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Tandem multicomponent/click reactions: synthesis of functionalized oxazoles and tetrazoles from acyl cyanides

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Abstract—The combination of multicomponent condensations with post-condensation dipolar cycloaddition reactions provides a useful route to densely functionalized oxazoles and tetrazoles in just two synthetic steps.

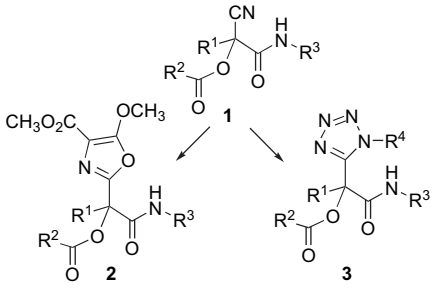
1. Introduction

In the past decade, multicomponent reactions (MCRs), have played an increasingly important role in the synthesis of drug candidates,[1] and especially heterocyclic compounds,[2] by facilitating access to whole libraries of structurally diverse compound family types for SAR studies. Several strategies have been developed to enhance the structural complexity that can be achieved using MCRs. For example, uniting two known MCRs led to a seven-component Asinger–Ugi coupling that produced pentasubstituted thiazoles.[3] Post-condensation modifications of MCR products by both intermolecular and intramolecular reactions have also been widely used to build out molecular complexity.[4]

The scope and versatility of click chemistry has recently been mined to introduce additional structural modifications to MCR products. For example, dihydropyrimidinones (DHPMs) prepared by the three-component Biginelli reaction have been subsequently functionalized with azide groups, thus setting the stage for an azide–alkyne coupling to create triazole-substituted DHPMs.[5] In a complementary strategy, several 2(1*H*)-pyrazinones prepared by multicomponent condensation were subsequently derivatized with alkyne groups in preparation for azide cycloadditions leading to triazolo-pyrazinones.[6]

We were interested in multicomponent reaction products that might directly undergo click reactions without intervening synthetic manipulations so as to streamline the overall process. To our knowledge, only one example of this type of two-step protocol has been described leading to a spirocyclic triazole.[7]

We recently reported that acyl cyanides undergo smooth Passerini condensations with carboxylic acids and isocyanides to afford products **1** (Scheme 1) that can be directly transformed into β-aminoacid diamide (β-peptide) structures.[8]



Scheme 1.

By combining that modified Passerini protocol with post-condensation dipolar cycloaddition reactions using either diazomalonic esters or alkyl azides, we here demonstrate that acyl cyanides may be transformed into functionally complex 1,3-oxazoles **2** or tetrazoles **3**, respectively. In the case of tetrazoles, the transposed sequence of reactions (click-then-MCR) provides an equally convenient route to target structures **3**.

Besides being active pharmacophores in their own right,[9] oxazole rings are found in a number of natural products, including virginiamycins,[10] disorazoles,[11] and ulapualides.[12] Tetrazoles function as peptide bond surrogates for the cis amide bond,[13] and have been incorporated into cis-constrained hydroxyethylamine isosteres as a new class of HIV-1 protease inhibitors.[14]

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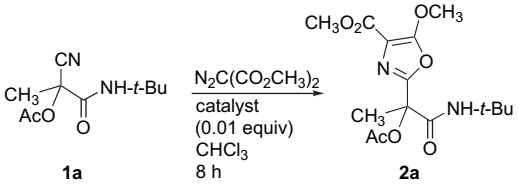
2. Results and discussion

Several years ago Helquist et al. developed a useful route to 4-carbomethoxy-5-methoxy-1,3-oxazoles by the transition metal-catalyzed dipolar cycloaddition of dimethyl diazomalonate with nitriles.[15] After investigating several catalysts for activity, the authors concluded that $Rh_2(OAc)_4$ afforded 1,3-oxazoles in the best yield. Because of possible side reactions involving the additional functionality in more complex nitriles like **1** we elected to screen a representative group of copper and rhodium complexes in cycloadditions of dimethyl diazomalonate using **1a**, prepared from pyruvonitrile, acetic acid and *tert*-butylisocyanide, as a test case (Scheme 2).



