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Oxa-ene Reaction of Enols of Amides with 4-Phenyl-1,2,4-triazoline-3,5-dione†

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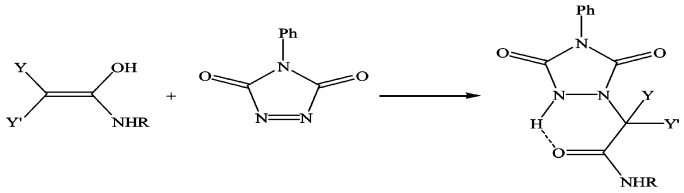

The reaction of 16 enols of amides with 4-phenyl-1,2,4-triazoline-1,3-dione gave open chain adducts rather than the [2 + 2] cycloadducts with a hemiaminal moiety, both in solid state and in solution. This assignment is based on X-ray crystallography, ^{1}H and ^{13}C NMR data, and IR spectra. The suggested mechanism involves hydroxyl proton loss in a formal oxa-ene reaction. Mechanistic details and a possible alternative are discussed.

Introduction

In recent years, we have prepared a large number of the rare enols (**1**) of the well-known tautomeric amides (**2**), where Y and Y′ are electron-withdrawing groups (EWGs). We studied their properties, mostly ^{1}H and ^{13}C NMR, their solid state and solution structure, their intramolecular hydrogen bonding, and especially the **1** ⇌ **2** equilibria, defined by K_{enol} = [**1**]/[**2**] as a function of Y, Y′, R, the solvent, and the temperature.[1,2]

Y'YC=C(OH)NHR
1

Y'YCHCONHR
2

Species **1** contain the OH, NHR, C═C, Y, and Y′ functional groups and seem to be interesting synthones. However, except for the very fast **1** ⇌ **2** reaction, the only study of their reaction is with CH_2N_2,[3] which reacts with different systems on either the OH, the NHR, or the C═C groups. In the present work, we extended this study to a possible reaction of the double bond of the enol with the azo functionality in 4-phenyl-1,2,4-triazoline-3,5-dione (PTAD) **3**.[4] This very reactive enophile[5] was used as a reaction partner in [2 + 4][5,6] and [2 + 2][7] cycloadditions and in ene reactions.[8] We desired to find out if PTAD's reaction with **1** would give the [2 + 2] cycloadducts 1,2-diazetidines **4**, their isomeric open chain 1,2 adducts **5**, or both, or other species such as the enol imine **6**.[9]

Results and Discussion

The reaction of 16 enols of amides **1** activated by different combinations of two β-EWGs with PTAD **3** gave adducts (eq

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† Preliminary report: Basheer, A.; Rappoport, Z. The 69th Meeting of the Israel Chemical Society, Tel Aviv, Israel, February 2−3, 2004, Abstract PB116.

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(9) Elimination of water from **4** will give a substituted 3-imino-1,5-diazabicyclo[3.2.0]heptane derivative.

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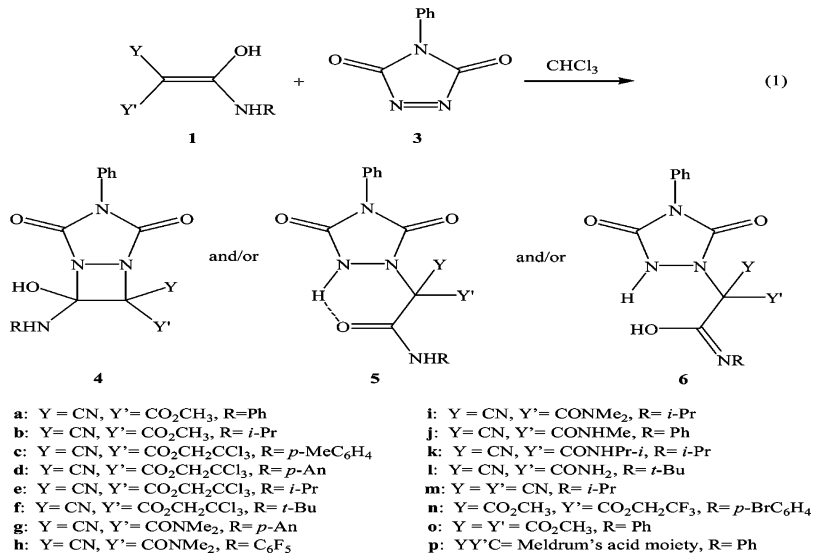


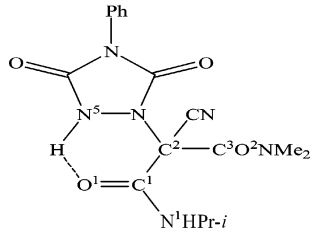
a: Y = CN, Y'= CO_2CH_3, R=Ph
b: Y= CN, Y'= CO_2CH_3, R= *i*-Pr
c: Y = CN, Y'= $CO_2CH_2CCl_3$, R= *p*-MeC_6H_4
d: Y= CN, Y'= $CO_2CH_2CCl_3$, R= *p*-An
e: Y = CN, Y'= $CO_2CH_2CCl_3$, R= *i*-Pr
f: Y= CN, Y'= $CO_2CH_2CCl_3$, R= *t*-Bu
g: Y = CN, Y'= $CONMe_2$, R= *p*-An
h: Y= CN, Y'= $CONMe_2$, R= C_6F_5
i: Y = CN, Y'= $CONMe_2$, R= *i*-Pr
j: Y= CN, Y'= CONHMe, R= Ph
k: Y = CN, Y'= CONHPr-*i*, R= *i*-Pr
l: Y= CN, Y'= $CONH_2$, R= *t*-Bu
m: Y = Y'= CN, R= *i*-Pr
n: Y= CO_2CH_3, Y'= $CO_2CH_2CF_3$, R= *p*-BrC_6H_4
o: Y = Y' = CO_2CH_3, R= Ph
p: YY'C= Meldrum's acid moiety, R= Ph

