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$BF_3 \cdot Et_2O$-Promoted Decomposition of Cyclic α-Diazo-β-Hydroxy Ketones: Novel Insights into Mechanistic Aspects

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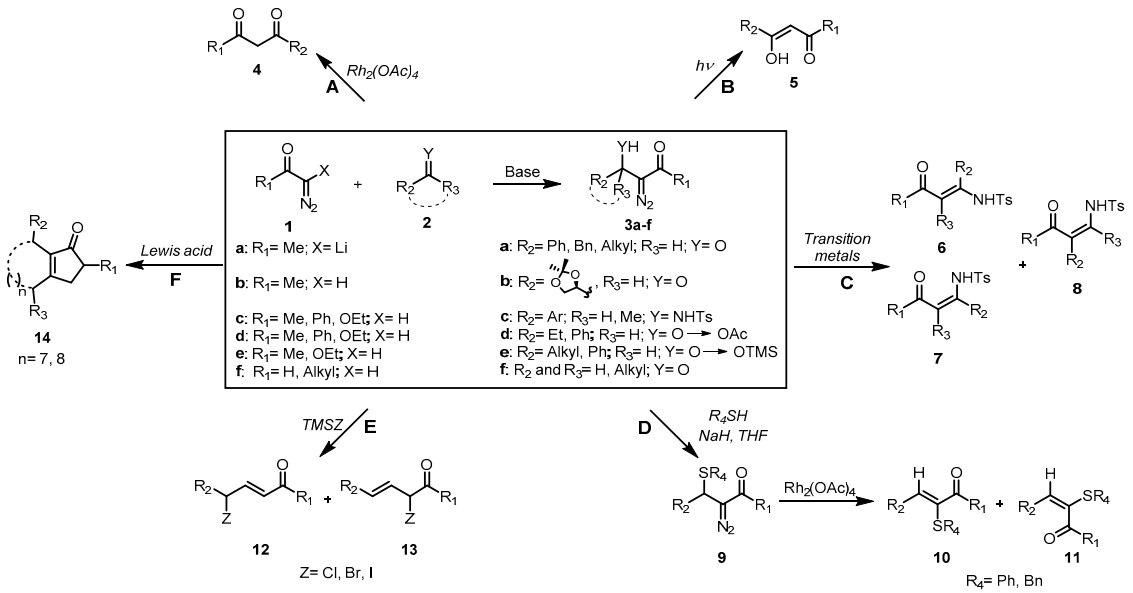
Abstract: We report novel insights into the cascade rearrangement of destabilized vinyl cations deriving from the $BF_3 \cdot Et_2O$-induced decomposition of cyclic α-diazo-β-hydroxy ketones in turn prepared by aldol-type condensation of cycloalkanones with diazoacetone. Complexation of the hydroxy group of the α-diazo-β-hydroxy compound with the Lewis acid is the first event, followed by the generation of the cycloalkanylidenediazonium salt that, after nitrogen loss, produces the highly reactive vinyl cation. The subsequent ring expansion results in the formation of a cycloalkenyl vinyl cation that affords the allylic cation by 1,2-methylene shift and ring contraction. The cation can then trap the solvent, the fluoride or the hydroxide released from the $[BF_3OH]^-$ to afford different reaction products. The effect of both solvent and substrate ring size on products types and ratios were analyzed and discussed from a mechanistic point of view.

Keywords: α-diazo-β-hydroxy ketones; decomposition; vinyl cation cascade; diazoacetone; borontrifluoride

1. Introduction

Since Curtius's pioneering work on the diazotization of glycine in 1883 [1], α-diazocarbonyl compounds have represented versatile reagents for myriad chemical transformations including the homologation reaction of carbonyl compounds, cyclopropanation of olefins, aziridination, bond insertion reactions, sigmatropic rearrangements, 1,3-dipolar and Staudinger cycloaddition [2–7]. In most of these reactions, transition metals able to stabilize the highly reactive carbene intermediate are employed, including copper, rhodium, ruthenium, iridium, palladium, cobalt and iron species [8]. While the literature illustrates several examples and applications on α-diazo-β-hydroxy esters, especially in the homologation reaction of acyclic and cyclic ketones [2,3], only few reports concern the use of α-diazo-β-hydroxy ketones (Scheme 1). In 1981, we reported the $Rh_2(OAc)_4$-catalyzed decomposition of α-diazo-β-hydroxy ketones **3a**, prepared from diazo lithioacetone (LiDAA, **1a**) and aldehydes **2a**, affording β-diketones **4** in 68–81% isolated yield (Scheme 1A) [9]. Notably, this two-step approach was adopted for the synthesis of the natural product β-damascone [9], and later for the preparation of β-diketones [10] and chiral *N*-protected α-amino-β-diketones [11].



Scheme 1. Main synthetic applications of α-diazo-β-hydroxy ketones and analogs.

More recently, López-Herrera and Sarabia-García studied the photochemical decomposition of α-diazo ketone **3b** prepared from 2,3-*O*-isopropylidene-D-glyceraldehyde (**2b**) and diazoacetone (DAA, **1b**) to determine those factors that favor the Wolf rearrangement over the 1,2-hydride shift (Scheme 1B) [12–14]. In line with this work, Wang and co-workers reported a mechanistic study on the decomposition reaction of β-(*N*-tosyl)amino diazocarbonyl compounds **3c** [15–17]. With the aim to define the main factors affecting the formation of 1,2-aryl migration products (**6** and **7**) over the 1,2-hydride migration adduct (**8**) (Scheme 1C), the diazo ketone decomposition reaction is conducted under various catalytic systems and the results analyzed by means of Hammett correlation. In 2005, the same authors showed a novel decomposition process of β-thio-substituted α-diazo carbonyls (**9**) (Scheme 1D) [18]. Interestingly, the treatment of **9** with catalytic amounts of $Rh_2(OAc)_4$ in CH_2Cl_2 at 0 °C leads to only the 1,2-thio group migration products (*Z*)-**10** and (*E*)-**11** [18]. Similarly, β-trimethylsiloxy α-diazo carbonyls **3e** are reacted with a stoichiometric amount of trimethylsilyl halides in CH_2Cl_2 at 0 °C affording a nearly equimolar mixture of α- and γ-halide substituted unsaturated carbonyl products (**12** and **13**) (Scheme 1E) [19]. To the best of our knowledge, only two research groups shed light on the mechanistic aspects of α-diazo-β-hydroxy ketones rearrangements. In 1981, Miyauchi et al. reported the acid-catalyzed decomposition of 3-aryl-2-diazo-3-hydroxy-1-phenylpropanones in different solvents [20]. Interestingly, more polar solvents favor the formation of aryl migration adducts over the products deriving from the hydrogen migration, while *p*-toluensulfonic acid (TsOH) is found to be an efficient catalyst for promoting the aryl shift. In 2017, Cleary et al. described the Lewis acid-catalyzed vinyl cation rearrangement of α-diazo-β-hydroxy ketones **1f** by 1,2-shift and subsequent C–H insertion at non-activated γ C–H bond [21]. This reaction allows the preparation of synthetic versatile bicyclic cyclopentenones fused with seven- and eight-membered rings (**14**) (Scheme 1F) [21].

