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A Potassium Carbonate-Catalyzed Efficient and Straightforward Synthesis of Dihydro-2-oxopyrrole (DPO) Building Blocks

Yan-Shun Zhang,[a] Hou-Ze Gui,[a] Yin Wei,[b] Min Shi*[a,b]

Abstract: An inorganic base K_2CO_3-catalyzed cascade dimerization and cyclization reactions of 2-sulfonaminoacrylates to give dihydro-2-oxopyrrole (DPO) derivatives has been disclosed in this paper. This straightforward and atom-economic transformation featured by a simple experimental operation with easily available starting materials and broad substrate scope as well as good functional group tolerance, giving the desired DPO building blocks in moderate to good yields.

Introduction

Dihydro-2-oxopyrrole (DPO) moiety is a common element within many biologically active natural products and pharmacologically important compounds such as *Oteromycin*,[1] a HIV integrase inhibitor and a antagonist of endothelin receptor; *Pyrrocidine*,[2] a potential antibiotic; *Ypaoamide*,[3] a feeding deterrent; and *Glimepiride*,[4] an antidiabetes drug (Figure 1). Moreover, many DPO's derivatives themselves also exhibited useful bioactive characters such as antimalarial,[5] pesticidal,[6] herbicidal,[7] etc.

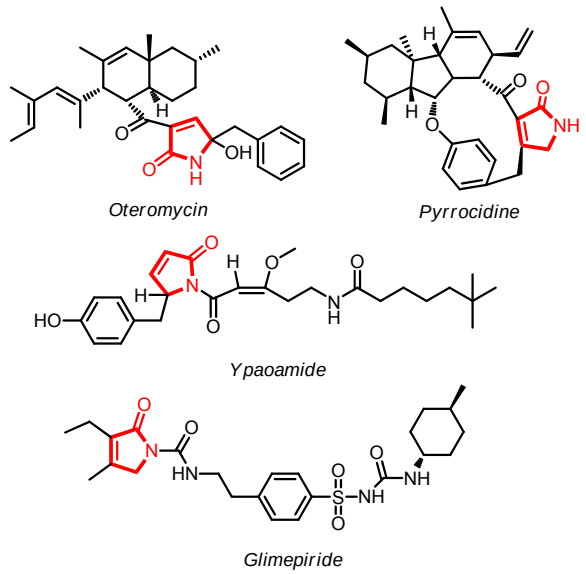
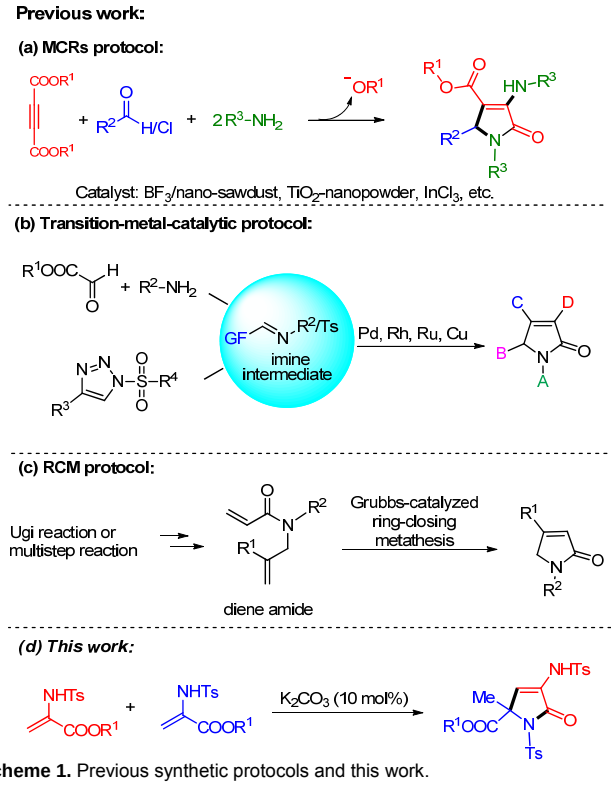


Figure 1. Some natural products and commercially available drugs containing DPO moiety.

Due to the significant usefulness of DPO derivatives, a number of synthetic methods for the preparation of functionalized DPO scaffolds have been developed by organic chemists. As shown in Scheme 1, the main synthetic methodologies to access DPO derivatives have been summarized (previous work).



Scheme 1. Previous synthetic protocols and this work.

The first synthetic approach is multicomponent reactions (MCRs)[8] using electron-deficient alkynes, aldehydes/acyl chlorides, and amines as substrates in the presence of Lewis acids. In these MCRs, the reactions generally started from the condensation of aldehydes and amines to generate imine intermediates, which then reacted with alkenes to afford the desired products (Scheme 1, a). During the last decades, transition-metal-catalytic methods have become powerful synthetic tools in the synthesis of DPO derivatives. Transition-metal-catalysts such as Pd,[9] Ru,[10] Rh,[11] Cu[12] etc have been applied for the synthesis of DPO derivatives *via* the reactions of metal-activated alkenes or aldehydes with *in situ* generated imines from the reactions of activated aldehydes and amines or triazoles (Scheme 1, b). Moreover, ring-closing metathesis (RCM)[13] is a common technique for crafting heterocycles and carbocycles. Keum and his co-workers[13a] have reported a novel synthetic methodology through RCM reaction of diene amide, which was prepared *via* four components Ugi reaction, to afford DPO scaffolds in one step. In 2016, Gondal's group[13c] reported another example for obtaining DPO derivatives *via* RCM reaction of 4-step prepared diene amides starting from commercially available allyl chloride (Scheme 1, c). However, all of these synthetic methods had their shortages and limitations such as the use of expensive metal catalysts and multistep synthesis of starting materials.

