



HAL
open science

Synthesis of 3-Amino-5-fluoroalkylfurans by Intramolecular Cyclization

Clotilde Plaçais, Morgan Donnard, Armen Panossian, Jean-Pierre Vors, David
Bernier, Sergii Pazenok, Frédéric R. Leroux

► **To cite this version:**

Clotilde Plaçais, Morgan Donnard, Armen Panossian, Jean-Pierre Vors, David Bernier, et al.. Synthesis of 3-Amino-5-fluoroalkylfurans by Intramolecular Cyclization. *Organic Letters*, 2021, 23 (12), pp.4915-4919. 10.1021/acs.orglett.1c01672 . hal-03325240

HAL Id: hal-03325240

<https://hal.science/hal-03325240>

Submitted on 24 Aug 2021

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

Synthesis of 3-amino-5-fluoroalkylfurans by intramolecular cyclization.

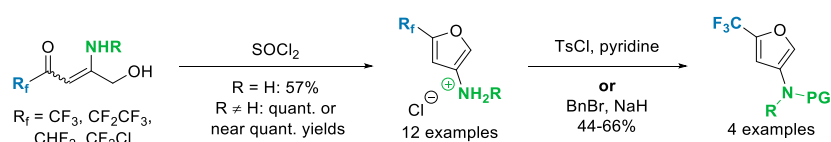
Clotilde Plaçais,^I Morgan Donnard,^I Armen Panossian,^I Jean-Pierre Vors,^{II} David Bernier,^{II} Sergii Pazenok,^{III} and Frédéric R. Leroux*,^I

^I Université de Strasbourg, Université de Haute-Alsace, CNRS, UMR 7042-LIMA, ECPM, 25 Rue Becquerel, Strasbourg 67087, France

^{II} Bayer S.A.S., 14 Impasse Pierre Baizet, BP99163, 69263 Lyon Cedex 09, France

^{III} Bayer CropScience AG, Alfred-Nobel-Strasse 50, 40789 Monheim, Germany

Supporting Information Placeholder



ABSTRACT: A synthesis to access rarely described 3-amino-5-fluoroalkylfurans has been developed by cyclization of easily accessible fluorovinamides. This method is rapid and simple and affords the desired furans as hydrochloride salts in quantitative or near quantitative yields. It is compatible with four different fluorinated groups: $-CF_3$, $-CF_2CF_3$, $-CHF_2$ and $-CF_2Cl$, and a wide range of substituents on the amine.

Fluorine is widely used in both agrochemical and pharmaceutical industries. 18% of pharmaceutical¹ and 16% of pesticides² commercialized at the present day contain fluorine, and the proportion of fluorine-containing molecules launched on the market has been growing steadily in the last decades, to become a majority for agrochemicals. Introduction of fluorine or fluorinated groups into a molecule allow to modulate its physico-chemical and biological properties, such as its pKa or lipophilicity, and can protect molecules against metabolism.³⁻⁷

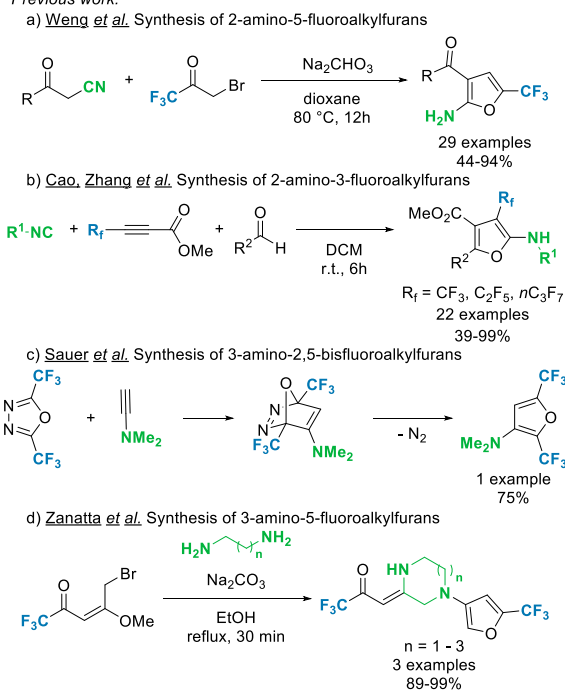
Furans are a very important class of heterocycles and can be found in natural products, pharmaceutical and agrochemical molecules, and as intermediates in organic chemistry.¹¹⁻¹⁶ Fluorinated furans can have enhanced biological properties and their use in drugs and pesticides have often been described.¹⁷⁻²¹ For instance, furans, usually poorly stable under acidic conditions, can be stabilized by a fluorinated group, due to its strong electron withdrawing property. Those structures can be synthesized using two different strategies. The first one consists in introducing the fluorinated group onto the furan ring. This method suffers from low regio- and chemoselectivity, as it relies on the use of highly reactive fluoroalkylating reagents. The second strategy, circumventing those drawbacks, relies on the use of fluorinated building blocks during the heterocyclization. A review on the synthesis of fluoro and perfluoroalkyl furans was published in 2010,²² and a variety of other methods have been developed since, which are in most cases limited to $-CF_3$ furans.²³⁻²⁸