Herein, as a continuation of our interest in diazo chemistry [9,22–31], we investigated the cascade rearrangement of destabilized vinyl cations deriving from the $BF_3{\cdot}Et_2O$-induced decomposition of α-diazo-β-hydroxy ketones, prepared by aldol-type condensation of cyclic ketones with DAA (**1**). In particular, the effect of solvent and ring size on products distribution and mechanism paths were analyzed and discussed.

2. Results and Discussion

Preparation and decomposition reaction of hydroxycycloalkyl diazoacetones. Although DAA (**1**) can be easily obtained by acylation of diazomethane (**15**) with acetylchloride (**16**), its isolation

from the crude reaction mixture is shown to be inefficient following the poor detailed experimental procedure reported in the original paper [32]. Indeed, the removal of the excess of ethereal diazomethane results in the loss of most highly volatile DAA (**1**). To overcome this problem, we first distilled off diethyl ether and the excess of diazomethane (**15**) under atmospheric pressure and the resulting residue was then distilled under reduced pressure. Thus, a solution of **16** was added dropwise to an ethereal solution of **15** at −10 °C affording DAA (**1**) in nearly quantitative conversion. Et_2O and the excess of diazomethane (**15**) were then distilled off (50 °C, 760 mmHg) through a glass spheres-packed (silver shell) column connected to a Friedrich condenser (Figure 1) [33]. DAA (**1**) was isolated in 81% yield and high purity after re-distillation (49 °C, 13 mmHg).

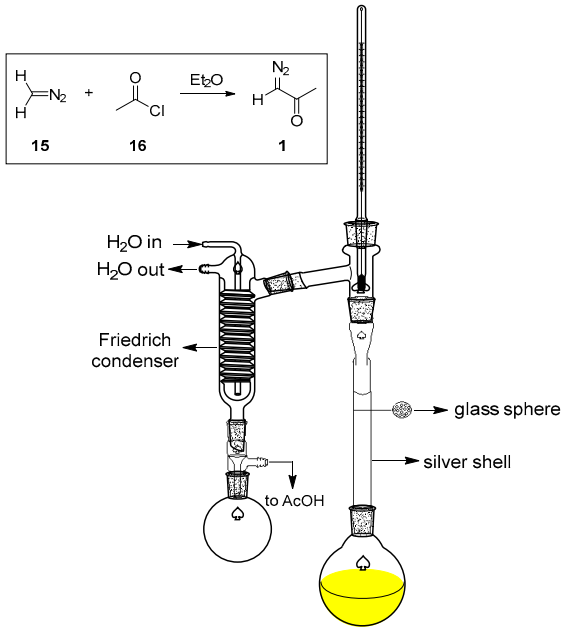
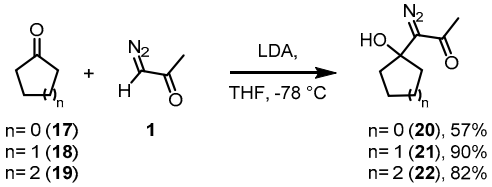


Figure 1. Apparatus used for the preparation and isolation of diazoacetone (**1**).

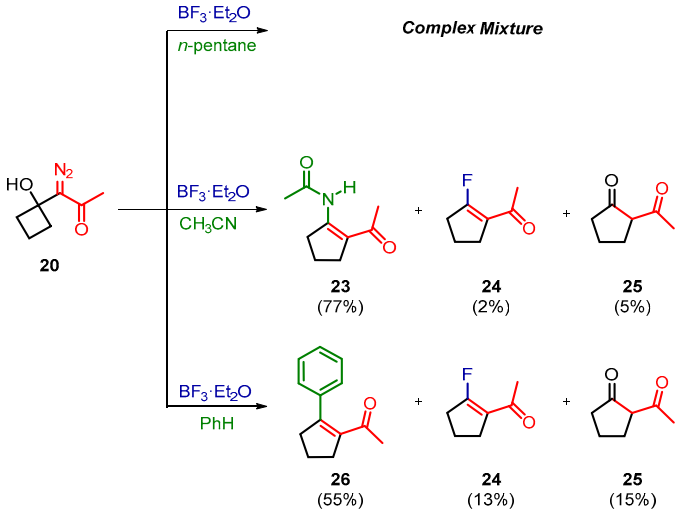
DAA (**1**) was readily submitted to aldol-type condensations with cyclobutanone (**17**, n = 0), cyclopentanone (**18**, n = 1), and cyclohexanone (**19**, n = 2) in presence of lithium diisopropylamide (LDA) as the base. The corresponding 1-diazo-1-(1-hydroxycycloalkyl)propan-2-ones **20**–**22** were obtained in moderate to good yields after purification of the crude reaction mixture by aluminum oxide (Brockmann activity IV) flash chromatography (Scheme 2).



Scheme 2. Synthesis of 1-diazo-1-(1-hydroxycycloalkyl)acetones **20**–**22**.

