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Synthetic Route to Phenyl Diazenes and Pyridazinium Salts from Phenylazosulfonates

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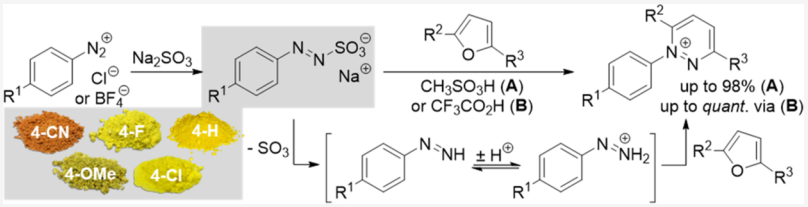

ABSTRACT: The synthesis of pyridazinium salts was achieved from readily available phenylazosulfonates in a single reaction step. The reaction proceeds *via* the formation of short-lived phenyldiazenes, which—owing to the strongly acidic conditions—are partially protonated. The phenyldiazenes then undergo a rapid cycloaddition to furans to give pyridazinium salts *via* elimination of water. The fact that the pyridazinium synthesis shows a low sensitivity toward oxygen, although phenyldiazenes occur as intermediates, can be explained by the very fast cycloaddition step and the partial protonation of the phenyldiazene.

INTRODUCTION

Heterocyclic compounds play an important role in many fields of application,[1] including medicinal chemistry,[1b,2] agrochemistry,[3] and advanced materials.[4] While pyridazinones[2] are well established among the six-membered nitrogen-containing compounds—regarding both synthesis and application,[2] the closely related group of pyridazinium salts[5] has so far received only little attention. This is however not astonishing taking into account their yet limited preparative accessibility. Early routes to pyridazinium salts of type **1** were reported by Carlson,[6] Hartnagel,[7] and Himmelspach,[8] either starting from diazonium salts **2** or phenylhydrazines **3** (Scheme 1). While the methodology by Hartnagel and Carlson was only applied to a few 1,3-dienes **4**, the strategy by Himmelspach suffers from the drawback that furfuryl alcohol **5** or 1,4-dicarbonyl derivatives are required as precursors, which significantly limits the product scope.

Within our research on reactions of aryldiazonium salts under reductive conditions,[9] we recently found that phenyldiazenes **6** are unstable but nevertheless highly useful intermediates for the preparation of pyridazinium salts **1** when combined in a reaction with furans **7**. Phenyldiazenes **6** had before been studied intensively by Nicholson,[10] Chattaway,[11] and Kosower,[12] whereat broad data on the properties and behavior of these compounds were collected, but an efficient trapping reaction—such as the one with furans **7** to give **1**—remained unknown for a long time.

Against this background, we focused on an improved access to phenyldiazenes **6** since this would not only make these promising compounds more easily available for future synthetic studies and applications but also render the preparative pathway to pyridazinium salts **1** more attractive. For the synthesis of **1**, the phenyldiazenes **6** were so far generated from phenylazocarboxylate salts **8** *via* protonation,[13] which however requires a phenylhydrazine **3** as the initial starting material and three additional steps comprising Boc protection, oxidation to the azo compound, and alkaline hydrolysis to obtain the azocarboxylate **8**. In the light of that, a direct access to phenyldiazenes **6** either *via* selective oxidation of phenylhydrazines **3**[14] or *via* controlled reduction of aryldiazonium salts **2** would be highly desirable (Scheme 1).

In this work, we now report the preparation of pyridazinium salts **1** *via* a straightforward sequence using readily available diazonium salts **2** as initial precursors. The abovementioned controlled reduction of diazonium salts **2** to phenyldiazenes **6** was achieved by choosing a synthetic sequence *via* phenylazosulfonates **9**, which have not yet been described as sources of phenyldiazenes **6** and pyridazinium salts **1**.

RESULTS AND DISCUSSION

In our first attempts to generate phenyldiazenes **6** as reactive intermediates to prepare pyridazinium salts **1**, we focused on the controlled oxidation of phenylhydrazines **3** (Scheme 1). Based on an earlier mechanistic control experiment conducted within a study aimed at radical carbofluorination,[14] phenyl-

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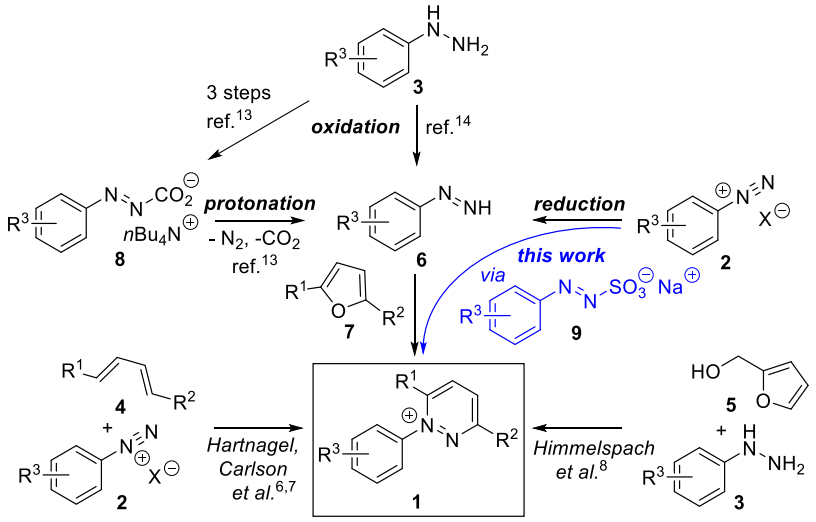
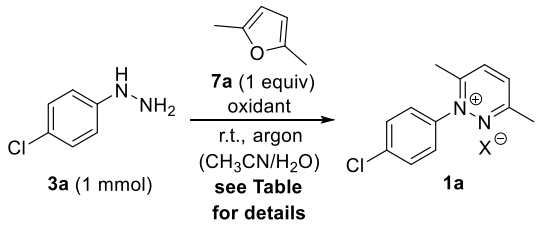
Scheme 1. Synthetic Access to Substituted Pyridazinium Salts 1



hydrazine **3a** was oxidized by Selectfluor in the presence of 2,5-dimethylfuran (**7a**) to give the respective pyridazinium salt **1a** (see Table 1, entry 1).[14]

Table 1. Synthesis of Pyridazinium Salt 1a *via* Oxidation of 4-Chlorophenylhydrazine (3a) in the Presence of 2,5-Dimethylfuran (7a)



entry	oxidant	*t* (min)	yield[a]
1	Selectfluor (1 equiv)	10	57%
2	MnO_2 (2 equiv)	10	n.d.
3	MnO_2 (2 equiv)[b]	10	n.d.
4	$KMnO_4$ (1 equiv)	10	n.d.
5	N-bromosuccinimide (2 equiv)[c]	30	8%
6	*N*-chlorosuccinimide (2 equiv)[d]	30	22%
7	$Ce(SO_4)_2$ (1 equiv)	10	35%
8	$(NH_4)_2[Ce(NO_2)_6]$ (1 equiv)	10	31%

[a]Yields determined by ^{1}H NMR using dimethyl terephthalate as the internal standard. [b]2 Equivalents of acetic acid added. [c]CH_2Cl_2 used as the solvent. [d]CH_3CN used as the solvent.

However, all further attempts to improve the yield of this oxidative access to pyridazinium salt **1a** remained unsuccessful (Table 1). In the experiments aimed at optimization, Selectfluor was replaced by such diverse oxidants as MnO_2, $KMnO_4$, *N*-bromosuccinimide, *N*-chlorosuccinimide, $Ce(SO_4)_2$, and $(NH_4)_2[Ce(NO_2)_6]$ (entries 2–8), but none of these reagents led to a yield superior to that initially achieved with Selectfluor (entry 1). Regarding these results, it appears that oxidative conditions most probably lead to an extremely short lifetime of the phenyldiazenes **6**, which is—albeit the efficient cycloaddition of phenyldiazenes to furans—still too short to enable a high-yielding formation of pyridazinium salts **1**.

To achieve the formation of phenyldiazenes from aryldiazonium salts **2** *via* controlled reduction, we then considered the known transformation of diazonium salts to phenylhydrazines *via* bis-sulfite adducts as a prototype.[15] If bis-sulfite adducts of aromatic diazonium salts can serve as precursors for phenylhydrazines as part of a formal four-electron reduction, then a monosulfite adduct—namely, a phenylazosulfonate salt—could possibly provide the desired phenyldiazene as part of a formal two-electron transfer process. As the formation of monosulfite adducts from diazonium salts has however been reported to be reversible,[16] suitable conditions favoring the reduction over the reverse reaction would be required.

To investigate the feasibility of the envisaged strategy involving phenylazosulfonates **9**, the 4-chloro substituted derivative **9a** was prepared from 4-chlorophenyldiazonium chloride (**2a**) according to established procedures (Table 2).[17] Directly following diazotization,[2a] the diazonium chloride **2a** was treated with a mixture of sodium sulfite and sodium carbonate. This step was carried out at reaction times between 2 and 3.5 h to preferentially obtain the azosulfonate **9a** as a thermodynamically more stable *trans* isomer instead of the *cis* isomer, which has been reported to be the less stable kinetic product.[17] Regarding purification, we found that the phenylazosulfonate **9a** can be easily purified by precipitation and washing with water. When stored at −32 °C, the phenylazosulfonate turned out to be stable for several months. In comparison to the available literature protocol,[17] an improvement in the synthesis of **9a** was achieved by prolonging the time for precipitation and crystallization.

