Chemical Science

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Cite this: *Chem. Sci.*, 2015, **6**, 5964

Gold-catalyzed formal [4π + 2π]-cycloadditions of propiolate derivatives with unactivated nitriles†

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Received 1st June 2015
Accepted 17th July 2015

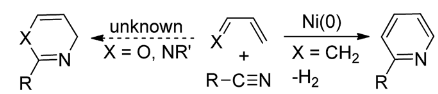
DOI: 10.1039/c5sc01950h

www.rsc.org/chemicalscience

Gold-catalyzed hetero-[4π + 2π]-cycloadditions of *tert*-butyl propiolates with unactivated nitriles are described; the resulting 6*H*-1,3-oxazin-6-ones are not easily accessible *via* conventional methods. This new finding enables a one-pot gold-catalyzed synthesis of highly substituted pyridines through sequential gold-catalyzed reactions of *tert*-butyl propiolates with nitriles, and then with electron-deficient alkynes in the same solvent. The utility of these [4 + 2]-cycloadditions is further expanded with various aldehydes, ketones and 2-phenyloxetane, yielding satisfactory yields of cycloadducts.

Introduction

Metal-catalyzed [4π + 2π]-cycloadditions are powerful tools for the construction of carbo- or heterocyclic frameworks.[1,2] Although common nitriles and alkynes represent common triple bond motifs, nitriles are generally less reactive than alkynes in catalytic [4π + 2π]-cycloadditions; the chemical stability of nitriles is reflected by their bond energy (854 kJ mol^{-1}), being larger than that of alkynes (835 kJ mol^{-1}).[3] For instance, thermal [4π + 2π]-cycloadditions of dienes with unactivated nitriles required 600 °C (2 min) to give pyridine derivatives in 0.1–0.5% yields.[4a] In the context of catalytic [4π + 2π]-cycloadditions, not surprisingly, only one literature report documents both nitrile/1,3-diene and nitrile/1,3-enyne systems (eqn (1) and (2)).[4b,c] Ogoshi reported the first formal [4 + 2]-cycloadditions of common nitriles with dienes using Ni(0) catalysts (eqn (1)).[4b] Although Barluenga and Aguilar reported formal [4π + 2π]-cycloadditions of some 3-en-1-ynes with unactivated nitriles,[4c] such highly functionalized 3-en-1-ynes (X = *cis*-unsaturated ester, Z = alkoxy) are too specialized to reflect the reaction generality (eqn (2)). The [4π + 2π]-nitrile cycloadditions still remain an unsolved task for O- and N-substituted analogues of 1,3-dienes and 1,3-enynes (X = O, NR′, eqn (1) and (2)).[5] In a significant advance, we here report the gold-catalyzed formal hetero-[4π + 2π]-cycloadditions[6,7] of various propiolates with nitriles to afford 6*H*-1,3-oxazin-6-ones efficiently (eqn (3)).[8] These findings enable the development of new cascade cycloadditions using three π-motifs including propiolates, nitriles and alkynes, yielding highly substituted pyridine derivatives. Notably, 6*H*-1,3-oxazin-6-ones are useful intermediates in various organic reactions whereas highly substituted pyridines are important structural cores commonly found in many bioactive molecules (see ESI Fig. S1†);[9,10] their availability from convenient *t*-butyl propiolates increases the synthetic utility of this gold catalysis.



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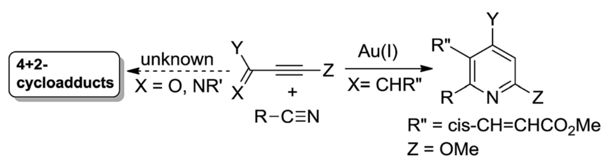

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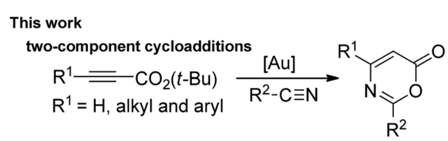

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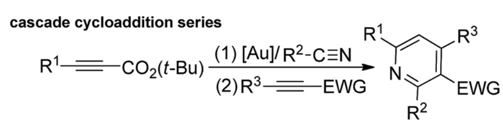

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Results and discussion

We envisage that direct [4π + 2π]-cycloadditions of propiolate derivatives with nitriles provide the most convenient synthesis of 6*H*-1,3-oxazin-6-ones such as **3**; the current procedures rely mainly on thermal rearrangement of *N*-acyl β-