Recently, 2-aminoacrylate **1** has become an extremely useful synthon in organic synthesis based on its unique electronic properties and multifunctional groups. When the protecting group (PG) of amino moiety was an acyl group (Ac), 2-aminoacrylate could sever as a Michael acceptor to undertake an addition of a nucleophile in the presence of *N*-heterocyclic carbene (NHC) catalyst.[14] However, 2-aminoacrylate could also display its potential nucleophilicity under the same conditions when the PG

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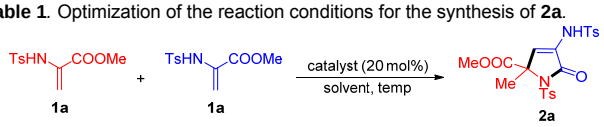
was a sulfonyl group.[15] Furthermore, the sulfonyl group protected 2-aminoacrylate could *in situ* isomerize to its imine equivalent to participate in the reaction as an electrophile,[16] avoiding the instability and limitations of imine substance.[17] On the basis of these findings, we envisaged that sulfonyl group protected 2-aminoacrylates could undergo cascade intermolecular nucleophilic dimerization and cyclization to afford the desired DPO skeleton in the presence of a base. Herein, we wish to report a facile synthetic approach for the rapid construction of dihydro-2-oxopyrrole (DPO) building blocks from easily accessible methyl 2-sulfonaminoacrylates using K_2CO_3 (10 mol%) as the catalyst (Scheme 1, *this work*).

Results and Discussion

We started the investigation on the reaction of **1a** (0.4 mmol) and PBu_3 (20 mol%) in toluene (4.0 mL) at 75 °C and found that the desired product **2a** was given in 58% yield after 4 h through a cascade dimerization and cyclization (Table 1, entry 1). A range of alkyl and aryl phosphines were then examined and we identified that PEt_3, $P(4\text{-}MeOC_6H_4)_3$, PPh_2Me, $PPhMe_2$ and dppm could catalyze the reaction, giving **2a** in moderate yields ranging from 30%-46%, but less nucleophilic PPh_3 and $P(4\text{-}CF_3C_6H_4)_3$ could not trigger the reaction (entries 2-8). Moreover, the use of nitrogen-containing Lewis base DABCO instead of PBu_3 produced **2a** in 36% yield (entry 9). The examination of solvent effects using PBu_3 as the catalyst with ethyl acetate (EA), 1,2-dichloroethane (DCE), and 1,4-dioxane revealed that these solvents did not facilitate the production of **2a** (entries 10-12). Interestingly, when 100 mol% of AgOAc was used as the catalyst at 83 °C (boiling point of DCE), the desired product **2a** was obtained in 71% yield (entry 13). Encouraged by this result, we tried to decrease the amount of AgOAc to 20 mol% or 10 mol%, but found that **2a** was afforded in lower yields as 25% respectively (entries 14 and 15). The use of other metal salts such as AgOTf, $Cu(OTf)_2$ or $AgSbF_6$ had no catalytic activity for this reaction, suggesting that the counter ion with strong basicity might play an important role in this transformation (entries 16-18).

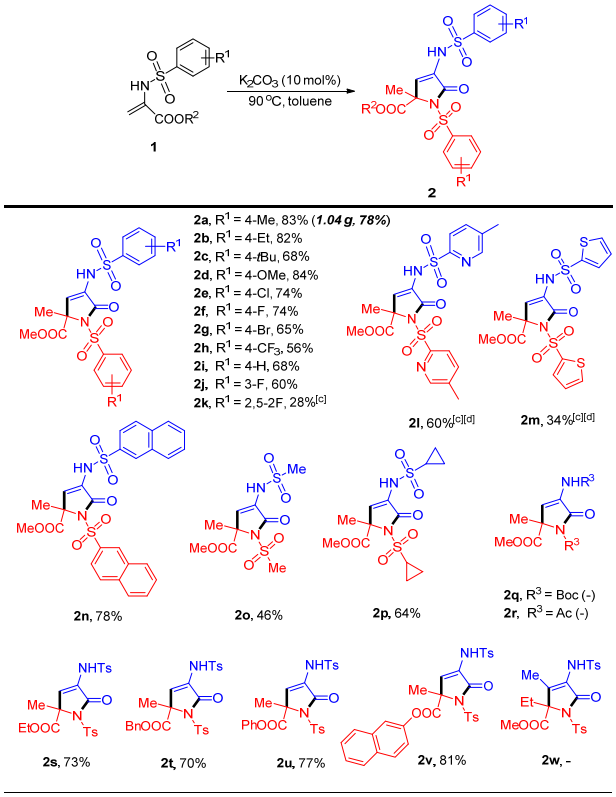
Table 1. Optimization of the reaction conditions for the synthesis of **2a**.



entry[a]	catalyst	solvent	temp (°C)	yield (%)[b]
1	PBu_3	PhMe	75	58
2	PEt_3	PhMe	75	42
3	PPh_3	PhMe	75	0
4	$P(4\text{-}CF_3C_6H_4)_3$	PhMe	75	0
5	$P(4\text{-}MeOC_6H_4)_3$	PhMe	75	39
6	PPh_2Me	PhMe	75	36
7	$PPhMe_2$	PhMe	75	46
8	dppm	PhMe	75	30
9	DABCO	PhMe	75	36
10	PBu_3	EA	75	33
11	PBu_3	DCE	75	53
12	PBu_3	dioxane	75	44
13[c]	AgOAc	DCE	83	71
14	AgOAc	DCE	83	25
15[d]	AgOAc	DCE	83	25
16[d]	AgOTf	DCE	83	< 5
17[d]	$Cu(OTf)_2$	DCE	83	< 5
18[d]	$AgSbF_6$	DCE	83	< 5
19[d]	K_2CO_3	PhMe	90	83
20[d]	Cs_2CO_3	PhMe	90	82
21[e]	K_2CO_3	PhMe	90	82
22[d, f]	K_2CO_3	DCE	90	80

[a] All reactions were carried out with **1a** (0.4 mmol) and catalyst (20.0 mol%) in solvent (4.0 mL) at indicated temperature. [b] Isolate yield. [c] 100 mol% AgOAc was used. [d] 10 mol% catalyst was used. [e] 100 mol% K_2CO_3 was used. [f] The reaction was carried out in a sealed tube.