In the next step, the conversion of azosulfonate **9a** to pyridazinium salt **1a**—which implies 4-chlorophenyldiazene as the intermediate—was investigated. From three series of optimization experiments using azosulfonate **9a** and 2,5-dimethylfuran (**7a**) as starting materials (Table 2), two basically suitable reaction conditions **A** (entry 5) and **B** (entry 12) were identified, which differ in the type of acid used and in the reaction time and temperature. While under conditions **A**, and employing methanesulfonic acid, a high yield of 95% was achieved at room temperature after only 10 min (entry 5), conditions **B** involving the weaker trifluoroacetic

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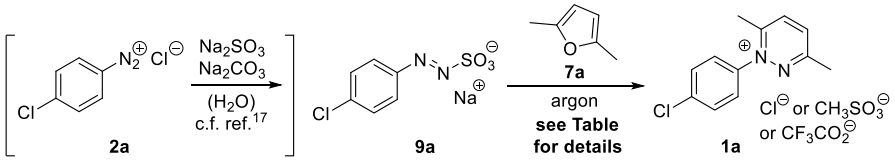
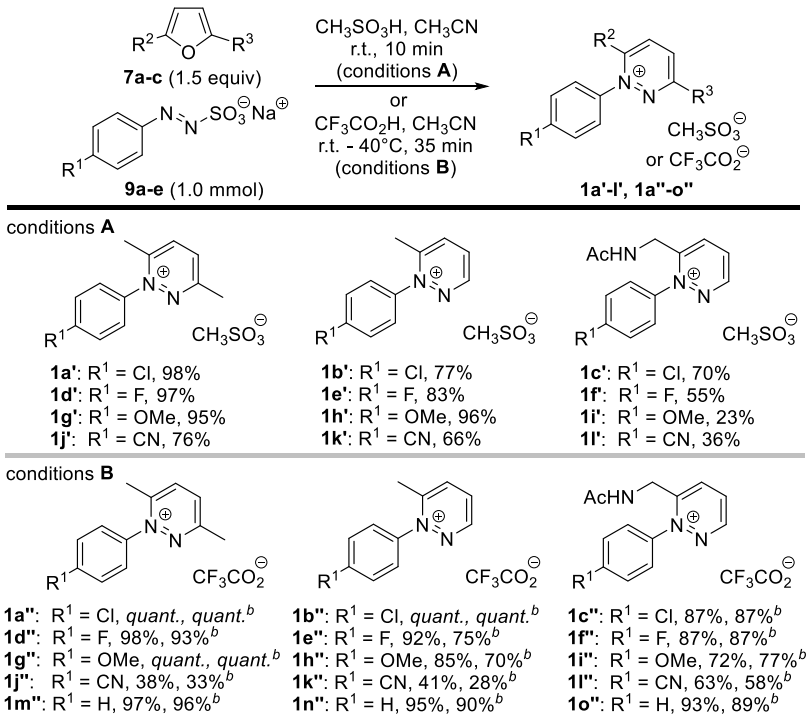
Table 2. Optimization of Reaction Conditions for the Synthesis of Pyridazinium Salt 1a from Phenylazosulfonate 9a



entry	solvent mixture (v/v)	T (°C)	**7a** (equiv)	t (min)	yield[a]
1	CH_3CN/HCl (5:1)	23	2	90	18%
2	CH_3CN/H_2O/HCl (4:1:1)	23	10	960	31%
3	CH_3CN/CH_3SO_3H (4:1)	23	10	960	96%
4	CH_3CN/CH_3SO_3H (4:1)	23	1	960	*quant.*
5	CH_3CN/CH_3SO_3H (4:1)	**23**	**1.5**	**10**	**95%**
6	CH_3CN/CF_3CO_2H (4:1)	23	1	960	56%
7	CH_3CN/CF_3CO_2H (4:1)	60	1	10	51%
8	CH_3CN/CF_3CO_2H (4:1)	40	1	10	63%
9	CH_3CN/CF_3CO_2H (4:1)	40	1.5	60	66%
10	CH_3CN/CF_3CO_2H (4:1)	40	1.5	20	64%
11	CH_3CN/CF_3CO_2H (4:1)	40	1.5	10	72%
12	CH_3CN/CF_3CO_2H (4:1)	**23−40**	**1.5**	**5 + 30**[b]	**79%**

[a]Yields determined by ^{1}H NMR spectroscopy using dimethyl terephthalate as the internal standard. Reactions conducted on 0.1 mmol scale regarding azosulfonate **9a**. [b]5 minutes at 23 °C, followed by 30 min at 40 °C.

Scheme 2. Synthesis of Pyridazinium Methanesulfonates 1a′−l′ and Trifluoroacetates 1a″−o″[a]



[a]Yields determined by ^{1}H NMR spectroscopy using dimethyl terephthalate as the internal standard. [b]Yields after purification by column chromatography.

acid (TFA) provided the best result at a longer reaction time of 35 min and at a marginally increased temperature (entry 12).

Regarding the optimized conditions **A** (entry 5), the higher amount of 1.5 equivalents of **7a** was chosen (cf. entries 3 and 4), as, when turning to the first experiments to determine the reaction scope, we realized that the use of only 1 equivalent of the furan 7 may lead to even longer reaction times than 960 min (16 h) to obtain high yields also with other substitution patterns. By increasing the amount of 7 to 1.5 equivalents, as in entry 5 (Table 2), reliable and convenient conditions for diverse substitution patterns could be established. Moreover, the increased amount of 7 enabled a better comparison of conditions **A** and **B** (see below).

The results from the evaluation of the scope including the donor-, more or less electron-neutral, and acceptor-substituted phenylazosulfonates **9a−e** in combination with 2,5-dimethylfuran (**7a**), 2-methylfuran (**7b**), and *N*-acetyl furfurylamine (**7c**) are summarized in Scheme 2. Upon increasing the reaction scale from 0.1 mmol (Table 2) to 1.0 mmol of azosulfonate **9** for the experiments summarized in Scheme 2,

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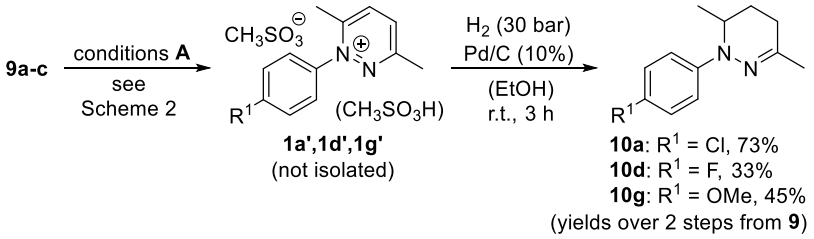
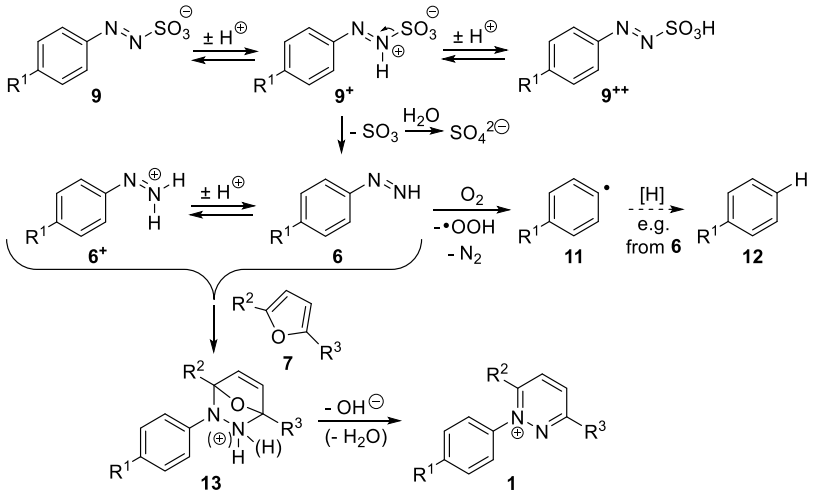
Scheme 3. Hydrogenation of Pyridazinium Methanesulfonates 1a′, 1d′, and 1g′ to Tetrahydropyridazines 10a, 10d, and 10g[a]



[a]Yields after purification by column chromatography.

Scheme 4. Plausible Reaction Pathways and Intermediates in the Formation of Pyridazinium Salts 1 from Phenylazosulfonates 9 and Furans 7



we were pleased to find that, in particular, the yields resulting from conditions **B** increased significantly. For this reason, no additional optimization experiments were conducted to further improve the outcome obtained with TFA. A possible explanation for the improvement of the yields on larger scale is the sensitivity of the TFA-mediated reactions to temperature (entries 9−12, Table 2). When starting at 23 °C and then heating to 40 °C, as under the optimized conditions **B** in entry 12, a larger reaction scale results in a slower temperature increase in the reaction mixture, what apparently improves the yield.

The regioselectivity of the reactions with the monosubstituted furans **7b,c** could be confirmed by comparison of the ^{1}H NMR spectra with literature data[7,13] and by selective nuclear Overhauser effect (NOE) experiments (see the Supporting Information). To distinguish between the different counter ions resulting from conditions **A** and **B**, the pyridazinium methanesulfonates are further on labeled as **1′** and the trifluoroacetates as **1″**.

All reactions conducted under conditions **A** suffered from the general drawback that the excess of methanesulfonic acid turned out to be difficult to remove in its full quantity during workup. Several attempts to separate the pyridazinium salt from the remaining acid—including column chromatography, precipitation of the excess of methanesulfonic acid with pyridine,[18] and precipitation of the pyridazinium salt with TFA—resulted in severe losses in yield so that the conditions **A** only appear suitable if a potential follow-up reaction of the pyridazinium salt is largely insensitive to methanesulfonic acid. Against this background, only the yields determined by ^{1}H NMR spectroscopy are reported for conditions **A** in Scheme 2. Performing the reaction under conditions **B** and using trifluoroacetic instead of methanesulfonic acid, has the advantage that the excess of acid can be readily removed under reduced pressure, which also allows recovery of the acid. Afterward, the crude pyridazinium salts could be submitted to column chromatography so that both a ^{1}H NMR yield and an isolated yield can be given for these examples. To ensure that the pyridazinium salts **1a″−o″** are present as trifluoroacetates after column chromatography, additional TFA was used as the additive to the solvent mixture (0.5 vol %).