1) having a 1:1 composition of the two reagents. The 1:2 adducts, similar to those observed in the addition of **3** to diphenylketene,[10] were not observed. The products can be the [2 + 2] cycloadducts **4a**−**p**, or the open chain isomeric tautomeric adducts **5a**−**p**, or **6a**−**p**. The only previously reported product was presented as **5o**.[11] The reactions of 0.25 M **3** with 5% molar excess of **1** in $CHCl_3$ were rapid, mostly finished in <1 min as judged by the disappearance of the red color of **3**, which was accompanied by a slower appearance of a precipitate. To obtain approximate information on the relative rates of several enols, these mixtures were diluted and the time required for complete disappearance of the color of **3** was recorded. For **1d**, the color disappeared immediately even on 100-fold dilution and in 3 and 17 min on 1000- and 2000-fold dilution, respectively. With **1h**, the color disappeared in 1, 5, 9, and 150 min, respectively, on 10-, 50-, 100-, and 1000-fold dilution. For the slowest compound, **1o**, the color of the undiluted solution disappeared in 45 min, whereas 2-, 5-, and 10-fold dilution caused its disappearance in 85, 285, and 7200 min, respectively. With the Meldrum's acid derivative **1p**, the color disappeared in 15 min, 170 min, overnight, and 8 days, respectively, with the original solution and its 2-, 5-, and 10-fold diluted solutions.

On the basis of these data and that of Table S5, the semiquantitative reactivity order of the enols is **1p** < **1o** < **1n** < **1g** < (**1i**, **1j**, and **1k**) < **1h** < **1d** < other enols **1**. The corresponding K_{enol} ($CDCl_3$) values are **1p** ($\geq 50^{2a}$), **1o** (0.07^{2a}), **1n** (0.41^{2d}), **1g** (4.0^{2h}), **1i** (4.0^{2h}), **1j** (9.0^{2h}), **1k** (8.1^{2h}), **1h** (13.3^{2h}), **1d** ($\geq 50^{2g}$), **1a** ($\geq 50^{2b}$), **1b** ($\geq 50^{2e}$), **1c** ($\geq 50^{2g}$), **1e** ($\geq 50^{2g}$), **1f** ($\geq 50^{2g}$), **1l** ($\geq 50^{2b}$), and **1m** ($\geq 50^{2e}$). Hence, the qualitative reaction rates depend mostly on the % enol in the enol/amide mixture in $CDCl_3$. The color disappeared immediately with enols whose equilibrium percentage with the amide **2** (e.g., **2e**) in chloroform is high. For systems with a lower K_{enol} value, its complete disappearance took from a few minutes to 45 min at 0.25 M concentration. Exceptions are the Meldrum's acid enol **1p**, which is fully enolic in $CHCl_3$ but reacted more slowly than most other enols, and the enol of nitromalonamide, which is fully enolic in THF but did not react at all with **3**.

Under these reaction conditions, no reaction was observed between **1b** and cyclopentadiene or tetraphenylcyclopentadiene and between **1f** and tetraphenylcyclopentadienone or tetracyanoethylene (TCNE). This is not surprising since **3** is ca. 10^2 to 10^4 more reactive than TCNE in Diels−Alder reactions with 1,4-diphenyl- and 2-chloro-1,4-butadienes.[5]

Structure Assignment. **(a) In the Solid State.** The solid state structure of derivative **i** was determined by X-ray crystallography to be that of the open chain adduct **5i**. The ORTEP drawing and the full data are given in the Supporting Information. This structure (for atom numbering, see the following designation) is unequivocally deduced from the C1−O1 and C3−O2 bond lengths of 1.2081 (17) and 1.2137 (18) Å, which indicate that they are C═O bonds. In both cases, no C−O bond lengthening due to the amide resonance was observed. Likewise, the C1−C2 and C2−C3 bonds are even longer (1.5669 (19) and 1.5518 (19) Å, respectively) than a normal C−C bond,[12] although C2−C3 is a $C_{sp^3}-C_{sp^2}$ bond. A relevant comparison is with the amide **2i**, $Me_2NCOCH(CN)CONHPr$-*i*, where the C1−C2 and C2−C3 bond lengths are 1.545(3) and 1.532 (4) Å, respectively, and the C1−O1 and C3−O2 bond lengths are 1.232 (3) and 1.220(3) Å, respectively. The remarkable similarity in the bond lengths exclude structure **6i**, and the N5−C1 distance of 2.473 Å excludes structure **4i**.



