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# TBAF-Triggered Aldol-Type Addition of α-Triethylsilyl-α-diazoacetone

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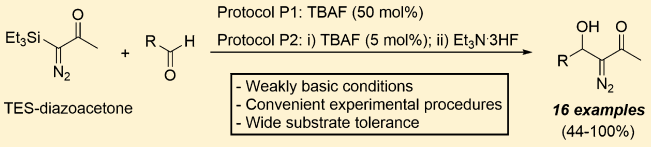
Supporting Information

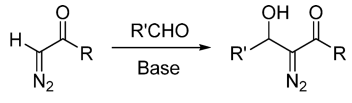
**ABSTRACT:** Aldol-type addition of α-triethylsilyl-α-diazoacetone was achieved under nucleophilic activation by tetrabutylammonium fluoride (TBAF). The use of a semi-stoichiometric amount of TBAF (protocol P1) provided the corresponding β-hydroxy-α-diazoacetone as the sole product. Alternatively, the use of a catalytic amount of TBAF led to a mixture of β-hydroxy- and β-silyloxy-α-diazoacetone products, which was cleanly desilylated with $Et_3N{\cdot}3HF$ (protocol P2). The weakly basic conditions employed tolerate a wide range of substrates and constitute a high-yielding, convenient complementary procedure to the low-temperature LDA-promoted aldol-type addition of diazoacetone.




## INTRODUCTION

α-Diazocarbonyl scaffolds play an important role in organic synthesis. The C═$N_2$ function undergoes a large array of transformations, including oxidations, reductions, cyclopropanations, and C−C, C−H, or heteroatom−H insertions.[1] This remarkable reactivity profile makes α-diazocarbonyl compounds valuable intermediates for organic synthesis, and numerous strategies have been developed to elaborate them.[2] The aldol-type addition of (diazomethyl)carbonyl moieties **A** with various aldehydes provides a convergent route to β-hydroxy-α-diazocarbonyl intermediates **B** (Scheme 1). This reaction is usually achieved under strongly basic conditions (KOH,[3] NaOH,[4] LDA,[5] $CH_3MgBr$,[6] DBU[7]). This methodology takes advantage of the good stability displayed by the diazo moiety of diazocarbonyl compounds in basic media. The diazocarbonyl anions thus generated display unique properties, with respect to their specific geometry and electronic structure. They proved to be highly reactive toward imines and aldehydes, tolerating hindered and sensitive substrates.[8]

**Scheme 1. Base-Induced Aldol-Type Addition of (Diazomethyl)carbonyl Compounds**




**A** **B**

$A_1$: R = OAlkyl
$A_2$: R = Alkyl, Aryl

α-Diazocarbonyl compounds involved in such nucleophilic additions are mainly diazoacetates ($A_1$, Scheme 1). Intrinsically less reactive α-diazoketones ($A_2$, Scheme 1) have been much less studied. Yet, high structural diversity can be expected for the β-hydroxy-α-diazoketone products, leading recently to important applications in multistep synthesis.[8c,9] We have recently reported a new methodology focused on the base-promoted chemistry of α-triethylsilyl-α-diazoacetone (TES-diazoacetone) (Scheme 2, eq 1).[10] While α-trialkylsilyl-α-diazoketones have been synthesized and used for a long time as silylketene precursors,[11] they had never been involved in aldol processes. In order to elaborate diversely substituted 5-hydroxy-1,3-diketones **E** in a convergent way, our strategy was based on the insertion of the three-carbon building-block TES-diazoacetone into a functionalized carbon chain via a base-induced double cross-aldol addition sequence (Scheme 2, eq 1). Due to the sensitivity of diazoaldols **B** (Scheme 1), particularly prone to retroaldolization, the TES group was introduced on diazoacetone to protect the most reactive *diazo-side*, allowing us to carry out the *methyl-side* aldolization first. Indeed, TES-diazoacetone underwent an unprecedented LDA-promoted methyl-side aldolization. Complete removal of the TES protecting group by methanolysis provided diazoaldol **C**. The latter was involved in a LDA-mediated diazo-side aldol-type addition, leading to diversely substituted 2-diazo-3-oxo-1,5-diols **D**. Clean 1,2-H migration induced by $Rh_2(OAc)_4$ provided the corresponding 5-hydroxy-1,3-diketones **E**, mainly

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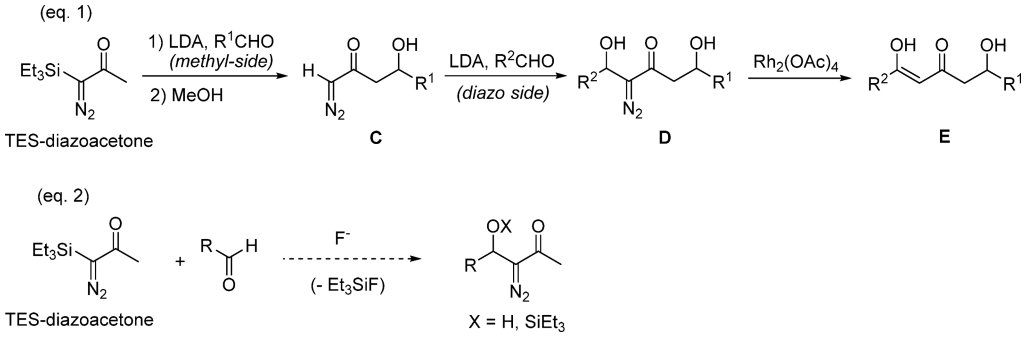
**Scheme 2. Aldol-Type Additions of TES-Diazoacetone**



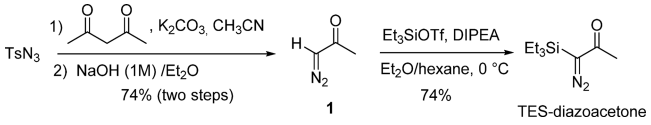

as their keto−enol tautomeric form. These results prompted us to investigate further the synthetic interest of the triethylsilyl moiety of TES-diazoacetone, particularly in the field of the fluoride-induced aldol-type additions (Scheme 2, eq 2).

The fluoride-promoted generation of a nucleophilic intermediate from an organotrimethylsilane precursor is well-known.[12] This nucleophilic activation has been successfully applied to the addition of trimethylsilyl enol ethers[13] and dienol ethers,[14] allyltrimethylsilane,[15] benzyltrimethylsilane,[16] and trimethylsilylalkynes[17] on carbonyl compounds and/or imines. Aldol-type additions induced by an ammonium fluoride display interesting features: (i) the mild generation of reactive and "soft" ammonium enolates, (ii) the rapid trapping of silicon by the aldol anion, allowing for the displacement of the equilibrium and the use of a catalytic amount of the fluoride source. The application of this methodology to α-trialkylsilyl-α-diazocarbonyl compounds is restricted to a unique paper from Kanemasa et al., reporting the TBAF-catalyzed aldol reaction between ethyl trimethylsilyldiazoacetate (TMS-DZA) and various aldehydes (40−99% yields).[18] Although synthetically promising, this approach has never been studied with α-trialkylsilyl-α-diazoketones. We report here the development of a mild and efficient TBAF-induced aldol-type addition of TES-diazoacetone.