When comparing the ^{1}H NMR yields for the individual compounds with respect to the conditions under which they were prepared, it becomes obvious that conditions **A** may only be advantageous in the case of pyridazinium salts **1h′**, **1j′**, and **1k′**, for which yields of 96, 76, and 66% were reached instead of 85, 38, and 41% for **1h″**, **1j″**, and **1k″** under conditions **B**, respectively. For all other examples, the use of TFA provides similar or better yields than methanesulfonic acid, and it has the abovementioned advantage of a facilitated workup.

Concerning the substituent effects on the phenylazosulfonates **9a−e**, the lowest yield in almost every series was found for the nitrile derivative (R^1 = CN), with the minor exception of the pyridazinium salt **1l′** obtained under conditions **A**. This overall trend can be plausibly explained by the mechanism (see below). Regarding the substituents on the furan, the 2,5-disubstituted furan **7a** typically provides higher product yields than the monosubstituted furans **7b** and **7c**, with a single exception in the row of pyridazinium salts **1j″**, **1k″**, and **1l″** prepared under conditions **B**. The overall trend that 2,5-

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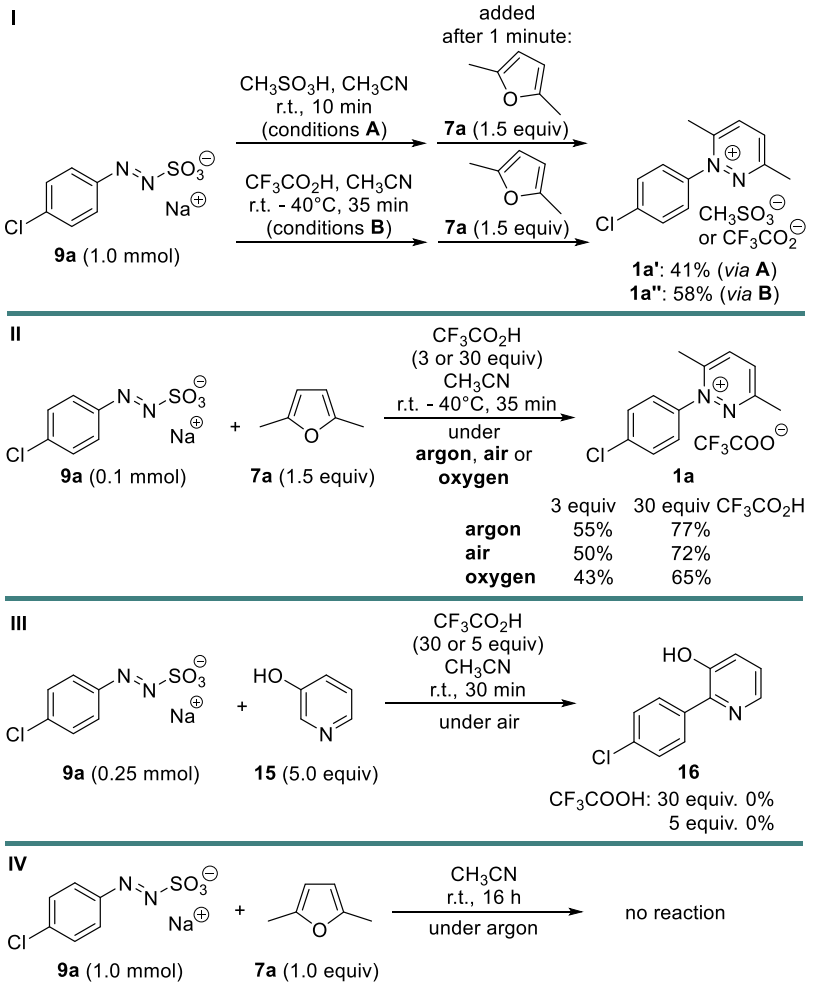
Scheme 5. Control Experiments[a]



[a]Yields determined by ^{1}H NMR using dimethyl terephthalate as the internal standard.

disubstitution on the furan is more favorable than 2-substitution is in agreement with our earlier studies, in which the pyridazinium salts were prepared from phenylazocarboxylates **8** (see Scheme 1).[13] This trend is also plausible with regard to the mechanism, in which elimination of water from the oxo-bridged cycloadduct is likely to be favored by 2,5-disubstitution (see below).

As an application of the pyridazinium salts, we examined the catalytic hydrogenation to tetrahydropyridazine derivatives **10** (Scheme 3). Since palladium-catalyzed hydrogenation can be considered to be largely insensitive to additional methanesulfonic acid,[19] as it is present in the pyridazinium salts **1′** prepared under conditions **A** (Scheme 2), the pyridazinium methanesulfonates **1a′**, **1d′**, and **1g′** were chosen as starting materials for this study. The reaction conditions used for the hydrogenation reactions were adopted from a procedure reported for the conversion of *N*-alkyl pyridinium salts to tetrahydropyridines in ethanolic solution.[20]

The three successful hydrogenations to the yet unknown tetrahydropyridazines **10a,d,g** show that conditions **A** to prepare pyridazinium salts can indeed be useful if the follow-up reaction tolerates the remaining methanesulfonic acid. During alkaline work-up after hydrogenation, the additional acid was then easily removed by extraction of the methanesulfonate into the aqueous phase. Such simple removal is not possible at the stage of the pyridazinium salt **1** as the pyridazinium salts cannot be extracted into an organic phase due to their high polarity.

In the next step, we turned to get deeper insights into the underlying reaction mechanism (Scheme 4). Under strongly acidic conditions, phenylazosulfonate **9** can be considered to be present in an equilibrium with protonated forms such as $\mathbf{9}^+$ and $\mathbf{9}^{++}$. Among these, the zwitterionic intermediate $\mathbf{9}^+$ is likely to cleave sulfur trioxide to generate the phenyldiazene **6**. A closely related cleavage mechanism, which also involves protonation at the *β*-nitrogen atom (relative to the aryl unit), has earlier been reported by Kosower[12] for the formation of phenyldiazenes **6** from phenylazocarboxylates **8** under acidic conditions (cf. Scheme 1). The assumption that sulfur trioxide and—along with that—sulfate are liberated in the cleavage step of the present reaction was verified by the successful precipitation of barium sulfate.

To investigate the formation of the phenyldiazene **6** more closely, we conducted two control experiments in which the furan **7a** was not added at the beginning but 1 min after the azosulfonate **9a** had been exposed to either methanesulfonic or TFA (Scheme 5, I). In the original version, both conditions **A** and **B** would give the pyridazinium salts **1a′** and **1a″** in essentially quantitative yields (Scheme 2). Under the modified conditions (Scheme 5, I), the yield under conditions **A** was

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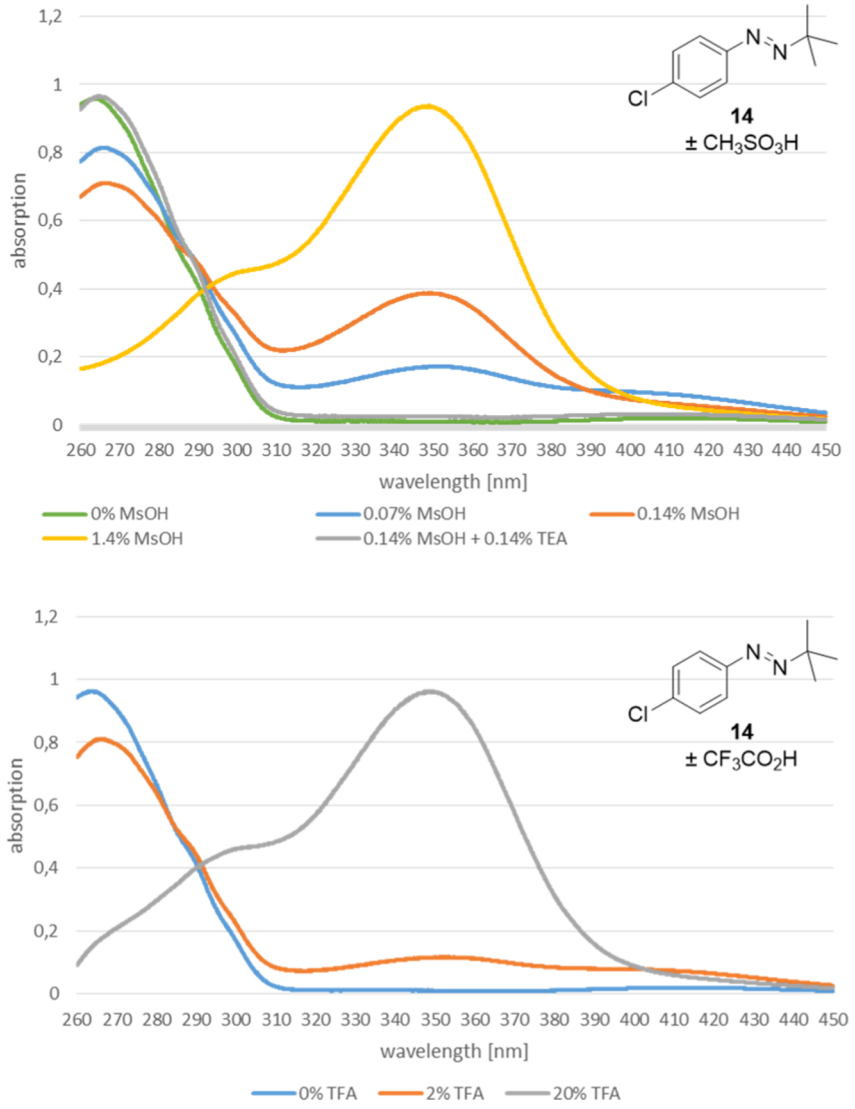

Figure 1. UV−vis spectra of *N-tert*-butyl phenyldiazene (**14**) in the absence and presence of methanesulfonic or TFA.

reduced to 41% and that under conditions **B** to 58%. This shows that already after 1 min, and under both conditions **A** and **B**, roughly half of the azosulfonate **9a** has reacted in a way that it can no longer contribute to pyridazinium formation. As all intermediates up to **6** and its protonated derivative $\mathbf{6}^+$ would however be able to still give **1** *via* the oxo-bridged intermediate **13**, not only the formation of **6** and $\mathbf{6}^+$ has to be very rapid but also their decomposition under the strongly acidic conditions if no furan **7** is present as a trapping reagent (Scheme 4). This is in agreement with earlier findings by Kosower and Huang,[12c] who reported the more rapid decay of phenyldiazenes **6** in increasingly acidic media.