Among furans, aminofurans are very important precursors of agrochemicals and pharmaceuticals.²⁹ Although several methods have been developed to synthesize them, fluorinated amino furans are still scarcely described. While 3-aminofurans are

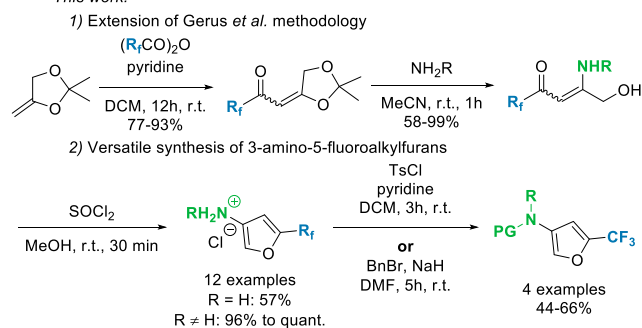
reported more stable than those substituted in the 2 position,²⁹ the syntheses of fluorinated 2-aminofurans are the most described. Weng *et al.* reported the cyclization of β -ketonitriles with 3-bromo-1,1,1-trifluoroacetone using a base (Scheme 1, a).³⁰ Cao, Zhang *et al.* described a multicomponent reaction using methyl perfluoroalk-2-ynoates, isocyanides and aldehydes to give 2-amino-3-perfluoroalkylfurans (Scheme 1, b).³¹ To the best of our knowledge, only two methods have been reported to access fluorinated 3-aminofurans, and both have a very limited scope. The first one was developed by Sauer *et al.*, and affords a 3-amino-2,5-bisfluoroalkyl furan via an hetero-Diels-Alder reaction followed by N_2 extrusion (Scheme 1, c).³² The second method was described by Zanatta *et al.* to form *N*-pyrrolyl(furanyl)-piperazines, 1,4-diazepanes, and 1,4-diazocanes by cyclization of a bromo trifluoroenone with a diamine (Scheme 1, d).³³ However, this method is only described for three examples of furans, and is only applicable to those very specific structures. In this work, we report on a simple synthesis of 3-amino-5-fluoroalkylfurans from fluoromethylated enones whose synthesis was reported by Gerus *et al.*, starting from easily accessible 4-methylene-1,3-dioxolane and using fluorinated acetic anhydride derivatives as the source of fluoroalkyl group (Scheme 1, *This work*).³⁴

Scheme 1. Synthesis of fluorinated aminofurans.

Previous work:



This work:



We first tried to cyclize trifluoroenone **1a**, bearing an isopropyl group on the amine, using HCl in methanol. After 30 minutes of stirring at room temperature, we could observe the hydrochloride salt of the desired furan **2a**, in an encouraging 54% yield (Table 1, entry 1). However, the reaction did not proceed cleanly, and we decided to increase the transient nucleofugality of the hydroxy group. Using thionyl chloride in DCM afforded the product in an improved yield of 84% (entry 2). Other activating agents such as oxalyl chloride (entry 3) or acetic anhydride (entry 4) led to a complex mixture or no conversion respectively. Notably, with trifluoroacetic anhydride we only obtained the uncyclized product of alcohol esterification (entry 5). Next, we evaluated the influence of the solvent on the thionyl chloride-activated reaction. To our delight, both in methanol and ethanol and after simple evaporation of the reaction mixture, we quantitatively obtained the product **2a** (entries 6-7) without the need for further purification. The reaction also performed in diethyl ether and ethyl acetate, but in lower yields of 53 and 56%, respectively (entries 8-9). THF, acetone and acetonitrile were not suitable for this cyclization and afforded complex mixtures (entries 10-12). Finally, reducing the amount of thionyl chloride from 1.5 equiv. to 1 equiv. led quantitatively to the targeted product **2a** (entry 13).