## RESULTS AND DISCUSSION

**Fluoride-Induced Aldol-Type Addition of TES-Diazoacetone with Benzaldehyde.** TES-diazoacetone was prepared by silylation of diazoacetone **1**,[19] readily synthesized in two steps via diazo transfer from tosyl azide to acetylacetone,[20] followed by rapid alkaline hydrolysis (Scheme 3).[10] This route was conveniently carried out on a multigram scale, affording pure TES-diazoacetone in good yield.[21]

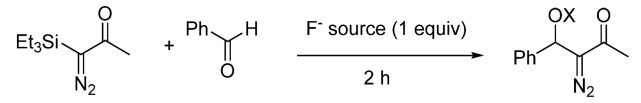
**Scheme 3. Preparation of TES-Diazoacetone**




The study of both the feasibility and optimization of the aldolization process was carried out on the TES-diazoacetone/benzaldehyde system (Table 1).[22] While the reaction did not proceed without fluoride activation (Table 1, entry 1), a stoichiometric amount of commercial TBAF (1 M/THF) in dry diethyl ether at 0 °C led to the expected diazoaldol **2a** in 79% yield after 2 h (entry 2). These conditions were initially chosen with regards to the optimal conditions developed previously for TMS-DZA.[18] The influence of the temperature and the nature of the fluoride source was next studied. Increasing the reaction temperature to rt resulted in a drastic drop of the yield (32%), due to a retroaldolization process (entry 3). To the contrary, we were delighted to observe that decreasing the temperature to −16 °C while adding 4 Å molecular sieves to the reaction mixture[23] allowed us to reach a 98% yield of diazoaldol **2a** (entry 4).[24] Other sources of fluoride were involved (entries 5−8), highlighting that TBAF was the most effective one. Indeed, anhydrous tetrabutylammonium triphenyldifluorosilicate (TBAT)[25] (entries 5 and 6) and KF·18-crown-6 ether complex[26] (entries 7 and 8) led to moderate to good yields at −16 °C and low yields at rt.

We investigated next the influence of the amount of fluoride on the course of the aldolization process (Table 2). Pleasingly, we discovered that 5 mol % of TBAF was sufficient to induce the addition in good to excellent yields (Table 2, entries 1−5). A mixture of the diazoaldol **2a** and the *O*-TES-protected diazoaldol **2b** was obtained and easily separated by column chromatography. Decreasing the temperature from rt to −16 °C while adding 4 Å molecular sieves[23] allowed for an increase in the global yield of the isolated aldols **2a** and **2b** from 75 to 96% (entries 1−3). The influence of the reaction time was next

**Table 1. Fluoride-Induced Aldol-Type Addition Using a Stoichiometric Amount of Fluoride Source**




| entry | F⁻ source | solvent | $T$ (°C) | **2a**/**2b** ratio[a] | isolated yield (%) |
|---|---|---|---|---|---|
| 1 | | $Et_2O$ or neat | rt | | 0[b] |
| 2 | TBAF[c] | $Et_2O$ | 0 | 100/0 | 79 |
| 3 | TBAF | $Et_2O$ | rt | 98/2 | 32 |
| 4 | TBAF, 4 Å MS | $Et_2O$ | −16 | 100/0 | 98 |
| 5 | TBAT | THF[d] | rt | 100/0 | 17 |
| 6 | TBAT | THF | −16 | 100/0 | 53 |
| 7 | KF·18-crown-6 ether[e] | THF[d] | rt | 100/0 | 35 |
| 8 | KF·18-crown-6 ether[e] | THF | −16 | 100/0 | 84 |

[a]From the $^1$H NMR spectrum of the crude product. [b]Reaction time: 3 days. [c]1 M/THF, commercial source. [d]For solubility reasons, THF was chosen as the solvent. [e]Under the same reaction conditions, at −16 °C and rt, CsF·18-crown-6 ether complex, prepared according to ref 26, led to irreproducible yields (32−86%).



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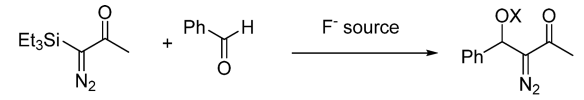
**Table 2. Influence of the amount of TBAF on the aldol-type addition of TES-diazoacetone**




TES-diazoacetone 1.1 equiv

**2a**: X = H
**2b:** X = $SiEt_3$

| entry | F⁻ source | fluoride amount (mol %) | T (°C) | time (min) | 2a/2b ratio[a] | global yield (%) of isolated 2a + isolated 2b |
|---|---|---|---|---|---|---|
| 1 | TBAF[b] | 5 | rt | 120 | 28/72 | 75 |
| 2 | TBAF | 5 | 0 | 120 | 37/63 | 85 |
| 3 | TBAF, 4 Å MS | 5 | −16 | 120 | 35/65 | 96 |
| 4 | TBAF, 4 Å MS | 5 | −16 | 60 | 27/73 | 92 |
| 5 | TBAF, 4 Å MS | 5 | −16 | 10 | 35/65 | 90 |
| | | | | | 41/59[c] | 80[c] |
| 6 | TBAF, 4 Å MS | 25 | −16 | 120 | 77/23 | 95 |
| 7 | TBAF, 4 Å MS | 50[d] | −16 | 120[e] | 100/0 | 97 |

[a]From the $^1$H NMR spectrum of the crude product. [b]1 M/THF, commercial source. [c]Without addition of molecular sieves. [d]Conditions of entry 7 constitute protocol P1. [e]A mixture of **2a** and **2b** was obtained when decreasing the reaction time (10 min: **2a**/**2b** = 82:18; 30 min: **2a**/**2b** = 94:6).

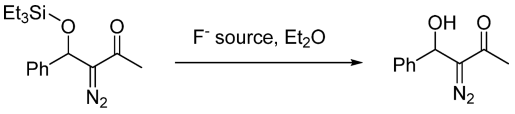
considered. The global yield of aldols (**2a** + **2b**) slightly decreased when the reaction time was shortened (60 min, entry 4; 10 min, entry 5). Under the latter experimental conditions, the absence of molecular sieves resulted in a 10% drop of the yield along with a higher amount of **2a** in the product mixture.

Expectedly, increasing the amount of TBAF (entries 6 and 7) favored the formation of the *O*-desilylated aldol **2a**. Pleasingly, we observed that a semistoichiometric amount of TBAF allowed for the exclusive formation of **2a** with an excellent 97% yield (entry 7, thereafter called protocol P1).

***O*-Desilylation of Aldol 2b.** *O*-TES-protected diazoaldols are interesting substrates for further diazo transformation.[27] It was, however, important to design a clean and high-yielding *O*-desilylation of aldol **2b**, enabling one to obtain aldol **2a** as the unique product after TBAF-catalyzed aldol-type addition. Various acidic conditions were first applied to aldol **2b** (AcOH/$CH_2Cl_2$,[28a] TFA/AcOH/$H_2O$,[28b] PPTS/MeOH/$CH_2Cl_2$[28c]). These conditions resulted in degradation and/or low conversions, preventing us from achieving a convenient *O*-desilylating acidic workup of the aldolization reaction mixture. Different sources of fluoride were thus considered (Table 3).

The TBAF-induced *O*-desilylation of aldol **2b** could not be carried out at rt (Table 3, entry 1). Extensive degradation of the substrate was observed, due to retroaldolization. When the reaction was carried out at 0 °C, aldol **2a** could be isolated in a moderate 67% yield (entry 2), while retroaldolization was still evidenced by the NMR signal of the aldehydic proton. Decreasing the temperature to −16 °C and the reaction time to 10 min led to an optimal 79% yield of aldol **2a** (entry 3). Interestingly, when the basicity of the reaction mixture was buffered by the addition of an equimolar amount of glacial acetic acid to TBAF,[29] the *O*-desilylation could be performed at rt, affording aldol **2a** in 77% yield (entry 4).