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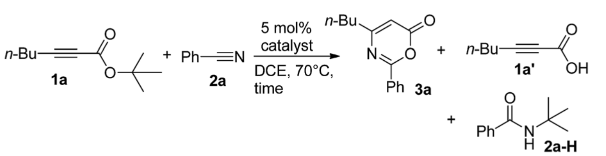
† Electronic supplementary information (ESI) available. CCDC 1062512, 1062513 and 1062772. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c5sc01950h

lactams.[8a–d] To test the feasibility, as shown in Table 1, *tert*-butyl hept-2-ynoate (**1a**, 1 equiv.) was treated with benzonitrile **2a** (3 equiv.) and $AuCl_3$ (5 mol%) in hot DCE (70 °C, 16 h), affording the desired product **3a** in only a small yield (5%) together with the initial **1a** in 45% recovery (entry 1). The use of $PPh_3AuCl/AgSbF_6$ significantly increased the yield of the desired **3a** to 51% (entry 2). We also examined other cationic gold catalysts (5 mol%) including $IPrAuCl/AgSbF_6$ and $P(t\text{-Bu})_2(o\text{-biphenyl})AuCl/AgSbF_6$, yielding compound **3a** in 64% and 85% yields, respectively (see entries 3 and 4). With the alteration of the silver salts as in $P(t\text{-Bu})_2$-(o-biphenyl)AuCl/AgX (X = NTf_2 and OTf), the product yields slightly decreased to 77% and 72%, respectively (entries 5 and 6). $AgSbF_6$ (70 °C, 24 h) and $Zn(OTf)_2$ (19 h) were found to be inactive in DCE, leading to a recovery of the starting compound **1a** in 72–75% yield (entries 7 and 8). The use of $In(OTf)_3$, $Sc(OTf)_3$ and TfOH in DCE gave hept-2-ynoic acid **1a′** in 65–72% yield and amide species **2a-H** (25–35% yield) along with unreacted starting compound **1a** (5–15% yield, entries 9–11). The yields of compound **3a** varied with the solvents (70 °C), with 65% in toluene (22 h), 82% in C_6H_5Cl (18 h) and 56% in 1,4-dioxane (19 h, entries 12–14).

Table 2 assesses the reaction generality using various propiolate derivatives with varied nitriles. We first examined the reactions with unsubstituted propiolate species **1b**; its cycloaddition with benzonitrile **2a** proceeded smoothly to form the formal cycloadduct **3b** in 65% yield (entry 1). The reaction scope is extensible to aliphatically substituted propiolate species **1c–1e** (R = isopropyl, cyclopropyl and cyclohexyl), yielding the desired products **3c–3e** in satisfactory yields (77–85%, entries 2–4). This formal cycloaddition is also applicable to alkenyl-substituted propiolate **1f** to afford the corresponding product **3f** in 68% yield (entry 5). We tested the reactions on various phenyl-substituted propiolate species **1g–1j** bearing various *para*-substituents (X = H, OMe, F and Cl); their resulting cycloadducts **3g–3j** were obtained in satisfactory yields (65–72%, entries 6–9). We performed an X-ray diffraction study of product **3g** to confirm its molecular structure.[11] We also prepared 2- and 3-thienyl-substituted propiolate derivatives **1k** and **1l**; their reactions with benzonitrile afforded cycloadducts **3k** and **3l** in reasonable yields (entries 10 and 11, 55–58%). Entries 12–15 show the tests of *tert*-butyl hept-2-ynoate **1a** with benzonitriles **2b–2e** bearing various *para*-substituents (X = OMe, Me, CO_2Me, Cl) that afforded the desired cycloadducts **3m–3p** in satisfactory yields (62–76%). These catalytic cycloadditions were compatible with disparate nitriles including cyclohexyl nitrile (**2f**), cinnamonitrile (**2g**) and 3-thienyl nitrile (**2h**), affording the expected products **3q–3s** in satisfactory yields (66–78%, entries 16–18).