Table 1. Optimization of the reaction conditions.^a

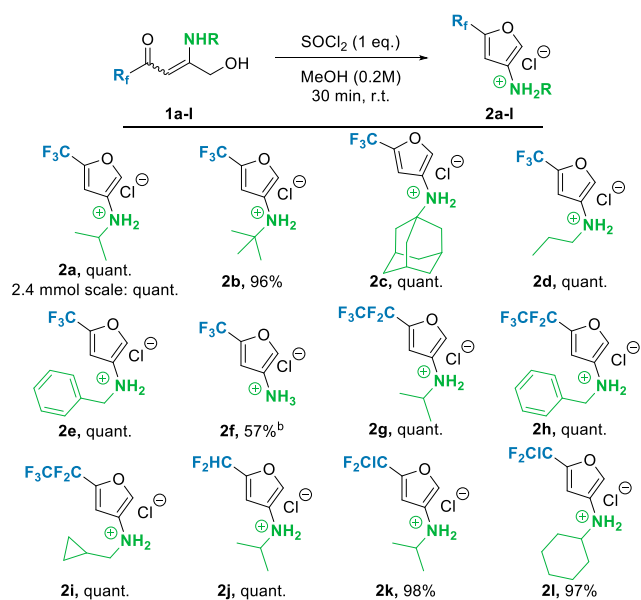
Entry	Solvent	Additive	NMR yield ^b
1	MeOH	HCl (1.5 eq.)	54%
2	DCM	SOCl ₂ (1.5 eq.)	84%
3	DCM	(COCl) ₂ (1.5 eq.)	10%
4	DCM	Ac ₂ O (1.5 eq.)	0%
5	DCM	TFAA (1.5 eq.)	0%
6	MeOH	SOCl ₂ (1.5 eq.)	quant. ^c
7	EtOH	SOCl ₂ (1.5 eq.)	quant. ^c
8	Diethyl ether	SOCl ₂ (1.5 eq.)	53%
9	EtOAc	SOCl ₂ (1.5 eq.)	56%
10	THF	SOCl ₂ (1.5 eq.)	0%
11	Acetone	SOCl ₂ (1.5 eq.)	0%
12	Acetonitrile	SOCl ₂ (1.5 eq.)	0%
13	MeOH	SOCl ₂ (1 eq.)	quant. ^c

^aReaction conditions: **1a** (0.2 mmol), additive, solvent (1 mL), 30 min. at room temperature under argon. ^bYield determined by ¹⁹F NMR using fluorobenzene as an internal standard. The conversion was complete in all cases except for entries 1 (80% conversion), and 4 (no conversion). ^cIsolated yield.

With optimal conditions in hand, we then explored the scope of the reaction (Scheme 2). We first modified the substituent on the amino group and the corresponding substrates were obtained in quantitative or near quantitative yields. Both more hindered substituents (*N-t*-butyl for **2b** and *N*-adamantyl for **2c**) and a less hindered substituent (*N*-propyl for **2d**) were efficient for this reaction. To our delight, the substrate bearing a potentially removable benzyl substituent led entirely to the corresponding furan **2e**. If the reaction with a primary amine gave the expected furan **2f**, it was too unstable to be fully characterized, and only a NMR yield could be determined.

We then wanted to extend the reaction to other fluorinated groups. The synthesis of the starting material is only reported for -CF₃ groups, using trifluoroacetic anhydride as the source, but we were able to extend it to -CF₂CF₃, -CHF₂ and -CF₂Cl groups using the corresponding anhydrides. The synthesis of these new fluorinated groups, through an extension of Gerus' methodology can be found in the supporting information. For each of these fluorinated substituents, using substrates bearing an isopropylamino group, we obtained the corresponding furans (**2g**, **2j** and **2k**) in excellent yields. In the case of -CF₂CF₃, switching the amino group to benzylamino (**2h**) or cyclopropylmethylamino (**2i**) did not affect the efficiency of the reaction. Similarly, substituting the isopropylamino by a cyclohexylamino in the case of the -CF₂Cl group (**2l**) led to equivalent results. However, furans bearing -CHF₂ groups were extremely unstable, with both more and less hindered amino groups, and we obtained in most cases either complex mixtures or very rapidly decomposing furans, and thus no other example of CHF₂-substituted furans could be synthesized.