**Table 3. *O*-Desilylation of Aldol 2b**




**2b** **2a**

| entry | F⁻ source | T (°C) | time | 2a isolated yield (%) |
|---|---|---|---|---|
| 1 | TBAF[a] (1.1 equiv) | rt | 3.5 h | degradation |
| 2 | TBAF (1.1 equiv) | 0 | 30 min | 67 |
| 3 | TBAF (1.1 equiv) | −16 | 10 min | 79 |
| 4 | TBAF/AcOH 1/1 (1.1 equiv) | rt | 5 h | 77 |
| 5 | HF·pyridine (2.2 equiv) | rt | 22 h | degradation |
| 6 | $Et_3N$·3HF (1.1 equiv) | rt | 3 h | 100 |

[a]1 M/THF, commercial source.

Degradation of the substrate was observed when treated with the HF·pyridine complex at rt, certainly due to the acidity of the medium (entry 5). To the contrary, 1.1 equiv of the mild and neutral $Et_3N$·3HF complex achieved quantitative *O*-desilylation of aldol **2b** in $Et_2O$ after 3 h at rt (entry 6).[30] An attempt was then made to perform the one-pot sequence: 5 mol % of TBAF-induced aldol-type addition followed by the addition of $Et_3N$·3HF to achieve *O*-desilylation. Unfortunately, complete desilylation could not be achieved under these conditions, even with 3 equiv of $Et_3N$·3HF complex (**2a**/**2b** = 60:40). However, we were pleased to observe that *O*-desilylation was complete when conducted on the crude mixture of aldols (**2a** + **2b**), in the more appropriate solvent THF, at rt (Scheme 4). Aldol **2a** was thus isolated as the unique product in 88% global yield for the two-step sequence, thereafter called protocol P2.

**TBAF-Induced Aldol-Type Addition of TES-Diazoacetone: Scope of the Reaction.** The methodology was next extended to a range of aldehydes in order to obtain the corresponding *O*-desilylated aldols in high yields (Table 4). The one-step protocol P1, involving a semistoichiometric amount of TBAF, was thus primarily carried out. When the yields proved to be unsatisfactory, the milder two-step protocol P2, involving 5 mol % of TBAF, was conducted.

Following protocol P1, electron-poor *p*-$CF_3$-, *p*-Cl-, and *o*-Cl-benzaldehyde afforded high yields of the corresponding aldols **3a**−**5a**. For *o*-Cl-benzaldehyde, while a mixture of aldols **5a** and **5b** was formed in an 88:12 ratio after 2 h, extending the reaction time to 6 h allowed complete *O*-desilylation to be achieved. To the contrary, *m*-Cl-benzaldehyde led to disappointing results. Protocol P1 led to a **6a**/**6b** mixture, even after an extended reaction time (6 h: **6a**/**6b** = 88:12; 40 h: **6a**/**6b** = 93:7), and $Et_3N$·3HF treatment of the crude mixture resulted in degradation. This limitation is probably due to the propensity of electron-poor aromatic aldehydes to undergo oxidation in the presence of fluoride sources.[31,32] Protocol P2 proved to be appropriate for the electron-rich anisaldehyde (**7a**, 82%), furfural (**8a**, 97%), and thiophene carbaldehyde (**9a**, 83%). A significant 11−25% increase of the yield was observed when compared to that of protocol P1. Hindered and/or enolizable alkyl aldehydes (**10a**−**12a**) and octynal (**13a**) led to excellent yields (92−100%) following protocol P1. For citronellal, the milder protocol P2 was the most efficient, affording the expected aldol **14a** in 85% yield. The reactivity of α,β-unsaturated aldehydes was also studied. Protocol P2 was



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**Scheme 4. TBAF-Catalyzed Two-Step Access to Aldol 2a**

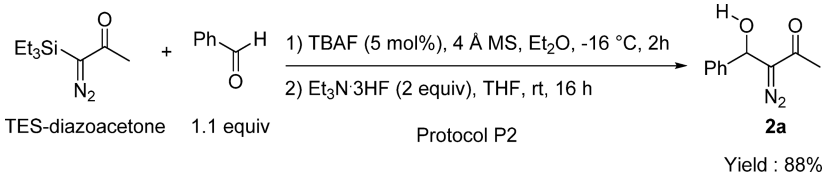
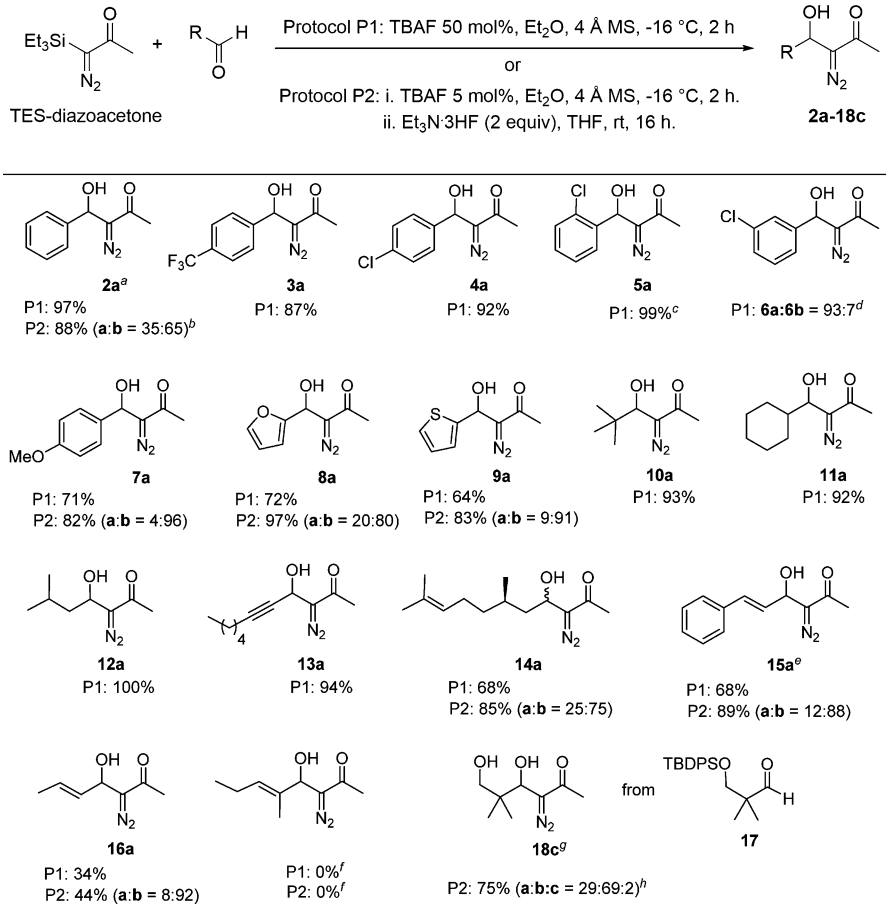



**Table 4. Extension of the TBAF-Induced Aldol-Type Addition of TES-Diazoacetone to a Range of Aldehydes**




[a]Literature yield: 79%.[27b] [b]Ratio of **a**/**b** determined before $Et_3N·3HF$ treatment from the $^1H$ NMR spectrum of the crude product. [c]Reaction time: 6 h (**5a**/**5b** = 88:12 after 2 h). [d]Reaction time: 40 h; $Et_3N·3HF$ treatment on the crude mixture (**6a** + **6b**) resulted in degradation [e]Literature yield: 92%.[5c] [f]No conversion. [g]**18c** is the diol product resulting from desilylation of the TBDPS ether. [h]Ratio of **a**/**b**/**c** determined before $Et_3N·3HF$ treatment from the $^1H$ NMR spectrum of the crude product.

more appropriate than protocol P1 for this class of compounds, but the yields proved to be highly substrate-dependent. Indeed, while a high yield of aldol **15a** was obtained with cinnamaldehyde, crotonaldehyde afforded a modest 44% yield of the corresponding aldol **16a**. It is noteworthy that no trace of Michael addition product was observed in this case. A limitation appeared with the less reactive 2-methyl-2-pentenal, for which no conversion was observed, whatever the protocol used. We finally investigated the behavior of the hindered aldehyde **17**,[33] displaying a TBDPS ether. Satisfyingly, the TBAF-catalyzed protocol P2 proved to be efficient, affording the expected aldol **18c** in 75% yield after treatment with $Et_3N·3HF$ (2 equiv), resulting from concomitant removal of the TBDPS primary alcohol protection.