As inferred from the chemistry of 2*H*-pyran-2-ones,[12,13] one representative compound **3a** (1 equiv.) was treated with diethyl but-2-ynedioate (4 equiv.) in hot *p*-xylene (150 °C, 10 h) to afford tetrasubstituted pyridine **5a** in 96% yield; this reaction sequence presumably proceeds with intermediate **I** that is prone to a loss of CO_2 (eqn (5)). As chlorobenzene is also an effective solvent for such a nitrile/propiolate cycloaddition (Table 1, entry 9), we developed a

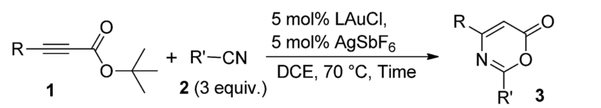
Table 1 Tests of propiolate derivatives with gold catalysts

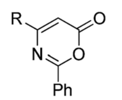


Entries	Catalyst	Solvent	Time (h)	Yields[a,b] (%) 1a	3a	1a′	2a-H
1	$AuCl_3$	DCE	16	45	5	—	—
2	$Ph_3PAuCl/AgSbF_6$	DCE	12	—	51	—	—
3	$IPrAuCl/AgSbF_6$	DCE	19	—	64	—	—
4	$LAuCl/AgSbF_6$	DCE	18	—	85	—	—
5	$LAuCl/AgNTf_2$	DCE	20	—	77	—	—
6	LAuCl/AgOTf	DCE	22	—	72	—	—
7	$AgSbF_6$	DCE	24	75	—		
8	$Zn(OTf)_2$[c]	DCE	19	72	—	—	—
9	$In(OTf)_3$[c]	DCE	18	15	—	72	35
10	$Sc(OTf)_3$[c]	DCE	22	10	—	65	32
11	HOTf[c]	DCE	15	5	—	67	25
12	$LAuCl/AgSbF_6$	Toluene	22	—	65	—	—
13	$LAuCl/AgSbF_6$	C_6H_5Cl	18	—	82	—	—
14	$LAuCl/AgSbF_6$	1,4-Dioxane	19	—	56	—	—

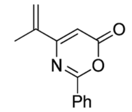
[a] [**1a**] = 0.18 M. [b] Product yields are reported after purification using a silica column. IPr = 1,3-bis(diisopropyl phenyl)-imidazol-2-ylidene, L = $P(t\text{-Bu})_2(o\text{-biphenyl})$, Tf = trifluoromethansesulfonyl. [c] Reactions carried out at room temperature.

Table 2 Formal cycloadditions of various propiolates with nitriles

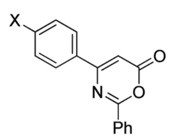




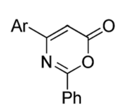
(1) R = H (**3b**, 17 h, 65%)[a,b]
(2) R = isopropyl (**3c**, 20 h, 77%)
(3) R = cyclopropyl (**3d**, 16 h, 85%)
(4) R = cyclohexyl (**3e**, 22 h, 82%)



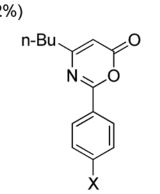
(5) **3f** (25 h, 68%)



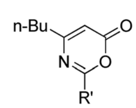
(6) X = H (**3g**, 24 h, 68%)
(7) X = OMe (**3h**, 24 h, 65%)
(8) X = F (**3i**, 19 h, 72%)
(9) X = Cl (**3j**, 20 h, 70%)



(10) Ar = 2-thienyl (**3k**, 35 h, 55%)
(11) Ar = 3-thienyl (**3l**, 35 h, 58%)



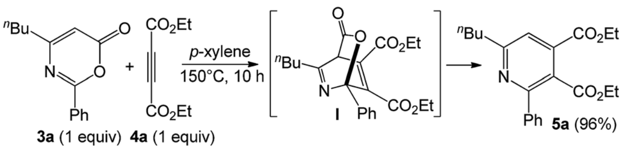
(12) X = OMe (**3m**, 16 h, 72%)
(13) X = Me (**3n**, 21 h, 76%)
(14) X = CO_2Me (**3o**, 24 h, 62%)
(15) X = Cl (**3p**, 25 h, 70%)



(16) R' = Cyclohexyl (**3q**, 25 h, 70%)
(17) R' = *trans*-styryl (**3r**, 48 h, 78%)
(18) R' = 3-thienyl (**3s**, 36 h, 66%)

[a] **2** (3 equiv.), [**1**] = 0.18 M. [b] Product yields are reported after purification using a silica column. L = $P(t\text{-Bu})_2(o\text{-biphenyl})$.