Scheme 2.

As the data in Table 1 indicate, $Rh_2(OAc)_4$ proved to be the catalyst of choice. The yield of oxazole **2a** was further improved to 52% using a catalyst loading of 0.05 equiv (instead of the 0.01 equiv used by Helquist) and 1.5 equiv of dimethyl diazomalonate added over 8 h.

Table 1. Catalyzed cycloadditions of $N_2C(CO_2CH_3)_2$ with **1a**

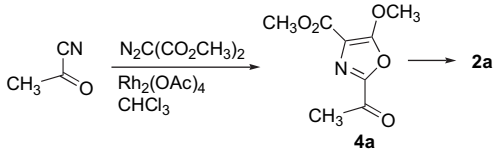
Catalyst	Temp (°C)	**2a** (% Yield)
$Cu(tfacac)_2$	45	0
$Cu(hfacac)_2$	70	20
$Cu(acac)_2$	70	25
$Rh_2(OAc)_4$	70	42

The scope of this cycloaddition was surveyed using representative examples of the Passerini-derived nitriles **1**. As data summarized in Table 2 indicate, the cycloaddition of dimethyl diazomalonate appears to accommodate a variety of substitution patterns in **1**.

Table 2. MCR/cycloaddition route to substituted oxazoles **2**

R^1	R^2	R^3	Product (% yield)
CH_3	CH_3	*t*-Bu	**2a** (52)
CH_3	CH_3	*n*-Bu	**2b** (50)
n-C_6H_{11}	$PhCH_2CH_2$	*n*-C_6H_{11}	**2c** (42)
CH_3	CH_3	EtO_2CCH_2	**2d** (31)

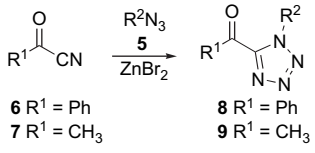
It was also of interest to determine whether the yield of products **2a–d** obtained by the two-step reaction sequence shown above might be improved by inverting the order of steps. Although dipolar cycloaddition reactions of diazomalonate with nitriles have been well-studied, comparable reactions with acyl cyanides have not been reported. To test this sequence, dimethyl diazomalonate (1 equiv–3 equiv) was added to a solution of pyruvonitrile and $Rh_2(OAc)_4$ (0.01 equiv–0.05 equiv) in $CHCl_3$ at reflux over 8 h. Concentration and flash chromatography of the product afforded the desired 2-methyl-4-carbomethoxy-5-methoxyacyloxazole **4a** (Scheme 3, 25%–40%) along with the diazoester-derived dimer, tetramethyl ethene-1,1,2,2-tetracarboxylate, which was co-eluted with **4a** and could not be separated using standard techniques. When reacted with acetic acid and *tert*-butylisocyanide, impure acyloxazole **4a** did afford substituted oxazole **2a**; however, the rate of Passerini condensation of the acyloxazole was significantly slower than that of the corresponding acyl cyanide. In view of that finding, the alternative route to oxazoles **2** was not pursued further.



Scheme 3.

We next explored the cycloaddition of Passerini-derived nitriles **1** with alkyl azides as a route to multiply-functionalized tetrazoles. Sharpless et al. have shown that such 'click chemistry' processes can be successfully applied to a wide range of nitriles,[16] including acyl cyanides.[17] However, attempted cycloaddition of either benzyl azide or cyclohexyl azide with nitrile **1a** in the presence of the standard zinc catalysts[18] led to recovered starting material in near-quantitative yield in all cases. We reasoned that the low reactivity of the nitrile group in **1a** was likely due to its sterically congested environment. Consequently, we decided to reverse the order of steps and first perform the click reaction on the acyl cyanide component.

