

Amines tuned controllable carbonylation for the synthesis of γ -lactones and 1,4-diones

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Yuanrui Wang^{1,2,5}, Youzhi Xu^{3,5}, Xin Qi^{1,2}, Le-Cheng Wang^{1,4}, Chao Xu^{1,2}, Genping Huang^{1,2,3}✉ & Xiao-Feng Wu^{1,2,4}✉

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In divergent carbonylative transformations using identical starting substrates, ligand-assisted transition metal catalysis has dominated selectively controllable transformations. However, achieving precise control of CO insertion in transition-metal-free systems remains a challenge. Herein, we disclose a divergent radical tandem carbonylation of multi-substituted homoallylic alcohols for the synthesis of γ -lactones and 1,4-diones. Utilizing quinuclidine as an electron donor steers the reaction towards lactonization, whereas the employment of DIPEA results in the migration of the aryl group to the carbonyl carbon. The key to tune the chemoselectivity lies in the ability of tertiary amines with different structures to precisely control the form of the active carbonyl intermediate, thereby inducing two distinct reaction pathways. Mechanistic studies reveal that the tertiary amine not only serves as an electron-transfer mediator but also functions as a tuner to govern chemoselectivity. The insights obtained from this study offer valuable enlightenment for selectively obtaining two types of carbonyl compounds, both advancing the performance exploring of electron donors in EDA complexes, fostering selective carbonylation development.

Embedding CO into small organic molecules provides an effective pathway for the construction of diverse molecular skeletons containing carbonyl functional groups^{1–6}. Obviously, selectivity-related challenges also gradually emerged with the development of carbonylation reactions. In particular, whether regioselectivity or chemoselectivity can be effectively controlled has become a common focus in the field of selective carbonylative synthesis^{7,8}. In the past few years, selective carbonylation^{9–12} (linear and branched) of unsaturated bonds represented by hydroformylation have achieved remarkable results. The practicality of these strategies can be attributed to the selective activation of the substrate by the ligand-chelated metal species^{13–15}. In these cases, whether the selectivity can be effectively controlled is often determined at the beginning stage of the reaction^{16,17} (Fig. 1a). For ligand-assisted metal-catalyzed systems, to enable the selective activation of diverse sites, its high demand on the specific steric and/or electronic properties of the ligands increasing the challenge of the

methodology. Therefore, there is an urgent need at present to develop innovative strategies for selective carbonylation in transition-metal-free systems. Whether there exists a key factor that can determine the direction of the carbonylation reaction by controlling the carbonyl intermediate in the late stage has triggered our meditation. The concept we envision is that different acyl intermediates induce the reaction in their respective channels. The challenge is how to obtain acyl intermediates with different reactivity in a controllable manner (Fig. 1b).

Over the past few years, organic transformations promoted by small organic molecules have provided complementary strategies for traditional transition metal-catalyzed coupling reactions, especially the exploration of electron donor-acceptor (EDA) complexes reaction system¹⁸, which has successfully attracted much attention of organic chemistry researchers^{19–22}. Triarylamines are electron-rich due to the presence of their lone pair electrons and are therefore often used in

¹Dalian National Laboratory for Clean Energy, Dalian Institute of Chemical Physics, Chinese Academy of Sciences, Dalian, Liaoning, China. ²University of Chinese Academy of Sciences, Beijing, China. ³Department of Chemistry, School of Science, Tianjin University, Tianjin, China. ⁴Leibniz-Institut für Katalyse e.V., Rostock, Germany. ⁵These authors contributed equally: Yuanrui Wang, Youzhi Xu. ✉ e-mail: gphuang@tju.edu.cn; xwu2020@dicp.ac.cn