5i

The triazolidine N5−H bond length is normal at 0.84 (2) Å, and the hydrogen is hydrogen bonded to the amide (formerly enol) oxygen O1 with an H···O1 hydrogen bond of 2.134 (19) Å.

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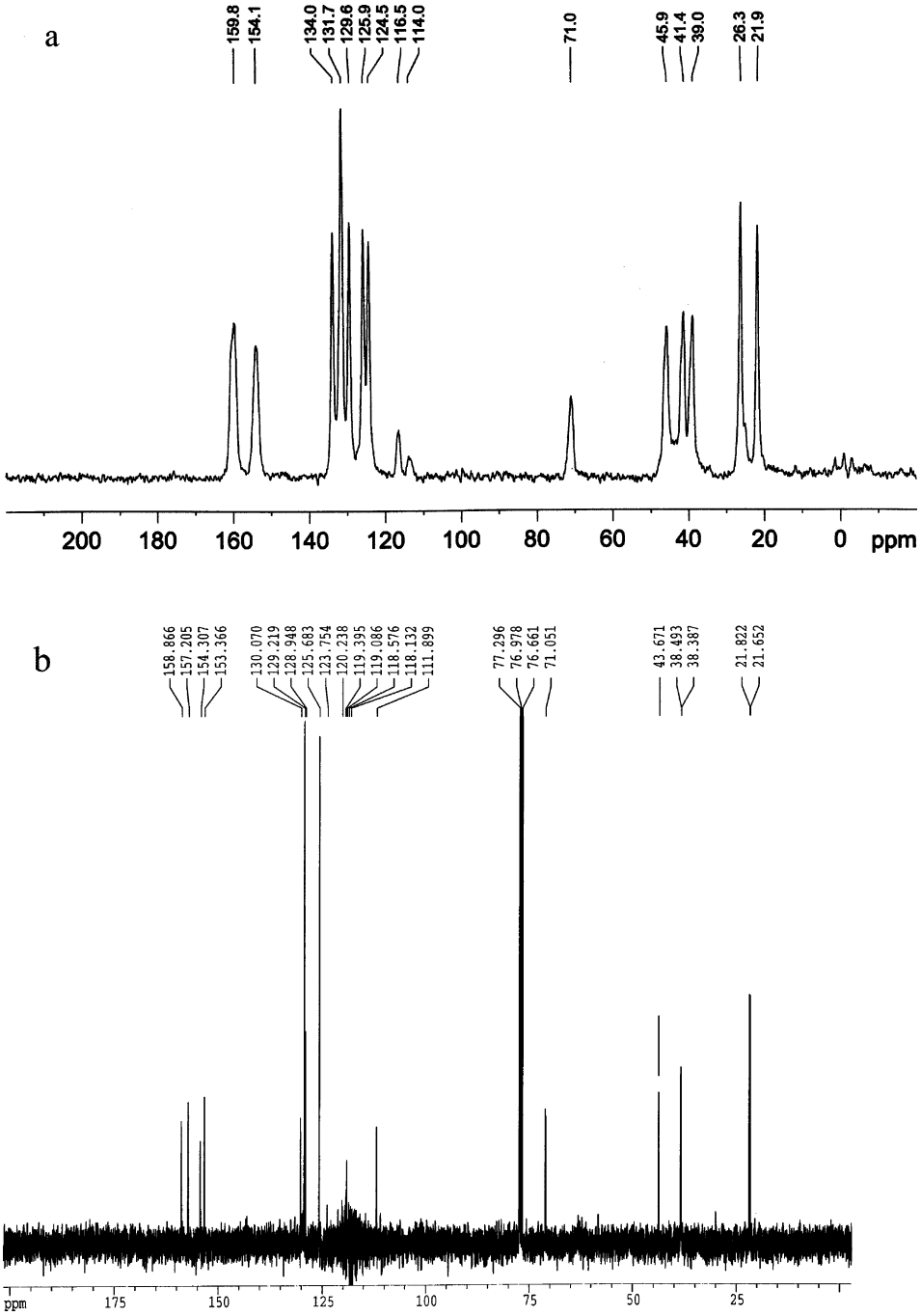

FIGURE 1. ^{13}C spectra of **5i**. (a) In the solid state and (b) in $CDCl_3$ solution.

The N5···O1 nonbonded distance of 2.6763 (17) Å indicates a moderately strong hydrogen bond, and the N5HO1 angle is 121.8 (16)°. The second N−H group is intermolecularly bonded to the amido-carbonyl of another molecule of **5i** with the following parameters: N1−H 0.810 (19) Å, N1···O2$^{\#1}$ 2.037 (19) Å, and N1···O2 2.8286 (17) Å and an NHO angle of 165.4 (17)°, where #1 denotes a symmetry transformation used to generate equivalent atoms: $-X + 1, -Y + 1, -Z$.

The solid state ^{13}C CPMAS NMR spectrum of **5i** displayed signals at 21.9, 26.3, 39.0, 41.4, 45.9, 71.0, 114.0, 116.5, 124.5, 125.9, 129.6, 131.7, 134.0, 154.1, and 159.8 ppm (Figure 1a). The NMR spectra in $CDCl_3$ displayed signals at 21.65, 21.82, 38.39, 38.49, 43.7, 71.1, 111.9, 125.7, 128.95, 129.22, 130.1, 153.4, 154.3, 157.2, and 158.9 ppm (Figure 1b). In general, the spectra look much the same, except that the solid state spectrum shows the two molecules observed in the X-ray diffraction and is poorly resolved in the 155−160 ppm region as compared to the solution spectrum.