To get an impression on the role of the free phenyldiazene **6** in the mechanism, two further series of control experiments were carried out (Scheme 5, II). Here, it is important to note that the phenyldiazene **6** can be considered to be the only intermediate in the mechanism (Scheme 4), which is highly sensitive toward oxygen. The related decomposition pathway is known to proceed *via* hydrogen abstraction and formation of aryl radicals **11**,[12,13] whereat this undesired side reaction is even more critical as the aryl radicals **11** may induce further decomposition of **6** through hydrogen atom abstraction. In this way, the reduced benzene derivative **12** can effectively be formed from **6** *via* a chain reaction, requiring only little initiation. Coming back to the results summarized in Scheme 5 (section II), one can conclude that both series show only a weak sensitivity toward air and that the reactions containing more TFA (30 equiv) are slightly less sensitive (comparing relative decrease in yield) than those conducted with 3 equivalents. These trends can be explained by the partial protonation of diazene **6** to give $\mathbf{6}^+$, which does not increase the overall lifetime of **6** (see accelerated decomposition, above) but which apparently reduces the sensitivity of the overall transformation toward oxygen. The actual protonation of **6** under the reaction conditions of Scheme 2, either by methanesulfonic or TFA, could be supported by UV−vis studies using *N-tert*-butyl phenyldiazene (**14**)[21] as a closely related analogue (Figure 1).

In comparison, and in agreement with reported pK_A values,[22] protonation of the azo compound **14** can be achieved with much lower amounts of methanesulfonic acid (MsOH) than TFA, whereat—according to the UV−vis spectra—the same protonated species (λ_{max} = 350 nm) is formed (Figure 1). The fact that the observed shift in absorption is not due to decomposition could be verified by an experiment in which **14** was first treated with methanesulfonic acid (0.14%) and then

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with an equal amount of triethylamine to give back the unprotonated species (Figure 1, upper part). A plausible result of the increased protonation of phenyldiazene **6** with methanesulfonic acid, which is generally most difficult to achieve for the acceptor-substituted 4-cyano derivative, are the strongly improved yields for **1j′** and **1k′** compared to **1j″** and **1k″** (Scheme 2). For **1l′** and **1l″**, which show the opposite trend, the lower stability of the *N*-acetyl substituted pyridazinium salt **1l′** in the presence of methanesulfonic acid could play a role.

Against the background of low sensitivity toward oxygen, the newly developed access to phenyldiazenes **6** from azosulfonates **9** under strongly acidic should not be useful for the generation of aryl radicals since these can only arise from the free phenyldiazene **6**. To verify this hypothesis, phenylazosulfonate **9a** was treated with TFA in the presence of 3-hydroxypyridine (**15**), which is known as a highly reactive scavenger for aryl radicals under acidic conditions (Scheme 5, III).[9b,23] Although conducting these control reactions under air to favor aryl radical formation, no detectable yields for biaryl **16** were obtained with 5 and 30 equivalents of TFA, respectively. This further underlines that free phenyldiazenes **6** are only formed in a low stationary concentration under the newly developed conditions.

Finally, and to support the assumption that the cycloaddition occurs between a phenyldiazene **6**, or its protonated form $\mathbf{6}^+$, and a furan derivative **7**, we conducted a control experiment with azosulfonate **9a** at a significantly prolonged reaction time of 16 h. This experiment did not show any conversion and failed to give an oxo-bridged cycloadduct **13** or pyridazinium salt **1** (Scheme 5, IV). As it is however difficult to design a practical surrogate for the protonated azosulfonate $\mathbf{9}^+$ (Scheme 4), we can currently not fully exclude some participation of such an intermediate in the cycloaddition reaction.

CONCLUSIONS

In summary, it has been shown that phenylazosulfonates **9**, which are readily available from phenyldiazonium salts, may serve as direct precursors in a novel straightforward access to pyridazinium salts **1**. Based on the initial conversion of the phenylazosulfonates **9** to phenyldiazenes **6**, the pyridazinium salts **1** then arise from a very rapid cycloaddition of the phenyldiazenes **6** to furan derivatives **7**. Notably, this new access to phenyldiazenes **6** does not provide these intermediates in a free form at a high concentration but owing to the strongly acidic conditions as short-lived, partially protonated species. While the low stationary concentration of free phenyldiazenes **6** in the reaction course has the beneficial effect of rendering the overall transformation largely insensitive toward oxygen, the additional presence of the also short-lived, protonated diazenium species $\mathbf{6}^+$ does apparently not impede—and may even promote—the desired cycloaddition to furans **7**. As a result, most pyridazinium salts **1** were obtained in high up to quantitative yields.

EXPERIMENTAL SECTION

General Experimental Section. Solvents and reagents were obtained from commercial sources and used as received. ^{1}H NMR and ^{13}C NMR spectra were recorded on Bruker Avance 600 (^{1}H: 600 MHz, ^{13}C: 151 MHz) and Bruker 400 (^{1}H: 400 MHz, ^{13}C: 101 MHz, and ^{19}F: 377 MHz) spectrometers. For ^{1}H NMR spectra, $CDCl_3$, CD_3OD, CD_3CN, and $(CD_3)_2SO$ were used as solvents referenced to TMS (0 ppm), $CDCl_3$ (7.26 ppm), CD_3OD (3.31 ppm), CD_3CN (1.94 ppm), and $(CD_3)_2SO$ (2.05 ppm). For ^{13}C NMR, $CDCl_3$, CD_3OD, CD_3CN, and $(CD_3)_2SO$ were used as solvents with $CDCl_3$ (77.16 ppm), CD_3OD (49.00 ppm), CD_3CN (1.94 ppm), and $(CD_3)_2SO$ (39.52 ppm) as the standard. For ^{19}F NMR, CCl_3F (0.65 ppm) was used as the standard. Chemical shifts were reported in parts per million (ppm). Coupling constants were reported in Hertz (Hz). The following abbreviations are used for the description of signals: s (singlet), d (doublet), t (triplet), q (quadruplet), m (multiplet), and b (broad). Mass spectra were recorded on Bruker micrOTOF DOTTONIK using electron spray ionization (ESI) or atmospheric pressure photoionization (APPI) and a sector field mass analyzer or time of flight (TOF) for HRMS measurements. Analytical thin-layer chromatography was carried out on Merck silica gel plates using short-wave (254 nm) UV light and ninhydrin (400 mg ninhydrin in 200 mL EtOH) to visualize components. Silica gel (Kieselgel 60, grain size 40−63 μm, Merck) was used for column chromatography. UV−vis spectra were recorded on a Specord 200 Plus device.

General Procedure for Synthesis of Phenylazosulfonates *via* Phenyldiazonium Chlorides (GP1). The respective aniline (10.0 mmol, 1.00 equiv) was dissolved in water (14 mL) and HCl (5 M, 6 mL). After degassing with nitrogen and cooling to 0 °C, a solution of sodium nitrite (10.0 mmol, 690 mg, 1.00 equiv) in water (5 mL) was added by using a syringe pump over a period of 10 min followed by additional 20 min of stirring at 0 °C. To a vigorously stirred solution of sodium sulfite (10.0 mmol, 1.26 g, 1.00 equiv) and sodium carbonate (5.66 mmol, 650 mg, 5.70 equiv) in water (8 mL), a 25 mL aliquot of the phenyldiazonium salt solution was added quickly and stirred for 2−3.5 h at RT. The solution was concentrated under reduced pressure until precipitation of the product started, and the reaction mixture was subsequently stored in a refrigerator overnight. The phenylazosulfonate **9** was filtered and washed with methyl *tert*-butyl ether (3 × 30 mL) and cold water (15 mL) and dried *in vacuo*. The purity was determined by ^{1}H NMR spectroscopy using 1,3,5-trimethoxybenzene as the internal standard. The phenylazosulfonates **9** can be stored at −32 °C for several weeks.

*Sodium 2-(4-Chlorophenyl)diazene-1-sulfonate (**9a**).* Compound **9a** was synthesized following GP1, starting from 4-chloroaniline (1.28 g, 10.0 mmol) with a reaction time of 3.5 h. Compound **9a** was obtained as a yellow solid (1.78 g, 7.32 mmol, 52%) in a purity of 97%. R_f = 0.3 (CH_2Cl_2/MeOH = 4:1) (UV). ^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm) = 7.79−7.74 (m, 2H), 7.66−7.61 (m, 2H). DEPTQ (100 MHz, DMSO-d_6): δ (ppm) = 148.9 (C_q), 136.5 (C_q), 129.6 (2 × CH), 124.3 (2 × CH). IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 1590 (w), 1580 (w), 1502 (m), 1404 (w), 1291 (s), 1228 (s), 1153 (w), 1103 (w), 1090 (w), 1074 (s), 1009 (m), 962 (w), 895 (m), 838 (s), 783 (m), 691 (s).