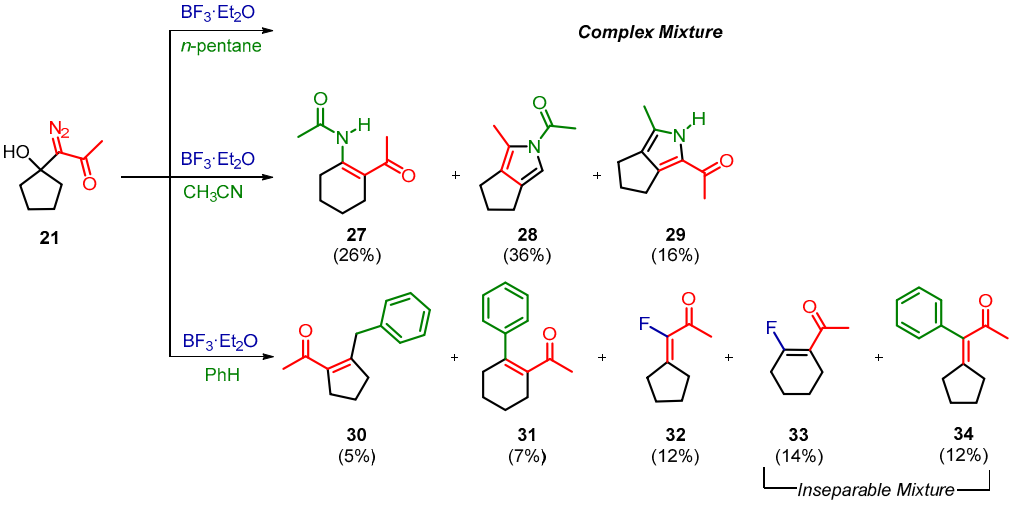
The lowest yield (57%) was observed for the cyclobutyl adduct **17** (n = 0), probably because of its relative instability also under weak acidic media, e.g., during chromatography (a partial decomposition was observed also in $CDCl_3$ during the NMR analysis). The freshly synthesized α-diazo-β-hydroxy ketones **20**–**22** thus obtained were dissolved in the solvent chosen for the decomposition (freshly distilled *n*-pentane, acetonitrile or benzene) and the resulting solution was added dropwise at room temperature to a solution of freshly distilled $BF_3{\cdot}Et_2O$ (1.5 equivalents) in the same solvent.

Cyclobutyl derivatives. While the treatment of cyclobutyl analog **20** with $BF_3 \cdot Et_2O$ in *n*-pentane resulted in a complex mixture of products, the same reaction performed in acetonitrile afforded *N*-(2-acetylcyclopent-1-en-1-yl)acetamide (**23**) (77%) as the major product accompanied by small amounts of 1-(2-fluorocyclopent-1-en-1-yl)ethanone (**24**) (2%) and 2-acetylcyclopentanone (**25**) (5%) (Scheme 3). A similar product distribution was observed using benzene as the solvent. Indeed, also in this case, the adduct **26** derived from the solvent addition resulted to be the main reaction product (55%), while compounds **24** and **25** were isolated in 13% and 15% yields, respectively (Scheme 3).



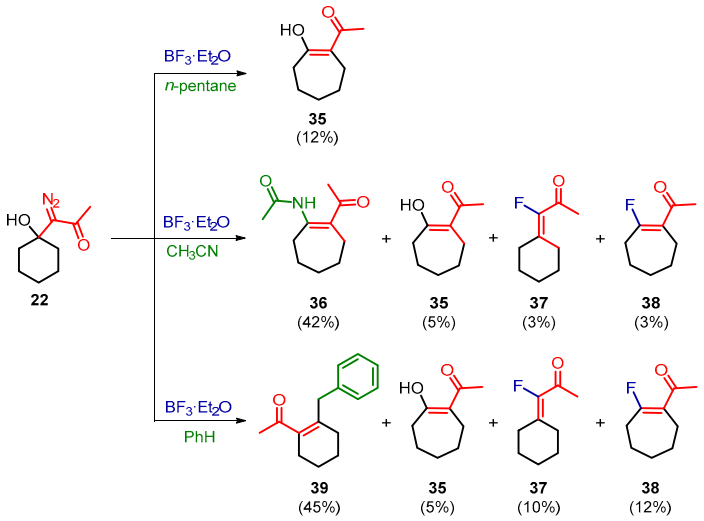
Scheme 3. $BF_3 \cdot Et_2O$-induced decomposition of 1-diazo-1-(1-hydroxycyclobutyl)propan-2-one (**20**).

Cyclopentyl derivatives. Exposure of 1-diazo-1-(1-hydroxycyclopentyl)propan-2-one (**21**) to freshly distilled $BF_3 \cdot Et_2O$ in *n*-pentane afforded a complex and inseparable mixture of products (Scheme 4). When the reaction was carried out in acetonitrile, β-enamino ketone **27**, 1-(1-methyl-5,6-dihydrocyclopenta[*c*]pyrrol-2(4*H*)-yl)ethan-1-one (**28**) and 1-(3-methyl-2,4,5,6-tetrahydrocyclopenta[*c*]pyrrol-1-yl)ethanone (**29**) were isolated in 26%, 36% and 16% yields, respectively, while adducts deriving from fluorine trapping were not observed (Scheme 4). Solvent-adducts, namely 1-(2-benzylcyclopent-1-en-1-yl)ethanone (**30**) and 1-(2-phenylcyclohex-1-en-1-yl)ethanone (**31**); 1-cyclopentylidene-1-fluoropropan-2-one (**32**); and the inseparable mixture of 1-(2-fluorocyclohex-1-en-1-yl)ethanone (**33**) and 1-cyclopentylidene-1-phenylacetone (**34**) were isolated using benzene as the solvent (Scheme 4).



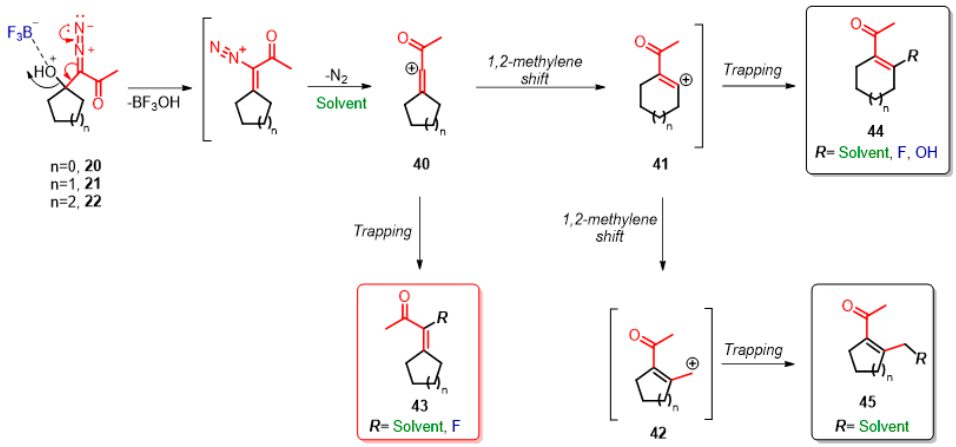
Scheme 4. $BF_3 \cdot Et_2O$-induced decomposition of 1-diazo-1-(1-hydroxycyclopentyl)propan-2-one (**21**).