Therefore, we next attempted to use K_2CO_3 (10 mol%) and Cs_2CO_3 (10 mol%) as the catalysts in this reaction and found that carrying out the reaction in toluene at 90 °C afforded **2a** in 83% and 82% yields, respectively (entries 19 and 20). Using 100 mol% of K_2CO_3 gave **2a** in 82% yield as well (entry 21). Performing the reaction in DCE at 90 °C (in a sealed reaction tube) provided **2a** in 80% yield (entry 22). Thus, the optimal conditions are identified as that this cascade dimerization and cyclization should be carried out with **1a** (0.4 mmol) in toluene (4.0 mL) at 90 °C for 4 h in the presence of K_2CO_3 (10 mol%) (for more information on the optimization of the reaction conditions, see Table S1 in the Supporting Information).



[a] Reaction conditions: **1** (0.4 mmol) and K_2CO_3 (10 mol%) in 4.0 mL toluene at 90 °C for 4 hours. [b] Isolated yield. [c] Reaction was carried out overnight. [d] Using DCE as solvent.

Scheme 2. Substrate scope for the production of **2**.[a],[b]

With the optimized reaction conditions in hand, the substrate scope of this reaction was then explored. The results are summarized in Scheme 2. First, a number of *para*-substituted aryl sulfonamides were examined. For substrates **1a**-**1h** bearing either an electron-deficient or electron-rich aromatic ring, the reaction proceeded smoothly, affording the corresponding products **2a**-**2h** in moderate to good yields ranging from 56% to 84%. The structure of **2a** has been unambiguously determined by X-ray diffraction.[18] The ORTEP drawing is shown in Figure 2 and the CIF data are presented in the Supporting Information. Substrate **1i**, in which the aromatic ring had no substituent (R^1 = H), gave the corresponding product **2i** in 68% yield, suggesting that the electronic property of aromatic ring did not have significant impact on the reaction outcome. As can be seen from Scheme 2, substrate **1j**, bearing a *meta*-substituted aromatic ring, furnished the desired product **2j** in 60% yield. In the case of substrate **1k**, in which two substituents were both introduced at the *ortho*- and *meta*-positions of the benzene ring, the desired product **2k** was obtained in 28% yield if the reaction was performed overnight, perhaps due to the steric effect. Moreover, substrates **1l** and **1m** bearing heteroaromatic rings such as substituted pyridine and thiophene as well as substrate **1n** having a fused naphthalene in their sulfonamide moieties were also tolerated, giving the corresponding products **2l**-**2n** in 60%, 34% and 78% yields, respectively. Furthermore, we also found that the reaction proceeded smoothly when the sulfonamide moiety was a methylsulfonyl group (substrate **1o**) and cyclopropylsulfonyl group (substrate **1p**), affording the desired products **2o** and **2p** in 46% and 64% yields, respectively. However, no reaction occurred when R^3 was an acyl or a Boc protecting group (substrates **1r** and **1s**), presumably due to the electronic effect. The reaction also

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had good substrate compatibility for ester moiety R^2. Replacing methyl ester with ethyl ester (substrate **1s**), benzyl ester (substrate **1t**), phenyl ester (substrate **1u**) and naphthyl ester (substrate **1v**) gave the corresponding products **2s**-**2v** in good yields ranging from 70% to 81%. Moreover, we have also investigated the reactivity of trisubstituted olefin substrate **1w** in this reaction. Unfortunately, none of the desired product could be formed under the standard conditions presumably due to the steric effect. It should be noted that this transformation could be carried out in a gram scale, delivering **2a** in 78% yield, indicating the practical usefulness of this new synthetic protocol (Scheme 2).

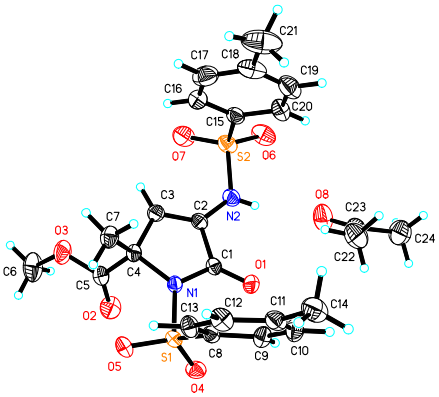
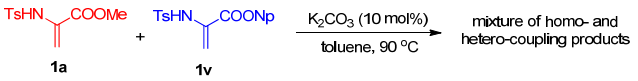


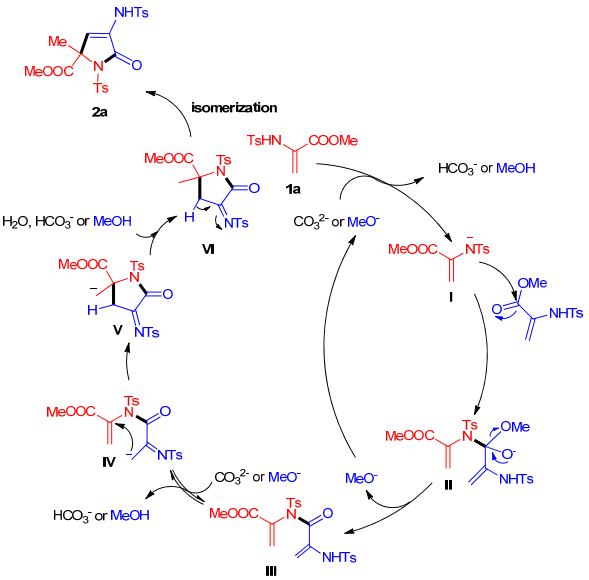
Figure 2. X-ray crystal structure of product **2a**

A hetero-dimerization reaction was also examined with substrates **1a** and **1v**, but a complex mixture was obtained without the selectivity (Scheme 3).