*Sodium 2-(4-Fluorophenyl)diazene-1-sulfonate (**9b**).* Compound **9b** was synthesized following GP1, starting from 4-fluoroaniline (1.11 g, 10.0 mmol) with a reaction time of 2.5 h. Compound **9b** was obtained as a yellow solid (692 mg, 3.06 mmol, 19%) in a purity of 100%. R_f = 0.3 (CH_2Cl_2/MeOH = 4:1) (UV). ^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm) = 7.85−7.81 (m, 2H), 7.44−7.38 (m, 2H). DEPTQ (151 MHz, DMSO-d_6): δ (ppm) = 165.3 (C_q), 125.0 (C_q), 116.6 (2 × CH), 116.4 (2 × CH). ^{19}F NMR (377 MHz, DMSO-d_6): δ (ppm) = −109.29 (s, 1F). IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 1595 (w), 1511 (w), 1260 (m), 1248 (m), 1230 (s), 1141 (w), 1073 (m), 1059 (s), 842 (s).

*Sodium 2-(4-Methoxyphenyl)diazene-1-sulfonate (**9c**).* Compound **9c** was synthesized following GP1, starting from 4-anisidine (1.23 g, 10.0 mmol) with a reaction time of 2 h. Compound **9c** was obtained as a yellow solid (1.92 g, 8.05 mmol, 62%) in a purity of 100%. R_f = 0.3 (CH_2Cl_2/MeOH = 4:1) (UV). ^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm) = 7.79−7.70 (m, 2H), 7.17−7.06 (m, 2H), 3.86 (s, 3H). DEPTQ (100 MHz, DMSO-d_6): δ (ppm) = 162.3 (C_q), 144.1 (C_q), 124.64 (2 × CH), 114.6 (2 × CH), 39.5 (CH_3). IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 2963 (w), 1603 (m), 1587 (m), 1509 (m), 1466 (w), 1439 (w), 1419 (w), 1290 (s), 1228 (s), 1175 (w), 1155 (m), 1112 (w), 1074 (s), 1025 (m), 951 (w), 893 (w), 836 (s), 824 (m), 816 (w), 805 (m), 737 (m), 642 (s), 630 (s).

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*Sodium 2-(4-cyanophenyl)diazene-1-sulfonate (**9d**).* Compound **9d** was synthesized following GP1, starting from 4-aminobenzonitrile (1.18 g, 10.0 mmol) with a reaction time of 3 h. Compound **9d** was obtained as an orange solid (1.19 g, 5.10 mmol, 51%) in a purity of 82%. R_f = 0.5 (CH_2Cl_2/MeOH = 4:1) (UV). ^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm) = 8.10−8.03 (m, 2H), 7.92−7.85 (m, 2H). DEPTQ (100 MHz, DMSO-d_6): δ (ppm) = 152.7 (C_q), 133.9 (2 × CH), 123.1 (2 × CH), 118.2 (C_q), 113.9 (C_q). IR (ATR): $\tilde{\upsilon}$ (cm^{-1}) = 2280 (w), 1641 (w), 1507 (w), 1405 (w), 1267 (m), 1250 (m), 1229 (s), 1154 (w), 1058 (s), 1010 (m), 896 (w), 845 (m), 791 (m), 709 (m), 645 (w), 606 (s).

*Sodium 2-Phenyldiazene-1-sulfonate (**9e**).* Compound **9e** was synthesized following GP1, starting from aniline (0.931 g, 10.0 mmol) with a reaction time of 3 h. Compound **9e** was obtained as a yellow solid (0.785 g, 3.8 mmol, 38%) in a purity of 85%. R_f = 0.2 (CH_2Cl_2/MeOH = 4:1) (UV). ^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm) = 7.77−7.70 (m, 2H), 7.62−7.54 (m, 3H). DEPTQ (100 MHz, DMSO-d_6): δ (ppm) = 150.40 (C_q), 131.91 (CH), 129.53 (2 × CH), 122.51 (2 × CH). IR (ATR): $\tilde{\upsilon}$ (cm^{-1}) = 2360 (w), 1508 (w), 1450 (w), 1290 (s), 1230 (s), 1150 (m), 1060 (s), 927 (m) 889 (m), 757 (s), 684 (s), 657 (s).

General Procedure for Synthesis of Pyridazinium Methanesulfonates (GP2) (Conditions A). A Schlenk flask was equipped with the respective phenylazosulfonate sodium salt **9** (1.00 mmol, 1.00 equiv) and an argon balloon. After evacuation and flushing with argon, a degassed solution of the respective furan derivative **7** (1.50 mmol, 1.50 equiv) in CH_3CN (8 mL) was added. To this vigorously stirred solution, $MeSO_3H$ (2 mL) was added, and the resulting mixture was stirred for 10 min at RT. The solvent was evaporated under reduced pressure. An authentic sample of this mixture was analyzed and the yield determined by ^{1}H NMR using dimethyl terephthalate as the internal standard.

General Procedure for Synthesis of Pyridazinium Trifluoroactates (GP3) (Conditions B). A Schlenk flask was equipped with the respective phenylazosulfonate sodium salt **9** (1.00 mmol, 1.00 equiv) and an argon balloon. After evacuation and flushing with argon, a degassed solution of the respective furan derivative **7** (1.50 mmol, 1.50 equiv) in CH_3CN (8 mL) was added. To the vigorously stirred solution, CF_3CO_2H (2 mL) was added, and stirring at RT was continued for 5 min, followed by 30 min at 40 °C. The solvent was evaporated under reduced pressure. An authentic sample of this mixture was analyzed and the yield determined by ^{1}H NMR using dimethyl terephthalate as the internal standard. Purification of the crude product by column chromatography (SiO_2, CH_2Cl_2/MeOH = 20:1 → CH_2Cl_2/MeOH = 5:1 + 0.5% TFA) gave the respective pyridazinium trifluoroacetate **1″**.

*1-(4-Chlorophenyl)-3,6-dimethylpyridazin-1-ium Trifluoroacetate (**1a″**).* Compound **1a″** was synthesized following GP3 and starting from sodium 2-(4-chlorophenyl)diazen-1-sulfonate (**9a**) (242 mg, 1.0 mmol) and 2,5-dimethylfuran (**7a**) (144 mg, 160 μL, 1.50 mmol). Purification gave **1a″** (332 mg, 1.00 mmol, *quant.*) as a brown oil. R_f = 0.4 (CH_2Cl_2/MeOH = 5:1) (ninhydrin). ^{1}H NMR (400 MHz, CD_3CN): δ (ppm) = 8.33 (d, J = 8.7 Hz, 1H), 8.27 (d, J = 8.7 Hz, 1H), 7.76−7.70 (m, 2H), 7.60−7.53 (m, 2H), 2.77 (s, 3H), 2.68 (s, 3H). DEPTQ (151 MHz, CD_3CN): δ (ppm) = 163.7 (C_q), 161.7 (C_q), 141.9 (C_q), 138.9 (CH), 138.4 (C_q), 138.3 (CH), 131.4 (2 × CH), 127.7 (2 × CH), 22.4 (CH_3), 21.8 (CH_3) (two C_q signals of F_3CCOO^- missing). ^{19}F NMR (377 MHz, CD_3CN): δ (ppm) = 74.81 (s, 3F). HRMS (ESI-TOF) m/z: $[M]^+$ calcd for $C_{12}H_{12}ClN_2^+$, 219.0689; found, 219.0683.

*1-(4-Chlorophenyl)-6-methylpyridazin-1-ium Trifluoroacetate (**1b″**).* Compound **1b″** was synthesized following GP3 and starting from sodium 2-(4-chlorophenyl)diazen-1-sulfonate (**9a**) (242 mg, 1.00 mmol) and 2-methylfuran (**7b**) (123 mg, 138 μL, 1.50 mmol). Purification gave **1b″** (318 mg, 1.00 mmol, *quant.*) as a red oil.[13] R_f = 0.5 (CH_2Cl_2/MeOH = 5:1) (ninhydrin). ^{1}H NMR (400 MHz, CD_3CN): δ (ppm) = 9.35 (dd, J = 4.8, 1.8 Hz, 1H), 8.50 (dd, J = 8.6, 1.8 Hz, 1H), 8.43 (dd, J = 8.6, 4.8 Hz, 1H), 7.77−7.70 (m, 2H), 7.64−7.54 (m, 2H), 2.74 (s, 3H). DEPTQ (151 MHz, CD_3CN): δ (ppm) = 164.4 (C_q), 153.0 (CH), 141.8 (C_q), 139.3 (CH), 138.5 (C_q), 137.9 (CH), 131.5 (2 × CH), 127.8 (2 × CH), 22.9 (CH_3) (two C_q signals of F_3CCOO^- missing). ^{19}F NMR (377 MHz, CD_3CN): δ (ppm) = −74.63 (s, 3F). HRMS (ESI-TOF) m/z: $[M]^+$ calcd for $C_{11}H_{10}ClN_2^+$, 205.0533; found, 205.0527.

*6-(Acetamidomethyl)-1-(4-chlorophenyl)pyridazin-1-ium Trifluoroacetate (**1c″**).* Compound **1c″** was synthesized following GP3 and starting from sodium 2-(4-chlorophenyl)diazen-1-sulfonate (**9a**) (242 mg, 1.00 mmol) and *N*-(furan-2-ylmethyl)acetamide (**7c**) (209 mg, 1.50 mmol). Purification gave **1c″** (325 mg, 0.87 mmol, 87%) as a brown oil. R_f = 0.5 (CH_2Cl_2/MeOH = 5:1) (ninhydrin). ^{1}H NMR (400 MHz, CD_3CN): δ (ppm) = 9.40 (dd, J = 4.8, 1.8 Hz, 1H), 8.58 (dd, J = 8.7, 1.8 Hz, 1H), 8.50 (dd, J = 8.7, 4.8 Hz, 1H), 7.78−7.69 (m, 2H), 7.69−7.63 (m, 2H), 4.53 (d, J = 5.5 Hz, 2H), 1.97 (s, 3H). DEPTQ (151 MHz, CD_3CN): δ (ppm) = 173.3 (C_q), 163.9 (C_q), 153.0 (CH), 140.8 (C_q), 138.4 (C_q), 138.0 (CH), 136.2 (CH), 131.1 (2 × CH), 127.4 (2 × CH), 42.5 (CH_2), 21.8 (CH_3) (two C_q signals of F_3CCOO^- missing). ^{19}F NMR (377 MHz, CD_3CN): δ (ppm) = −74.63 (s, 3F). HRMS (ESI-TOF) m/z: $[M]^+$ calcd for $C_{13}H_{13}ClN_3O^+$, 262.0747; found, 262.0740.