one-pot reaction involving the prior heating of a chlorobenzene solution of propiolate derivative **1a**, benzonitrile (3 equiv.) and P(t-Bu)$_2$(o-biphenyl) AuCl/AgSbF$_6$ (5 mol%) at 70 °C (18 h) in a sealed tube to ensure a complete consumption of starting compound **1a**; to this solution was added diethyl but-2-ynedioate (4 equiv.) with further heating at 150 °C for 20 h. This one-pot process delivered the desired pyridine **5a** in 80% yield (eqn (6)). If the three reactants in the same proportions were heated together with a gold catalyst in hot chlorobenzene (150 °C, 20 h), the yield of **5a** was decreased to 38% yield.



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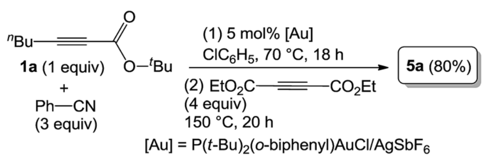
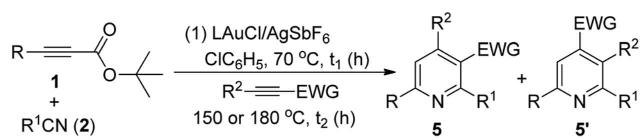


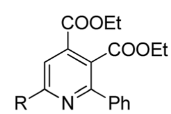
(6)

The easy operation of this one-pot reaction inspires us to examine the scope of the reaction using various propiolates, nitriles and alkynes; the results are summarized in Table 3. The procedures follow exactly that described in eqn (6). In the second stage of heating, the temperature is 150 °C for entries 1–7 and 180 °C for entries 8–12. Entry 1 shows the compatibility of these cycloadditions with unsubstituted propiolate derivative **1b** (R = H) that reacted sequentially with benzonitrile (**2a**) and diethyl but-2-ynedioate (**4a**) to yield the desired pyridine **5b** in 45% yield. We also tested the reactions on various alkyl-substituted propiolates **1c–1e** (R = isopropyl, cyclopropyl and cyclohexyl) that reacted with the same alkyne and benzonitrile to afford the desired pyridine species **5c–5e** in 73–76% yields (entries 2–4). The reaction is further applicable to aryl-substituted propiolates **1g** and **1l** (R = Ph, 3-thienyl) to deliver the desired pyridines **5f** and **5g** in 61% and 51% yield, respectively (entries 5 and 6). We tested the reactions of model propiolate (**1a**) and diethyl but-2-ynedioate (**4a**) with various nitriles (R^1 = cyclohexyl, 3-thienyl and *trans*-styryl), affording the expected pyridine products **5h–5j** in satisfactory yields (68–75%, entries 7–9). The reactions were extensible to various unsymmetric alkynes **4b–4f** that reacted with propiolate (**1a**) and benzonitrile (**2a**) with excellent or high regioselectivity (entries 11–15). The reactions worked well for terminal alkynes **4b** (EWG = COOMe) and **4c** (EWG = COPh) to afford the desired pyridines **5k** and **5l** as single regioisomers, with respective yields of 83% and 76% (entries 10 and 11). For n-butyl propiolate **4d**, this one-pot sequence gave two inseparable isomeric products **5m**/**5m′** = 4/1, in a combined 82% yield (entry 12). For the other n-butyl and phenyl-substituted ynones **4e** and **4f** (EWG = COPh), their reactions afforded **5n** and **5o** with excellent regioselectivity and satisfactory yields (81–84%) (entries 13–14). The structures of representative compounds **5m** and **5n** were confirmed by proton NOE effects whereas the structure of cycloadduct **5o** was elucidated with an HMBC experiment (see ESI†).