Sharpless reported that acyl cyanides formed 1-substituted-5-acyltetrazoles by regioselective [2+3] cycloaddition when heated in slight excess (1.5 equiv) with azides neat at 120 °C. Benzoyl cyanide **6** (Scheme 4) cyclized cleanly with benzyl azide **5a** (R^2=Bn) to afford 1-benzyl-5-benzoyltetrazole **8a** (R^2=Bn).



Scheme 4.

However, Sharpless noted that acyl cyanides like pyruvonitrile **7** having a hydrogen at the α position were unstable during the prolonged heating required for tetrazole formation. We therefore developed an improved protocol for the formation of 5-acetyltetrazoles. The use of $ZnBr_2$ (1 equiv) made it possible to run the cycloaddition of **7** with benzyl azide (10 equiv) at rt, which improved the yield of 1-benzyl-5-acetyltetrazole **9a** (R^2=Bn, 65%) and increased the purity of the product.

This modified cycloaddition protocol for **7** was successful with several different azides and afforded 5-acetyltetrazoles

9 as summarized in Table 3. Reactions were run neat in a tightly capped vial for 48 h at rt. Stirring of the crude reaction mixture with aqueous potassium carbonate, extraction with ethyl acetate, and flash chromatography afforded the pure 5-acetyltetrazoles.

Table 3. Formation of 1-substituted-5-acetyltetrazoles **9**

5 (R^2=)	**9** (% Yield)
Bn	**9a** R^2=Bn (65)
C_8H_{17}	**9b** R^2=C_8H_{17} (73)
C_6H_{11}	**9c** R^2=C_6H_{11} (49)
PhCH=CHCH$_2$	**9d** R^2=PhCH=CHCH$_2$ (11)

The 5-acetyltetrazoles **9a–d** functioned as reactive carbonyl components in Passerini reactions using various carboxylic acids and isocyanides. The expected MCR products **3a–g** (Fig. 1) were obtained in moderate to good yields.

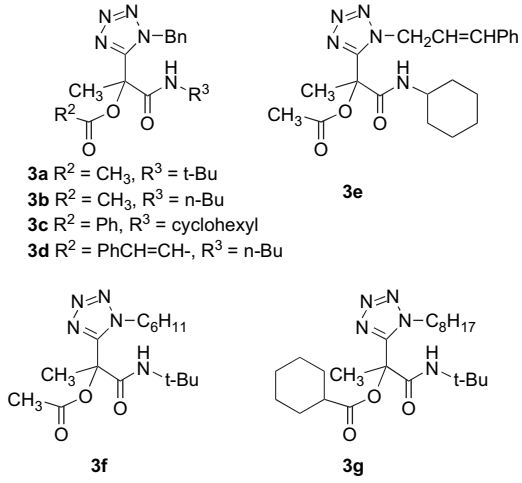


Figure 1.

In summary, we have shown that merging multicomponent condensations with dipolar cycloadditions can broaden the diversity of complex heterocycle-containing scaffolds that are readily accessible in two steps. Click chemistry reactions are easy to perform using readily available reagents that are insensitive to air and moisture, and thus are ideally suited partners for MCRs. The densely functionalized oxazole and tetrazole products described here represent just a few of the readily conceived examples of complexity-generating MCR-based strategies. Our findings suggest that there may be numerous opportunities to apply this approach to diversity-based chemical synthesis.