**Mechanistic Aspects.** The observation that 5 mol % of TBAF was sufficient to afford the expected aldols in good yields, mainly in the *O*-silylated form **b**, strongly suggested that a fluoride-triggered autocatalytic mechanism was involved (Scheme 5). It parallels the mechanism widely accepted for the fluoride-triggered Sakurai–Hosomi reaction and the related reaction of allyltrimethylsilane with imines, thoroughly investigated by Hou et al.[15] Accordingly, we suggest that TBAF behaves as an initiator, reacting with TES-diazoacetone to generate triethylsilylfluoride and carbanion (**I**). This anionic species undergoes reversible aldol-type addition with the aldehyde, producing the ammonium alkoxy anion intermediate (**II**). The latter is nucleophilic enough to trap the triethylsilyl moiety from another TES-diazoacetone substrate. This non-reversible step affords the *O*-silylated aldol **2b** while generating a new carbanion (**I**), which in turn undergoes reversible aldol-type addition. We could notice that aldolate **II** induced the desilylation of TES-diazoacetone more rapidly than TBAF. Indeed, when the aldol-type addition with benzaldehyde was carried out according to protocol P1 (50 mol % of TBAF),



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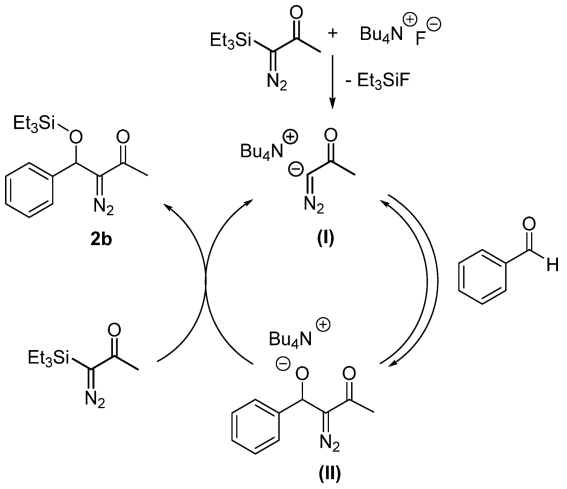
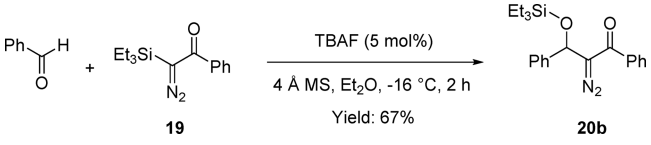
**Scheme 5. Mechanistic Rationale for the Formation of Aldol 2b**




decreasing the reaction time resulted in the isolation of a **2a**/**2b** mixture (Table 2, entry 7). Similarly, the reaction with *o*-chlorobenzaldehyde following protocol P1 required 6 h in order for the TBAF, still present in the medium, to achieve complete *O*-desilylation of aldol **5b** (Table 4). Considering the autocatalytic mechanism involved, we evaluated next if hydroxide or alkoxide ions could be used with the same efficiency as TBAF. Sodium methoxide and potassium trimethylsilanolate led to low conversion (<15%) or degradation when a stoichiometric amount was used. The use of 5 mol % of a commercial methanolic solution of tetrabutylammonium hydroxide proved to be more efficient, affording a mixture of aldols **2a** and **2b** (94:6 ratio), albeit with a modest 63% global yield. These attempts showed the superiority of the less basic and highly soluble TBAF to trigger the aldol-type addition of TES-diazoacetone.

A surprising feature of the fluoride-induced aldol-type addition described here is that a semistoichiometric amount of TBAF was sufficient to afford the sole aldols **a** (protocol P1). Additionally, a highly substrate-dependent **a**/**b** ratio was obtained with protocol P2, varying from 4:96 to 37:63, where a 5:95 ratio was expected. Having evidenced that (i) no deprotection of *O*-TES-aldol **2b** occurred during the aqueous workup[34] and (ii) intramolecular 1,5-(*O*→*O*) TES migration did not take place on aldol **2b** to provide **2a**,[35] the mechanism leading to aldol **a** remains unclear. Among the parameters influencing the **a**/**b** ratio, the ketone substituent of the TES-diazoketone substrate proved to be important. Indeed, the aldol-type addition with 5 mol % of TBAF between benzaldehyde and TES-diazoacetophenone **19**,[19b] prepared by silylation of 2-diazo-1-phenyl-ethan-1-one,[36] resulted in the isolation of the unique *O*-silylated aldol **20b** in 67% yield (Scheme 6).

**Scheme 6. TBAF-Catalyzed Aldol-Type Addition of TES-Diazoacetophenone 19**




## CONCLUSION

We described here the TBAF-induced aldol-type addition between α-triethylsilyl-α-diazoacetone and various aldehydes. A large range of β-hydroxy-α-diazoacetone scaffolds could be obtained in high yields. The nucleophilic, weakly basic conditions employed allowed us to set up convenient experimental protocols, which constitute complementary procedures to the available low-temperature LDA-promoted aldol-type addition of diazoacetone. A fluoride-triggered autocatalytic mechanism has been shown to occur, allowing for the use of a catalytic amount of TBAF, while producing the *O*-TES-protected aldols. The latter underwent clean and quantitative desilylation when treated with $Et_3N{\cdot}3HF$. This study highlights the similar reactivity profile displayed by TES-diazoacetone and TMS-enol ethers toward the fluoride ion. The major prospect of this methodology is to carry out its organocatalytic asymmetric extension using a chiral ammonium cation, in a context where no enantioselective aldol-type addition of either diazoketones or trialkylsilyldiazoketones is available so far.

## EXPERIMENTAL SECTION

**Caution:** Although we never had any trouble in handling the diazo compounds described in this study, diazo compounds are potentially explosive and should be handled with care in a well-ventilated fumehood.

**General Information.** All reactions were performed under an argon atmosphere. $Et_2O$ and THF were dried through activated alumina columns. DIPEA and $CH_3CN$ were distilled over $CaH_2$. Commercial aldehydes were distilled or recrystallized before use. TBAF (1 M/THF, 50 mL) was used as received. Molecular sieves 4 Å, powder, were activated by heating under vacuum. Reactions at −16 °C were performed using an ice/NaCl bath or using a bath cooled by cryogenic flow. Melting points are uncorrected. Column chromatography was performed using 60 μm silica gel. Thin-layer chromatography was performed with silica gel $60F_{254}$ precoated TLC sheets, and products were detected by UV light or vanillin ethanolic solution. $^1H$ NMR (200 or 400 MHz) and $^{13}C$ NMR (100 MHz) spectra were recorded in $CDCl_3$. Chemical shifts were reported as parts per million (ppm) relative to $Me_4Si$, and coupling constants were expressed in hertz (Hz). The splitting patterns were designated as follows: s, singlet; br s, broad singlet; d, doublet; t, triplet; q, quartet; m, multiplet. Proton and carbon assignments were established using COSY, HSQC, and DEPT-Q experiments. IR spectra were recorded on a FTIR spectrometer equipped with an ATR unit. The wavenumbers of representative absorption peaks were given in $cm^{-1}$. High-resolution mass spectra were recorded on an ESI-QTOF apparatus.