(b) Structure in Solution. The ^1H NMR spectra in solution (Table S1 in the Supporting Information) were determined in $CDCl_3$, THF-d_8, or DMSO-d_6 and showed only the number of signals expected for a single compound. When Y ≠ Y′, both C_α and C_β are chiral, and **4** may display pairs of diastereomers, whereas in compounds **5**, only one set of signals is expected in achiral medium. We conclude that either **4** does not exist in

solution or if it is formed, its chiral C_α center is lost by a rapid **4** ⇌ **5** equilibration.

The ^{1}H NMR spectra show Ph, N−Ar or N−Alk, and Y,Y′ signals and two additional protons: one for the NHR group, and one is either the OH of **4** or the NH of **5**. Of these, one broad singlet is at the lowest field observed at room temperature. The other is usually a singlet or a doublet for the NH−Pr-*i* derivatives due to C*H*−N*H* coupling. Since when R is *i*-Pr or *t*-Bu, the δ(NH) value is smaller than when R is Ar, and assignment of this proton is clear. Its δ value of 7.65−11.58 is much higher than that of hemiaminal C(OH)NHR protons. Comparison with the amides **2** in the same solvent mostly show a good correspondence with the higher field proton of the adduct: adduct, δ(NH-**4** or **5**), δ(NH-**2**) ppm: **4c**/**5c**, 8.14, 9.28;[2g] **4d**/**5d**, 10.83, 10.30;[2g] **4e**/**5e**, 6.31, 6.37[2g] ($CDCl_3$), and 8.83, 8.31[2g] (DMSO-d_6); **4f**/**5f**, 6.22, 5.95;[2g] **4g**/**5g**, 8.10, 9.14;[2h] **4h**/**5h**, 8.77, 9.40;[2h] **4i**/**5i**, 6.61, 6.68[2h] ($CDCl_3$) and 7.60, 7.31[2h] (THF-d_8); **4j**/**5j** 10.46, 10.38;[2h] **4k**/**5k** 6.36, 6.88;[2h] **4o**/**5o** 7.98, 9.26;[2a] and **4p**/**5p**, 8.90, 10.99[2a]. We conclude that all compounds have structure **5**.

^{1}H NOESY and COSY NMR spectra in $CDCl_3$ and THF-d_8 show a correlation between the *i*-Pr−H (δ 4.05 and 4.02) and the N−H (δ 7.75 and 7.89) in **4b**/**5b**/**6b** and **4i**/**5i**/**6i**, respectively. Hence, structure **6** is excluded. It is further excluded since the NMR data for **4k**/**5k**/**6k** show identical *i*-PrNHCO groups.

The ^{13}C NMR spectra in solution (Table S2 in the Supporting Information) display the expected signals. The triazolidinyl group behaves as a strong EWG, as deduced by the strong shift of C_β to a lower field as compared to the amides **2**. The major difference expected between **4** and **5** (including **4i** and **5i**) is in $\delta(C_\alpha)$, which is a carbonyl in **5i** and an hemiaminal (**C**(OH)-NHR) carbon in **4i**. The adducts displayed three to five carbonyl groups at 153.4−163.9 ppm. The two triazolidinedione C═O groups are singlets <2 ppm apart at 153.6−156.1 ppm. In **3**, they are at 158 ppm.[13] The CONRR′ carbonyls are at 155−161 ppm, and the ester carbonyls are at 158.6−165 ppm. The differences are substituent- and solvent-dependent. More than half of the amido carbonyls are doublets or multiplets with J values of 2.5−4.0 ppm, due to coupling with the NH. The RCONRR′ (R = Alk, Ar) carbonyls resonate mostly at 160−168 ppm (sometimes up to 171 ppm),[14] in line with the δ values in structures **5**.

Hemiaminals are mostly unstable species that frequently eliminate water to form an imine, but several of them are stable. δ^{13}C values for 14 R^1R^2(OH)NHR compounds (R^1,R^2 = alkyl, $PhCH_2$ and R = H, NH_2, NMe_2, N(*c*-$(CH_2)_5$) appear at 80.6−86.9 ppm (75.4 ppm when R^1 = Me and R^2 = R = H).[15a] The values for δ(^{13}C(RNH)(OH)$(CF_3)CO_2$Me) (R = Ph, *o*-Tol, Ph_2-CH, $PhCH_2$) with C$(EWG)_2$, which are closer models for δ-(^{13}C)(**4**), are 84.5−87.3 ppm.[15b] We ascribe the unassigned ^{1}H NMR broad singlets at 4.31−4.66 and 4.66−2.46 ppm to the OH and NH since they are affected by a temperature change: δ($F_3C^{13}CH$(OH)NRR′) is 84.5 ppm.[15c] For an hemiaminal Rh^+ complex, δ(^{13}C) is 84.6, δ(NH) is 5.16, and δ(OH) is 2.27 ppm.[16] We conclude that δ(**C**(OH)NH) is 75−88 ppm, mostly ca. 85 ppm, and that δ(OH) and δ(NHR) are at the 2.5−5.2 ppm region. Since our compounds display only one ^{13}C NMR singlet at 69−79 ppm, assigned to C_β, and no unidentified ^{1}H NMR signals at 2.5−5.2 ppm, we exclude structure **4**.