Scheme 3. Investigation on the hetero-dimerization

A plausible reaction mechanism for this reaction is shown in Scheme 4 using **1a** as a model substrate. K_2CO_3 abstracted a proton from NHTs group of **1a** to generate intermediate **I**, which attacked the ester moiety of another substrate **1a** to afford intermediate **II**. The release of MeO^- from intermediate **II** produced the dienyl amide compound **III**, which subsequently underwent deprotonation and isomerization to give intermediate **IV**. An intramolecular cyclization of intermediate **IV** took place to produce intermediate **V**, which could be reprotonated to give the precursor **VI**. Isomerization of **VI** produced the desired product **2a** *via* a proton migration. The *in situ* generated MeO^- or intermediate **V** could act as a base as well in the catalytic cycle, rendering that the use of catalytic amount of K_2CO_3 is possible for this novel cascade dimerization and cyclization process.



Scheme 4. Proposed reaction mechanism.

Conclusions

In summary, we have disclosed a novel and efficient inorganic base K_2CO_3-catalyzed cascade dimerization and cyclization reactions of 2-sulfonaminoacrylate derivatives to synthesize dihydro-2-oxopyrrole (DPO) derivatives in moderate to good yields in one step. In this atom-economic and metal-free transformation, the starting materials are easily available and the experimental operations are simple along with broad substrate scope and good functional group tolerance. Furthermore, gram-scale synthesis makes this protocol to be more efficient and practical. Further investigations on the application of this protocol to the synthesis of biologically active DPO derivatives are underway.

Experimental Section

General methods: Proton nuclear magnetic resonance (^{1}H NMR) spectra, carbon nuclear magnetic resonance (^{13}C NMR) spectra and fluorous nuclear magnetic resonance (^{19}F NMR) spectra were recorded at 400, 100 and 367 MHz, respectively. Data are presented as follows: chemical shift (ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constants in Hertz (Hz) and integration. Mass and High Resolution Mass Spectra (HRMS) spectra were recorded by DART or ESI method. The employed solvents were dry up by standard methods when necessary. Commercially obtained reagents were used without further purification. For thin-layer chromatography (TLC), silica gel plates (Huanghai GF254) were used. Flash column chromatography was carried out using 300-400 mesh silica gel at increased pressure.

General Procedure for the Synthesis of 1: To a 100 mL round-bottom flask was added sulfonamide (22.0 mmol), methyl pyruvate (20.0 mmol), *p*-toluenesulfonic acid (0.2 mmol), *p*-methoxyphenol (0.2 mmol) and toluene (50 mL). The resulting mixture was stirred and heated under reflux for 18 hours. Then, the solvent was removed under reduced pressure and the residue was purified by a flash column chromatography (eluent: petroleum ether/ethyl acetate = 4/1) to give the corresponding product **1**.

General Procedure for the Synthesis of 2: To a 10 mL Schlenk tube was added substrate **1** (0.4 mmol, 2.0 eq.) and K_2CO_3 (0.02 mmol, 10 mol%) and then toluene (4.0 mL) was added into tube. The resulting reaction mixture was stirred at 90 °C. Upon reaction completion, the mixture was filtered through a celite. The filtrate

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was concentrated under reduced pressure and the residue was purified by a silica gel flash chromatography (eluent: petroleum ether/ethyl acetate = 2/1) to afford the desired products **2** in moderate to good yields.

Compound *2a*: 80 mg, yield: 83%; white solid. MP: 155-157 °C. ^{1}H NMR (CD_3COCD_3, 400 MHz, TMS) δ 1.84 (s, 3H), 2.40 (s, 3H), 2.43 (s, 3H), 3.71 (s, 3H), 6.08 (s, 1H), 7.39 (d, *J* = 8.0 Hz, 2H), 7.43 (d, *J* = 8.0 Hz, 2H), 7.82 (d, *J* = 8.4 Hz, 2H), 7.93 (d, *J* = 8.4 Hz, 2H), 9.04 (s, 1H). ^{13}C NMR (CD_3COCD_3, 100 MHz, TMS) δ 20.6, 20.7, 21.2, 52.7, 69.1, 123.8, 127.4, 128.7, 129.4, 129.7, 129.8, 135.8, 136.1, 144.7, 145.7, 163.2, 168.8. IR (neat) ν 3228, 1732, 1658, 1435, 1359, 1287, 1154, 1117, 867, 810, 660 cm^{-1}. HRMS (ESI) calcd. for $C_{21}H_{26}N_3O_7S_2$: 496.1207, found: 496.1210.

Compound *2b*: 83 mg, yield: 82%; yellow oil. ^{1}H NMR (CD_3COCD_3, 400 MHz, TMS) δ 1.71-1.23 (m, 6H), 1.85 (s, 3H), 2.70 (q, *J* = 7.6 Hz, 2H), 2.72 (q, *J* = 7.6 Hz, 2H), 3.71 (s, 3H), 6.69 (s, 1H), 7.42 (d, *J* = 8.4 Hz, 2H), 7.46 (d, *J* = 8.4 Hz, 2H), 7.86 (d, *J* = 8.4 Hz, 2H), 7.87 (d, *J* = 8.4 Hz, 2H), 9.13 (s, 1H). ^{13}C NMR (CD_3COCD_3, 100 MHz, TMS) δ 14.5, 14.6, 21.3, 28.4, 28.5, 52.8, 69.1, 123.7, 127.5, 128.4, 128.6, 128.8, 129.4, 129.9, 135.8, 136.0, 136.3, 150.7, 151.7, 163.2, 168.8. IR (neat) ν 3240, 2928, 1731, 1361, 1255, 1165, 1087, 834, 778 cm^{-1}. HRMS (ESI) calcd. for $C_{23}H_{30}N_3O_7S_2$: 524.1520, found: 524.1522.