**1. Preparation of α-Triethylsilyl-α-diazoacetone.** *Diazoacetone (1).*[10] To a solution of 3-diazopentane-2,4-dione[20] (2.47 g, 19.6 mmol, 1.0 equiv) in diethyl ether (122 mL) was added an aqueous NaOH solution (1 M, 94 mL), and the reaction mixture was stirred at rt for 3.5 h. $H_2O$ (50 mL) was added, and the aqueous phase was extracted with dichloromethane (4 × 80 mL). The combined organic layer was dried over $Na_2SO_4$ and filtered, and the filtrate was concentrated under reduced pressure ($T$ = 20 °C, $P \geq 250$ mbar) to afford diazoacetone as a volatile yellow liquid (1.55 g, 94% yield): IR (film) $\nu_{max}$ ($cm^{-1}$) 3089, 2095 ($\nu_{C=N2}$), 1640 ($\nu_{C=O}$), 1330, 1180, 970, 630; $^1H$ NMR (200 MHz, $CDCl_3$) $\delta$ (ppm) 2.10 (s, 3H), 5.28 (br s, 1H).

*1-Diazo-1-(triethylsilyl)propan-2-one (TES-Diazoacetone).*[19a] To a stirred solution of diazoacetone (**1**) (1 g, 11.9 mmol) in a 1:1 mixture of anhydrous $Et_2O$/hexane (90 mL) at 0 °C were added DIPEA (2.7 mL, 15.5 mmol, 1.3 equiv) and TESOTf (2.8 mL, 13.1 mmol, 1.1 equiv). After being stirred for 90 min at 0 °C under an argon atmosphere, the reaction mixture was quenched by the addition of a saturated aqueous $NaHCO_3$ solution (100 mL). The organic layer



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was washed with saturated aqueous $NH_4Cl$ (2 × 50 mL) and brine (100 mL), dried over $Na_2SO_4$, and filtered, and the filtrate was concentrated under reduced pressure. The oily residue was chromatographed (silica gel, cyclohexane/ethyl acetate = 99:1) to afford TES-diazoacetone as a yellow oil (1.74 g, 74% yield): $R_f$ = 0.65 (petroleum ether/ethyl acetate =80/20); IR (film) $\nu_{max}$ ($cm^{-1}$) 2954, 2876, 2060 ($\nu_{C=N2}$), 1637 ($\nu_{C=O}$), 1463, 1414, 1358, 1267, 1240, 1199, 1005, 964, 721; $^1H$ NMR (200 MHz, $CDCl_3$) $\delta$ (ppm) 2.26 (s, 3H), 0.98 (t, 9H, $J$ = 7.7 Hz), 0.77 (q, 6H, $J$ = 7.7 Hz).

**2. General Procedures for the Fluoride-Induced Aldol-Type Addition of TES-Diazoacetone.** *Protocol P1.* To a stirred solution of TES-diazoacetone (0.5 mmol, 1 equiv), aldehyde (0.55 mmol, 1.1 equiv), and 4 Å molecular sieves (250 mg, 500 mg/mmol) in anhydrous $Et_2O$ (4 mL) at −16 °C was slowly added TBAF (1 M/THF, 0.25 mmol, 50 mol %). After being stirred for 120 min at −16 °C under Ar, the reaction mixture was quenched by the addition of a saturated aqueous $NH_4Cl$ solution (8 mL). The aqueous layer was extracted with diethyl ether (3 × 10 mL), and the combined organic layer was dried over $Na_2SO_4$ and filtered, and the filtrate was concentrated under reduced pressure. The oily residue was purified by column chromatography (silica gel, cyclohexane/ethyl acetate = 95:5 to 60:40) to afford the expected *O*-desilylated aldol.

*Protocol P2.* To a stirred solution of TES-diazoacetone (0.5 mmol, 1 equiv), aldehyde (0.55 mmol, 1.1 equiv), and 4 Å molecular sieves (250 mg, 500 mg/mmol) in anhydrous $Et_2O$ (4 mL) at −16 °C was slowly added TBAF (1 M/THF, 0.025 mmol, 5 mol %). After being stirred for 120 min at −16 °C under Ar, the reaction mixture was quenched by the addition of a saturated aqueous $NH_4Cl$ solution (8 mL). The aqueous layer was extracted with diethyl ether (3 × 10 mL), and the combined organic layer was dried over $Na_2SO_4$ and filtered, and the filtrate was concentrated under reduced pressure. The oily residue was dissolved in anhydrous THF (5 mL/mmol), and triethylamine trihydrofluoride complex (0.16 mL, 1.0 mmol, 2 equiv) was added dropwise. After being stirred for 16 h at room temperature under Ar, the reaction mixture was quenched with saturated aqueous $NaHCO_3$ (8 mL). The aqueous layer was extracted with diethyl ether (3 × 10 mL), and the combined organic layer was dried over $Na_2SO_4$ and filtered, and the filtrate was concentrated under reduced pressure. The oily residue was purified by column chromatography (silica gel, cyclohexane/ethyl acetate = 95:5 to 60:40) to afford the expected *O*-desilylated aldol.

*TBAT Protocol.* To a stirred solution of TES-diazoacetone (0.25 mmol, 1 equiv) and aldehyde (0.27 mmol, 1.1 equiv) in anhydrous THF (2 mL) at −16 °C under argon was slowly added TBAT (0.25 mmol, 1 equiv). After being stirred for 120 min at −16 °C under Ar, the reaction mixture was quenched by the addition of saturated aqueous $NH_4Cl$ (4 mL). The aqueous layer was extracted with diethyl ether (3 × 5 mL), and the combined organic layer was dried over $Na_2SO_4$ and filtered, and the filtrate was concentrated under reduced pressure. The oily residue was purified by column chromatography (silica gel, cyclohexane/ethyl acetate = 95:5 to 60:40) to afford *O*-desilylated aldol **2a** (25.2 mg, 53% yield).

*KF·18-Crown-6 Ether Protocol.* To a stirred solution of TES-diazoacetone (0.5 mmol, 1 equiv) and aldehyde (0.55 mmol, 1.1 equiv) in anhydrous THF (4 mL) at −16 °C under argon was slowly added KF·18-crown-6 ether complex, prepared according to ref 26 (0.5 mmol, 1 equiv). After being stirred for 120 min at −16 °C under Ar, the reaction mixture was quenched by the addition of saturated aqueous $NH_4Cl$ (8 mL). The aqueous layer was extracted with diethyl ether (3 × 10 mL), and the combined organic layer was dried over $Na_2SO_4$ and filtered, and the filtrate was concentrated under reduced pressure. The oily residue was purified by column chromatography (silica gel, cyclohexane/ethyl acetate = 95:5 to 60:40) to afford *O*-desilylated aldol **2a** (80 mg, 84% yield).