In Table S3 in the Supporting Information, δ(^{13}C) values for the amides **2** and the corresponding adducts **5** ($\Delta_{adduct-amide}$) in the same solvent are compared. The major influence is on C_β, which is attached to the triazolidinyl group. The differences in parts per million are nearly constant, being 25.9 ± 0.9 for the cyanomalonamides, 23.5 ± 1.4 for the cyanoester amides, and 18.9 ± 0.50 for the amido diesters. The latter lower values are due to much higher δ values of **5**, as compared to those for **2**. For all other groups, δ(**5**) are at a higher field than δ(**2**). They are −0.75 to −2.17 for the CN and −0.63 −to −3.31 for the amide CO with no apparent trend. In sum, the spectra of the two species resemble each other reasonably, considering the presence of the triazolidinyl group. Moreover, the strong effect of the latter group on the $\delta(C_\beta)$ differences is not observed at all for C_α, suggesting that C_α is not bonded to this group (i.e., the structure is **5** and not **4**). NOESY, COSY, and ^{1}H−^{13}C HSQC NMR spectra in THF-d_8 indicate (by two N−H couplings) that the acyclic **5i** was obtained.

(c) IR Spectra. IR spectra of **5c**, **5f**, **5h**, **5i**, **and 5l−o** in $CHCl_3$ (Table S4 in the Supporting Information) display one or two broad peaks at 3250−3357 cm^{-1}, which are ascribed to N−H absorptions,[17] and most of the peaks appear at ca. 2880 or 2800 cm^{-1}. C═O peaks for all compounds are at 1740−1800 cm^{-1} (those for **3** are at 1780 and 1760 ppm)[6a] and 1680−1730 cm^{-1}. The weak CN absorptions observed at 2250 cm^{-1} for **5f** and **5m** are typical for CN systems substituted by strong EWGs,[18] but they are absent or very weak for most other compounds. Only **5l**, which is the only system with an unsubstituted NH_2 group, displays peaks at high wave numbers of 3637 and 3553 cm^{-1}, in addition to the other peaks, and no compound has shown a peak >3360 cm^{-1}, the range assigned to O−H absorptions.[17]

Solvent Effect. Whereas the reaction of **1c** with **3** in $CHCl_3$ is complete in <1 min, at approximately the same concentrations, the color disappeared in 2−3 min and after 17 min in THF and in CH_3CN, respectively, and was not completely discharged in DMF-d_7 even after 15 h. The percent enol of **1c** at equilibrium with **2c** is 100, 89, 62, and 0 in $CDCl_3$, THF-d_8, CD_3CN, and DMF-d_7, respectively. From the limited data, the increase in solvent polarity reduces strongly the reaction rate with **3**. If the reaction intermediate is a polar aziridinium imide,[8] we expect a rate increase for an ene reaction starting with two neutral molecules. However, judging from literature data, this is not the case. In the reaction of **3** with several alkenes, the reactivity order in solvents CH_2Cl_2 > $ClCH_2CH_2Cl$ > $PhNO_2$ > C_6H_6 > EtOAc > THF with a 50-fold difference between the extremes[19] does not correlate with the solvent polarity. The effect was tentatively ascribed to strong donor−acceptor interac-