*1-(4-Fluorophenyl)-3,6-dimethylpyridazin-1-ium Trifluoroacetate (**1d″**).* Compound **1d″** was synthesized following GP3 and starting from sodium 2-(4-fluorophenyl)diazen-1-sulfonate (**9b**) (226 mg, 1.00 mmol) and 2,5-dimethylfuran (**7a**) (144 mg, 160 μL, 1.50 mmol). Purification gave **1d″** (293 mg, 0.927 mmol, 93%) as a brown oil. R_f = 0.5 (CH_2Cl_2/MeOH = 5:1) (ninhydrin). ^{1}H NMR (400 MHz, CD_3CN): δ (ppm) = 8.33 (d, J = 8.6 Hz, 1H), 8.28 (d, J = 8.6 Hz, 1H), 7.62 (dd, J = 8.7, 4.6 Hz, 2H), 7.45 (dd, J = 8.7, 8.6 Hz, 2H), 2.77 (s, 3H), 2.68 (s, 3H). DEPTQ (151 MHz, CD_3CN): δ (ppm) = 164.8 (d, $^1J_{C-F}$ = 251.0 Hz, C_q), 163.6 (C_q), 161.7 (C_q), 139.5 (C_q), 138.7 (CH), 138.2 (CH), 128.4 (d, $^3J_{C-F}$ = 9.6 Hz, 2 × CH), 118.2 (d, $^2J_{C-F}$ = 24.1 Hz, 2 × CH), 22.4 (CH_3), 21.7 (CH_3) (two C_q signals of F_3CCOO^- missing). ^{19}F NMR (377 MHz, CD_3CN): δ (ppm) = −74.65 (s, 3F), −107.49 (s, 1F). HRMS (ESI-TOF) m/z: $[M]^+$ calcd for $C_{12}H_{12}FN_2^+$, 203.0985; found, 203.0982.

*1-(4-Fluorophenyl)-6-methylpyridazin-1-ium Trifluoroacetate (**1e″**).* Compound **1e″** was synthesized following GP3 and starting from sodium 2-(4-fluorophenyl)diazen-1-sulfonate (**9b**) (226 mg, 1.00 mmol) and 2-methylfuran (**7b**) (123 mg, 138 μL, 1.50 mmol). Purification gave **1e″** (227 mg, 0.750 mmol, 75%) as a dark-brown oil. R_f = 0.4 (CH_2Cl_2/MeOH = 5:1) (ninhydrin). ^{1}H NMR (400 MHz, CD_3CN): δ (ppm) = 9.36 (s, 1H), 8.54 (d, J = 7.3 Hz, 1H), 8.45 (d, J = 7.6 Hz, 1H), 7.67 (dd, J = 8.7, 4.4 Hz, 2H), 7.45 (dd, J = 8.5, 8.2 Hz, 2H), 2.75 (s, 3H). DEPTQ (151 MHz, CD_3CN): δ (ppm) = 164.6 (d, $^1J_{C-F}$ = 251.0 Hz, C_q), 164.2 (C_q), 152.8 (CH), 139.3 (C_q), 139.1 (CH), 137.6 (CH), 128.4 (d, $^3J_{C-F}$ = 9.5 Hz, 2 × CH), 118.1 (d, $^2J_{C-F}$ = 24.1 Hz, 2 × CH), 22.7 (CH_3) (two C_q signals of F_3CCOO^- missing). ^{19}F NMR (377 MHz, CD_3CN): δ (ppm) = −74.24 (s, 3F), −107.29 (s, 1F). HRMS (ESI-TOF) m/z: $[M]^+$ calcd for $C_{11}H_{10}FN_2^+$, 189.0828; found, 189.0822.

*6-(Acetamidomethyl)-1-(4-fluorophenyl)pyridazin-1-ium Trifluoroacetate (**1f″**).* Compound **1f″** was synthesized following GP3 and starting from sodium 2-(4-fluorophenyl)diazen-1-sulfonate (**9b**) (226 mg, 1.00 mmol) and *N*-(furan-2-ylmethyl)acetamide (**7c**) (209 mg, 1.50 mmol). Purification gave **1f″** (313 mg, 0.87 mmol, 87%) as a dark-violet oil. R_f = 0.4 (CH_2Cl_2/MeOH = 5:1) (ninhydrin). ^{1}H NMR (400 MHz, CD_3CN): δ (ppm) = 9.40 (dd, J = 4.8, 1.8 Hz, 1H), 8.59 (dd, J = 8.7, 1.8 Hz, 1H), 8.51 (dd, J = 8.7, 4.8 Hz, 1H), 7.71 (dd, J = 8.9, 4.5 Hz, 2H), 7.46 (dd, J = 8.9, 8.7 Hz, 2H), 4.56 (d, J = 5.6 Hz, 2H), 2.03 (s, 3H). DEPTQ (101 MHz, CD_3CN): δ (ppm) = 172.6 (C_q), 164.0 (d, $^1J_{C-F}$ = 251.7 Hz, C_q), 163.1 (C_q), 159.2 (q, $^2J_{C-F}$ = 38.2 Hz, F_3CCOO^-), 152.3 (CH), 137.7 (d, $^4J_{C-F}$ = 3.2 Hz, C_q), 137.2 (CH), 135.4 (CH), 127.5 (d, $^3J_{C-F}$ = 9.7 Hz, 2 × CH), 117.2 (d, $^2J_{C-F}$ = 24.0 Hz, 2 × CH), 115.5 (q, $^1J_{C-F}$ = 288.1 Hz, F_3CCOO^-), 41.8 (CH_2), 21.0 (CH_3). ^{19}F NMR (377 MHz, CD_3CN): δ (ppm) = −74.50 (s, 3F), −106.92 (s, 1F). HRMS (ESI-TOF) m/z: $[M]^+$ calcd for $C_{13}H_{13}FN_3O^+$, 246.1043; found, 246.1037.

*1-(4-Methoxyphenyl)-3,6-dimethylpyridazin-1-ium Trifluoroacetate (**1g″**).* Compound **1g″** was synthesized following GP3 and starting from sodium 2-(4-methoxyphenyl)diazen-1-sulfonate (**9c**)

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(238 mg, 1.00 mmol) and 2,5-dimethylfuran (**7a**) (144 mg, 160 μL, 1.50 mmol). Purification gave **1g″** (328 mg, 1.00 mmol, *quant.*) as an orange oil. R_f = 0.4 (CH_2Cl_2/MeOH = 5:1) (ninhydrin). ^{1}H NMR (400 MHz, CD_3CN): δ (ppm) = 8.31 (d, *J* = 8.5 Hz, 1H), 8.24 (d, *J* = 8.5 Hz, 1H), 7.49 (d, *J* = 8.6 Hz, 2H), 7.19 (d, *J* = 8.6 Hz, 2H), 3.91 (s, 3H), 2.76 (s, 3H), 2.69 (s, 3H). DEPTQ (151 MHz, CD_3CN): δ (ppm) = 163.4 (C_q), 162.7 (C_q), 161.2 (C_q), 138.1 (CH), 136.2 (C_q), 127.3 (2 × CH), 116.0 (2 × CH), 56.6 (OCH_3), 22.4 (CH_3), 21.7 (CH_3) (three C_q signals missing, including two C_q signals of F_3CCOO^- and one CH due to overlap). ^{19}F NMR (377 MHz, CD_3CN): δ (ppm) = −74.81 (s, 3F). HRMS (ESI-TOF) *m*/*z*: $[M]^+$ calcd for $C_{13}H_{15}N_2O^+$, 215.1184; found, 215.1179.

*1-(4-Methoxyphenyl)-6-methylpyridazin-1-ium Trifluoroacetate (**1h″**).* Compound **1h″** was synthesized following GP3 and starting from sodium 2-(4-methoxyphenyl)diazen-1-sulfonate (**9c**) (238 mg, 1.00 mmol) and 2-methylfuran (**7b**) (123 mg, 138 μL, 1.50 mmol). Purification gave **1h″** (221 mg, 0.70 mmol, 70%) as a brown oil. R_f = 0.5 (CH_2Cl_2/MeOH = 4:1) (ninhydrin). ^{1}H NMR (400 MHz, CD_3CN): δ (ppm) = 9.32 (d, *J* = 4.2 Hz, 1H), 8.47 (d, *J* = 8.3 Hz, 1H), 8.38 (dd, *J* = 8.3, 4.2 Hz, 1H), 7.52 (d, *J* = 8.7 Hz, 2H), 7.19 (d, *J* = 8.7 Hz, 2H), 3.91 (s, 3H), 2.74 (s, 3H). DEPTQ (151 MHz, CD_3CN): δ (ppm) = 163.9 (C_q), 162.8 (C_q), 152.9 (CH), 139.1 (CH), 137.2 (CH), 136.1 (C_q), 127.4 (2 × CH), 116.0 (2 × CH), 56.6 (OCH_3), 23.0 (CH_3). ^{19}F NMR (377 MHz, CD_3CN): δ (ppm) = −74.76 (s, 3F). HRMS (ESI-TOF) *m*/*z*: $[M]^+$ calcd for $C_{12}H_{13}N_2O^+$, 201.1028; found, 201.1023.

