0·74
144	MC	273	0·016	0·112	0·83
146	MC	273	0·041	0·094	0·81
46	PhBr	298	0·075	0·140	0·34
48	PhBr	298	0·047	0·070	0·38
38	PhD	293	0·024	0·064	0·21
40	PhD	293	0·027	0·064	0·08
76	PhD	293	0·035	0·070	0·16

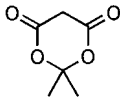
[a] See Table 1.
[b] fr$(\mathbf{I})_{max}$ is th ratio of the maximum [**I**] to that of the limiting reagent.



Scheme 2

benzene and bromobenzene than in the chlorinated solvents. Small amounts of **I** could also be observed in toluene and xylene, and the overall addition rate is comparable to that in benzene, although detailed kinetic studies were not done. **M** proved to react too rapidly with THF[6] and with alcohols for these solvents to be usable for studying additions of **M** to **A**. Intermediate **I** was not observed to build up in deuterated acetone, acetonitrile or nitromethane, and the rate of **P** formation was qualitatively no faster than for bromobenzene, making it clear that solvent polarity does not correlate significantly with the rate of diazetidine formation, despite the fact that polar intermediates between the starting materials and the product almost certainly occur. Similar observations were made for the phenyltriazolinedione addition to **A** by Cheng *et al*.[2] (see Introduction).

The relatively rapid rates of **P** formation in chloroform and methylene chloride do not correlate with solvent polarity, but do correspond to significantly larger K_{eq} values for **I** formation. As noted above, **I** is presumably not directly involved in the formation of **P**; its formation is a reversible side reaction on the pathway to **P** formation. Some factor not only correlated with solvent polarity apparently stabilizes the transition state for **P** formation [lowering the energy gap between (**A**+**M**) and the k_3 transition state of Scheme 2] in chloroform more than in methylene chloride, and both are significantly lower than in the aromatic solvents. We suggest that the rough parallel between the free energy gaps between (**A**+**M**), the observed **I** and the transition state for **X** closure to **P** occurs because of the structural similarity between **I** and **X**; both have urea anion character in the heterocyclic ring, and they differ principally by the degree of bonding of the nitrogen bonded to one adamantyl C-2 carbon to the other adamantyl C-2 carbon. It seems likely that factors which stabilize **I** relative to (**A**+**M**) will also stabilize **X**, and therefore also its transition state for **P** formation, leading to the qualitative correlation observed between K_{eq} for **I** formation and the overall rate of addition of **A** to **M** to give **P**.



1

It occurred to us that hydrogen bonding to these intermediates by $CDCl_3$ and CD_2Cl_2 might be involved. Weak hydrogen bonding to the relatively accessible partially negatively charged carbonyl group in both **X** and **I** might stabilize them, which ought to lower the barrier for formation of **P** from **X** relative to a solvent in which **X** and **I** are not so stabilized. Although compounds with hydroxyl groups would form much stronger hydrogen bonds than these chlorinated solvents, as noted above, they proved to react too rapidly with **M** to allow their use. We found that addition of Meldrum's acid (**1**) to **M**+**A** reactions in benzene increases the rate constant for **M** disappearance as measured by monitoring the absorbance at 536 nm using optical spectrometry, that a plot of k_{obs} vs equivalents of **1** is curved, the rate increase 'saturating' as more **1** is added, and that the increase in k_{obs} is roughly a factor of 15 when 9–13 mol of **1** per mole of **M** are added (see Figure 2). Control experiments demonstrated that **1** does not detectably decompose **M** during the times of these reactions in the absence of **A**, but that it does decompose **M** in acetone (possibly because the enol content is higher?), so this solvent could not be used for similar studies. The catalysis

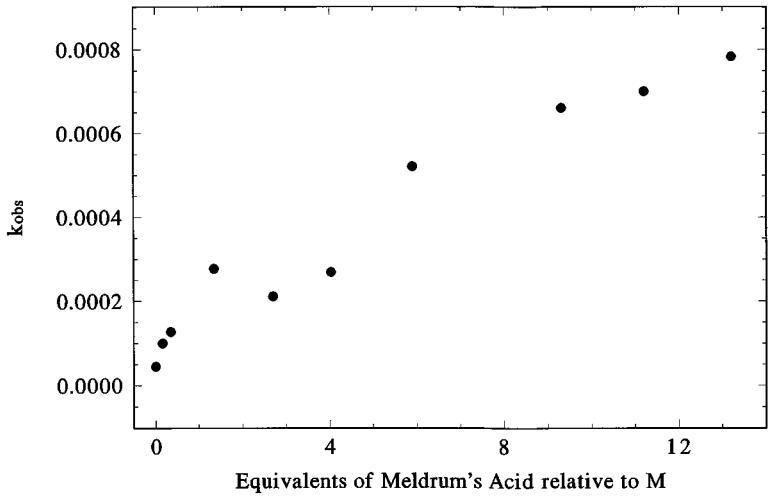


Figure 2. Plot of k_{obs} measured by **M** disappearance versus equivalents of **1** relative to **M** for the reaction of **A** with **M** in benzene at room temperature

Table 3. Chemical shifts of signals used for quantification of concentrations in kinetic runs

Species	Peak	CD_2Cl_2	$CDCl_3$	C_6D_5Br	C_6D_6
M	NMe (3H)	3·18	3·18	2·45	1·98
A	H_{Br} (4H)	2·85	2·85	Unresolved	2·96
I	H_{Br} (2H)	2·71	2·71	2·92	Unresolved
I	NMe (3H)	3·01	3·01	2·92	2·84
P	NMe (3H)	2·99	2·99	2·85	2·79

of **P** formation by addition of Meldrum's acid is consistent with the hydrogen bonding idea mentioned above, although it does not prove it. The poor reproducibility we have been able to obtain for the NMR kinetics of these reactions unfortunately precludes probing small effects. CH hydrogen bonding is clearly detected in solid state structures,[7] and the relative hydrogen bonding ability of chloroform, methylene chloride and alcohols have been studied by both NMR and IR methods,[8] but we have not seen CH hydrogen bonding proposed previously to cause significant changes in the rates of reactions in solution. Although replacing CD by CH in chloroform and methylene chloride and CH by CD in Meldrum's acid might be expected to have some effect on hydrogen bonding, a primary isotope effect would not be involved, and we would not expect to be able to measure the very small effect expected (Ref. 8b, p. 16). Acetonitrile and nitromethane appear not to have significant rate-enhancing effects, but CH hydrogen bonding by methyl groups appears to be considerably less important than that by tri- and dihalogenated methanes (Ref. 8b. p. 53).

EXPERIMENTAL

NMR kinetics. Stock solutions of an NMR standard (*tert*-butylbenzene or methlene chloride) and of freshly sublimed *N*-methyltriazolinedione[9] were added by syringe to a biadamantylidene[10] solution in a cooled NMR tube, which was quickly inserted into a temperature pre-equilbrated and shimmed AM-360 NMR probe. The quality of shimming was the most important factor affecting the quality of the integrations. The regions integrated to determine the concentrations as a function of time are summarized in Table 3. Each spectrum was transformed, phased and integrated five separate times and the results averaged.

ACKNOWLEDGEMENTS

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