Cyclohexyl derivatives. Reaction of 1-diazo-1-(1-hydroxycyclohexyl)propan-2-one (**22**) with $BF_3{\cdot}Et_2O$ in *n*-pentane resulted again in a complex crude mixture whose purification allowed the exclusive isolation of 1-(2-hydroxycyclohept-1-en-1-yl)ethanone (**35**) in 12% yield (Scheme 5). When the same reaction was performed in acetonitrile, the enamino ketone **36** was obtained in 42% yield along with minor amounts of **35** (5% isolated yield) and the isomeric products deriving from the fluoride addition, namely 1-cyclohexylidene-1-fluoroacetone (**37**) and 1-(2-fluorocyclohept-1-en-1-yl)ethanone (**38**) (Scheme 5). Finally, decomposition of **22** in benzene gave 1-(2-benzylcyclohex-1-en-1-yl)ethanone (**39**) (45% isolated yield) as the main reaction product with poor amounts of fluorinated adducts **37** and **38**, and the ketoenol **35** (Scheme 5).



Scheme 5. $BF_3{\cdot}Et_2O$-induced decomposition of 1-diazo-1-(1-hydroxycyclohexyl)propan-2-one (**22**).

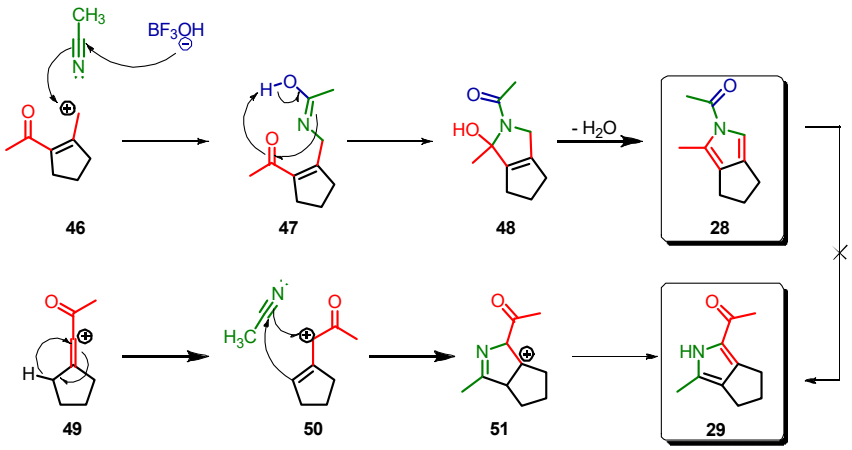
Proposed reaction mechanism. A mechanism which nicely accommodates the various products isolated in the diverse reactions is outlined in Scheme 6. The complexation of the alcohol functionality of α-diazo-β-hydroxy ketones **20**–**22** with $BF_3{\cdot}Et_2O$ occurs first, followed by the generation of the cycloalkanylidenediazonium salt, which after loss of nitrogen produces the highly reactive and destabilized vinyl cation **40**. Rearrangement of **40** via 1,2-methylene shift results in a ring expansion and in the formation of a cyclic vinyl cation **41** that, after 1,2-methylene shift and ring contraction, affords the allylic cation **42** (Scheme 6). As previously reported for α-diazo-β-hydroxy esters [28], these cations can trap solvent, fluoride or hydroxide from the $[BF_3OH]^-$ specie, generating the corresponding derivatives **43**, **44** and **45** (Scheme 6).



Scheme 6. Carbocation cascade in the $BF_3{\cdot}Et_2O$-promoted decomposition of α-diazo-β-hydroxy ketones **20**–**22**.

It is worth noting that the main differences in terms of reactivity between α-diazo-β-hydroxy esters and ketones are related to the different stabilizing/destabilizing effects of carbonyl in comparison to carboxyl group in the vinyl cation cascade [28]. In general, α-carbonyl vinyl cations result less stable and, therefore, more reactive with respect to α-carboxyl vinyl cations, thus resulting in a more complex array of products. However, in presence of more polar solvents such as acetonitrile, the stabilization of the cation intermediate and the subsequent trapping of the solvent results to be the favored process, with the exception of compound **20**, for which the presence of a highly constrained four-membered vinyl cation gives rise of the ring expansion as the exclusive rearrangement process.

A further discussion is needed to explain the formation of tetrahydrocyclopenta[*c*]pyrroles **28** and **29** by $BF_3{\cdot}Et_2O$-promoted decomposition of **21** in acetonitrile (Scheme 7). The formation of **28** is driven by acetonitrile trapping of the allyl cation intermediate **46**, followed by an intramolecular cyclization involving the carbonyl group and the adjacent nitrogen. The obtained hydroxypyrrolidine **48** undergoes dehydration and aromatization leading to tetrahydrocyclopenta[*c*]pyrrole **28** (Scheme 7). Similarly, the α-carbonyl cation intermediate **50**, generated from the 1,3-hydride shift of the linear vinyl cation **49**, undergoes a dipolar cycloaddition with acetonitrile, resulting in the formation of **51**. Deprotonation and aromatization of the cycloadduct **51** finally leads the product **29** (Scheme 7).



Scheme 7. Proposed reaction mechanism for the formation of tetrahydrocyclopenta[*c*]pyrrole derivatives **28** and **29** from the $BF_3{\cdot}Et_2O$-promoted decomposition of 1-diazo-1-(1-hydroxycyclopentyl)propan-2-one (**21**) in acetonitrile.