Compound *2c*: 76 mg, yield: 68%; yellow oil. ^{1}H NMR (CD_3COCD_3, 400 MHz, TMS) δ 1.32 (s, 9H), 1.34 (s, 9H), 1.85 (s, 3H), 3.70 (s, 3H), 6.68 (s, 1H), 7.62-7.69 (m, 4H), 7.88 (d, *J* = 8.4 Hz, 2H), 7.98 (d, *J* = 8.4 Hz, 2H), 9.14 (s, 1H). ^{13}C NMR (CD_3COCD_3, 100 MHz, TMS) δ 26.4, 35.4, 35.5, 40.1, 40.2, 57.9, 74.3, 128.5, 131.1, 131.2, 132.4, 133.7, 135.0, 141.0, 141.2, 162.5, 163.5, 168.4, 173.9. IR (neat) ν 3245, 2920, 1743, 1666, 1391, 1137, 1116, 831, 761 cm^{-1}. HRMS (ESI) calcd. for $C_{27}H_{38}N_3O_7S_2$: 580.2146, found: 580.2154.

Compound *2d*: 86 mg, yield: 84%; yellow oil. ^{1}H NMR (CD_3COCD_3, 400 MHz, TMS) δ 1.85 (s, 3H), 3.73 (s, 3H), 3.90 (s, 3H), 6.66 (s, 1H), 7.08 (d, *J* = 8.8 Hz, 2H), 7.11 (d, *J* = 8.8 Hz, 2H), 7.88 (d, *J* = 8.8 Hz, 2H), 7.99 (d, *J* = 8.8 Hz, 2H). ^{13}C NMR (CD_3COCD_3, 100 MHz, TMS) δ 26.5, 58.0, 60.5, 60.6, 74.2, 119.2, 119.4, 128.6, 134.8, 135.1, 135.5, 136.2, 136.3, 168.4, 168.9, 169.6, 174.1. IR (neat) ν 2922, 2852, 1730, 1594, 1497, 1355, 1258, 1152, 1115, 1087, 832, 803 cm^{-1}. HRMS (ESI) calcd. for $C_{21}H_{26}N_3O_9S_2$: 528.1106, found: 528.1109.

Compound *2e*: 77 mg, yield: 74%; yellow solid. MP: 162-164 °C. ^{1}H NMR (CD_3COCD_3, 400 MHz, TMS) δ 1.87 (s, 3H), 3.74 (s, 3H), 6.74 (s, 1H), 7.63 (d, *J* = 8.4 Hz, 2H), 7.68 (d, *J* = 8.4 Hz, 2H), 7.95 (d, *J* = 8.8 Hz, 2H), 8.05 (d, *J* = 8.8 Hz, 2H). ^{13}C NMR (CD_3COCD_3, 100 MHz, TMS) δ 21.1, 52.9, 69.4, 124.7, 129.1, 129.2, 129.4, 129.7, 130.5, 137.2, 137.7, 139.4, 140.4, 163.2, 168.6. IR (neat) ν 3102, 2922, 1730, 1704, 1476, 1366, 1285, 1170, 1084, 859, 827, 753 cm^{-1}. HRMS (ESI) calcd. for $C_{19}H_{20}Cl_2N_3O_7S_2$: 536.0114, found: 536.0114.

Compound *2f*: 72 mg, yield: 74%; yellow oil. ^{1}H NMR (CD_3COCD_3, 400 MHz, TMS) δ 1.87 (s, 3H), 3.75 (s, 3H), 6.75 (s, 1H), 7.37 (d, *J* = 8.8 Hz, 2H), 7.42 (d, *J* = 8.8 Hz, 2H), 8.04 (dd, *J* = 8.4, 5.2 Hz, 2H), 8.14 (dd, *J* = 8.4, 5.2 Hz, 2H). ^{13}C NMR (CD_3COCD_3, 100 MHz, TMS) δ 21.2, 52.9, 69.3, 116.0, 116.2, 116.4, 124.5, 129.7, 130.5 (d, $J_{C\text{-}F}$ = 9.7 Hz), 132.0 (d, $J_{C\text{-}F}$ = 13.6 Hz), 134.7 (d, $J_{C\text{-}F}$ = 2.9 Hz), 135.2 (d, $J_{C\text{-}F}$ = 3.2 Hz), 164.5 (d, $J_{C\text{-}F}$ = 52.6 Hz), 167.6 (d, $J_{C\text{-}F}$ = 54.2 Hz), 168.7. ^{19}F NMR (376 MHz, CD_3COCD_3, $CFCl_3$) δ -105.02 ~ -104.99 (m, 1F), -103.56 ~ -103.50 (m, 1F). IR (neat) ν 2913, 2851, 1733, 1590, 1493, 1364, 1154, 1086, 837, 690 cm^{-1}. HRMS (ESI) calcd. for $C_{19}H_{20}F_2N_3O_7S_2$: 504.0705, found: 504.0709.

Compound *2g*: 79 mg, yield: 65%; yellow oil. ^{1}H NMR (CD_3COCD_3, 400 MHz, TMS) δ 1.88 (s, 3H), 3.75 (s, 3H), 6.77 (s, 1H), 7.79 (d, *J* = 8.4 Hz, 2H), 7.84 (d, *J* = 8.4 Hz, 2H), 7.89 (d, *J* = 8.4 Hz, 2H), 7.98 (d, *J* = 8.4 Hz, 2H). ^{13}C NMR (CD_3COCD_3, 100 MHz, TMS) δ 21.1, 52.9, 69.4, 124.7, 128.1, 129.2, 129.6, 130.5, 132.2, 132.4, 137.7, 138.1, 163.2, 168.6. IR (neat) ν 3290, 1707, 1645, 1441, 1353, 1254, 1153, 1078, 833, 777 cm^{-1}. HRMS (ESI) calcd. for $C_{19}H_{20}Br_2N_3O_7S_2$: 623.9104, found: 623.9092.