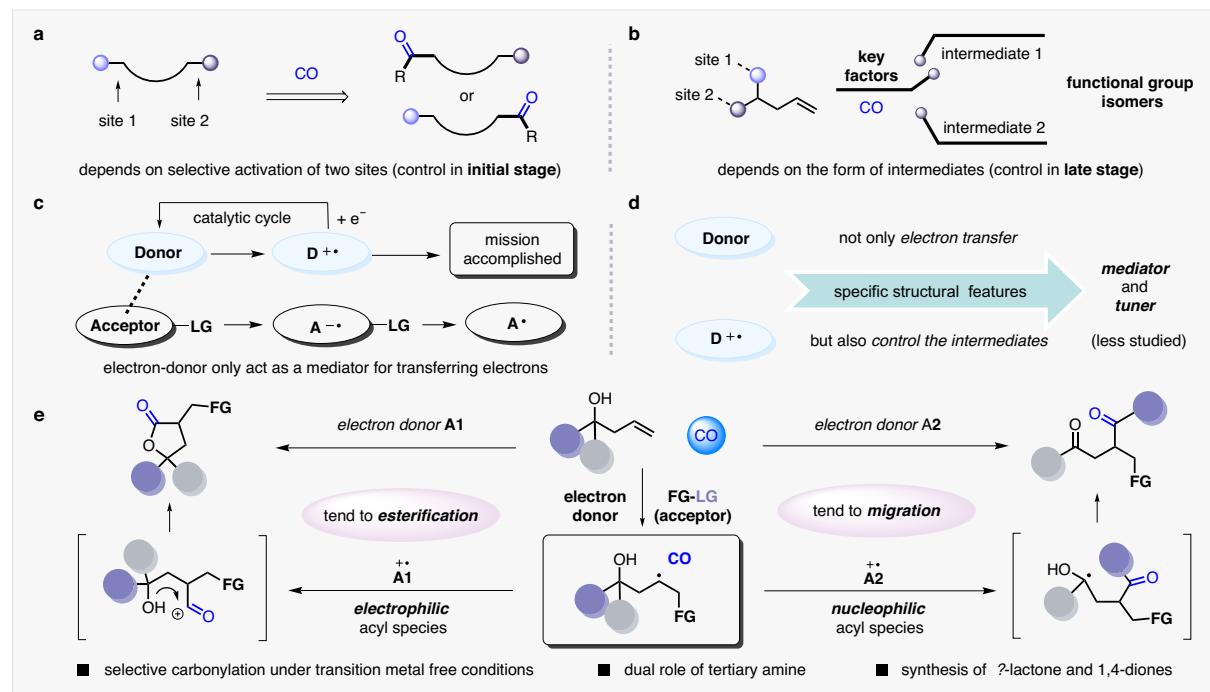


Fig. 1 | Chemoselective carbonylation and EDA chemistry related to amine species. **a** Tunable divergent carbonylation via site-selective activation strategy. **b** Our concept: chemoselective carbonylation enabled by controlling acyl intermediates. **c** Traditional EDA complex model in which amine species play a single

role. **d** Our design of dual functionality of amine species in EDA chemistry. **e** Tertiary amine regulated divergent carbonylation for the synthesis of 1,4-diones and γ -lactones.

EDA complexes as electron donors to induce the generation of radical species through single-electron transfer. For example, in 2022, Procter and co-workers developed an EDA complex for the alkylation and cyanation of arenes²³. In this system, newly designed amines act as an electron donor, promoting triarylsulfonium salts to produce aromatic radicals. Recently, Li's group also reported a novel EDA complex employing tris(4-methoxyphenyl) amine as a catalytic electron donor for the sulfonylation of alkenes²⁴. These representative studies demonstrated that amines have great development potential as electron donors in EDA complex chemistry^{25,26} (Fig. 1c). In traditional EDA chemistry, for tertiary amines, whether they act as a stoichiometric electron donor or a catalytic electron donor, during the reaction process, apart from undertaking the responsibility of electron transfer, they do not play an additional role, such as controlling the chemoselectivity of the reaction²⁷. The unique properties of amine cation radicals generated by tertiary amines with different structures have been ignored. Amine cation radicals with different electronic properties may become the key elements for controlling reaction intermediates. Especially in selective carbonylation transformations, if amines can not only transfer electrons but also play a second role in controlling the form of the acyl intermediate, it will provide a new platform for divergent carbonylation. (Fig. 1d). Although amine cation radicals show great potential in controlling the chemoselectivity of reactions, yet there remains less explored on tertiary amines that take on two functions in one process and achieve chemoselective transformations.

A variety of reactive carbonyl intermediates are the basis for achieving chemoselectivity in carbonylation reactions, but how to precisely control the production of a particular intermediate is a challenge. We try to overcome this obstacle, so we envision a model in which tertiary amines as electron donors. Carbon radical is produced by the EDA complex, then captures CO to obtain an acyl radical species. Meanwhile, the amine loses one electron and is transformed into

an amine radical cation, and the radical cations with different structures or electronic properties will determine the form of the acyl intermediate. Specifically, when the steric hindrance is small, the acyl radical species could be oxidized to acyl cations²⁸, but when the steric hindrance is large, the acyl radical could be exposed. While two active groups, a nucleophilic hydroxyl group and an aryl group that can be added by radical, competing in one molecule, the acyl intermediate will selectively react with one of them. Electrophilic acyl cations tend to undergo lactonization with the hydroxyl group, while nucleophilic acyl radicals tend to allow the aryl group to complete radical long-distance migration²⁹ (Fig. 1e).