With the aim to support this mechanistic hypothesis and exclude the formation of **29** by 1,2-acetyl shift of **28** (Scheme 7), the decomposition reaction of **21** was carried out in CD_3CN. According to Scheme 4, three deuterated derivatives **27**-d_3, **28**-d_3 and **29**-d_3 were obtained. Next, ^{1}H-^{13}C Heteronuclear Multiple-Quantum Correlation (HMQC) experiments were carried out evidencing that singlets at 2.52 and 2.34 ppm correspond to the methyl at C-3 position and the acetyl at C-1 position, respectively. The comparison of the ^{1}H-NMR spectra of **29** and **29**-d_3 clearly confirms the structure and mechanistic hypothesis as derived from dipolar cycloaddition of CD_3CN to cation **50** (Figure 2).

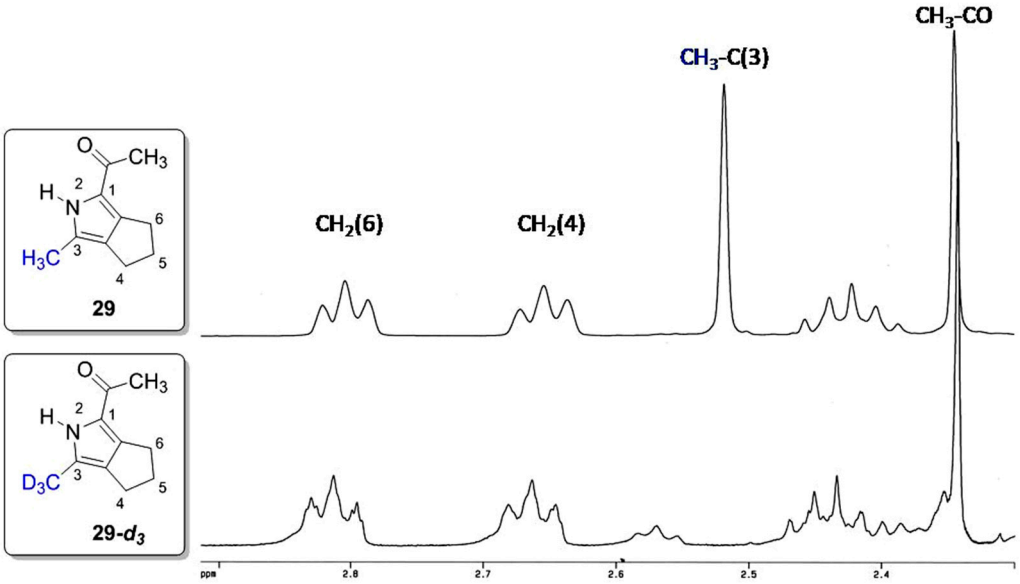


Figure 2. Comparison of the ^{1}H-NMR spectra of **29** and **29**-d_3.

3. Materials and Methods

All the chemicals were purchased from Sigma-Aldrich (Saint Louis, MO, US). All dry solvents were distilled under argon immediately prior to use. Acetonitrile was distilled from P_2O_5. Benzene and *n*-pentane were distilled from sodium. *N*,*N*-diisopropylamine and $BF_3{\cdot}Et_2O$ were distilled from CaH_2. Cyclobutanone (**17**), cyclopentanone (**18**) and cyclohexanone (**19**) were distilled in vacuo from molecular sieves (4 Å). All reactions were conducted in flame-dried glassware under a positive pressure of argon. NMR spectra were recorded on a Bruker AC 400 MHz spectrometer (Bruker, Madison, WI, USA) in the indicated solvent. Chemical shifts are reported in parts per million (ppm) using tetramethylsilane (TMS) as internal standard and are relative to $CDCl_3$ (7.26 and 77.0 ppm) or acetone-d_6 (2.05, 29.84, and 206.26 ppm). The abbreviations used are as follows: s, singlet; brs, broad singlet; d, doublet; dd, double of doublets; dt, doublet of triplets; t, triplet; q, quartet; qui, quintet; m, multiplet; and brm, broad multiplet. Coupling constants (*J*) are reported in Hertz (Hz). Flash column chromatography was performed using silica gel (40–63 μm, Merck, Darmstadt, Germany). Thin-layer chromatography (TLC) was performed on aluminum backed silica plates (silica gel 60 F254, Merck, Darmstadt, Germany). Spots were visualized by UV detector (λ = 254 nm) and/or by staining and warming with potassium permanganate. GC-MS analyses were performed using an Agilent Technologies 6890N GC system (Santa Clara, CA, USA) interfaced with a 5973N mass selective detector. An Agilent J&W capillary column (30 m length, 0.32 mm diameter, 0.25 μm film) was employed with a splitless injection (250 °C inlet, 8.8 psi), an initial 70 °C hold (2 min) and ramped for 15 min to 230 °C.

3.1. Preparation of DAA (**1**)

A 1 L single-neck round bottom flask, equipped with a magnetic stirring bar and a 25 mL pressure-equalizing dropping funnel fitted with an argon inlet, was charged a freshly prepared etheral solution of diazomethane (**15**, title: 2.3% *w*/*v*, 427 mmol, 780 mL) [33]. The flask was cooled to −10 °C and acetyl chloride (**16**, 143 mmol, 10 mL) was added dropwise over 2 h. After the addition was complete, the reaction mixture was stirred at −10 °C for additional 30 min. Then, the dropping funnel was removed and the flask was fitted with a vacuum-insulated silvered column (20 cm length, 1 cm i.d.) packed with glass helices (size 2.3 mm) and connected to a water-cooled Friedrich condenser (Figure 1). The cooling bath was removed and replaced by a heating mantel. The temperature was gently increased up to 50 °C. A first yellow fraction, containing the excess of **15**, was collected (ca. 100 mL) followed by clear Et_2O. The residue yellow liquid was transferred to a 25 mL single-neck round bottom flask and

redistilled in vacuo (49 °C, 13 mmHg) cooling at −10 °C, with both the collecting flask (pig adapter) and the two traps placed between the vacuum pump and the distillation head. Thus, DAA (**1**) (9.7 g, 115 mmol, 81% yield) was obtained in high purity.