*6-(Acetamidomethyl)-1-(4-methoxyphenyl)pyridazin-1-ium Trifluoroacetate (**1i″**).* Compound **1i″** was synthesized following GP3 and starting from sodium 2-(4-methoxyphenyl)diazen-1-sulfonate (**9c**) (238 mg, 1.00 mmol) and *N*-(furan-2-ylmethyl)acetamide (**7c**) (209 mg, 1.50 mmol). Purification gave **1i″** (287.6 mg, 0.77 mmol, 77%) as a brown solid. R_f = 0.4 (CH_2Cl_2/MeOH = 5:1) (ninhydrin). ^{1}H NMR (400 MHz, CD_3CN): δ (ppm) = 9.35 (dd, *J* = 4.9, 1.7 Hz, 1H), 8.53 (dd, *J* = 8.8, 1.7 Hz, 1H), 8.44 (dd, *J* = 8.8, 4.9 Hz, 1H), 7.61−7.53 (m, 2H), 7.24−7.15 (m, 2H), 4.52 (d, *J* = 5.5 Hz, 2H), 3.90 (s, 3H), 1.96 (s, 3H). DEPTQ (101 MHz, CD_3CN): δ (ppm) = 172.7 (C_q), 163.4 (C_q), 162.4 (C_q), 152.5 (CH), 137.0 (CH), 135.6 (CH), 134.7 (C_q), 126.8 (2 × CH), 115.5 (2 × CH), 56.0 (OCH_3), 42.2 (CH_2), 21.6 (CH_3) (two C_q signals of F_3CCOO^- missing). ^{19}F NMR (377 MHz, CD_3CN): δ (ppm) = −74.81 (3F). HRMS (ESI-TOF) *m*/*z*: $[M]^+$ calcd for $C_{14}H_{16}N_3O_2^+$, 258.1243; found, 258.1236.

*1-(4-Cyanophenyl)-3,6-dimethylpyridazin-1-ium Trifluoroacetate (**1j″**).* Compound **1j″** was synthesized following GP3 and starting from sodium 2-(4-cyanophenyl)diazen-1-sulfonate (**9d**) (233 mg, 1.00 mmol) and 2,5-dimethylfuran (**7a**) (144 mg, 160 μL, 1.50 mmol). Purification gave **1j″** (107 mg, 0.33 mmol, 33%) as an orange-brown oil. R_f = 0.3 (CH_2Cl_2/MeOH = 4:1) (ninhydrin). ^{1}H NMR (400 MHz, CD_3CN): δ (ppm) = 8.37 (d, *J* = 8.8 Hz, 1H), 8.32 (d, *J* = 8.8 Hz, 1H), 8.12−8.04 (m, 2H), 7.80−7.72 (m, 2H), 2.77 (s, 3H), 2.68 (s, 3H). DEPTQ (151 MHz, CD_3CN): δ (ppm) = 163.8 (C_q), 161.8 (C_q), 160.3 (q, $^2J_{C-F}$ = 36.2 Hz, F_3CCOO^-), 146.0 (C_q), 139.2 (CH), 138.3 (CH), 135.5 (2 × CH), 127.2 (2 × CH), 116.5 (C_q), 115.6 (C_q), 22.3 (CH_3), 21.8 (CH_3) (one C_q signal of F_3CCOO^- missing). ^{19}F NMR (377 MHz, CD_3CN): δ (ppm) = −75.45 (s, 3F). HRMS (ESI-TOF) *m*/*z*: $[M]^+$ calcd for $C_{13}H_{12}N_3^+$, 210.1026; found, 210.1026.

*1-(4-Cyanophenyl)-6-methylpyridazin-1-ium Trifluoroacetate (**1k″**).* Compound **1k″** was synthesized following GP3 and starting from sodium 2-(4-cyanophenyl)diazen-1-sulfonate (**9d**) (233 mg, 1.00 mmol) and 2-methylfuran (**7b**) (123 mg, 138 μL, 1.50 mmol). Purification gave **1k″** (86 mg, 0.28 mmol, 28%) as a brown oil. R_f = 0.4 (CH_2Cl_2/MeOH = 4:1) (ninhydrin). ^{1}H NMR (400 MHz, CD_3CN): δ (ppm) = 9.40 (dd, *J* = 4.8, 1.8 Hz, 1H), 8.57 (dd, *J* = 8.6, 1.8 Hz, 1H), 8.50 (dd, *J* = 8.6, 4.8 Hz, 1H), 8.15−8.08 (m, 2H), 7.85−7.79 (m, 2H), 2.77 (s, 3H). DEPTQ (151 MHz, CD_3CN): δ (ppm) = 163.6 (C_q), 159.3 (q, $^2J_{C-F}$ = 37.2 Hz, F_3CCOO^-), 152.2 (CH), 145.0 (C_q), 138.5 (CH), 137.4 (CH), 134.6 (2 × CH), 126.4 (2 × CH), 115.7 (C_q), 114.6 (C_q), 21.9 (CH_3) (one C_q signal of F_3CCOO^- missing). ^{19}F NMR (377 MHz, CD_3CN): δ (ppm) = −75.37 (s, 3F). HRMS (ESI-TOF) *m*/*z*: $[M]^+$ calcd for $C_{12}H_{10}N_3^+$, 196.0869; found, 196.0871.

*6-(Acetamidomethyl)-1-(4-cyanophenyl)pyridazin-1-ium Trifluoroacetate (**1l″**).* Compound **1l″** was synthesized following GP3 and starting from sodium 2-(4-cyanophenyl)diazen-1-sulfonate (**9d**) (233 mg, 1.00 mmol) and *N*-(furan-2-ylmethyl)acetamide (**7c**) (209 mg, 1.50 mmol). Purification gave **1l″** (213 mg, 0.58 mmol, 58%) as a green-blue oil. R_f = 0.2 (CH_2Cl_2/MeOH = 4:1) (ninhydrin). ^{1}H NMR (400 MHz, CD_3CN): δ (ppm) = 9.39 (dd, *J* = 4.8, 1.7 Hz, 1H), 8.63 (dd, *J* = 8.7, 1.7 Hz, 1H), 8.51 (dd, *J* = 8.7, 4.8 Hz, 1H), 8.18−8.02 (m, 2H), 7.92−7.81 (m, 2H), 4.50 (d, *J* = 5.5 Hz, 2H) (CH_3 signal missing due to overlap with CD_2HCN). DEPTQ (151 MHz, CD_3CN): δ (ppm) = 171.4 (C_q), 163.7 (C_q), 159.3 (q, $^2J_{C-F}$ = 36.2 Hz, F_3CCOO^-), 152.6 (CH), 144.4 (C_q), 137.8 (CH), 135.8 (CH), 134.7 (2 × CH), 126.4 (2 × CH), 116.0 (C_q), 114.7 (C_q), 41.9 (CH_2), 21.4 (CH_3) (one C_q signal of F_3CCOO^- missing). HRMS (ESI-TOF) *m*/*z*: $[M]^+$ calcd for $C_{14}H_{13}N_4O^+$, 253.1084; found, 253.1086.

*3,6-Dimethyl-1-phenylpyridazin-1-ium Trifluoroacetate (**1m″**).* Compound **1m″** was synthesized following GP3 and starting from sodium 2-phenyldiazene-1-sulfonate (**9e**) (208 mg, 1.00 mmol) and 2,5-dimethylfuran (**7a**) (144 mg, 160 μL, 1.50 mmol). Purification gave **1m″** (285 mg, 0.96 mmol, 96%) as a red-brown oil. R_f = 0.3 (CH_2Cl_2/MeOH = 4:1) (ninhydrin). ^{1}H NMR (400 MHz, CD_3CN): δ (ppm) = 8.33 (d, *J* = 8.7 Hz, 1H), 8.27 (d, *J* = 8.7 Hz, 1H), 7.78−7.69 (m, 3H), 7.59−7.54 (m, 2H), 2.77 (s, 3H), 2.67 (s, 3H). DEPTQ (101 MHz, CD_3CN): δ (ppm) = 163.5 (C_q), 161.3 (C_q), 143.4 (C_q), 138.6 (CH), 138.1 (CH), 132.7 (CH), 131.2 (2 × CH), 125.8 (2 × CH), 22.3 (CH_3), 21.8 (CH_3) (two C_q signals of F_3CCOO^- missing). ^{19}F NMR (377 MHz, CD_3CN): δ (ppm) = −76.30 (s, 3F). HRMS (ESI-TOF) *m*/*z*: $[M]^+$ calcd for $C_{12}H_{13}N_2^+$, 185.1073; found, 185.1074.

*6-Methyl-1-phenylpyridazin-1-ium Trifluoroacetate (**1n″**).* Compound **1n″** was synthesized following GP3 and starting from sodium 2-phenyldiazene-1-sulfonate (**9e**) (208 mg, 1.00 mmol) and 2-methylfuran (**7b**) (123 mg, 138 μL, 1.50 mmol). Purification gave **1n″** (256 mg, 0.90 mmol, 90%) as a red-brown oil. R_f = 0.1 (CH_2Cl_2/MeOH = 4:1) (ninhydrin). ^{1}H NMR (400 MHz, CD_3CN): δ (ppm) = 9.35 (dd, *J* = 4.9, 1.8 Hz, 1H), 8.49 (dd, *J* = 8.6, 1.8 Hz, 1H), 8.42 (dd, *J* = 8.6, 4.9 Hz, 1H), 7.81−7.69 (m, 3H), 7.62−7.56 (m, 2H), 2.73 (s, 3H). DEPTQ (101 MHz, CD_3CN): δ (ppm) = 164.0 (C_q), 152.9 (CH), 143.3 (C_q), 139.2 (CH), 137.6 (CH), 132.8 (CH), 131.3 (2 × CH), 125.8 (2 × CH), 22.9 (CH_3) (two C_q signals of F_3CCOO^- missing). ^{19}F NMR (377 MHz, CD_3CN): δ (ppm) = −76.46 (s, 3F). HRMS (ESI-TOF) *m*/*z*: $[M]^+$ calcd for $C_{11}H_{11}N_2^+$, 171.0917; found, 171.0917.