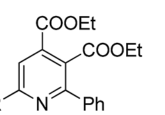
As nitriles are weakly nucleophilic, we envisage that aldehydes and ketones might be applicable substrates. To our pleasure, gold-catalyzed reactions of 3-phenylpropiolate **1g** with benzaldehyde, phenyl methyl ketone and acetone in hot dichloroethane (DCE) proceeded smoothly to afford formal cycloadducts **6a–6c** in high yields (86–89%, eqn (7)). The structure of compound **6a** was determined by X-ray diffraction.[11] These carbonyl cycloadditions were also applicable to alkyl-substituted propiolates (**1a**) and (**1e**), yielding the desired compounds **6d** and **6e** in 87% and 77% yield, respectively (eqn (8)). Such a reaction was, notably, accessible to an eight-membered oxacyclic compound **6f** with 2.5 mol% 1,3-bis(diisopropyl phenyl)-imidazol-2-ylidene AuSbF$_6$; it was isolated as a single regioisomer with 67% yield with 2-phenyloxetane (3 equiv.) and its molecular structure has been confirmed by X-ray diffraction.[11] The compatibility of this gold catalysis with aldehydes, ketones and oxetanes truly reflects a broad applicability of these cycloadditions.

Table 3 One-pot operations with nitriles, propiolates and alkynes

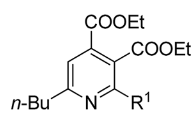




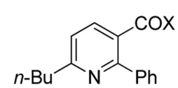
(1) R = H (**5b**, 17/20 h, 45%)[a,b]
(2) R = isopropyl (**5c**, 20/18 h, 74%)
(3) R = cyclopropyl (**5d**, 16/18 h, 76%)
(4) R = cyclohexyl (**5e**, 22/25 h, 73%)



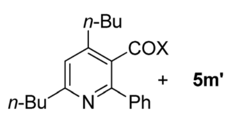
(5) R = Ph (**5f**, 24/20 h, 61%)
(6) R = 3-thienyl (**5g**, 35/27 h, 51%)



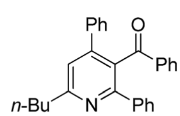
(7) R^1 = cyclohexyl (**5h**, 25/26 h, 75%)
(8) R^1 = 3-thienyl (**5i** 36/19 h, 68%)
(9) R^1 = *trans*-styryl (**5j**, 48/30 h, 72%)



(10) X = OMe (**5k**, 18/35 h, 83%)
(11) X = Ph (**5l**, 18/33 h, 76%)

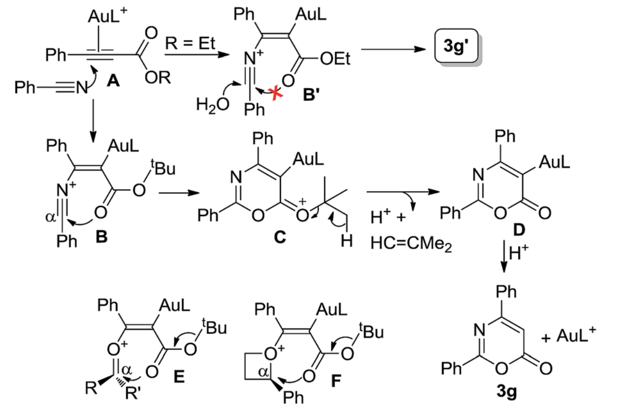


(12) X = OEt (**5m/5m′** = 4/1, 18/120 h, 82%)
(13) X = Ph ((**5n**, 18/47 h, 81%)

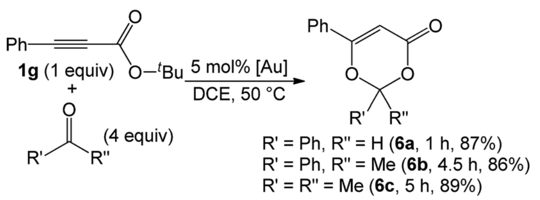


(14) **5o** (18/35 h, 84%)

[a] 5 mol% gold catalyst, L = P(t-Bu)$_2$(o-biphenyl), R^{1}CN (3 equiv.), R^{2}CC–EWG (4 equiv.), 150 °C for entries 1–9 and 180 °C for entries 10–14. [b] These data correspond to the reaction time t_1/t_2.



Scheme 1 A postulated reaction mechanism.