*3-Diazo-4-hydroxy-4-phenyl-butan-2-one (**2a**).*[27b] Prepared from TES-diazoacetone and benzaldehyde according to the general protocol P1. The *O*-desilylated aldol **2a** was obtained after column chromatography (cyclohexane/ethyl acetate = 95:5 to 60:40) as a yellow solid (92 mg, 97% yield): m p = 69−72 °C; $R_f$ = 0.14 (petroleum ether/ethyl acetate = 80/20); IR (film) $\nu_{max}$ ($cm^{-1}$) 3312 ($\nu_{OH}$), 2922, 2086 ($\nu_{C=N2}$), 1618 ($\nu_{C=O}$), 1340, 1022, 733; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ (ppm) 7.32−7.40 (m, 5H), 6.02 (br s, 1H), 3.72 (br s, 1H), 2.28 (s, 3H); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ (ppm) 191.2, 138.5, 128.8, 128.5, 125.7, 74.0, 68.2, and 25.8; HRMS $m/z$ calcd for $C_{10}H_{10}N_2NaO_2$ $[M + Na]^+$ 213,0634, found 213,0636.

*3-Diazo-4-phenyl-4-(triethylsilyloxy)-butan-2-one (**2b**).* A solution of TES-diazoacetone, benzaldehyde (0.55 mmol, 1.1 equiv), and 4 Å molecular sieves (250 mg, 500 mg/mmol) in anhydrous $Et_2O$ (4 mL) was cooled at −16 °C under Ar. TBAF (1 M/THF, 0.025 mmol, 5 mol %) was added slowly. After being stirred for 120 min −16 °C, the reaction mixture was quenched by the addition of saturated aqueous $NH_4Cl$ (8 mL). The aqueous layer was extracted with diethyl ether (3 × 10 mL), and the combined organic layer was dried over $Na_2SO_4$ and filtered, and the filtrate was concentrated under reduced pressure. The crude mixture of aldols **2** (**2a**/**2b** = 35:65) was purified by column chromatography (cyclohexane/ethyl acetate = 95:5), affording aldol **2b** (91 mg, 60% yield) as a yellow oil and aldol **2a** (34 mg, 36% yield) as a yellow solid. Aldol **2b**: $R_f$ = 0.82 (petroleum ether/ethyl acetate = 80:20); IR (film) $\nu_{max}$ ($cm^{-1}$) 2956, 2079 ($\nu_{C=N2}$), 1644 ($\nu_{C=O}$), 1338, 1090, 734; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ (ppm) 7.26−7.39 (m, 5H), 5.98 (br s, 1H), 2.21 (s, 3H), 0.92 (t, 9H, $J$ = 8.0 Hz), 0.63 (q, 6H, $J$ = 8.0 Hz); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ (ppm) 188.5, 141.6, 128.5, 127.8, 125.2, 75.4, 67.0, 25.8, 6.7, and 4.6; HRMS $m/z$ calcd for $C_{16}H_{24}N_2NaO_2Si$ $[M + Na]^+$ 327.1499, found 327.1498.

*3-Diazo-4-hydroxy-4-(4-trifluoromethyl)phenyl)-butan-2-one (**3a**).* Prepared from TES-diazoacetone and 4-(trifluoromethyl)-benzaldehyde according to general protocol P1. Aldol **3a** was obtained after column chromatography (cyclohexane/ethyl acetate = 95:5 to 60:40) as a yellow solid (112 mg, 87% yield): m p = 79 °C; $R_f$ = 0.08 (petroleum ether/ethyl acetate = 80:20); IR (film) $\nu_{max}$ ($cm^{-1}$) 3371 ($\nu_{OH}$), 2082 ($\nu_{C=N2}$), 1614 ($\nu_{C=O}$), 1320, 1110, 1015, 830, 787; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ (ppm) 7.64 (d, 2H, $J$ = 8.2 Hz), 7.54 (d, 2H, $J$ = 8.2 Hz), 6.07 (br s, 1H), 2.28 (s, 3H); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ (ppm) 190.9, 143.2, 130.5 (q, $^2J_{CF}$ = 32.4 Hz), 126.1, 125.7 (q, $^3J_{CF}$ = 3.5 Hz), 123.9 (q, $^1J_{CF}$ = 272.4 Hz), 74.3, 67.0, and 25.7; HRMS $m/z$ calcd for $C_{11}H_9F_3N_2NaO_2$ $[M + Na]^+$ 281.0508, found 281.0513.

*4-(4-Chlorophenyl)-3-diazo-4-hydroxybutan-2-one (**4a**).* Prepared from TES-diazoacetone and 4-chlorobenzaldehyde according to general protocol P1. Aldol **4a** was obtained after column chromatography (cyclohexane/ethyl acetate = 95:5 to 60:40) as a yellow solid (103 mg, 92% yield): m p = 60−62 °C; $R_f$ = 0.14 (petroleum ether/ethyl acetate = 80/20); IR (film) $\nu_{max}$ ($cm^{-1}$) 3379 ($\nu_{OH}$), 2085 ($\nu_{C=N2}$), 1635 ($\nu_{C=O}$), 1265; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ (ppm) 7.36 (s, 4H), 5.99 (br s, 1H), 3.68 (br s, 1H, OH), 2.27 (s, 3H); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ (ppm) 191.0, 137.4, 134.2, 129.0, 127.2, 73.8, 67.4, and 25.8; HRMS $m/z$ calcd for $C_{10}H_9ClN_2NaO_2$ $[M + Na]^+$ 247.0245, found 247.0237.

*4-(2-Chlorophenyl)-3-diazo-4-hydroxybutan-2-one (**5a**).* Prepared from TES-diazoacetone and *o*-chlorobenzaldehyde according to general protocol P1. Aldol **5a** was obtained after column chromatography (cyclohexane/ethyl acetate = 95:5 to 60:40) as a yellow solid (111 mg, 99% yield): m p = 89 °C; $R_f$ = 0.23 (petroleum ether/ethyl acetate = 80:20); IR (film) $\nu_{max}$ ($cm^{-1}$) 3369 ($\nu_{OH}$), 2082 ($\nu_{C=N2}$), 1615 ($\nu_{C=O}$), 1025, 735, 703; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ (ppm) 7.71 (dd, 1H, $J$ = 7.6, 2.0 Hz), 7.33−7.39 (m, 2H), 7.28 (dd, 1H, $J$ = 7.6, 1.8 Hz), 6.20 (br s, 1H), 2.28 (s, 3H); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ (ppm) 191.3, 136.3, 131.6, 129.6, 129.4, 127.5, 127.2, 72.9, 65.8, and 25.7; HRMS $m/z$ calcd for $C_{10}H_9ClN_2NaO_2$ $[M + Na]^+$ 247.0245, found 247.0236.

*3-Diazo-4-hydroxy-4-(4-methoxyphenyl)-butan-2-one (**7a**).* Prepared from TES-diazoacetone and 4-methoxybenzaldehyde according to general protocol P2. Aldol **7a** was obtained after column chromatography (cyclohexane/ethyl acetate = 95:5 to 60:40) as a yellow solid (90 mg, 82% yield): m p = 97−100 °C; $R_f$ = 0.07 (petroleum ether/ethyl acetate = 80:20); IR (film) $\nu_{max}$ ($cm^{-1}$) 3414 ($\nu_{OH}$), 2086 ($\nu_{C=N2}$), 1613 ($\nu_{C=O}$), 1370; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ (ppm) 7.33 (d, 2H, $J$ = 8.6 Hz), 6.91 (d, 2H, $J$ = 8.6 Hz), 5.96 (br s, 1H), 3.81 (s, 3H), 2.27 (s, 3H); $^{13}C$ NMR (100 MHz,



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$CDCl_3$) $\delta$ (ppm) 191.3, 159.6, 130.7, 127.1, 114.1, 74.0, 67.8, 55.3, and 25.8; HRMS $m/z$ calcd for $C_{11}H_{12}N_2NaO_3$ $[M + Na]^+$ 243.0740, found 243.0739.