Compound *2h*: 66 mg, yield: 56%; yellow oil. ^{1}H NMR (CD_3COCD_3, 400 MHz, TMS) δ 1.90 (s, 3H), 3.75 (s, 3H), 6.83 (s, 1H), 7.97 (d, *J* = 8.4 Hz, 2H), 8.01 (d, *J* = 8.4 Hz, 2H), 8.19 (d, *J* = 8.4 Hz, 2H), 8.28 (d, *J* = 8.4 Hz, 2H). ^{13}C NMR (CD_3COCD_3, 100 MHz, TMS) δ 21.0, 52.9, 69.6, 123.4 (q, $J_{C\text{-}F}$ = 275.0 Hz), 123.5 (q, $J_{C\text{-}F}$ = 270.5 Hz), 125.1, 126.2 (q, $J_{C\text{-}F}$ = 3.7 Hz), 126.4 (q, $J_{C\text{-}F}$ = 3.8 Hz), 128.2, 129.5, 129.6, 134.6 (q, $J_{C\text{-}F}$ = 32.7 Hz), 135.0 (q, $J_{C\text{-}F}$ = 32.5 Hz), 142.1, 142.6, 163.2, 168.5. ^{19}F NMR (376 MHz, CD_3COCD_3, $CFCl_3$) δ -58.67 (s, 3F), -58.57 (s, 3F). IR (neat) ν 3230, 1746, 1723, 1406, 1321, 1169, 1129, 1110, 1061, 842, 713 cm^{-1}. HRMS (ESI) calcd. for $C_{21}H_{20}F_6N_3O_7S_2$: 604.0641, found: 604.0649.

Compound *2i*: 62 mg, yield: 68%; yellow oil. ^{1}H NMR (CD_3COCD_3, 400 MHz, TMS) δ 1.85 (s, 3H), 3.71 (s, 3H), 6.72 (s, 1H), 7.57-7.61 (m, 2H), 7.62-7.65 (m, 2H), 7.67-7.70 (m, 2H), 7.73-7.77 (m, 2H), 7.95 (d, *J* = 7.6 Hz, 2H), 8.06 (d, *J* = 7.6 Hz, 2H), 9.21 (s, 1H). ^{13}C NMR (CD_3COCD_3, 100 MHz, TMS) δ 21.2, 52.8, 69.2, 124.2, 127.3, 128.5, 129.0, 129.2, 129.8, 133.7, 134.5, 138.7, 138.9, 163.2, 168.7. IR (neat) ν 3199, 1723, 1660, 1448, 1365, 1270, 1153, 1086, 878, 760 cm^{-1}. HRMS (ESI) calcd. for $C_{19}H_{22}N_3O_7S_2$: 468.0894, found: 468.0896.

Compound *2j*: 58 mg, yield: 60%; yellow oil. ^{1}H NMR (CD_3COCD_3, 400 MHz, TMS) δ 1.89 (s, 3H), 3.75 (s, 3H), 6.83 (s, 1H), 7.49 (td, *J* = 8.8, 2.4Hz, 1H), 7.56 (td, *J* = 8.8, 2.4Hz, 1H), 7.64-7.72 (m, 3H), 7.80 (d, *J* = 8.0 Hz, 2H), 7.90 (d, *J* = 8.0 Hz, 1H), 9.36 (s, 1H). ^{13}C NMR (CD_3COCD_3, 100 MHz, TMS) δ 21.0, 52.9, 69.5, 114.4 (d, $J_{C\text{-}F}$ = 24.7 Hz), 115.6 (d, $J_{C\text{-}F}$ = 25.4 Hz), 120.8 (d, $J_{C\text{-}F}$ = 21.2 Hz), 121,7 (d, $J_{C\text{-}F}$ = 21.2 Hz), 123.4 (d, $J_{C\text{-}F}$ = 3.3 Hz), 124.6 (d, $J_{C\text{-}F}$ = 3.3 Hz), 125.1, 129.5, 131.3 (d, $J_{C\text{-}F}$ = 7.8 Hz), 131.5 (d, $J_{C\text{-}F}$ = 8.0 Hz), 140.4 (d, $J_{C\text{-}F}$ = 7.4 Hz), 140.9 (d, $J_{C\text{-}F}$ = 6.9 Hz), 160.8 (d, $J_{C\text{-}F}$ = 36.0 Hz), 163.2, 163.3 (d, $J_{C\text{-}F}$ = 36.5 Hz), 168.5. ^{19}F NMR (376 MHz, CD_3COCD_3, $CFCl_3$) δ -110.67 (s, 1F), -110.46 (s, 1F). IR (neat) ν 3249, 1759, 1703, 1472, 1368, 1294, 1166, 780, 695, 679 cm^{-1}. HRMS (ESI) calcd. for $C_{19}H_{16}F_2N_2O_7NaS_2$: 509.0259, found: 509.0262.

Compound *2k*: 30 mg, yield: 28%; yellow oil. ^{1}H NMR (CD_3COCD_3, 400 MHz, TMS) δ 1.90 (s, 3H), 3.71 (s, 3H), 6.82 (s, 1H), 7.42-7.51 (m, 2H), 7.55-7.68 (m, 2H), 7.69-7.73 (m, 1H), 7.81-7.85 (m,1H). ^{13}C NMR (CD_3COCD_3, 100 MHz, TMS) δ 20.4, 52.9, 70.0, 117.4 (d, $J_{C\text{-}F}$ = 27.3 Hz), 118.7 (d, $J_{C\text{-}F}$ = 27.7 Hz), 119.3 (d, $J_{C\text{-}F}$ = 7.4 Hz), 119,5 (d, $J_{C\text{-}F}$ = 7.8 Hz), 122.9 (dd, $J_{C\text{-}F}$ = 24.1, 8.9 Hz), 124.1 (dd, $J_{C\text{-}F}$ = 24.1, 8.9 Hz), 126.5, 127.2 (dd, $J_{C\text{-}F}$ = 14.4, 7.7 Hz), 127.8 (dd, $J_{C\text{-}F}$ = 16.6, 7.4 Hz), 129.0, 153.9 (dd, $J_{C\text{-}F}$ = 17.9, 2.7 Hz), 156.3 (dd, $J_{C\text{-}F}$ = 21.1, 2.7 Hz), 156.5 (dd, $J_{C\text{-}F}$ = 18.6, 2.5 Hz), 158.8 (dd, $J_{C\text{-}F}$ = 18.6, 2.5 Hz), 163.4, 168.3. ^{19}F NMR (376 MHz, CD_3COCD_3, $CFCl_3$) δ -114.24- -114.04 (m, 2F), -113.03- -112.89 (m, 1F), -112.07- -112.01 (m, 1F). IR (neat) ν 3262, 1732, 1490, 1253, 1161, 1117, 1088, 820, 693, 661 cm^{-1}. HRMS (ESI) calcd. for $C_{19}H_{18}F_4N_3O_7S_2$: 540.0517, found: 540.0520.