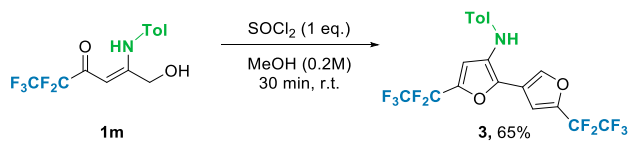
Scheme 2. Substrate scope.^a



^aReaction conditions: **1a-k** (0.4 mmol), SOCl_2 (0.4 mmol), MeOH (2 mL), 30 min at room temperature under argon. Products were obtained pure after simple evaporation of the solvent. ^bYield determined by ^{19}F NMR using fluorobenzene as an internal standard, due to the high instability of the product obtained.

When using aromatic amines, we observed no traces of the expected furan. Instead, we were surprised to observe the formation of pseudodimers such as product **3** (Scheme 3), resulting from an intermolecular electrophilic substitution. This reaction was not as clean as the furan formation, and the pseudodimer was not obtained pure directly after evaporation of the solvent. However, it was also more stable and the mixture could be easily separated on silica to give pure compound **3** in a 65% yield.

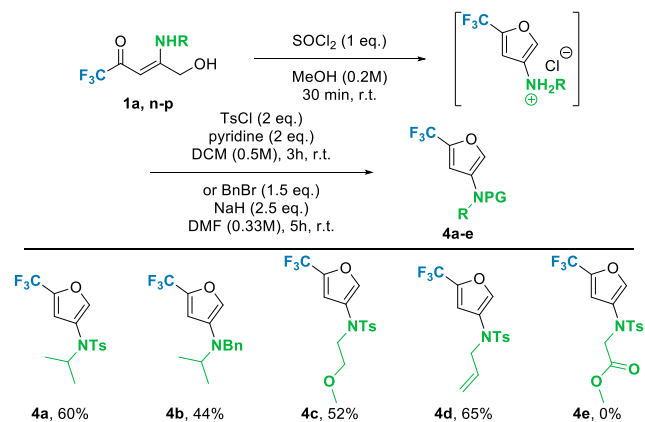
Scheme 3. Cyclization using an aromatic amine.



^aReaction conditions: **1m** (0.4 mmol), SOCl_2 (0.4 mmol), MeOH (2 mL) at room temperature under argon.

Next, we decided to investigate the protection of the amino groups on the newly formed furans, in order to stabilize them so as to facilitate potential post-functionalization (Scheme 4). Using our model substrate **1a**, we found that both tosyl (**4a**) and benzyl (**4b**) protecting groups were suitable, affording the products in 60% and 44% yields respectively. During our initial exploration of the substrate scope, we obtained in some cases impure furans that we were not able to purify due to their instability. Nicely, once protected with a tosyl group, these furans revealed to be stabilized and could be easily purified by chromatography on silica. For instance, compounds **4c** bearing a methoxide and **4d** bearing an allyl group were obtained in good 52% and 65% yields respectively. However, esters were not suitable with this methodology, and a complex mixture was obtained (**4e**).

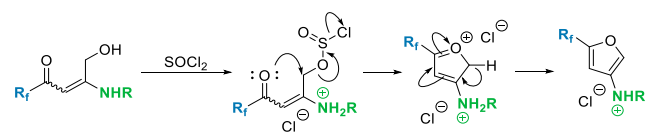
Scheme 4. Protection of the amine and extension of the substrate scope.^a



^aReaction conditions: As in Scheme 2, followed by evaporation of methanol, dissolving of the reaction mixture in DCM or DMF, and addition of the base and protecting agent.

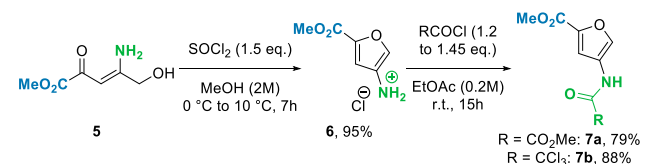
Regarding the mechanism of the cyclization, we envision that the reaction is initiated by activation of the alcohol by thionyl chloride (Scheme 5). Under acidic conditions without SOCl_2 , the alcohol is probably only activated by protonation. The carbon in α position of the activated alcohol is then attacked by the double bond on the oxygen atom of the enone, to form a five-membered ring, followed by aromatization to obtain the furan.