3. Experimental section

3.1. Representative procedure for the synthesis of substituted oxazoles 2a–d

3.1.1. Synthesis of 2a. A heterogeneous mixture of $Rh_2(OAc)_4$ (7.9 mg, 0.02 mmol), α-acyloxy-α-cyanoamide **1a** (76 mg, 0.36 mmol), and $CHCl_3$ (0.5 mL) was heated to reflux under argon. A solution of dimethyl diazomalonate (83 mg, 0.52 mmol) in $CHCl_3$ (0.3 mL) was gradually added to the reaction mixture over 8 h. After addition, the solution was cooled to rt and concentrated in vacuo. The remaining oil was purified by silica gel flash column chromatography (1:1 petroleum ether/ethyl acetate and 1:2 petroleum ether/ethyl acetate) to give a yellow oil (63 mg, 52%): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30 (s, 1H), 4.16 (s, 3H), 3.85 (s, 3H), 2.17 (s, 3H), 1.93 (s, 3H), 1.39 (s, 9H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 169.02, 166.29, 161.67, 161.52, 151.05, 106.75, 60.09, 51.94, 51.89, 28.55, 23.04, 21.40; IR (neat) 2957 (w), 2361 (w), 2255 (m), 1753 (m), 1719 (m), 1634 (m), 1522 (w), 1456 (w), 1398 (w), 1370 (w), 1221 (m), 1096 (m), 909 (s), 735 (s), 650 (m), 424 (w) cm^{-1}; CIMS (methane) *m/z*: 343 (M+H), 283.

3.1.2. Oxazole 2b. The product was purified by silica gel flash column chromatography (1:2 hexanes/ethyl acetate) to give a brown oil (35 mg, 50%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 (m, 1H), 4.17 (s, 3H), 3.86 (s, 3H), 3.33 (m, 2H), 2.18 (s, 3H), 1.92 (s, 3H), 1.56 (m, 2H), 1.38 (m, 2H), 0.94 (t, 3H, *J*=7 Hz); ^{13}C NMR (500 MHz, $CDCl_3$) δ 169.17, 167.30, 161.67, 161.61, 151.02, 106.85, 60.20, 52.00, 39.82, 31.53, 23.27, 21.36, 20.20, 13.92; IR (neat) 3435 (br), 2957 (m), 2874 (w), 1751 (w), 1721 (m), 1676 (m), 1630 (s), 1534 (m), 1456 (m), 1398 (m), 1233 (s), 1119 (m), 1078 (s) cm^{-1}; CIMS (methane) *m/z*: 343 (M+H), 283.

3.1.3. Oxazole 2c. The product was purified by silica gel flash column chromatography (3:1 hexanes/ethyl acetate and 1:1 hexanes/ethyl acetate) to give a yellow oil (22 mg, 42%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.64 (m, 1H), 7.19–7.30 (m, 5H), 3.86 (m, 7H), 3.00 (m, 2H), 2.83 (m, 2H), 0.78–2.09 (m, 21H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 172.17, 164.54, 161.61, 161.28, 150.84, 140.62, 128.67, 128.55, 126.45, 106.18, 81.90, 60.02, 51.99, 48.62, 46.88, 35.45, 32.66, 32.34, 30.62, 27.61, 26.92, 26.19, 26.08, 26.04, 25.81, 24.44; IR (neat) 3428 (br), 2930 (m), 2855 (w), 1748 (m), 1686 (m), 1634 (s), 1551 (w), 1452 (w), 1397 (w), 1250 (w), 1142 (w), 1090 (w), 980 (w), 637 (br) cm^{-1}; CIMS (methane) *m/z*: 527 (M+H), 377.

3.1.4. Oxazole 2d. The product was purified by silica gel flash column chromatography (1:3 hexanes/ethyl acetate and 1:5 hexanes/ethyl acetate) to give a green oil (16 mg, 31%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (m, 1H), 4.24 (q, 2H, *J*=7 Hz), 4.18 (s, 3H), 4.09 (t, 2H, *J*=5 Hz), 3.87 (s, 3H), 2.19 (s, 3H), 2.00 (s, 3H), 1.30 (t, 3H, *J*=8 Hz); ^{13}C NMR (500 MHz, $CDCl_3$) δ 169.37, 169.02, 167.75, 161.70, 161.64, 150.46, 106.99, 61.85, 60.25, 52.00, 41.89, 22.91, 21.32, 14.30; IR (neat) 3424 (br), 1719 (br), 1630 (s), 1541 (w), 1456 (w), 1398 (w), 1217 (m), 1078 (w), 1018 (w) cm^{-1}; CIMS (methane) *m/z*: 373 (M+H), 313.