Aryl-substituted homoallyl alcohol compounds, which can be obtained from various ketones through simple transformation, come into our view. The structural characteristics of both hydroxyl and aromatic groups make it the best choice for us to test the regulation of chemoselective carbonylation by controlling intermediates. Note that, although unsaturated alcohols have been widely studied in intramolecular cyclization and remote functional group migration reactions^{30–33}, homoallylic alcohols are not candidates for aromatic migration due to their short carbon chain. CO insertion enables intramolecular cyclization and remote group migration because of carbon chain can be extended. We expect to rely on the control of the acyl intermediate species by the electron donor to synthesize 1,4-diketones and γ -lactones from the same substrate, respectively. 1,4-diketones^{34–38} and γ -lactones^{39–41} are two important carbonyl-containing compounds that are isomers of each other, and their skeleton structures are widely present in natural products and drug molecules. This platform, which only relies on switchable tertiary amines as electron donors, offers valuable enlightenment for selectively obtaining two compounds containing different types of carbonyl functional groups, both advancing the performance exploring of electron donors in EDA complexes and fostering selective carbonylation development.

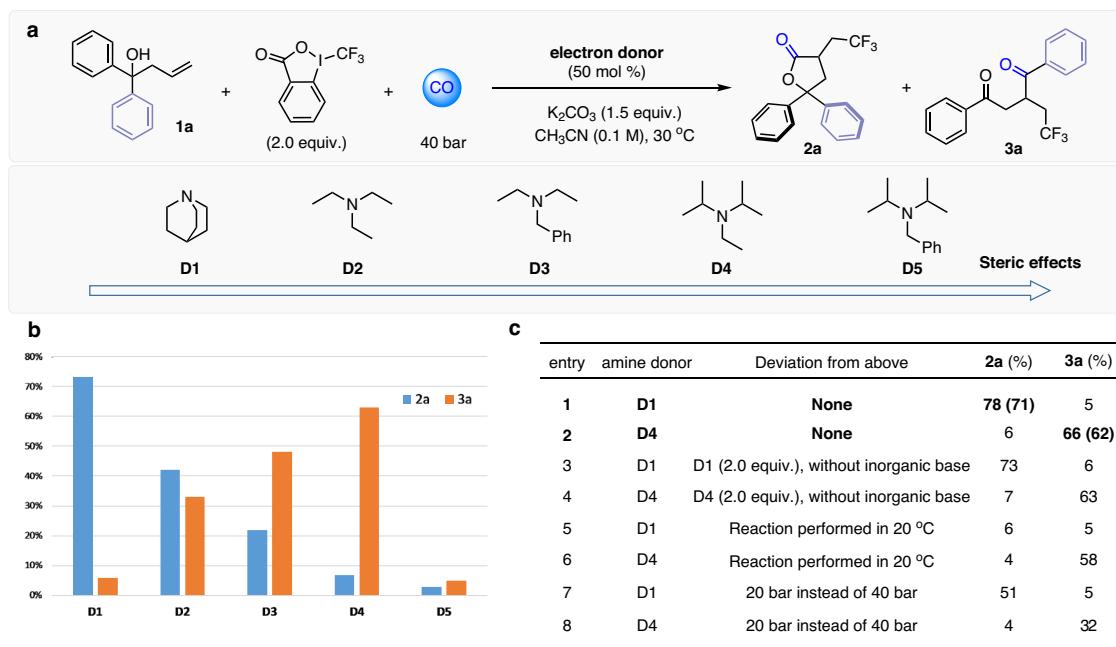


Fig. 2 | Optimization of the reaction conditions. **a** Reaction conditions: **1a** (0.2 mmol), Togni reagent (II) (0.4 mmol), donor (50 mol %), K_2CO_3 (1.5 equiv.) in solvent (2 mL) at 30 °C for 36 h under CO (40 bar). **b** Comparison of the effects of typical amines on selectivity between lactonization and migration. Reaction conditions: **1a** (0.2 mmol), Togni reagent (II) (0.4 mmol), donor (0.4 mmol), in solvent

(2 mL) at 30 °C for 36 h under CO (40 bar), yields were determined by GC-FID. **c** Effect of others on tunable chemoselective carbonylation, yields were determined by GC-FID analysis using *n*-hexadecane as internal standard. Isolated yields are given in brackets.