Scheme 5. Proposed mechanism



Since fluoroalkyl groups exhibit an electroattractive character, we wondered about the possibility to extend our methodology to other electroattractive groups. We were delighted to see that this methodology is also applicable to esters such as CO_2Me and led to the corresponding furan **6** in a 95% yield. The obtained furan is shelf stable and could be acylated, which was not possible with the fluoroalkylfurans. These structures are of interest for the agrochemical³⁵ and pharmaceutical³⁶ industries, and the only two previously reported syntheses rely on the use of metal catalysts³⁷ or explosive azides³⁸ and are not suitable for large scale synthesis. Further experimentations are in progress and will be reported in due course.

Scheme 6. Extension of the methodology



To conclude, we developed a highly efficient synthesis of 3-amino-5-fluoroalkylfurans in quantitative or near quantitative yields. This reaction is efficient with different fluorinated groups and is starting from easily accessible fluoroenones. It is compatible with a variety of substitutions on the amine, and the use of aromatic substituents led to the formation of furan pseudodimers. Gratifyingly, less stable furans could be synthesized via protection of the amine in satisfying yields.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website.

Experimental procedures and characterization data (PDF)

AUTHOR INFORMATION

Corresponding Author

* E-mail: frederic.leroux@unistra.fr

Author Contributions

All authors have given approval to the final version of the manuscript.

Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENT

We thank the CNRS (Centre National de la Recherche Scientifique, France). We are grateful to Bayer S.A.S for a PhD grant to C.P. The French Fluorine Network (GIS Fluor) is also acknowledged.