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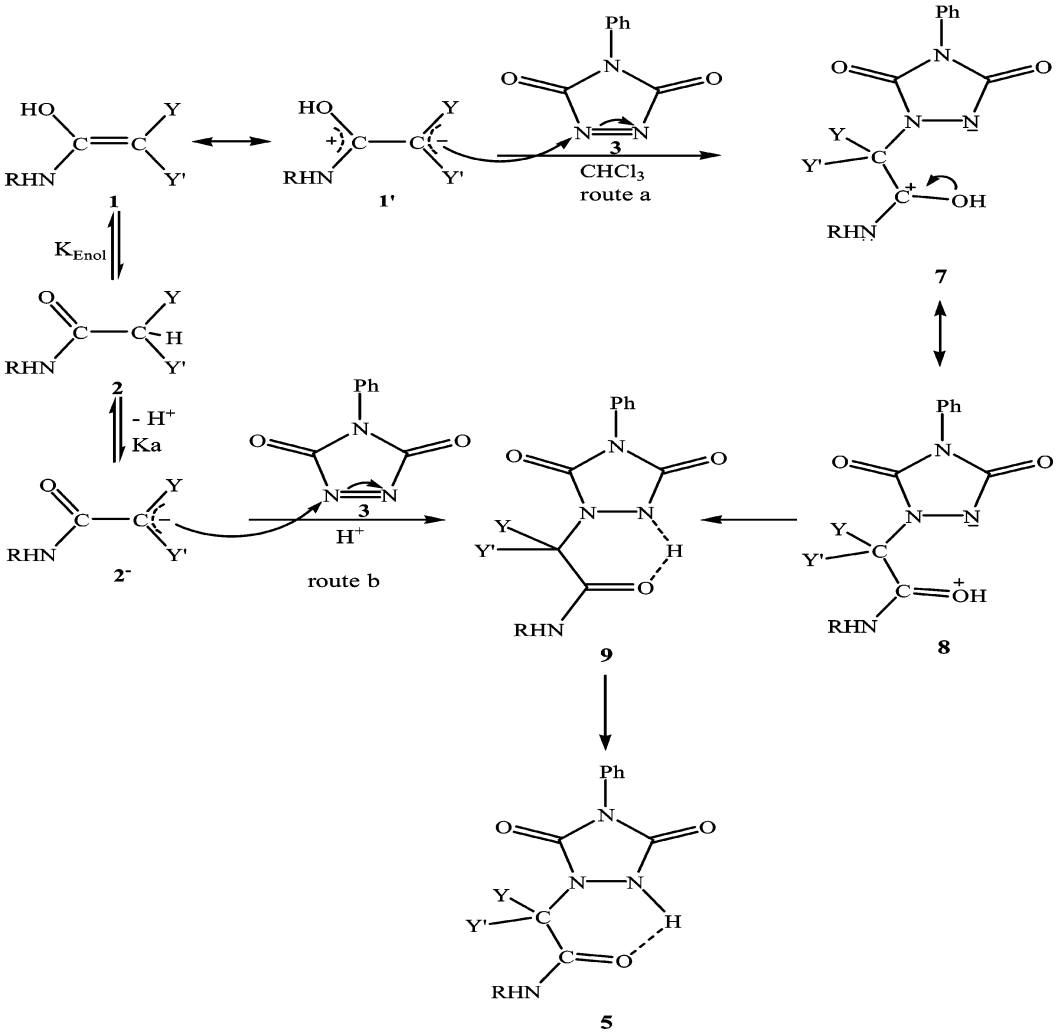
SCHEME 1. Suggested Mechanism for Formation of 5



tions between **3** and solvent. Greene et al.[20] found the following solvent effect on the ene reaction of **3** with tetramethylethylene: C_6H_6 > THF and CH_2Cl_2 > CH_3CN, and from this and literature data, they deduced a "lack of marked effect on solvent polarity" and no correlation with E_T. This was tentatively ascribed to a diffuse charge distribution in the transition state or to an unclarified solvent−solute interaction. A similar solvent effect ($CHCl_3$ > C_6H_6 > CH_3CN) was found on the rates with several C═C compounds.[21] The solvent effect was ascribed to the association of **3** with $CHCl_3$, which decreases its LUMO energy.

Suggested Mechanism. Since [2 + 2] cycloadditions of enophiles including **3** are well-documented,[5] but thermal [$_\pi 2_s$ + $_\pi 2_s$] reactions are symmetry forbidden,[22] two step reactions involving the intermediacy of aziridinium imides,[20,23] radicals,[24] or 1,4-dipoles[25] were invoked. Similar polar two step processes with a first step attack of the highly nucleophilic C_β of the zwitterion **1** ↔ **1′** on the enophile **3** will give a zwitterion **7** ↔ **8**. This can either undergo intramolecular charge recombination to give the [2 + 2] adduct **4** or transfer a proton from the OH group to the negatively charged nitrogen, either intramolecularly or stepwise via **9**, to give the 1,2 adduct **5** (Scheme 1, route a).

We note that an initially formed **4** can ring open in a retroaldolization to give **5**. The allowed photochemical variant of the [2 + 2] cycloaddition, found by de Mayo[26a] and Eaton[26c] gave in the reaction of cyclohexene with the enol of acetylacetone the bicyclic adduct, which was opened to give a C═O group from the former OH. Similar ring openings were recorded.[26d] A [2 + 2] adduct was considered as the intermediate on the way to the open chain adduct in the [2 + 2] addition of 1,1,4,4-tetramethylbutadiene to **3**,[6c] the [2 + 2] adduct of **3** with adamantylideneadamantane was suggested to undergo the reverse reaction,[20] and the [2 + 2] adduct of 2-methylindene

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gave the ene product on heating.[27] The previous discussion on the absence of NMR δ values of hemiaminals, or the absence of a coalescence signal of **5** with the [2 + 2] adduct in our system, exclude a significant concomitant concentrations of **4** and **5** in solution.

We view the formation of **5** as the oxa analogue of the extensively studied ene reaction with **3**, where an allylic hydrogen is lost.[8] In our variant, an enolic hydrogen is lost, and an amide C═O bond is formed. The enol is suggested as the alkene component (Scheme 1, route a) based on the faster reaction of enols with a higher percentage of enols in the amide/enol mixture (i.e., higher K_{enol} values) since at least half of the reactants used are ≥98% enolic in $CHCl_3$ or in the solid state. The slower reaction of the Meldrum's acid enol **1p** is ascribed to the loss of the very strong hydrogen bond, superimposed on a possible steric retardation in the formation of **7**.