3.2. General Procedures for the Preparation of 1-Diazo-1-(1-hydroxycycloalkyl)acetone Derivatives **20–22**

A solution of LDA was prepared by addition of *n*-BuLi (2.5 M in *n*-hexane, 1.2 mmol) to a solution of freshly distilled *N*,*N*-diisopropylamine (1.4 mmol) in freshly distilled tetrahydrofurane (THF) (3 mL) at −78 °C under nitrogen atmosphere. This cold solution was added, during 30 min, to a stirred solution of the appropriate distilled ketone **17–19** (1 mmol) and freshly prepared diazoacetone (**1**) (1 mmol) in dry THF (3 mL) at −78 °C. The mixture was stirred at −78 °C for 2 h, and then quenched with an aqueous saturated solution of NH_4Cl (30 mL) and extracted with EtOAc (3 × 20 mL). The combined organic extracts were washed with aqueous saturated solution of $NaHCO_3$ (30 mL) and brine (30 mL), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The crude residue was purified by silica gel flash chromatography (Eluent: *n*-hexane/EtOAc, from 100:0 to 90:10, *v*/*v*) affording the corresponding 1-diazo-1-(1-hydroxycycloalkyl)acetone derivatives **20–22**.

1-Diazo-1-(1-hydroxycyclobuthyl)acetone (20): Obtained in 57% yield as yellow oil. ^{1}H-NMR (400 MHz, acetone-d_6) δ: 1.67–1.71 (m, 2H), 1.75–1.95 (m, 2H), 2.19 (s, 3H), 2.37–2.43 (m, 2H), 4.60 (brs, 1H).

1-Diazo-1-(1-hydroxycyclopenthyl)acetone (21): Obtained in 90% yield as yellow oil. ^{1}H-NMR (400 MHz, acetone-d_6) δ: 1.66–1.69 (m, 2H), 1.80–1.96 (m, 6H), 2.22 (s, 3H), 4.35 (s, 1H). ^{13}C-NMR (100.6 MHz, acetone-d_6) δ: 22.9 (2x), 25.9, 38.5 (2x), 77.2, 190.8.

1-Diazo-1-(1-hydroxycyclohexyl)acetone (22) [34]**:** Obtained in 82% yield as yellow oil. ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 1.42–1.47 (m, 2H), 1.57–1.60 (m, 4H), 1.68–1.74 (m, 2H), 1.84–1.92 (m, 2H), 2.22 (s, 3H), 4.28 (brs, 1H). ^{13}C-NMR (100.6 MHz, $CDCl_3$) δ: 21.6 (2x), 25.2, 26.3, 36.1 (2x), 70.8, 193.6.

3.3. General Procedure for BF_3·Et_2O-Induced Decomposition of 1-Diazo-1-(1-hydroxycycloalkyl)acetone **20–22**

To a stirred solution of freshly distilled BF_3·Et_2O (1.66 mmol) in the selected anhydrous solvent (5 mL), a solution of **20–22** (1.11 mmol) in the same solvent (30 mL) was added at room temperature by using a syringe-pump (0.02 mmol min^{-1}). After the complete addition, the reaction mixture was stirred for an additional 30 min at room temperature and then poured into a saturated aqueous solution of $NaHCO_3$ (75 mL), extracted with EtOAc (3 × 25 mL), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The reaction crude was purified by flash chromatography.

***N*-(2-Acetylcyclopent-1-en-1-yl)acetamide (23):** Amorphous solid. ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 1.83–1.90 (m, 2H), 2.09 (s, 3H), 2.12 (s, 3H), 2.52–2.56 (m, 2H), 3.10–3.14 (m, 2H), 11.38 (brs, 1H). ^{13}C-NMR (100.6 MHz, $CDCl_3$) δ: 21.2, 24.7, 29.35, 29.36, 33.9, 115.2, 155.4, 169.1, 199.0. GC-MS: t_R = 19.627 min; *m*/*z* (%) = 167.2 ([M$^+$], 100).

1-(2-Fluorocyclopent-1-en-1-yl)ethan-1-one (24): Amorphous solid. ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 1.94–2.02 (m, 2H), 2.36 (s, 3H), 2.42–2.54 (m, 4H). ^{13}C-NMR (100.6 MHz, $CDCl_3$) δ: 27.2 (d, $J_{C\text{-}F}$ = 30.62 Hz), 27.7, 28.4 (d, $J_{C\text{-}F}$ = 8.74 Hz), 34.7 (d, $J_{C\text{-}F}$ = 1.62 Hz), 126.4 (d, $J_{C\text{-}F}$ = 12.84 Hz), 144.6 (d, $J_{C\text{-}F}$ = 118.47 Hz), 194.6 (d, $J_{C\text{-}F}$ = 36.2 Hz). ^{19}F-NMR (376 MHz, $CDCl_3$) δ: −67.1. GC-MS: t_R = 10.751 min; *m*/*z* (%) = 128.1 ([M]$^+$, 42), 113.1 (100), 85.1 (18), 65.1 (20), 59.1 (12).

2-Acetylcyclopentan-1-one (25) [35]**:** Colorless liquid. ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 2.13 (s, 3H), 2.13–2.40 (m, 6H), 2.92 (brs, 1H). ^{13}C-NMR (100.6 MHz, $CDCl_3$) δ: 20.2, 25.8, 30.2, 38.6, 62.8, 205.2, 212.8. GC-MS: t_R = 21.216 min; *m*/*z* (%) = 126.1 ([M$^+$], 100).

1-(2-Phenylcyclopent-1-en-1-yl)ethan-1-one (26) [36]**:** Colorless oil. ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 1.91 (s, 3H), 1.96 (qui, *J* = 7.70 Hz, 2H), 2.81 (tt, J_1 = 2.26 Hz, J_2 = 7.78 Hz, 2H), 2.87 (tt, J_1 = 2.23 Hz, J_2 = 7.50 Hz, 2H), 7.22–7.24 (m, 3H), 7.32–7.39 (m, 2H). ^{13}C-NMR (100.6 MHz, $CDCl_3$) δ: 21.9, 29.9, 35.1,

41.7, 127.7, 128.3, 128.6, 138.1, 139.7, 153.1, 200.2. GC-MS: t_R = 21.080 min; *m*/*z* (%) = 186.2 ([M + 1]$^+$, 50), 185.2 ([M]$^+$, 100), 171.2 (80), 143.2 (16), 128.1 (59), 115.1 (31), 91.2 (8), 77.1 (6), 63.1 (6), 50.1 (5).