REFERENCES

- (1) Inoue, M.; Sumii, Y.; Shibata, N. Contribution of Organofluorine Compounds to Pharmaceuticals. *ACS Omega*, **2020**, *5*, 10633–10640.
- (2) Ogawa, Y.; Tokunaga, E.; Kobayashi, O.; Hirai, K.; Shibata, N. Current Contributions of Organofluorine Compounds to the Agrochemical Industry. *iScience*, **2020**, *23*, 101467.
- (3) Gillis, E.P.; Eastman, K.J.; Hill, M.D.; Donnelly, D.J.; Meanwell, N.A. Applications of Fluorine in Medicinal Chemistry. *J. Med. Chem.*, **2015**, *58*, 8315–8359.
- (4) Meanwell, N.A. Fluorine and Fluorinated Motifs in the Design and Application of Bioisosteres for Drug Design. *J. Med. Chem.*, **2018**, *61*, 5822–5880.
- (5) Groult, H.; Leroux, F.; Tressaud, A. *Modern Synthesis Processes and Reactivity of Fluorinated Compounds*; Elsevier Science: London, **2017**.
- (6) Haufe, G.; Leroux, F. *Fluorine in Life Sciences: Pharmaceuticals, Medicinal Diagnostics, and Agrochemicals*; Academic press: London, **2019**.
- (7) Fujiwara, T.; O'Hagan, D. Successful Fluorine-Containing Herbicide Agrochemicals. *J. Fluorine Chem.*, **2014**, *167*, 16–29.
- (8) Pazenok, S.; Leroux, F.R. Modern Fluorine-Containing Agrochemicals. In: *Frontiers of Organofluorine Chemistry*; World Scientific, **2019**; pp. 695–732.
- (9) Zakharychev, V.V.; Kuzenkov, A.V.; Martsynkevich, A.M. Good Pyridine Hunting: A Biomimic Compound, a Modifier and a Unique Pharmacophore in Agrochemicals. *Chem Heterocycl. Comp.*, **2020**, *56*, 1491–1516.
- (10) Mykhailiuk, P.K. Fluorinated Pyrazoles: From Synthesis to Applications. *Chem. Rev.*, **2021**, *121*, 1670–1715.
- (11) Liu, Y.; Zhang, S.; Abreu, P.J.M. Heterocyclic Terpenes: Linear Furano- and Pyrroloterpenoids. *Nat. Prod. Rep.*, **2006**, *23*, 630.
- (12) Racané, L.; Tralić-Kulenović, V.; Kraljević Pavelić, S.; Ratkaj, I.; Peixoto, P.; Nhili, R.; Depauw, S.; Hildebrand, M.-P.; David-Cordonnier, M.-H.; Pavelić, K.; Karminski-Zamola, G. Novel Diamidino-Substituted Derivatives of Phenyl Benzothiazolyl and Dibenzothiazolyl Furans and Thiophenes: Synthesis, Antiproliferative and DNA Binding Properties. *J. Med. Chem.*, **2010**, *53*, 2418–2432.
- (13) Peterson, L.A. Reactive Metabolites in the Biotransformation of Molecules Containing a Furan Ring. *Chem. Res. Toxicol.*, **2013**, *26*, 6–25.
- (14) Hosoya, T.; Aoyama, H.; Ikemoto, T.; Kihara, Y.; Hiramatsu, T.; Endo, M.; Suzuki, M. Dantrolene Analogues Revisited: General Synthesis and Specific Functions Capable of Discriminating Two Kinds of Ca²⁺ Release from Sarcoplasmic Reticulum of Mouse Skeletal Muscle. *Bioorg. Med. Chem.*, **2003**, *11*, 663–673.
- (15) Ye, Q.-Z.; Xie, S.-X.; Huang, M.; Huang, W.-J.; Lu, J.-P.; Ma, Z.-Q. Metalloform-Selective Inhibitors of Escherichia Coli Methionine Aminopeptidase and X-Ray Structure of a Mn(II)-Form Enzyme Complexed with an Inhibitor. *J. Am. Chem. Soc.*, **2004**, *126*, 13940–13941.
- (16) Yamada, K.; Abe, Y.; Kato, Y.; Nakauchi, A.; Saito, Y.; Fuchi, S. September 6, **2019**.
- (17) Nenajdenko, V. *Fluorine in Heterocyclic Chemistry Volume I*; Springer International Publishing, **2014**.
- (18) Elworthy, T.R.; Brill, E.R.; Caires, C.C.; Kim, W.; Lach, L.K.; Tracy, J.L.; Chiou, S.-S. Lactams as Prostanoid Receptor Ligands. Part 4: 2-Piperidones as Selective EP4 Receptor Agonists. *Bioorg. Med. Chem. Lett.*, **2005**, *15*, 2523–2526.
- (19) Liddle, J.; Allen, M.J.; Borthwick, A.D.; Brooks, D.P.; Davies, D.E.; Edwards, R.M.; Exall, A.M.; Hamlett, C.; Irving, W.R.; Mason, A.M.; McCafferty, G.P.; Nerozzi, F.; Peace, S.; Philp, J.; Pollard, D.; Pullen, M.A.; Shabbir, S.S.; Sollis, S.L.; Westfall, T.D.; Woollard, P.M.; Wu, C.; Hickey, D.M.B. The Discovery of GSK221149A: A Potent and Selective Oxytocin Antagonist. *Bioorg. Med. Chem. Lett.*, **2008**, *18*, 90–94.
- (20) Mansfield, D.; Rieck, H.; Coqueron, P.-Y.; Desbordes, P.; Villier, A.; Grosjean-Cournoyer, M.-C.; Genix, P. WO2006108791A2, **2006**.
- (21) Vezouet, R.L.; Soergel, S.; Defieber, C.; Gross, S.; Koerber, K.; Anspaugh, D.D.; Culbertson, D.L.; Varina, F. US 8853214 B2, **2014**.
- (22) Serdyuk, O.; Butin, A.; Abaev, V. Synthesis of Fluorofurans and Perfluoroalkylfurans. *J. Fluorine Chem.*, **2010**, *131*, 296–319.
- (23) Chen, G.; He, G.; Xue, C.; Fu, C.; Ma, S. Diversified Assembly of Perfluoroalkyl-Substituted Furans and 2,5-Dihydrofuran-2-Ols. *Tetrahedron Lett.*, **2011**, *52*, 196–198.
- (24) Wang, Y.; Luo, Y.-C.; Hu, X.-Q.; Xu, P.-F. A Powerful Cascade Approach for Expedient Synthesis of Trifluoromethylated Furans. *Org. Lett.*, **2011**, *13*, 5346–5349.
- (25) Chong, Q.; Xin, X.; Wang, C.; Wu, F.; Wang, H.; Shi, J.; Wan, B. DABCO-Catalyzed Synthesis of Trifluoromethylated Furans from Propargyl Alcohols and Methyl 2-Perfluoroalkynoate. *J. Org. Chem.*, **2014**, *79*, 2105–2110.
- (26) De Saint Jores, C.; Mukan, I.; Yegorova, T.; Harakat, D.; Bouillon, J.-P. Straightforward Synthesis of Tri- and Tetra-Substituted 3-Trifluoromethylfurans by Heterocyclization Reaction of Perfluoroketene Dithioacetals. *Tetrahedron*, **2016**, *72*, 6807–6814.
- (27) Zhou, W.; Yue, Z.; Zhang, J. A Highly Efficient One-Pot Trifluoromethylation/Cyclization Reaction of Electron-Deficient 1,3-Conjugated Enynes: Modular Access to Trifluoromethylated Furans and 2,3-Dihydrofurans. *Org. Chem. Front.*, **2016**, *3*, 1416–1419.
- (28) Zhang, T.; Maekawa, H. Synthesis of 4-(Trifluoromethyl)Cyclopentenones and 2-(Trifluoromethyl)Furans by Reductive Trifluoroacetylation of Ynones. *Org. Lett.*, **2017**, *19*, 6602–6605.
- (29) Ramsden, C.A.; Milata, V. 2-Aminofurans and 3-Aminofurans. In: *Advances in Heterocyclic Chemistry*; Elsevier, **2006**; Vol. 92, pp. 1–54.
- (30) Wang, J.; Chen, S.; Wu, W.; Wen, S.; Weng, Z. Base-Mediated Tunable Synthesis of 2-Trifluoromethylated Furans and Dihydrofuranols: Extraordinary Stable in Sulfuric Acid. *J. Org. Chem.*, **2019**, *84*, 15685–15696.
- (31) Wang, Y.; Tao, L.; Chen, J.; He, W.; Deng, H.; Shao, M.; Zhang, H.; Cao, W. Isocyanide-Based Multicomponent