3.2. Representative procedure for the synthesis of 5-acetyltetrazoles 9a–d

3.2.1. Synthesis of 9a. A one-dram vial was charged with benzyl azide (174 mg, 1.3 mmol), $ZnBr_2$ (304 mg, 1.3 mmol), pyruvonitrile (0.9 mL, 13 mmol), and a stirbar and tightly capped. The reagents were stirred vigorously for 48 h at rt. The reaction mixture was then poured in a round bottom flask containing 15 mL aqueous $NaHCO_3$.

The vial was rinsed with ethyl acetate (3×2 mL) and the rinses were added to the round bottom flask. The two-phase mixture was stirred overnight at rt. The organic layer was then isolated and the aqueous layer was extracted with ethyl acetate (2×10 mL). The combined organic layers were dried over $MgSO_4$. After filtration and concentration, the brown oil was purified by silica gel flash column chromatography (3:1 hexanes/ethyl acetate) to afford the known[19] **9a** as a yellow oil (171 mg, 65%).

3.2.2. Acetyltetrazole 9b. The product was purified by silica gel flash column chromatography (6:1 hexanes/ethyl acetate) to give **9b** as a colorless oil (73%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.70 (t, 2H, J=8 Hz), 2.86 (s, 3H), 1.89 (m, 2H), 1.29 (m, 10H), 0.88 (t, 3H, J=7 Hz); ^{13}C NMR (500 MHz, $CDCl_3$) δ 188.51, 149.27, 50.00, 31.81, 29.93, 29.14, 29.08, 29.00, 26.37, 22.73, 14.21; IR (neat) 3449 (br), 2928 (s), 2857 (m), 1713 (s), 1636 (br), 1491 (w), 1449 (m), 1362 (m), 1262 (w), 1128 (m), 963 (w), 637 (m) cm^{-1}; CIMS (methane) *m/z*: 225 (M+H).

3.2.3. Acetyltetrazole 9c. The product was purified by silica gel flash column chromatography (3:1 hexanes/ethyl acetate) to afford the known[19] **9c** as a white solid (49%).

3.2.4. Acetyltetrazole 9d. The product was purified by silica gel flash column chromatography (3:1 hexanes/ethyl acetate) to afford **9d** as a yellow oil (11%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26–7.38 (m, 5H), 6.74 (d, 1H, J=16 Hz), 6.31 (m, 1H), 5.47 (dd, 2H, J=1 Hz, 6 Hz), 2.86 (s, 3H); ^{13}C NMR (500 MHz, $CDCl_3$) δ 188.52, 149.15, 136.76, 135.48, 128.91, 128.90, 126.99, 120.61, 51.81, 29.05; IR (neat) 3455 (br), 3059 (w), 2928 (w), 1713 (s), 1647 (br), 1495 (m), 1441 (m), 1362 (m), 1252 (w), 1125 (m), 966 (m), 762 (m), 691 (m), 637 (m) cm^{-1}; CIMS (methane) *m/z*: 229.1 (M+H), 157, 117.

3.3. Representative procedure for the synthesis of substituted oxazoles 3a–g

3.3.1. Synthesis of tetrazole 3a. A vial was charged with **9a** (81 mg, 0.4 mmol), acetic acid (20 μL, 0.4 mmol), and a stir-bar and tightly capped. The reagents were stirred for 10 min at 0 °C whereupon *tert*-butyl isocyanide (50 μL, 0.4 mmol) was added. After stirring for 10 min at 0 °C, the reaction mixture was warmed to rt and stirred for 24 h. After evaporation, the crude oil was purified by silica gel flash column chromatography (1:1 hexanes/ethyl acetate) to give a colorless oil (80 mg, 58%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 (s, 1H), 7.35 (m, 3H), 7.10 (m, 2H), 5.71 (dd, 2H, J=16 Hz, 33 Hz), 1.97 (s, 3H), 1.75 (s, 3H), 1.39 (s, 9H); ^{13}C NMR (500 MHz, $CDCl_3$) δ 168.87, 166.28, 154.55, 133.96, 129.20, 128.69, 126.96, 52.31, 52.20, 28.55, 24.08, 20.69; IR (neat) 3370 (br), 2972 (m), 2251 (w), 1757 (s), 1690 (s), 1526 (s), 1456 (s), 1370 (s), 1217 (s), 1138 (m), 1096 (m), 1014 (w), 907 (w), 729 (s) cm^{-1}; CIMS (methane) *m/z*: 346 (M+H).