*3-Diazo-4-(furan-2-yl)-4-hydroxybutan-2-one (**8a**).* Prepared from TES-diazoacetone and furfural according to general protocol P2. Aldol **8a** was obtained after column chromatography (cyclohexane/ethyl acetate = 95:5 to 60:40) as a yellow oil (87 mg, 97% yield): $R_f$ = 0.15 (petroleum ether/ethyl acetate = 80:20); IR (film) $\nu_{max}$ ($cm^{-1}$) 3347 ($\nu_{OH}$), 2085 ($\nu_{C=N2}$), 1614 ($\nu_{C=O}$), 1336, 1005, 737; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ (ppm) 7.40 (d, 1H, $J$ = 1.2 Hz), 6.36−6.40 (m, 2H), 5.93 (br s, 1H), 2.28 (s, 3H); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ (ppm) 190.6, 151.8, 142.8, 110.4, 107.6, 72.5, 62.5, and 25.6; HRMS $m/z$ calcd for $C_8H_8N_2NaO_3$ $[M + Na]^+$ 203.0427, found 203.0421.

*3-Diazo-4-hydroxy-4-(thiophen-2-yl)-butan-2-one (**9a**).* Prepared from TES-diazoacetone and 2-thiophenecarboxaldehyde according to general protocol P2. Aldol **9a** was obtained after column chromatography (cyclohexane/ethyl acetate = 95:5 to 60:40) as an orange oil (81 mg, 83% yield): $R_f$ = 0.13 (petroleum ether/ethyl acetate = 80:20); IR (film) $\nu_{max}$ ($cm^{-1}$) 3343 ($\nu_{OH}$), 2081 ($\nu_{C=N2}$), 1607 ($\nu_{C=O}$), 1335, 1285, 1014, 945, 853, 780; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ (ppm) 7.29 (dd, 1H, $J$ = 5.0, 1.2 Hz), 7.00−7.05 (m, 2H), 6.21 (br s, 1H), 3.69 (br s, 1H, OH), 2.28 (s, 3H); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ (ppm) 190.7, 142.8, 127.1, 125.4, 124.4, 74.4, 64.9, and 25.8; HRMS $m/z$ calcd for $C_8H_8N_2NaO_2S$ $[M + Na]^+$ 219.0199, found 219.0201.

*3-Diazo-4-hydroxy-5,5-dimethylhexan-2-one (**10a**).* Prepared from TES-diazoacetone and pivalaldehyde according to general protocol P1. Aldol **10a** was obtained after column chromatography (cyclohexane/ethyl acetate = 95:5 to 60:40) as a yellow solid (79 mg, 93% yield): m p = 86.5 °C; $R_f$ = 0.21 (petroleum ether/ethyl acetate = 80:20); IR (film) $\nu_{max}$ ($cm^{-1}$) 3406 ($\nu_{OH}$), 2086 ($\nu_{C=N2}$), 1627 ($\nu_{C=O}$), 1266, 739; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ (ppm) 4.36 (br s, 1H), 3.04 (br s, 1H, OH), 2.26 (s, 3H), 0.97 (s, 9H); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ (ppm) 191.3, 73.4, 69.8, 38.4, 25.7, and 25.6; HRMS $m/z$ calcd for $C_8H_{14}N_2NaO_2$ $[M + Na]^+$ 193.0947, found 193.0947.

*4-Cyclohexyl-3-diazo-4-hydroxybutan-2-one (**11a**).* Prepared from TES-diazoacetone and cyclohexanecarboxaldehyde according to general protocol P1. Aldol **11a** was obtained after column chromatography (cyclohexane/ethyl acetate = 95:5 to 60:40) as a yellow solid (90 mg, 92% yield): m p = 38 °C; $R_f$ = 0.24 (petroleum ether/ethyl acetate = 80:20); IR (film) $\nu_{max}$ ($cm^{-1}$) 3397 ($\nu_{OH}$), 2927, 2082 ($\nu_{C=N2}$), 1620 ($\nu_{C=O}$), 1371; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ (ppm) 4.40 (d, 1H, $J$ = 6.1 Hz), 2.79 (br s, 1H, OH), 2.25 (s, 3H), 2.01 (d, 1H, $J$ = 12.6 Hz), 1.52−1.80 (m, 5H), 1.00−1.29 (m, 5H); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ (ppm) 191.5, 71.0, 70.8, 42.0, 29.3, 29.1, 26.4, 26.0, 25.9, and 25.8; HRMS $m/z$ calcd for $C_{10}H_{16}N_2NaO_2$ $[M + Na]^+$ 219.1104, found 219.1110.

*3-Diazo-4-hydroxy-6-methylheptan-2-one (**12a**).* Prepared from TES-diazoacetone and isovaleraldehyde according to general protocol P1. Aldol **12a** was obtained after column chromatography (cyclohexane/ethyl acetate = 95:5 to 60:40) as a yellow oil (85 mg, 100% yield): $R_f$ = 0.14 (petroleum ether/ethyl acetate = 80:20); IR (film) $\nu_{max}$ ($cm^{-1}$) 3417 ($\nu_{OH}$), 3054, 2082 ($\nu_{C=N2}$), 1633 ($\nu_{C=O}$), 1265, 739; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ (ppm) 4.88 (dd, 1H, $J$ = 8.2, 5.7 Hz), 2.88 (br s, 1H, OH), 2.26 (s, 3H), 1.80 (m, 1H), 1.63−1.68 (m, 1H), 1.34−1.43 (m, 1H), 0.95 (d, 6H, $J$ = 6.6 Hz); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ (ppm) 191.6, 72.1, 64.2, 42.3, 25.8, 24.6, 23.0, and 22.0; HRMS $m/z$ calcd for $C_8H_{14}N_2NaO_2$ $[M + Na]^+$ 193.0947, found 193.0935.

*3-Diazo-4-hydroxyundec-5-yn-2-one (**13a**).* Prepared from TES-diazoacetone and 2-octynal according to general protocol P1. Aldol **13a** was obtained after column chromatography (cyclohexane/ethyl acetate = 95:5 to 60:40) as an orange oil (98 mg, 94% yield): $R_f$ = 0.23 (petroleum ether/ethyl acetate = 80:20); IR (film) $\nu_{max}$ ($cm^{-1}$) 3368 ($\nu_{OH}$), 2090 ($\nu_{C=N2}$), 1636 ($\nu_{C=O}$), 1339, 733; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ (ppm) 5.64 (br s, 1H), 3.77 (br s, 1H, OH), 2.27 (s, 3H), 2.22−2.25 (m, 2H), 1.48−1.55 (m, 2H), 1.27−1.40 (m, 4H), 0.90 (t, 3H, $J$ = 7.1 Hz); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ (ppm) 190.2, 88.9, 75.0, 73.4, 58.0, 31.0, 28.1, 25.7, 22.1, 18.5, and 13.9; HRMS $m/z$ calcd for $C_{11}H_{16}N_2NaO_2$ $[M + Na]^+$ 231.1104, found 231.1106.