Results

To test the validity of chemoselective carbonylation utilizing tertiary amine, we selected amines and Togni's reagent (II)⁴² as EDA complex models to investigate the intramolecular cyclization and distant aromatic migration of homoallylic alcohol **1a** in the presence of CO (Fig. 2a and Supplementary Tables 1–4). We started our study by stirring a mixture of **1a**, Togni's reagent (II) (2 equiv.), and TEA (triethylamine) (2 equiv.) in MeCN under CO atmosphere at 30 °C for 36 h. As expected, the intramolecular cyclization product **2a** and the phenyl migration product **3a** were obtained simultaneously in 42% and 33% yields, respectively. The most immediate challenge facing us was controlling chemoselectivity (lactonization vs migration). We tested a series of organic amines with different structures (D1–D5), which are considered to be potentially effective to solve this problem. Surprisingly, we found that the type of amine essential to regulate the chemoselectivity in this transformation (Fig. 2b). The specific situation is **2a** was delivered in 73% yield with exquisite selectivity when D1 (quinuclidine, 2 equiv.) was employed as the electron donor in this system (Fig. 2c, entry 3). When the electron donor was replaced with D4 (DIPEA, 2 equiv.), **3a** was successfully obtained with a yield of 63% (Fig. 2c, entry 4). According to the ratio of **2a** and **3a**, it can be confirmed that the amine with a small steric hindrance can promote the lactonization process to obtain **2a**, while the amine with a large steric hindrance is conducive to the migration of the phenyl group to obtain **3a**. It has been preliminarily proved that the change of steric hindrance helps to tune the selectivity.

In addition, we also attempted to add more amines, both commercially available and newly designed (Please see Supplementary Table 1 for more details). We found an interesting phenomenon that greater steric hindrance is not always more favorable for the formation of **3a**. For example, the results of the experiment in the presence of D5 showed that when the steric hindrance is too large, both lactonization and aromatic rearrangement will be inhibited, and the starting materials will be completely recovered. We speculated that compared with DIPEA after the ethyl group is replaced by the benzyl group, the lone

pairs of electrons on the nitrogen atom are subjected to a stronger shielding effect, the formation of the EDA complex is hindered, which retards the single-electron transfer and thus no radicals are generated. It is worth noting that the amount of amine donor cannot exceed that of the electron acceptor (Togni's reagent (II)); otherwise, the reaction will be completely inhibited, regardless of whether D1 or D4 was used.

After screening the dosage of amines, the temperature test of lactonization conversion^{43–46} was also carried out, it was found that when the temperature was reduced to 20 °C, the reaction system was completely inactivated (Fig. 2c, entry 5), and when the temperature was increased to 50 °C, the selectivity control effect was slightly reduced. Notably, the two reaction pathways have different sensitivities to temperature. When D4 was used for rearrangement transformation, the yield of **3a** did not fluctuate significantly in the range of 20 °C to 50 °C.

Reducing the CO pressure⁴⁷ is not conducive to carbonylation conversion (whether lactonization or migration), which is mainly due to the difficulty in capturing alkyl radicals by CO (Fig. 2c, entries 7 and 8)^{48–50}. Finally, the loading of the amine donor could be appropriately reduced by adding an additional inorganic base, and the reaction efficiency can be marginally improved. In particular, only amines play a decisive role in the selectivity of carbonylation conversion in the whole process, thus revealing that the EDA system we designed is indeed a suitable system, which can achieve unusual chemoselective carbonylation reactions under transition metal-free conditions by relying on the characteristics of amines.

As the lactonization and migration conditions have been optimized, we assessed the ability of this protocol to discriminate between lactonization and migration products by preparing a series of substrates to explore the effects of aromatic ring substitution (Fig. 3). First, homoallylic alcohols substituted with two symmetrical aromatic rings are well tolerated, especially when the *para*-position of the aromatic ring contains the same substituent (such as the Me, OMe, halogen, OTs.), whether it is an electron-withdrawing group or an electron-donating group. In condition A, the lactonization products **2a**–**2g** were