3.3.2. Tetrazole 3b. The product was purified by silica gel flash column chromatography (1:1 hexanes/ethyl acetate) to give a colorless oil (16 mg, 31%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (s, 1H), 7.35 (m, 3H), 7.12 (m, 2H), 5.72 (dd, 2H, J=16 Hz, 22 Hz), 3.32 (q, 2H, J=6 Hz), 1.97 (s, 3H), 1.79 (s, 3H), 1.55 (m, 2H), 1.36 (m, 2H), 0.93 (t, 3H, J=8 Hz); ^{13}C NMR (500 MHz, $CDCl_3$) δ 169.11, 167.35, 154.51, 133.91, 129.26, 128.79, 127.05, 52.38, 40.11, 31.46, 24.31, 20.71, 20.20, 13.90; IR (neat) 3351 (br), 2959 (m), 2874 (w), 1757 (s), 1682 (s), 1532 (m), 1456 (m), 1371 (m), 1219 (s), 1138 (m), 1015 (w), 947 (w), 878 (w), 729 (m), 604 (w) cm^{-1}; CIMS (methane) *m/z*: 346 (M+H), 304.

3.3.3. Tetrazole 3c. The product was purified by silica gel flash column chromatography (2:1 hexanes/ethyl acetate) to give a yellow oil (50 mg, 58%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (m, 1H), 7.84 (m, 2H), 7.58 (m, 1H), 7.39 (m, 2H), 7.19 (m, 3H), 7.02 (m, 2H), 5.64 (dd, 2H, J=16 Hz, 61 Hz), 3.80 (m, 1H), 1.97 (s, 3H), 1.90 (m, 1H), 1.74 (m, 2H), 1.61 (1H), 1.23–1.42 (m, 6H); ^{13}C NMR (500 MHz, $CDCl_3$) δ 166.38, 164.98, 154.68, 134.11, 133.49, 131.42, 130.15, 129.23, 129.19, 129.02, 128.73, 128.70, 128.46, 127.33, 127.00, 52.52, 49.34, 32.74, 32.66, 29.04, 25.64, 24.81, 24.75; IR (neat) 3437 (w), 3308 (m), 2936 (s), 2857 (m), 2253 (m), 1732 (s), 1682 (s), 1520 (m), 1452 (m), 1273 (s), 1103 (m), 1026 (w), 910 (s), 729 (s), 648 (m) cm^{-1}; CIMS (methane) *m/z*: 434 (M+H).

3.3.4. Tetrazole 3d. The product was purified by silica gel flash column chromatography (3:1 hexanes/ethyl acetate) to give a white solid (28 mg, 50%): mp=171–172 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (s, 1H), 7.53 (d, 1H, J=16 Hz), 7.41 (m, 5H), 7.20–7.31 (m, 3H), 7.12 (d, 2H, J=7 Hz), 6.14 (d, 1H, J=16 Hz), 5.72 (dd, 2H, J=16 Hz, 24 Hz), 3.34 (m, 2H), 1.97 (s, 3H), 1.57 (m, 2H), 1.38 (m, 2H), 0.94 (t, 3H, J=7 Hz); ^{13}C NMR (400 MHz, $CDCl_3$) δ 167.34, 165.05, 154.67, 147.63, 133.90, 133.88, 131.19, 129.14, 128.79, 128.58, 127.29, 115.62, 52.57, 40.17, 31.48, 24.59, 20.25, 13.93; IR (neat) 3410 (br), 3102 (w), 2926 (m), 2857 (m), 2368 (br), 1730 (s), 1682 (s), 1634 (s), 1530 (m), 1452 (m), 1422 (w), 1370 (w), 1331 (m), 1281 (w), 1204 (w), 1130 (s), 982 (w), 864 (w), 768 (m), 727 (s), 685 (w) cm^{-1}; CIMS (methane) *m/z*: 434 (M+H), 288.