*3-Diazo-4-hydroxy-6,10-dimethylundec-9-en-2-one (**14a**).* Prepared from TES-diazoacetone and citronellal according to general protocol P1. After column chromatography (cyclohexane/ethyl acetate = 95:5 to 60:40), aldol **14a** was obtained as a mixture of diastereoisomers, $\mathbf{14a}_{d1}$ and $\mathbf{14a}_{d2}$, as a yellow oil (101 mg, 85% yield): $R_f$ = 0.08 (petroleum ether/ethyl acetate = 80:20); IR (film) $\nu_{max}$ ($cm^{-1}$) 3398 ($\nu_{OH}$), 2962, 2915, 2082 ($\nu_{C=N2}$), 1614 ($\nu_{C=O}$), 1371, 1292, 617; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ (ppm) 5.10−5.06 (m, $1H_{d1+d2}$), 4.93−4.87 (m, $1H_{d1+d2}$), 2.88 (br s, 1H, $OH_{d1+d2}$), 2.26 (s, $3H_{d1}$), 2.25 (s, $3H_{d2}$), 2.08−1.91 (m, $2H_{d1+d2}$), 1.68 (s, $3H_{d1+d2}$), 1.77−1.68 (m, $1H_{d1+d2}$), 1.60 (s, $3H_{d1+d2}$), 1.58−1.52 (m, $1H_{d1+d2}$), 1.45−1.15 (m, $3H_{d1+d2}$), 0.95 (d, $3H_{d1}$, $J$ = 6.3 Hz), 0.94 (d, $3H_{d2}$, $J$ = 6.3 Hz); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ (ppm) 191.6, 191.4, 131.5, 131.4, 124.5, 124.4, 72.5, 72.1, 64.2, 63.7, 40.8, 40.7, 37.4, 36.7, 29.2, 28.8, 25.8, 25.7, 25.4, 25.3, 19.9, 18.9, 17.7, and 17.6; HRMS $m/z$ calcd for $C_{13}H_{22}N_2NaO_2$ $[M + Na]^+$ 261.1573, found 261.1572.

*3-Diazo-(E)-4-hydroxy-6-phenylhex-5-en-2-one (**15a**).*[5c] Prepared from TES-diazoacetone and (*E*)-cinnamaldehyde according to general protocol P2. Aldol **15a** was obtained after column chromatography (cyclohexane/ethyl acetate = 95:5 to 60:40) as an orange solid (96 mg, 89% yield): m p = 74 °C; $R_f$ = 0.15 (petroleum ether/ethyl acetate = 80/20); IR (film) $\nu_{max}$ ($cm^{-1}$) 3377 ($\nu_{OH}$), 2087 ($\nu_{C=N2}$), 1631 ($\nu_{C=O}$), 1369; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ (ppm) 7.24−7.40 (m, 5H), 6.80 (dd, 1H, $J$ = 16.0, 1.2 Hz), 6.23 (dd, 1H, $J$ = 16.0, 5.5 Hz), 5.54 (d, 1H, $J$ = 5.5 Hz), 2.28 (s, 3H); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ (ppm) 191.0, 135.9, 132.5, 128.7, 128.3, 126.7, 125.4, 72.2, 66.5, and 25.8; HRMS $m/z$ calcd for $C_{12}H_{12}N_2NaO_2$ $[M + Na]^+$ 239.0791, found 239.0781.

*3-Diazo-(E)-4-hydroxyhept-5-en-2-one (**16a**).* Prepared from TES-diazoacetone and (*E*)-crotonaldehyde according to general protocol P2. Aldol **16a** was obtained after column chromatography (cyclohexane/ethyl acetate = 95:5 to 60:40) as an orange oil (34 mg, 44% yield): $R_f$ = 0.11 (petroleum ether/ethyl acetate = 80:20); IR (film) $\nu_{max}$ ($cm^{-1}$) 3406 ($\nu_{OH}$), 2090 ($\nu_{C=N2}$), 1621 ($\nu_{C=O}$), 1371; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ (ppm) 5.91 (m, 1H), 5.53 (dd, 1H, $J$ = 15.5, 5.2 Hz), 5.30 (d, 1H, $J$ = 5.2 Hz), 3.12 (br s, 1H, OH), 2.26 (s, 3H), 1.75 (d, 3H, $J$ = 6.6 Hz); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ (ppm) 191.3, 129.8, 127.2, 72.0, 66.6, 25.7, and 17.7; HRMS $m/z$ calcd for $C_7H_{10}N_2NaO_2$ $[M + Na]^+$ 177.0634, found 177.0635.

*3-Diazo-4,6-dihydroxy-5,5-dimethylhexan-2-one (**18c**).* Prepared from TES-diazoacetone and 3-(*tert*-butyldiphenylsilyloxy)-2,2-dimethylpropanal according to general protocol P2. Aldol **18c** was obtained after column chromatography (cyclohexane/ethyl acetate = 95:5 to 50:50) as a yellow oil (70 mg, 75% yield): $R_f$ = 0.04 (petroleum ether/ethyl acetate = 80:20); IR (film) $\nu_{max}$ ($cm^{-1}$) 3362 ($\nu_{OH}$), 2963, 2876, 2085 ($\nu_{C=N2}$), 1607 ($\nu_{C=O}$), 1367, 1077, 1037, 730, 624; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ (ppm) 4.67 (br s, 1H), 3.48 (d, 1H, $J$ = 11.4 Hz), 3.39 (d, 1H, $J$ = 11.4 Hz), 2.29 (s, 3H), 1.06 (s, 3H), 0.86 (s, 3H); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ (ppm) 191.7, 72.1, 71.0, 70.0, 41.8, 25.6, 20.2, and 20.1; HRMS $m/z$ calcd for $C_8H_{15}N_2O_3$ $[M + H]^+$ 187.1083, found 187.1075.

*2-Diazo-1,3-diphenyl-3-(triethylsilyloxy)propan-1-one (**20b**).* A solution of TES-diazoacetophenone **19**, benzaldehyde (0.47 mmol, 1.1 equiv), and 4 Å molecular sieves (215 mg, 500 mg/mmol) in anhydrous $Et_2O$ (4 mL) was cooled at −16 °C under Ar. TBAF (1 M/THF, 0.021 mmol, 5 mol %) was added slowly. After being stirred for 120 min at −16 °C, the reaction mixture was quenched by the addition of saturated aqueous $NH_4Cl$ (8 mL). The aqueous layer was extracted with diethyl ether (3 × 10 mL), and the combined organic layer was dried over $Na_2SO_4$ and filtered, and the filtrate was concentrated under reduced pressure. Aldol **20b** was obtained after column chromatography (cyclohexane/ethyl acetate = 95:5) as an orange oil (105 mg, 67% yield): $R_f$ = 0.73 (petroleum ether/ethyl acetate = 80:20); IR (film) $\nu_{max}$ ($cm^{-1}$) 2953, 2875, 2079 ($\nu_{C=N2}$), 1621 ($\nu_{C=O}$), 1342, 1237, 1060, 1002, 840, 729; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ (ppm) 7.58−7.30 (m, 10H), 6.21 (s, 1H), 0.95 (m, 9H), 0.68 (m, 6H); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ (ppm) 186.8, 141.5, 131.6, 128.7, 128.5,


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128.5, 128.2, 127.9, 127.6, 127.1, 125.4, 74.9, 67.9, 6.7, and 4.6; HRMS $m/z$ calcd for $C_{21}H_{26}N_2NaO_2Si$ $[M + Na]^+$ 389.1656, found 389.1652.

## ■ ASSOCIATED CONTENT

### Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b01554.

$^1H$ and $^{13}C$ NMR spectra for all aldols (PDF)

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### Notes

The authors declare no competing financial interest.

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(21) TES-diazoacetone should not be contaminated with silylated residues in order to get optimal and reproducible yields in the following fluoride-induced aldol-type addition study.

(22) TMS-diazoacetone is known to be highly sensitive to protodesilylation and could not be isolated or handled; see ref 19c.

(23) Addition of activated powdered 4 Å molecular sieves to the reaction medium (250 mg/0.5 mmol of substrate) allowed reproducible yields of product to be obtained, whatever the quality of the commercial TBAF solution employed.

(24) The temperature of −16 °C was chosen as it is conveniently reached with an ice/NaCl bath.

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