***N*-(2-Acetylcyclohex-1-en-1-yl)acetamide (27)** [37]**:** Amorphous solid. ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 1.56–1.63 (m, 4H), 2.08 (s, 3H), 2.18 (s, 3H), 2.35–2.37 (m, 2H), 2.95–2.98 (m, 2H), 12.80 (brs, 1H). ^{13}C-NMR (100.6 MHz, $CDCl_3$) δ: 21.4, 22.0, 25.6, 26.3, 28.4, 28.9, 111.2, 152.8, 169.5, 202.5. GC-MS: t_R = 17.059 min; *m*/*z* (%) = 181.2 ([M]$^+$, 28), 139.2 (70), 138.2 (100), 124.1 (65), 111.1 (10), 96.2 (55), 79.1 (10), 68.1 (7), 54.1 (6).

1-(1-Methyl-5,6-dihydrocyclopenta[*c*]pyrrol-2(4*H*)-yl)ethan-1-one (28): Amorphous solid. ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 1.94 (qui, *J* = 7.42 Hz, 2H), 2.32 (s, 3H), 2.34 (s, 3H), 2.40–2.44 (m, 2H), 2.60–2.65 (m, 2H), 6.04–6.05 (m, 1H). ^{13}C-NMR (100.6 MHz, $CDCl_3$) δ: 11.4, 13.6, 23.4, 32.6, 33.4, 127.1, 132.0, 134.1, 142.9, 158.8. GC-MS: t_R = 13.889 min; *m*/*z* (%) = 164.2 ([M + 1]$^+$, 10), 163.2 ([M]$^+$, 91), 162.1 (59), 149.1 (10), 148.1 (100), 120.1 (21), 107.1 (32), 91.1 (10), 79.1 (38), 65.1 (7), 51.1 (11).

1-(3-Methyl-2,4,5,6-tetrahydrocyclopenta[*c*]pyrrol-1-yl)ethan-1-one (29) [38]**:** Amorphous solid. ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 2.34 (s, 3H), 2.42 (qui, *J* = 7.39 Hz, 2H), 2.52 (s, 3H), 2.65 (t, *J* = 7.14 Hz, 2H), 2.80 (t, *J* = 6.81 Hz, 2H), 8.42 (brs, 1H). ^{13}C-NMR (100.6 MHz, $CDCl_3$) δ: 14.7, 25.1, 27.5, 28.5, 29.6, 117.2, 127.3, 133.7, 138.2, 195.4. GC-MS: t_R = 18.953 min; *m*/*z* (%) = 164.1 ([M + 1]$^+$, 7), 163.1 ([M]$^+$, 56), 162.1 (9), 149.1 (11), 148.1 (100), 120.1 (19), 91.1 (6), 77.1 (9), 60.5 (4), 51.0 (3).

1-(2-Benzylcyclopent-1-en-1-yl)ethan-1-one (30): Amorphous solid. ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 1.73–1.82 (m, 2H), 2.27 (s, 3H), 2.37–2.41 (m, 2H), 2.69–2.73 (m, 2H), 3.90 (s, 2H), 7.18–7.21 (m, 2H), 7.25–7.29 (m, 3H). ^{13}C-NMR (100.6 MHz, $CDCl_3$) δ: 21.5, 23.6, 34.6, 36.2, 37.9, 126.1, 128.4, 128.8, 136.9, 139.0, 155.6, 198.6. GC-MS: t_R = 22.273 min; *m*/*z* (%) = 201.2 ([M + 1]$^+$, 15), 200.2 ([M]$^+$, 100), 185.1 (78), 167.1 (22), 157.1 (47), 141.1 (12), 129.1 (47), 118.1 (21), 109.1 (34), 91.1 (53), 77.1 (18), 65.1 (13), 51.1 (9).

1-(2-Phenylcyclohex-1-en-1-yl)ethan-1-one (31) [39]**:** Amorphous solid. ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 1.22–1.44 (m, 2H), 1.68–1.76 (m, 2H), 1.68 (s, 3H), 2.38–2.44 (m, 4H), 7.16–7.32 (m, 5H). ^{13}C-NMR (100.6 MHz, $CDCl_3$) δ: 22.0, 22.6, 26.4, 30.2, 32.4, 127.6, 127.8, 128.2, 137.6, 142.6, 143.4, 206.2. GC-MS: t_R = 21.135 min; *m*/*z* (%) = 200.2 ([M]$^+$, 9), 157.2 (98), 142.1 (15), 129.1 (100), 115.1 (45), 91.1 (51), 77.1 (12), 65.1 (5), 51.1 (5).

1-Cyclopentylidene-1-fluoropropan-2-one (32): Colorless oil. ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 1.67–1.76 (m, 4H), 2.26 (d, *J* = 4.80 Hz, 3H), 2.47–2.49 (m, 2H), 2.68–2.70 (m, 2H). ^{13}C-NMR (100.6 MHz, $CDCl_3$) δ: 25.5, 27.1, 27.2 (d, $J_{C\text{-}F}$ = 2.86 Hz), 30.7 (d, $J_{C\text{-}F}$ = 3.15 Hz), 31.3 (d, $J_{C\text{-}F}$ = 1.67 Hz), 140.0 (d, $J_{C\text{-}F}$ = 14.65 Hz), 149.3 (d, $J_{C\text{-}F}$ = 248.10 Hz), 193.3 (d, $J_{C\text{-}F}$ = 38.0 Hz). ^{19}F-NMR (376 MHz, $CDCl_3$) δ: −124.7. GC-MS: t_R = 12.593 min; *m*/*z* (%) = 143.1 ([M + 1]$^+$, 9), 142.1 ([M]$^+$, 100), 141.1 (19), 127.1 (37), 113.1 (43), 107.1 (83), 99.1 (20), 91.1 (6), 85.1 (4), 79.1 (53), 73.1 (5), 67.1 (9), 59.1 (11), 51.1 (17).

1-(2-Hydroxycyclohept-1-en-1-yl)ethan-1-one (35): Yellow oil. ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 1.58–1.64 (m, 6H), 2.24 (s, 3H), 2.36–2.38 (m, 2H), 2.48–2.56 (m, 2H), 15.86 (s, 1H). ^{13}C-NMR (100.6 MHz, $CDCl_3$) δ: 22.4, 24.2, 26.7, 27.2, 28.6, 38.4, 117.2, 138.4, 198.2. GC-MS: t_R = 18.953 min; *m*/*z* (%) = 163.1 ([M]$^+$, 100).