However, due to the enols **1** ⇌ amides **2** equilibria in $CHCl_3$, it could be argued that **2** itself is the reagent, giving **5** via $\mathbf{2}^-$ (Scheme 1, route b). The kinetic order will be the same in both alternatives since the amide and the enol concentrations are proportional, $[\mathbf{2}] = [\mathbf{1}]/K_{enol}$. The methine carbon of **2** is acidic due to its Y and Y′ and CONHR EWG substituents, and the conjugate base $\mathbf{2}^-$ formed even in the absence of an added base may be the nucleophile attacking **3**, forming **9** directly and then **5**. Alternatively, the proton formed by the ionization may first protonate the nitrogen of **3**, and $\mathbf{2}^-$ will then combine with $\mathbf{3}\cdot\mathbf{H}^+$.[28] Formation of **5o** from **2o** with **3** with no mechanistic discussion was reported.[11]

Moreover, the slower reaction is that of **1o**, whose equilibrium percentage with **2a** is only 7%.[2a] The lower reactivity of the most enolic substrate **1p**, by this route, is ascribed to the low percentage of amide **2p** and the relatively low nucleophilicity of its highly stable anion, in addition to a contribution from steric effects of the bulky anion of **1p**.

We attempted to probe this question. First, when the active methylene compounds CH_2YY' (Y = Y′ = CO_2Et, $C_4F_9SO_2$ and Y = CN, Y′ = CO_2Me, CONHR, and R = *i*-Pr, *t*-Bu) were added to **3** in $CHCl_3$, the color did not disappear overnight. Since the concentrations of the derived anions in the neutral solvent may be too low to give a sufficiently rapid reaction, we added Et_3N to the reaction mixture of the slow **1o** with **3.** The red color disappeared rapidly, but a control experiment showed that the reaction of Et_3N with **3** alone resulted in a rapid disappearance of color. Second, when 0.5−0.05 mL of AcOH was added to a mixture of **1c** with **3** in $CHCl_3$, the rapid color disappearance was not slowed down, indicating that protonation of the anion of **1c**, if any, does not reduce its concentration to affect sufficiently its reaction rate with **3**. A control experiment showed no apparent reaction of AcOH with **3**.

The strong decrease of the reaction rate with the increased solvent polarity is a better probe. As mentioned previously, the ene reactions of **3** showed an irregular change of the rate with solvent polarity, which was explained by a specific solvent−solute interaction. Comparison of the polarities of the precursors and the transition state of the reaction only suggested that the latter is not highly polar, despite the polar intermediates that follow it. Our system is more complicated since the enols are highly polar with a significant zwitterionic contribution to the ground state. Since **3** is also polar, and the transition state is also zwitterionic, the lower rate in more polar solvents can be accounted for by route a in Scheme 1 with more polar reactants than the transition state. Moreover, the percent enol decreases strongly in the more polar solvents,[2] and this should reduce the rate of route a (Scheme 1) in the more polar solvents. In contrast, if the reaction proceed via route b in Scheme 1, both the concentrations of the pre-equilibrium formed enolate ion and the concentrations of the amide will be higher in a more polar solvent, and the reaction rate will increase. This is in contrast to the observation. Consequently, route a in Scheme 1 is more consistent with the observed experimental data than route b. The hydrogen transfer step can be either concerted with the addition of **1** to **3** to form **7** or occur after it.[29]

Finally, is the aziridinium imide intermediate suggested in the ene reactions of **3**[8,20,23] relevant to the reaction of the enols with **3**? In contrast to most alkenes studied, which are not very polar, the enols have definite positive and negative centers on the formal alkene moiety. Whereas the interaction of the positive nitrogen in the transition state with the $^{\delta-}$CYY′ carbon is favorable, a simultaneous interaction with the positively polarized $^{\delta+}$C(OH)NHR carbon is unfavorable. A reaction of the electrophilic nitrogen of **3** with C_β of **1** to form **7** is favorable (Scheme 1) with no need for interaction with C_α.[30]

Conclusion

Reaction of enols of amides with PTAD gave adducts of CYY′CONHR and H to the N═N bond in an oxa-ene reaction. The suggested mechanism involves an initial nucleophilic attack of the $Y'YC^{\delta-}$ moiety of the enol to one PTAD nitrogen, followed or coupled with proton transfer to the other nitrogen.

Experimental Section

Materials and General Methods. The enols were available from our previous work.[2] Compound **3** is commercially available. Melting points are uncorrected. General methods are similar to those reported.[31]

Solid State NMR Spectroscopy. Solid state NMR spectroscopy with MAS was carried out on a 300 MHz spectrometer operating at 75.4 MHz for ^{13}C and employing a triple-resonance probe equipped with a 5 mm o.d. spinning module. The sample (78.6 mg) was packed into a high performance zirconium rotor and the MAS frequency was maintained at 10.000 ± 2 Hz. Chemical shifts were referenced to an external secondary standard ((2-^{13}C)-Gly = 44 ppm). The contact time for ^1H and ^{13}C Hartman−Hahn matched fields (50 kHz) was 3 ms. Refocused ^{13}C spectra were acquired, with delays set to one rotor period (100 μs) on each side of the 180° ^{13}C pulse. High power dipolar coupling (DD) on the proton channel (ca. 100 kHz) was used following the CP excitation. Acquisition was of 6000 points with a dwell time of 25 μs. The signal was averaged over 3072 transients with a repetition delay of 3 s. The FID was Fourier transformed with an exponential window function of 5 Hz.