*6-(Acetamidomethyl)-1-phenylpyridazin-1-ium Trifluoroacetate (**1o″**).* Compound **1o″** was synthesized following GP3 and starting from sodium 2-phenyldiazene-1-sulfonate (**9e**) (208 mg, 1.00 mmol) and *N*-(furan-2-ylmethyl)acetamide (**7c**) (209 mg, 1.50 mmol). Purification gave **1o″** (304 mg, 0.89 mmol, 89%) as a dark-turquoise oil. R_f = 0.5 (CH_2Cl_2/MeOH = 5:1) (ninhydrin). ^{1}H NMR (400 MHz, CD_3CN): δ (ppm) = 9.38 (dd, *J* = 4.8, 1.8 Hz, 1H), 8.55 (dd, *J* = 8.7, 1.8 Hz, 1H), 8.47 (dd, *J* = 8.7, 4.8 Hz, 1H), 7.83−7.69 (m, 3H), 7.69−7.59 (m, 2H), 7.39 (s, 1H), 4.48 (d, *J* = 5.6 Hz, 2H), 1.95 (s, 3H). DEPTQ (101 MHz, CD_3CN): δ (ppm) = 172.4 (C_q), 164.1 (C_q), 153.2 (CH), 142.6 (C_q), 138.0 (CH), 136.3 (CH), 133.1 (CH), 131.3 (2 × CH), 125.9 (2 × CH), 42.8 (CH_2), 22.3 (CH_3) (two C_q signals of F_3CCOO^- missing). ^{19}F NMR (377 MHz, CD_3CN): δ (ppm) = −76.29 (3F). HRMS (ESI-TOF) *m*/*z*: $[M]^+$ calcd for $C_{13}H_{14}N_3O^+$, 228.1131; found, 228.1130.

General Procedure for Synthesis of Tetrahydropyridines (GP4). The respective pyridazinium methanesulfonate **1a′**, **1d′**, or **1g′** was synthesized according to GP2, starting from the respective phenylazosulfonate **9a−c** (1.00 mmol). After removal of the solvent under reduced pressure, the crude product **1a′**, **1d′**, or **1g′** (containing remaining methanesulfonic acid) was dissolved in EtOH (15 mL) and transferred into the autoclave vessel. The solution was degassed with nitrogen and Pd/C (10%) (120 mg) was added, followed by further degassing with nitrogen. The reaction was

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performed under hydrogen pressure (30 bar) and stirring for 3 h. Afterward, the reaction mixture was filtered, transferred into a round-bottom flask, and the solvent was removed under reduced pressure. Saturated Na_2CO_3 solution (25 mL) was added to a pH value of 10, and the product was extracted with EtOAc (3 × 25 mL) and washed with H_2O (25 mL). The combined organic layers were dried over Na_2SO_4, filtered, and the solvent was removed under reduced pressure. Purification by column chromatography (SiO_2) (hexanes/EtOAc = 8:1) gave the respective tetrahydropyridazine **10a**, **10d**, or **10g**.

*1-(4-Chlorophenyl)-3,6-dimethyl-1,4,5,6-tetrahydropyridazine (**10a**).* Compound **10a** was synthesized following GP4 and starting from sodium 2-(4-chlorophenyl)diazen-1-sulfonate (**9a**) (0.50 mmol) *via* pyridazinium methanesulfonate **1a′**. Purification gave **10a** (83.5 mg, 0.375 mmol, 73%) as a red oil. R_f = 0.8 (hexanes/EtOAc = 8:1) (ninhydrin). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.20−7.14 (m, 2H), 7.13−7.08 (m, 2H), 4.21−4.04 (m, 1H), 2.32−2.18 (m, 1H), 2.11−1.91 (m, 2H), 1.98 (d, J = 1.1 Hz, 3H), 1.80 (dddd, J = 13.2, J = 7.5, 2.5, 1.3 Hz, 1H), 1.08 (dd, J = 6.6, J = 0.5 Hz, 3H). DEPTQ (101 MHz, CD_3CN): δ (ppm) = 146.6 (C_q), 144.9 (C_q), 129.5 (2 × CH), 123.0 (C_q), 114.9 (2 × CH), 45.8 (CH), 24.5 (CH_2), 24.3 (CH_3), 22.3 (CH_2), 14.6 (CH_3). HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{12}H_{16}ClN_2^+$, 223.0997; found, 223.0996.

*1-(4-Fluorophenyl)-3,6-dimethyl-1,4,5,6-tetrahydropyridazine (**10d**).* Compound **10d** was synthesized following GP4 and starting from sodium 2-(4-fluorophenyl)diazen-1-sulfonate (**9b**) (2.50 mmol) *via* pyridazinium methanesulfonate **1d′**. Purification gave **10d** (155 mg, 0.753 mmol, 33%) as a brown oil. R_f = 0.7 (hexanes/EtOAc = 8:1) (ninhydrin). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.16−7.10 (m, 2H), 6.99−6.92 (m, 2H), 4.16−4.04 (m, 1H), 2.34−2.21 (m, 1H), 2.14−2.02 (m, 2H), 2.00 (s, 3H), 1.86−1.79 (m, 1H), 1.09 (dd, J = 6.6, 0.5 Hz, 3H). DEPTQ (101 MHz, CD_3CN): δ (ppm) = 157.1 (d, $^1J_{C-F}$ = 234.1 Hz, C_q), 144.7 (d, $^4J_{C-F}$ = 1.8 Hz, C_q), 144.2 (C_q), 116.0 (d, $^2J_{C-F}$ = 22.1 Hz, 2 × CH), 115.0 (d, $^3J_{C-F}$ = 7.3 Hz, 2 × CH), 46.2 (CH), 24.8 (CH_2), 24.2 (CH_3), 22.4 (CH_2), 14.4 (CH_3). ^{19}F NMR (377 MHz, $CDCl_3$): δ (ppm) = −126.7 (s, 1F). HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{12}H_{16}FN_2^+$, 207.1292; found, 207.1293.

*1-(4-Methoxyphenyl)-3,6-dimethyl-1,4,5,6-tetrahydropyridazine (**10g**).* Compound **10g** was synthesized following GP4 and starting from sodium 2-(4-methoxyphenyl)diazen-1-sulfonate (**9c**) (1.00 mmol) *via* pyridazinium methanesulfonate **1g′**. Purification gave **10g** (99.2 mg, 0.454 mmol, 45%) as a brown oil. R_f = 0.3 (hexanes/EtOAc = 8:1) (ninhydrin). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.17−7.10 (m, 2H), 6.87−6.82 (m, 2H), 4.00 (qt, J = 6.8, 3.8 Hz, 1H), 3.77 (s, 3H), 2.33−2.21 (m, 1H), 2.16−2.02 (m, 2H), 2.01 (d, J = 1.0 Hz, 3H), 1.82 (dddd, J = 13.2, 7.6, 3.5, 2.3 Hz, 1H), 1.07 (d, J = 6.6 Hz, 3H). DEPTQ (101 MHz, CD_3CN): δ (ppm) = 153.7 (C_q), 143.1 (C_q), 142.5 (C_q), 115.8 (2 × CH), 115.1 (2 × CH), 56.0 (OCH_3), 46.7 (CH), 25.1 (CH_2), 24.1 (CH_3), 22.5 (CH_2), 14.5 (CH_3). HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{13}H_{19}ON_2^+$, 219.1492; found, 219.1491.

Control Experiments (Scheme 5). Experiments I were performed as described in GP3 (conditions **B**). 2,5-Dimethylfuran (**7a**) was added after 1 min of stirring at RT.

Experiments II were performed as described in GP3 (conditions **B**). Reactions were carried out under an argon, air, or oxygen atmosphere.

Experiments III were performed as described in GP3 (conditions **B**). To a stirring solution of azosulfonate **9a** (61 mg, 0.25 mmol) and 3-hydroxypyridine (**16**) (119 mg, 1.25 mmol) in CH_3CN (2 mL), 30 or 5 equiv of CF_3COOH was added.

Experiment IV was performed under conditions **B**, in the absence of methanesulfonic acid but at a significantly prolonged reaction time of 16 h.

UV/Vis Measurements. *1-(tert-Butyl)-2-(4-chlorophenyl)-diazene (**14**).* The synthesis of azo compound **14** was performed by following a literature procedure.[23] To an ice-cooled solution of 4-chloroaniline (510 mg, 4.00 mmol) in 10% H_2SO_4 in H_2O (6 mL), a solution of $NaNO_2$ (290 mg, 4.20 mmol) in H_2O (2 mL) was added dropwise. After stirring at 0 °C for 15 min, $FeSO_4 \times 7H_2O$ (2.22 g, 8.0 mmol) in DMSO (80 mL), 2-iodo-2-methylpropane (1.84 g, 1.19 mL, 10 mmol), and H_2O_2 (30% (m/v), 907 μL, 8.0 mmol) were added to the mixture. After stirring for 15 min at RT, water (100 mL) was added and the resulting mixture was extracted with hexanes (4 × 150 mL). Purification by column chromatography (SiO_2, hexanes/CH_2Cl_2 = 7:1) gave **14** (429 mg, 2.18 mmol, 55%) as a pale-yellow liquid. R_f = 0.5 (CH_2Cl_2/hexanes = 1:7) (UV). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.63−7.58 (m, 2H), 7.44−7.39 (m, 2H), 1.33 (s, 9 H). DEPTQ (101 MHz, $CDCl_3$): δ (ppm) = 150.79 (C_q), 135.94 (C_q), 129.21 (2 × CH), 123.43 (2 × CH), 68.06 (C_q), 27.08 (3 × CH_3). The analytical data obtained are in agreement with the data reported in the literature.[24]

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.1c00013.

Copies of ^{1}H NMR spectra for compounds **1a′−1l′** and copies of ^{1}H NMR and ^{13}C NMR spectra for compounds **1a″−1o″**, **9a−e**, **10a,d,g**, and **14** (PDF)

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Notes

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