***N*-(2-Acetylcyclohept-1-en-1-yl)acetamide (36):** Amorphous solid. ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 1.49–1.54 (m, 2H), 1.60–1.65 (m, 2H), 1.72–1.76 (m, 2H), 2.08 (s, 3H), 2.23 (s, 3H), 2.46–2.49 (m, 2H), 3.05–3.07 (m, 2H), 12.46 (brs, 1H). ^{13}C-NMR (100.6 MHz, $CDCl_3$) δ: 24.2, 25.7, 26.4, 27.9, 29.2, 29.9, 31.5, 119.4, 158.1, 170.0, 201.6. GC-MS: t_R = 17.500 min; *m*/*z* (%) = 195.2 ([M + 1]$^+$, 9), 162.1 (4), 153.2 (19), 152.2 (100), 138.1 (31), 124.1 (14), 110.2 (39), 93.1 (7), 82.1 (10), 54.1 (6).

1-Cyclohexylidene-1-fluoropropan-2-one (37) [40]**:** Colorless oil. ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 1.56–1.65 (m, 6H), 2.27–2.32 (m, 5H), 2.72–2.75 (m, 2H). ^{13}C-NMR (100.6 MHz, $CDCl_3$) δ: 26.0 (d, $J_{C\text{-}F}$ = 0.29 Hz), 27.2 (d, $J_{C\text{-}F}$ = 1.82 Hz), 27.3 (d, $J_{C\text{-}F}$ = 2.82 Hz), 27.4 (d, $J_{C\text{-}F}$ = 9.60 Hz), 27.5 (d, $J_{C\text{-}F}$ = 2.72 Hz), 28.3 (d, $J_{C\text{-}F}$ = 2.4 Hz), 134.8 (d, $J_{C\text{-}F}$ = 12.44 Hz), 148.3 (d, $J_{C\text{-}F}$ = 246.64 Hz), 194.7

($J_{C\text{-}F}$ = 42.11 Hz). ^{19}F-NMR (376 MHz, $CDCl_3$) δ: −127.48. GC-MS: t_R = 9.899 min; *m*/*z* (%) = 157.1 ([M + 1]$^+$, 9), 156.1 ([M]$^+$, 100), 141.1 (23), 135.1 (5), 127.1 (35), 121.1 (27), 113.1 (81), 102.1 (23), 93.1 (34), 85.1 (12), 77.1 (20), 67.1 (19), 59.1 (11), 51.1 (13).

1-(2-Fluorocyclohept-1-en-1-yl)ethan-1-one (38): Colorless oil. ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 1.49–1.53 (m, 2H), 1.64–1.69 (m, 2H), 1.71–1.75 (m, 2H), 2.36–2.40 (m, 5H), 2.52–2.55 (m, 1H), 2.56–2.59 (m, 1H). ^{13}C-NMR (100.6 MHz, $CDCl_3$) δ: 23.98 (d, $J_{C\text{-}F}$ = 2.77 Hz), 24.03 (d, $J_{C\text{-}F}$ = 6.01 Hz), 26.1 (d, $J_{C\text{-}F}$ = 1.58 Hz), 31.1, 32.0 (d, $J_{C\text{-}F}$ = 9.60 Hz), 32.9 (d, $J_{C\text{-}F}$ = 29.42 Hz), 121.6 (d, $J_{C\text{-}F}$ = 7.11 Hz), 172.5 (d, $J_{C\text{-}F}$ = 281.68 Hz), 197.2. ^{19}F-NMR (376 MHz, $CDCl_3$) δ: −70.87. GC-MS: t_R = 15.329 min; *m*/*z* (%) = 156.1 ([M]$^+$, 46), 141.1 (100), 128.1 (4), 121.1 (7), 113.1 (22), 93.1 (20), 83.0 (10), 77.1 (15), 67.1 (7), 59.1 (6), 51.1 (7).

1-(2-Benzylcyclohex-1-en-1-yl)ethan-1-one (39) [41]**:** Amorphous solid. ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 1.55–1.59 (m, 2H), 1.62–1.68 (m, 2H), 1.99–2.02 (m, 2H), 2.28 (s, 3H), 2.29–2.33 (m, 2H), 3.55 (s, 2H), 7.19–7.23 (m, 3H), 7.26–7.30 (m, 2H). ^{13}C-NMR (100.6 MHz, $CDCl_3$) δ: 22.0, 22.1, 26.9, 29.5, 29.6, 40.0, 125.9, 128.2, 128.7, 135.0, 139.6, 140.6, 204.8. GC-MS: t_R = 23.0219 min; *m*/*z* (%) = 215.2 ([M + 1]$^+$, 15), 214.2 ([M]$^+$, 89), 199.2 (98), 181.2 (12), 171.2 (32), 157.1 (62), 141.2 (19), 129.6 (61), 115.2 (34), 105.2 (12), 91.2 (100), 77.2 (24), 65.2 (22), 51.2 (11).

4. Conclusions

We studied the mechanistic hypotheses of the $BF_3{\cdot}Et_2O$-promoted decomposition reaction of cycloalkyl α-diazo-β-hydroxy ketones in various solvents. In line with previous findings on α-diazo-β-hydroxy esters [28], vinyl cation formation, rearrangement and carbenium ion trapping accommodate both products structure and distribution deriving from the different reaction pathways. Although ab initio computational studies are needed to confirm our mechanistic hypothesis, it is likely that the driving force for vinyl cations rearrangement is basically determined by the formation of a more stable carbenium ion. Interestingly, it can be ruled out that the main difference in reactivity between α-diazo-β-hydroxy esters and ketones derived from the different electronic characteristics of the carbonyl versus the carboxyl group. Indeed, they behaved differently in the stabilization/destabilization of the cation intermediates that, in turn, drive products type and distribution. It is worth noting that a novel reaction pathway was identified, yielding tetrahydrocyclopenta[*c*]pyrroles **28** and **29**, which represent relevant structural frameworks for the synthesis of biologically active compounds [42–45].

Supplementary Materials: The following are available online at http://www.mdpi.com/2073-4344/8/12/600/s1: NMR and GC-MS spectra of compounds **20**–**39**, and semiempirical, quantum mechanical calculations for intermediates **40**–**42**.

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