General Procedure for Reaction of Enols of Amides with 4-Phenyl-1,2,4-triazoline-3,5-dione. The procedure used with minor modifications regarding the reaction rate (deduced from the disappearance of the red color of **3** and the appearance of the precipitate) and the yields is demonstrated for 3-hydroxy-3-isopropylamino-2-dimethylaminocarbonylacrylonitrile. When a so-

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(28) We note that if the reaction proceeds via $\mathbf{2}^-$, $\mathbf{2}^-$ can also be formed initially from **1**.

(29) For a stepwise mechanism in the ene reaction of **3**, see: Elemes, Y.; Foote, C. S. *J. Am. Chem. Soc.* **1992**, *114*, 6044.

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lution of **1i** (197 mg, 1 mmol) and 4-phenyl-1,2,4-triazoline-3,5-dione (175 mg, 1 mmol) in chloroform (4 mL) was stirred for 1 min, the red color disappeared. The mixture was kept at room temperature overnight, and the white precipitate that formed was filtered and dried in air affording 320 mg (79%) of **5i**, mp 182 −3 °C. Anal. calcd for $C_{17}H_{20}N_6O_4$: C, 54.84; H, 5.38; N, 22.58 Found: C, 54.72; H, 5.44; N, 22.77. Suitable crystals for X-ray diffraction were obtained by dissolving crude **5i** in THF and slow evaporation of the solvent at room temperature.

^{1}H NMR ($CDCl_3$, 298 K, 400 MHz) δ: 1.17 (6H, d, J = 6.5 Hz); 3.08 (3H, s); 3.33 (3H, s); 4.10 (1H, octet, J = 6.8 Hz); 6.61 (d, J = 7.7 Hz); 7.38−7.45 (m); 8.41 (s, br). ^{13}C NMR ($CDCl_3$, 298 K, 400 MHz) δ: 21.65 (q, J = 1227.6 Hz); 21.82 (q, J = 126.5 Hz); 38.39 (q, J = 143.3 Hz); 38.49 (q, J = 143.8 Hz); 43.7 (d, J = 140.3 Hz); 71.1 (s); 111.90 (s); 125.7 (d, J = 164.4 Hz); 128.95 (dt, J_d = 162.0 Hz, J_t = 7.3 Hz); 129.22 (dd, J_1 = 163.1 Hz, J_2 = 5.6 Hz); 130.1 (m); 153.4(s); 154.3 (s); 157.2 (s); 158.9 (m, J = 3.2 Hz, C═O). ^{1}H NMR (THF-d_8, 298 K, 400 MHz) δ: 1.15 (3H, d, J = 6.4 Hz); 1.17 (3H, d, J = 4.6 Hz); 2.99 (3H, s); 3.27 (3H, s); 4.05 (1H, octet, 6.8 Hz); 7.33 (1H, t, J = 7.3 Hz); 7.42 (2H, t, J = 7.7 Hz); 7.52 (2H, d, J = 7.7 Hz); 7.60 (d, J = 8.1 Hz); 9.52 (s). ^{13}C NMR (THF-d_8, 298 K, 400 MHz)δ: 20.9 (q, J = 126.6 Hz); 36.91 (q, J = 138.0 Hz); 37.39 (q, J = 138.1 Hz); 42.9 (d, J = 140.7 Hz); 70.7 (s); 112.7 (s); 125.3 (dt, J_d = 163.8 Hz, J_t = 6.2 Hz); 127.7 (dt, J_d = 161.7 Hz, J_t = 7.5 Hz); 128.4 (dd, J_1 = 162.3 Hz, J_2 = 8.1 Hz); 131.7 (s); 153.5 (s); 155.0 (s); 157.99 (d, J = 3.2 Hz); 158.51 (m, J = 3.5 Hz).

The full spectral data for **5a**−**p** in several solvents are given in Tables S1 and S2 of the Supporting Information. Melting points, yields, and microanalyses are given in Table S5 of the Supporting Information.

Control Experiments. (a) No reaction was observed when several active methylene compounds (CH_2YY', Y = Y′ = $CO_2CH_2CCl_3$; Y = CN, Y′ = CO_2Me; Y = CN, Y′ = CONHPr-*i*, CONHBu-*t* (1.0 mmol)) were reacted with **3** (0.96 mmol) in $CHCl_3$. The red color persisted for >35 h, and the precursors were re-isolated.

(b) To a solution of **3** (212 mg, 0.12 mmol) in $CHCl_3$ (2 mL), two drops of triethylamine (ca. 0.3 mmol) were added. The red color disappeared immediately.

(c) When **1d** (0.125 mmol) was reacted with **3** (0.12 mmol) in $CHCl_3$ (2 mL) in the presence of excess acetic acid (0.5 mL), the red color disappeared immediately.

(d) To a solution of **3** (212 mg, 0.12 mmol) in $CHCl_3$ (2 mL), one to 10 drops of glacial acetic acid were added. The red color persisted for >35 h.

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Supporting Information Available: CIF and ORTEP of **5i**, Tables S1 and S2 of ^{1}H and ^{13}C NMR of all adducts, Table S3 of comparison of ^{13}C NMR of amides **1** and adducts **5**, Table S4 of IR spectra of **5**, and Table S5 of analytical data. This material is available free of charge via the Internet at http://pubs.acs.org.

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