- Reactions: A Concise Approach to 2-Amino-3-perfluoroalkylfurans Using Methyl Perfluoroalk-2-ynoates as Fluorinated Building Blocks. *Asian J. Org. Chem.*, **2019**, *8*, 710–715.
- (32) Thalhammer, F.; Wallfharer, U.; Sauer, J. 1,3,4-Oxadiazole Als Heterocyclische 4 π -Komponenten in Diels-Alder-Reaktionen. *Tetrahedron Lett.*, **1988**, *29*, 3231–3234.
- (33) Mittersteiner, M.; Andrade, V.P.; Zachow, L.L.; Frizzo, C.P.; Bonacorso, H.G.; Martins, M.A.P.; Zanatta, N. Synthesis of *N*-Pyrrolyl(Furanyl)-Substituted Piperazines, 1,4-Dizepanes, and 1,4-Diazocanes. *J. Org. Chem.*, **2019**, *84*, 8976–8983.
- (34) Gerus, I.I.; Balabon, O.A.; Pazenok, S.V.; Lui, N.; Kondratov, I.S.; Tarasenko, K.V.; Shaitanova, E.N.; Ivasyshyn, V.E.; Kukhar, V.P. Synthesis and Properties of Polyfunctional Cyclic β -Alkoxy- α,β -Unsaturated Ketones Based on 4-Methylene-1,3-Dioxolanes: Synthesis and Properties of Polyfunctional Cyclic β -Alkoxy- α,β -Unsaturated Ketones Based on 4-Methylene-1,3-Dioxolanes. *Eur. J. Org. Chem.*, **2018**, 3853–3861.
- (35) Peters, O.; Haaf, K.; Lindell, S.; Bojack, G.; Law, K.; Machettira, A.; Dietrich, H.; Gatzweiler, E.; Rosinger, C. WO2018228985, December 20, **2018**.
- (36) Woods, C.R.; Faucher, N.; Eschgfäller, B.; Bair, K.W.; Boger, D.L. Synthesis and DNA Binding Properties of Saturated Distantamycin Analogues. *Bioorg. Med. Chem. Lett.*, **2002**, *4*.
- (37) Brucoli, F.; Natoli, A.; Marimuthu, P.; Borrello, M.T.; Stapleton, P.; Gibbons, S.; Schätzlein, A. Efficient Synthesis and Biological Evaluation of Proximicins A, B and C. *Bioorg. Med. Chem.*, **2012**, *20*, 2019–2024.
- (38) Wolter, F.E.; Schneider, K.; Davies, B.P.; Socher, E.R.; Nicholson, G.; Seitz, O.; Süßmuth, R.D. Total Synthesis of Proximicin A–C and Synthesis of New Furan-Based DNA Binding Agents. *Org. Lett.*, **2009**, *11*, 2804–2807.
-