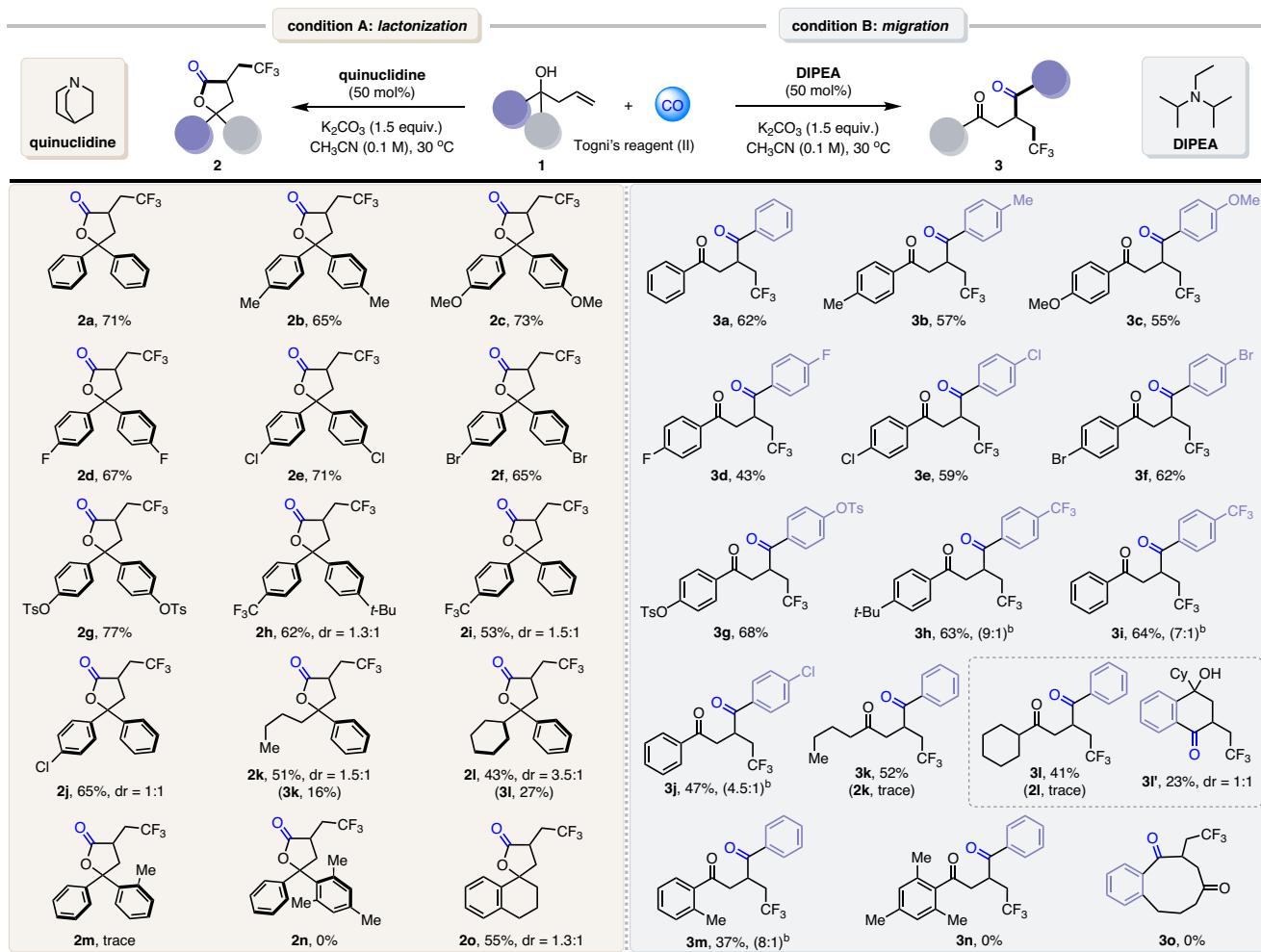


Fig. 3 | Scope of homoallylic tertiary alcohols in tunable carbonylation

reactions. ^aCondition A: **1** (0.2 mmol), Togni reagent (II) (0.4 mmol), quinuclidine (50 mol%), K_2CO_3 (1.5 equiv.) in CH_3CN (2 mL) at 30 °C for 36 h under CO (40 bar). Condition B: **1** (0.2 mmol), Togni reagent (II) (0.4 mmol), DIPEA (50 mol%), K_2CO_3