3.3.5. Tetrazole 3e. The product was purified by silica gel flash column chromatography (1:1 hexanes/ethyl acetate) to give an off-white solid (12 mg, 40%): mp=149 °C–152 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 (m, 1H), 7.26–7.37 (m, 5H), 6.53 (m, 1H), 6.31 (m, 1H), 5.30 (dd, 2H, J=1 Hz, 5 Hz), 3.76 (m, 1H), 2.13 (s, 3H), 2.10 (s, 3H), 1.85–1.96 (m, 2H), 1.68–1.75 (m, 2H), 1.19–1.40 (m, 6H); ^{13}C NMR (500 MHz, $CDCl_3$) δ 169.36, 166.66, 154.50, 135.74, 135.26, 129.24, 129.07, 127.11, 121.55, 51.40, 49.66, 33.03, 32.92, 25.89, 25.08, 25.03, 24.65, 21.70; IR (neat) 3117 (br), 2934 (m), 2857 (w), 1755 (m), 1678 (s), 1526 (m), 1451 (w), 1406 (s), 1371 (w), 1219 (m), 1152 (w), 968 (w), 731 (w), 692 (w) cm^{-1}; CIMS (methane) *m/z*: 398 (M+H), 117.

3.3.6. Tetrazole 3f. The product was purified by silica gel flash column chromatography (3:1 hexanes/ethyl acetate and 1:1 hexanes/ethyl acetate) to give a white solid (9 mg, 28%): mp=138 °C–141 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 (s, 1H), 4.63 (m, 1H), 2.18 (s, 3H), 2.09 (s, 3H), 1.89–2.07 (m, 6H), 1.77 (m, 1H), 1.26–1.43 (m, 12H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 168.66, 166.23, 153.28, 59.74, 52.38, 33.60, 33.14, 28.57, 25.82, 25.71, 25.03, 24.38, 21.33; IR (neat) 3422 (br), 2938 (m), 2861 (w), 1753 (m),

1686 (s), 1638 (w), 1524 (m), 1456 (m), 1370 (m), 1215 (s), 1138 (m), 1094 (m), 1011 (w) cm^{-1}; CIMS (methane) *m/z*: 338 (M+H), 256.

3.3.7. Tetrazole 3g. The product was purified by silica gel flash column chromatography (6:1 hexanes/ethyl acetate) to give a colorless oil (13 mg, 28%): ^1H NMR (400 MHz, $CDCl_3$) δ 7.26 (s, 1H), 4.40 (m, 2H), 2.41 (m, 1H), 2.07 (s, 3H), 1.98 (m, 4H), 1.81 (m, 2H), 1.67 (m, 2H), 1.22–1.49 (m, 23H), 0.88 (t, 3H, J=7 Hz); ^{13}C NMR (400 MHz, $CDCl_3$) δ 173.92, 166.27, 154.18, 52.21, 49.43, 43.36, 31.91, 29.97, 29.29, 29.28, 29.14, 28.91, 28.58, 26.89, 25.75, 25.49, 25.43, 24.32, 22.80, 14.28; IR (neat) 3412 (br), 2930 (s), 2857 (s), 1761 (s), 1692 (s), 1518 (m), 1456 (m), 1368 (m), 1223 (m), 1121 (s), 1020 (w), 619 (w) cm^{-1}; CIMS (methane) *m/z*: 436 (M+H), 225.

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