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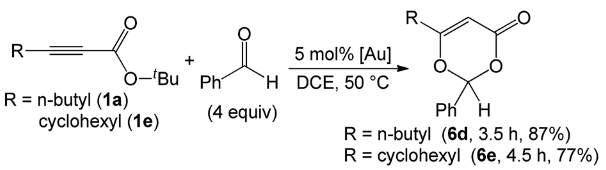

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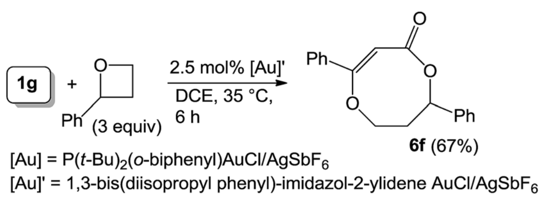
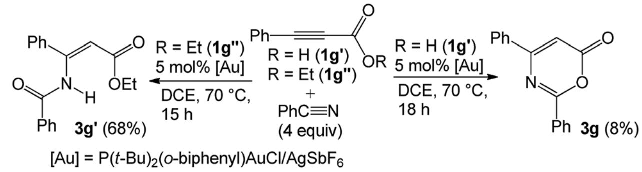


(9)

Prior to this work, Shin reported gold-catalyzed [4 + 2]-cycloadditions of alkenes with propiolic acid, which was, however, the only applicable substrate.[6a] Here, we employ diverse propiolate substrates to comply with not only nitriles but also aldehydes, ketones and oxetanes. To understand this discrepancy, we performed the reaction of 3-phenylpropiolic acid (**1g′**) with benzonitrile with the same gold catalyst in DCE, but the yield of the desired compound **1g** was only 8%, much smaller than that (68%) of its *tert*-butoxy derivative **1g** (Table 2, entry 5). Clearly, prior transformations of *t*-butoxy propiolates to the propiolate acids do not occur in the course of the reactions. For ethyl propiolate **1g″**, its corresponding reaction with benzonitrile gave the amide-addition product **3g′** in 68% yield (eqn (10)); under this condition, benzonitrile was not effectively transformed into benzamide with this gold catalyst.[14]



(10)

The control experiments in eqn (10) indicate a mechanism involving a prior formation of nitrilium species **B** *via* a π-alkyne activation, proceeding with an attack of nitrile at the gold-π-alkyne species **A**. As shown in Scheme 1, we postulate that the *tert*-butyoxy group of species **B** increases the nucleophilicity of a carbonyl group to attack this nitrilium moiety efficiently. This process releases a *tert*-butyl cation to induce a demetalation to form the observed cycloadduct **3g**. Beside nitriles, various aldehydes, ketones and oxetanes are more reactive than alkenes upon comparison of their applicable propiolates. We postulate that these nucleophiles generate intermediates **B**, **E** and **F** bearing a large positive charge on the reacting C_α-carbons because of their adjacent oxonium and ammonium centers. We envisage that the propiolate cycloadditions match well with those nucleophiles that can develop highly polarized carbocations through π-alkyne activations.

Conclusions

Unactivated nitriles are known to be stable triple-bond species, and their [4 + 2]-cycloadditions with 4π-bond motifs and other small molecules have few successful examples.[15] This work reports the hetero-[4π + 2π]-cycloadditions of *tert*-butyl propiolates and nitriles catalyzed by gold catalysts. Such formal cycloadditions are applicable to diverse *tert*-butyl propiolates and nitriles, yielding useful 6*H*-1,3-oxazin-6-ones, which are not readily prepared with current methods.[8] This new finding enables a one-pot gold-catalyzed synthesis of highly substituted pyridines through sequential reactions of *tert*-butyl propiolates with nitriles, and then with electron-deficient alkynes in the same solvent. The utility of these [4 + 2]-cycloadditions is further expanded with various aldehydes, ketones and 2-phenyloxetane, yielding satisfactory yields of cycloadducts. This work provides a new version of *tert*-butyl propiolates that feature useful four-atom building blocks with polar π-bond motifs such as nitriles, aldehydes and ketones, although their reactions with alkenes were reported to be restrictive.[8]

Acknowledgements

We thank the National Science Council, Taiwan, for financial support of this work.

Notes and references

1 For metal-catalyzed [4 + 2]-cycloaddition reactions, see selected reviews: (*a*) M. Lautens, W. Klute and W. Tam, *Chem. Rev.*, 1996, **96**, 49–92; (*b*) P. A. Inglesby and P. A. Evans, *Chem. Soc. Rev.*, 2010, **39**, 2791–2805; (*c*)

X. Jiang and R. Wang, *Chem. Rev.*, 2013, **113**, 5515–5546; (*d*) H. B. Kagan and O. Riant, *Chem. Rev.*, 1992, **92**, 1007–1019; (*e*) I. Bauer and H.-J. Knölker, *Chem. Rev.*, 2015, **115**, 3170–3387.