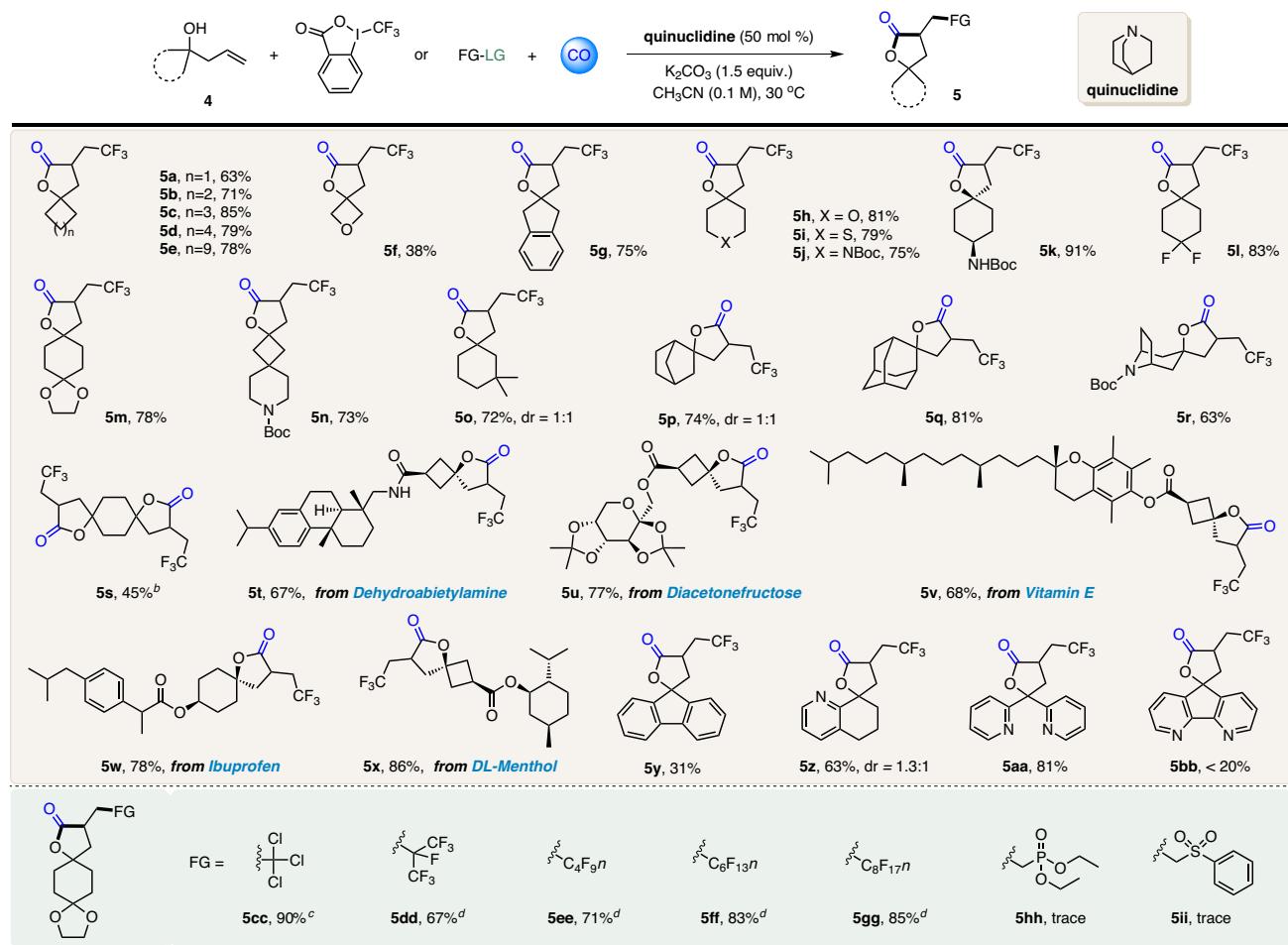
(1.5 equiv.) in CH_3CN (2 mL) at 30 °C for 36 h under CO (40 bar). ^bThe ratio of diastereoisomers (competition migration between two different aryl groups) was determined by ¹H NMR. The dr. ratio was determined by ¹H NMR. All yields are isolated yields.

delivered in 65–77% yields. In condition B, the migration products **3a**–**3g** were delivered in 43–68% yields. When the substituents on the substrate are replaced by two asymmetric aromatic rings, containing two different substituents at the *para*-position, **2h**–**2j** were obtained in 53–65% yields using the lactonization procedure. However, in the migration section, we found that there is a priority between the two asymmetric aromatic rings. For example, the ratio of electron-poor trifluoromethyl-substituted benzene ring to electron-rich *tert*-butyl substituted benzene ring is 9:1 (**3h**). However, the ratio of chlorine-substituted benzene rings to unsubstituted benzene rings is 4.5:1 (**3j**). This indicates that the more electron-deficient aromatic ring will migrate preferentially, and further extreme electronic effects of the two benzene rings are conducive to better selectivity. These results are consistent with the fact that acyl radicals are nucleophilic⁵¹. It's also important to mention that the diastereomers could not be separated to determine the major diastereomers for the compounds that have diastereomers due to their very similar polarity⁵².