Compound *2l*: 58 mg, yield: 60%; yellow oil. ^{1}H NMR (CD_3COCD_3, 400 MHz, TMS) δ 1.90 (s, 3H), 2.45 (s, 3H), 2.47 (s, 3H), 3.70 (s, 3H), 6.75 (s, 1H), 7.90-7.97 (m, 3H), 8.10 (d, *J* = 8.0 Hz, 1H), 8.50 (s, 1H), 8.57 (s, 1H). ^{13}C NMR (CD_3COCD_3, 100 MHz, TMS) δ 17.5, 17.6, 21.0, 52.7, 69.0, 122.3, 123.9, 125.6, 129.9, 138.2, 138.3, 138.6, 139.3, 150.5, 150.6, 152.9, 153.5, 163.2, 168.8. IR (neat) ν 2917, 1740, 1653, 1365, 1258, 1176, 1120, 1105, 874, 669 cm^{-1}. HRMS (ESI) calcd. for $C_{19}H_{21}N_4O_7S_2$: 481.0846, found: 481.0853.

Compound *2m*: 32 mg, yield: 34%; yellow oil. ^{1}H NMR (CD_3COCD_3, 400 MHz, TMS) δ 1.91 (s, 3H), 3.75 (s, 3H), 6.77 (s, 1H), 7.19-7.25 (m, 2H), 7.78-7.80 (m, 1H), 7.91-7.95 (m, 2H), 8.05-8.07 (m, 1H), 9.48 (s, 1H). ^{13}C NMR (CD_3COCD_3, 100 MHz, TMS) δ 21.1, 52.8, 69.6, 124.6, 127.5, 127.6, 129.6, 133.7, 133.9, 135.7, 135.9, 138.5, 138.9, 162.8, 168.6. IR (neat) v 3219, 1720, 1657, 1371, 1268, 1166, 1154, 1016, 862, 777 cm^{-1}. HRMS (ESI) calcd. for $C_{15}H_{18}N_3O_7S_4$: 480. 0022, found: 480.0025.

Compound *2n*: 86 mg, yield: 78%; yellow oil. ^{1}H NMR (CD_3COCD_3, 400 MHz, TMS) δ 1.88 (s, 3H), 3.57 (s, 3H), 6.84 (s, 1H), 7.66-7.72 (m, 4H), 7.88-8.05 (m, 6H), 8.09-8.13 (m, 2H), 8.59 (s, 1H), 8.66 (s, 1H), 9.29 (s, 1H). ^{13}C NMR (CD_3COCD_3, 100 MHz, TMS) δ 21.2, 52.7, 69.2, 122.1, 122.9, 124.4, 127.8, 127.9, 129.0, 129.2, 129.3, 129.6, 129.7, 129.8, 130.7, 131.7, 131.8, 135.1, 135.52, 135.56, 163.3, 168.8. IR (neat) v 3257, 2914, 1744, 1710, 1456, 1362, 1164, 1129, 1117, 813, 752 cm^{-1}. HRMS (ESI) calcd. for $C_{27}H_{26}N_3O_7S_2$: 568.1207, found: 568.1199.

Compound *2o*: 30 mg, yield: 46%; yellow oil. ^{1}H NMR (CD_3COCD_3, 400 MHz, TMS) δ 1.91 (s, 3H), 3.18 (s, 3H), 3.41 (s, 3H), 3.80 (s, 3H), 6.61 (s, 1H). ^{13}C NMR (CD_3COCD_3, 100 MHz, TMS) δ 26.7, 44.1, 46.0, 58.2, 74.8, 127.7, 135.6, 169.5, 174.3. IR (neat) v 3296, 1759, 1724, 1662, 1453, 1347, 1147, 1125, 983, 757 cm^{-1}. HRMS (ESI) calcd. for $C_9H_{14}N_2O_7NaS_2$: 349. 0135, found: 349.0132.

Compound *2p*: 48 mg, yield: 64%; yellow oil. ^{1}H NMR (CD_3COCD_3, 400 MHz, TMS) δ 1.07-1.121 (m, 6H), 1.33-1.36 (m, 2H), 1.88 (s, 3H), 2.83-2.88 (m, 1H), 3.06-3.12 (m, 1H), 3.77 (s, 3H), 6.63 (s, 1H), 8.79 (s, 1H). ^{13}C NMR (CD_3COCD_3, 100 MHz, TMS) δ 4.80, 4.82, 5.2, 5.8, 21.5, 30.1, 31.8, 52.8, 68.9, 122.9, 130.4 164.1, 169.0. IR (neat) v 3250, 1753, 1712, 1654, 1466, 1356, 1153, 1129, 885 cm^{-1}. HRMS (ESI) calcd. for $C_{13}H_{18}N_2O_7NaS_2$: 401. 0448, found: 401.0445.