2 For gold-catalyzed cycloaddition reactions see: (*a*) M. E. Muratore, A. Homs, C. Obradors and A. M. Echavarren, *Chem.–Asian J.*, 2014, **9**, 3066–3082; (*b*) F. López and J. L. Mascareñas, *Chem. Soc. Rev.*, 2014, **43**, 2904–2915; (*c*) F. López and J. L. Mascareñas, *Beilstein J. Org. Chem.*, 2013, **9**, 2250–2264; (*d*) N. T. Patil and Y. Yamamoto, *Chem. Rev.*, 2008, **108**, 3395–3442; (*e*) A. S. K. Hashmi, *Chem. Rev.*, 2007, **107**, 3180–3211; (*f*) D. Qian and J. Zhang, *Chem. Rec.*, 2014, **14**, 280–302; (*g*) J. Francos, F. Grande Carmona, H. Faustino, J. Iglesias Sigüenza, E. Díez, I. Alonso, R. Fernández, J. M. Lassaletta, F. López and J. L. Mascareñas, *J. Am. Chem. Soc.*, 2012, **134**, 14322–14325; (*h*) H. Faustino, F. López, L. Castedo and J. L. Mascareñas, *Chem. Sci.*, 2011, **2**, 633–637; (*i*) N. Huguet, D. Leboeuf and A. M. Echavarren, *Chem.–Eur. J.*, 2013, **19**, 6581–6585; (*j*) A. Homs, C. Obradors, D. Leboeuf and A. M. Echavarren, *Adv. Synth. Catal.*, 2014, **356**, 221–228.

3 (*a*) S. J. Blanksby and G. B. Ellison, *Acc. Chem. Res.*, 2003, **36**, 255–263; (*b*) M. B. Smith and J. March, *March's Advanced Organic Chemistry*, 2007, 6th edn, p. 29.

4 (*a*) C. S. Marvel and J. C. H. Hwa, *J. Org. Chem.*, 1950, **15**, 525–529; (*b*) M. Ohashi, I. Takeda, M. Ikawa and S. Ogoshi, *J. Am. Chem. Soc.*, 2014, **133**, 18018–18021; (*c*) J. Barluenga, M. A. Fernández-Rodríguez, P. García-García and E. Aguilar, *J. Am. Chem. Soc.*, 2008, **130**, 2764–2765.

5 For the cycloadditions of 1,3-dienes with activated nitriles, see the following examples; most instances refer to stoichiometric reactions: (*a*) W.-T. Li, F.-C. Lai, G.-H. Lee, S.-M. Peng and R.-S. Liu, *J. Am. Chem. Soc.*, 1998, **120**, 4520–4521; (*b*) J. Chen, Q. Song, C. Wang and Z. Xi, *J. Am. Chem. Soc.*, 2002, **124**, 6238–6239; (*c*) H. Junge and G. Oehme, *Tetrahedron*, 1998, **54**, 11027–11032; (*d*) I. Hussain, M. A. Yawer, M. Lalk, U. Lindequist, A. Villinger, C. Fischer and P. Langer, *Bioorg. Med. Chem. Lett.*, 2008, **16**, 9898–9903.

6 Although gold-catalyzed reactions of propiolic acids with alkenes or alkynes were reported, the mechanisms were distinct from those of this work: (*a*) H.-S. Yeom, J. Koo, H.-S. Park, Y. Wang, Y. Liang, Z.-X. Yu and S. Shin, *J. Am. Chem. Soc.*, 2012, **134**, 208–211; (*b*) T. Luo, M. Dai, S.-L. Zheng and S. L. Schreiber, *Org. Lett.*, 2011, **13**, 2834–2836.

7 For gold-catalyzed cycloadditions of common nitriles with other small molecules, see: (*a*) S. N. Karad and R. S. Liu, *Angew. Chem., Int. Ed.*, 2014, **53**, 9072–9076; (*b*) W. He, C. Li and L. Zhang, *J. Am. Chem. Soc.*, 2011, **133**, 8482–8485; (*c*) Y. Xiao and L. Zhang, *Org. Lett.*, 2012, **14**, 4662–4665; (*d*) G. Lonzi and L. A. Lopez, *Adv. Synth. Catal.*, 2013, **355**, 1948–1954.