Aside from double aromatic ring substitution, single aromatic ring substituted homoallylic alcohols were also used to perform exploration (**1k** and **1l**). **1k** was tested under condition A, lactone product **2k** was obtained in 51% and gave a 16% yield of the migration product **3k** (3.2:1 lactonization/migration). For cyclohexyl-substituted **1l**, the ratio of lactone products **2l** to migration products **3l** decreased to 1.6:1, but

2l was still the major product. Obviously, in condition A, alkyl substitution reduced the selectivity of lactonization. With condition B, **3l** and **3l'** can be obtained in moderate yield with good migration selectivity (52% and 41%). It is noteworthy that we isolated the acyl radical homolytic aromatic substitution product **3l'** in 23% yield. We speculate that the alkyl substitution hinders the *ipso*-addition of the acyl radical to the aromatic ring, so the acyl group was directly introduced into the benzene ring to complete the cycloketonization.

Interestingly, lactonization is more sensitive to the steric hindrance of the substrate than migration. When a methyl group was introduced at the *ortho*-position of one of the benzene rings of the model substrate **1a**, the lactonization was almost completely inhibited, only trace amounts of the target product **2m** were detected, and the raw material **1m** was recovered. Even increasing the reaction temperature could not overcome this obstacle. Although migration is also affected, **3m** can still be obtained at a yield of 37%. The benzene ring with less steric hindrance has an advantage over the competition for migration. Further increasing the steric hindrance of the substrate, such as **2n**, no matter which conditions are used, it cannot be made reactive, lactonization and migration are both completely inhibited. When we tried the cyclic substrates **1o**, surprisingly, the spiroolactone product **2o** could be obtained under condition A, but ring expansion by migration seemed extremely difficult.

**Fig. 4 | Scope of homoallylic tertiary alcohols in carbonylative lactonization.**

^aReaction conditions: **4** (0.2 mmol), Togni reagent (II) (0.4 mmol), quinuclidine (50 mol %), K_2CO_3 (1.5 equiv.) in CH_3CN (2 mL) at 30 °C for 36 h under CO (40 bar).

^b**4s** (0.2 mmol), Togni reagent (II) (0.8 mmol), quinuclidine (0.4 mmol), in solvent (2 mL) at 30 °C for 36 h under CO (40 bar). ^c**4m** (0.2 mmol), CCl_4 (2 mmol),

quinuclidine (0.4 mmol), CH_3CN (2.0 mL, 0.1 M), CO (40 bar), 390 nm LED (45 W), rt. and 24 h. ^d**4m** (0.2 mmol), R_FI (0.4 mmol), quinuclidine (0.4 mmol), Et_2O (2.0 mL, 0.1 M), CO (40 bar), white LED (30 W), rt. and 24 h. The dr. ratio was determined by 1H NMR. dr. diastereomeric ratio. All yields are isolated yields.

Inspired by the spironolactone **2o** obtained from **1o**, we next turned our attention to the spirolactonization promoted by quinuclidine. γ -Lactone fragment is found in myriad pharmaceuticals and natural biological molecules. Especially spironolactone, has a special efficacy in the treatment of certain diseases, such as spironolactone can be used to treat heart failure⁵³. Although some methods have been developed to synthesize spironolactones^{52,54}, existing strategies are difficult to avoid preparation for complex substrates or dependence on transition metal catalysis. The inside-out cyclization of α -oxygenated radicals is based on oxalyl chloride as the carbonyl source. However, there are less studies on utilizing cheap CO to construct spironolactone in transition-metal-free conditions (Fig. 4).