Compound *2s*: 72 mg, yield: 73%; yellow oil. ^{1}H NMR (CD_3COCD_3, 400 MHz, TMS) δ 1.14 (t, *J* = 7.2 Hz, 3H), 1.83 (s, 3H), 2.40 (s, 3H), 2.43 (s, 3H), 4.10-4.23 (m, 2H), 6.65 (s, 1H), 7.39 (d, *J* = 8.4 Hz, 2H), 7.43 (d, *J* = 8.4 Hz, 2H), 7.83 (d, *J* = 8.4 Hz, 2H), 7.94 (d, *J* = 8.4 Hz, 2H), 9.11 (s, 1H). ^{13}C NMR (CD_3COCD_3, 100 MHz, TMS) δ 13.3, 20.6, 20.7, 21.1, 62.2, 69.2, 123.6, 127.4, 128.6, 129.5, 129.7, 129.8, 135.9, 136.1, 144.7, 145.7, 163.2, 168.2. IR (neat) v 3222, 2925, 1732, 1663, 1439, 1290, 1166, 1110, 1090, 813, 708 cm^{-1}. HRMS (ESI) calcd. for $C_{22}H_{28}N_3O_7S_2$: 510.1363, found: 510.1368.

Compound *2t*: 78 mg, yield: 70%; yellow oil. ^{1}H NMR (CD_3Cl, 400 MHz, TMS) δ 1.89 (s, 3H), 2.34 (s, 3H), 2.38 (s, 3H), 5.18 (q, *J* = 12.8 Hz, 2H), 6.46 (s, 1H), 7.10 (s, 1H), 7.17 (d, *J* = 8.0 Hz, 2H), 7.23 (d, *J* = 8.0 Hz, 2H), 7.28 (t, *J* = 4.0 Hz, 2H), 7.34-7.36 (m, 3H), 7.65 (d, *J* = 8.0 Hz, 2H), 7.91 (d, *J* = 8.0 Hz, 2H). ^{13}C NMR (CD_3Cl, 100 MHz, TMS) δ 21.5, 21.6, 21.9, 68.3, 69.7, 122.1, 127.0, 128.0, 128.4, 128.5, 128.8, 129.0, 129.4, 129.8, 134.6, 135.0, 135.1, 144.9, 145.6, 163.4, 168.2. IR (neat) v 3400, 2964, 1746, 1729, 1456, 1258, 1165, 1083, 844, 812, 799 cm^{-1}. HRMS (ESI) calcd. for $C_{27}H_{30}N_3O_7S_2$: 572.1520, found: 572.1521.

Compound *2u*: 83 mg, yield: 77%; yellow oil. ^{1}H NMR (CD_3COCD_3, 400 MHz, TMS) δ 1.94 (s, 3H), 2.38 (s, 3H), 2.43 (s, 3H), 6.85 (s, 1H), 7.05 (d, *J* = 8.0 Hz, 2H), 7.31 (t, *J* = 7.2 Hz, 1H), 7.38 (d, *J* = 8.0 Hz, 2H), 7.43-7.48 (m, 4H), 7.90 (d, *J* = 8.4 Hz, 2H), 7.99 (d, *J* = 8.4 Hz, 2H), 9.27 (s, 1H). ^{13}C NMR (CD_3COCD_3, 100 MHz, TMS) δ 20.6, 20.7, 20.9, 69.0, 121.3, 122.8, 126.3, 127.5, 128.4, 129.5, 129.7, 129.8, 130.4, 135.8, 136.0, 144.7, 145.9, 150.8, 163.1, 167.3. IR (neat) v 3286, 2921, 1719, 1653, 1368, 1177, 1153, 1067, 842, 739, 700 cm^{-1}. HRMS (ESI) calcd. for $C_{26}H_{28}N_3O_7S_2$: 558.1363, found: 558.1373.

Compound *2v*: 96 mg, yield: 81%; red oil. ^{1}H NMR (CD_3COCD_3, 400 MHz, TMS) δ 1.99 (s, 3H), 2.28 (s, 3H), 2.39 (s, 3H), 6.95 (s, 1H), 7.22 (dd, *J* = 8.0, 2.0 Hz, 1H), 7.35 (d, *J* = 8.0 Hz, 2H), 7.41 (d, *J* = 8.0 Hz, 2H), 7.51-7.60 (m, 3H), 7.91-8.03 (m, 7H), 9.26 (s, 1H). ^{13}C NMR (CD_3COCD_3, 100 MHz, TMS) δ 25.8, 25.9, 26.2, 74.3, 123.5, 125.8, 128.0, 131.3, 132.1, 132.7, 132.9, 133.1, 133.6, 133.8, 134.9, 135.0, 135.7, 136.9, 138.9, 141.0, 141.2, 149.9, 151.1, 153.6, 168.4, 172.7. IR (neat) v 2916, 1730, 1716, 1287, 1150, 1122, 1087, 816, 720, 702, 687 cm^{-1}. HRMS (ESI) calcd. for $C_{30}H_{26}N_2O_7NaS_2$: 613.1074, found: 613.1059**.**

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[18] CCDC 1913944 (for **2a**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre.

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Inorganic base-catalysis

Yan-Shun Zhang, Hou-Ze Gui, Yin Wei and Min Shi* _____

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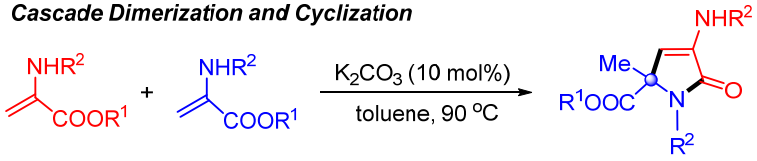
Cascade Dimerization and Cyclization



- *Simple operation and easily available materials*
- *Broad substrate scope and good functional tolerance*
- *Metal-free and atom-economic process*
- *Construction of quaternary carbon center*

20 examples
up to 84% yield

A Potassium Carbonate-Catalyzed Efficient and Straightforward Synthesis of Dihydro-2-oxopyrrole (DPO) Building Blocks

We have disclosed a novel and efficient inorganic base K_2CO_3-catalyzed cascade dimerization and cyclization reactions of 2-sulfonaminoacrylate derivatives to synthesize dihydro-2-oxopyrrole (DPO) derivatives in moderate to good yields in one step.