8 For reported synthetic procedures of 6*H*-1,3-oxazin-6-ones, see reported examples: (*a*) M. Alajarin, A. Vidal, P. Sánchez-Andrada, F. Tovar and G. Ochoa, *Org. Lett.*, 2000, **2**, 965–968; (*b*) M. Alajarin, P. Sánchez-Andrada, F. P. Cossio, A. Arrieta and B. Lecea, *J. Org. Chem.*, 2001, **66**, 8470–8477; (*c*) G. Cainelli, D. Giacomini, M. Gazzano, P. Galleti and A. Quintavalla, *Tetrahedron Lett.*, 2003, **44**, 6269–6272; (*d*) Z.-Y. Ge, Q.-M. Xu, X.-D. Fei, T. Tang, Y.-M. Zhu and S.-J. Ji, *J. Org. Chem.*, 2013, **78**, 4524–4529; (*e*) M. Chen, Z.-H. Ren, Y.-Y. Wang and Z.-H. Guan, *Angew. Chem., Int. Ed.*, 2013, **52**, 14196–14199; (*f*) A. D. Clark, W. K. Janowski and R. H. Prager, *Tetrahedron*, 1999, **55**, 3637–3648.

9 (*a*) L. Hedstrom, A. R. Moorman, J. Dobbs and R. H. Abeles, *Biochemistry*, 1984, **23**, 1753–1759; (*b*) R. L. Jarvest, M. J. Parratt, C. M. Debouck, J. G. Gorniak, J. L. Jennings, H. T. Serafinowska and J. E. Strickler, *Bioorg. Med. Chem. Lett.*, 1996, **6**, 2463–2466; (*c*) Q. Liu, P. Chen and G. Liu, *ACS Catal.*, 2013, **3**, 178–181; (*d*) M. Gütschow and U. Neumann, *Bioorg. Med. Chem.*, 1997, **5**, 1935–1942.

10 (*a*) A. M. F. Eissa and R. El-Sayed, *J. Heterocycl. Chem.*, 2006, **43**, 1161–1168; (*b*) U. Neumann, N. M. Schechter and M. Gütschow, *Bioorg. Med. Chem.*, 2001, **9**, 947–954; (*c*) P. Kopelman, A. Bryson, R. Hickling, A. Rissanen, S. Rossner, S. Toubro and P. Valensi, *Int. J. Obes.*, 2006, **31**, 494–499; (*d*) M. Baumann and I. R. Baxendale, *Beilstein J. Org. Chem.*, 2013, **9**, 2265–2319; (*e*) A. E. Goetz and N. K. Garg, *Nat. Chem.*, 2013, **5**, 54–60.

11 ESI†

12 For review, see: K. Afarinkia, V. Vinader, T. D. Nelson and G. H. Posner, *Tetrahedron*, 1992, **48**, 9111–9171.

13 (*a*) K. Kranjc, B. Štefane, S. Polanc and M. Kočevar, *J. Org. Chem.*, 2004, **69**, 3190–3193; (*b*) J. A. Reed, C. L. Schilling Jr, R. F. Tarvin, T. A. Rettig and J. K. Stille, *J. Org. Chem.*, 1969, **34**, 2188–2192; (*c*) Y. Kuninobu, H. Takata, A. Kawata and K. Takai, *Org. Lett.*, 2008, **10**, 3133–3135; (*d*) E. S. Kim, K. H. Kim, S. H. Kim and J. N. Kim, *Tetrahedron Lett.*, 2009, **50**, 5098–5101; (*e*) C. J. Moody, *J. Chem. Soc., Chem. Commun.*, 1984, 925–926.

14 In the absence of ethyl propiolate **1g′′**, treatment of benzonitrile with $P(t\text{-}Bu)_2(o\text{-biphenyl})AuCl/AgSbF_6$ (5 mol%) in hot DCE (70 °C, 15 h) gave benzamide in 34% yield with **1g′** recovered in 60% yield. A prior hydrolysis of benzonitrile could not be completed for the reaction in eqn (10).

15 Only one paper was noted for the [4 + 2]-cycloadditions of common nitriles with non-4π-conjugated species, see, B. A. Bhanu Prasad, A. Bisai and V. K. Singh, *Org. Lett.*, 2004, **6**, 4829–4831.