Relying on a quinuclidine-promoted lactonization strategy, we synthesized a series of cycloalkyl-substituted homoallyl alcohols **4** from cyclic ketones to produce a wide variety of spirolactonization products **5**. Trifluoromethyl-substituted γ -lactones with 4, 5, 6, 7, and even 12-membered carbon rings can be obtained in moderate to good yields (**5a**–**5e**, respectively). Oxetane-containing spirocyclic lactones **5f** that are difficult to construct by other methods can be synthesized using this strategy. 2-Indanone derivatives can also be used to construct spironolactone **5g**, containing aromatic rings. Six-membered heterocyclic rings containing oxygen, sulfur, or nitrogen also show good compatibility, spiro- γ -lactones (**5h**–**5j**) obtained in excellent

yields, requiring only the corresponding alcohols derived from cyclic ketones. When the *para*-position of the 6-membered carbon ring contained an amino or fluorine functional group, **5k** and **5l** were synthesized in 91% and 83% yields, respectively. Polycyclic and endocyclic structures are very attractive, so we hope to use this approach to introduce structures with important synthetic values, such as adamantane and tropane, into spironolactones. Fortunately, we successfully obtained products **5m**–**5r**. When the substrate contains two cyclization sites, molecule **5s** containing two lactone fragments can be constructed in one step. In addition, some complex substrates containing bioactive molecular fragments could also be employed, allowing for the formation of spironolactones **5t**–**5x** in good yields. Notably, **5aa** has two pyridine groups derived from di-2-pyridyl ketone, which is a potential ligand for selective C-H activation⁵⁵. Finally, by simply adjusting the conditions, we can replace the radical precursor and expand the types of radicals to trichloromethyl and various perfluoroalkyl (**5cc**–**5gg**).

To further demonstrate the practicality of using DIPEA as an electron donor to initiate remote group migration, after completing the above-mentioned studies, we attempted to replace the migrating group with a heterocycle (Fig. 5). Considering that heteroaryl groups are generally electron-deficient, the addition of the nucleophilic acyl radical to the heterocycle for dearomatization is more advantageous⁵⁶.

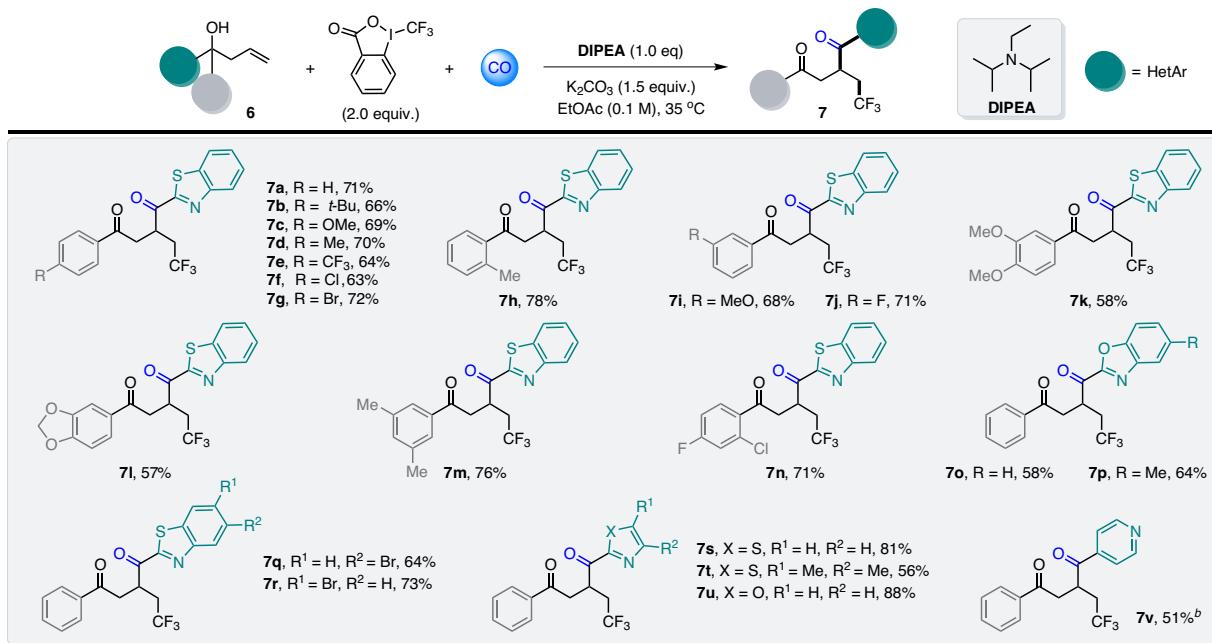


Fig. 5 | Scope of homoallylic tertiary alcohols in carbonylative heteroaryl migration. ^aReaction conditions: **6** (0.2 mmol), Togni reagent (II) (0.4 mmol), DIPEA (1.0 equiv.), K_2CO_3 (1.5 equiv.) in EtOAc (2 mL) at 35°C for 24 h under CO (40 bar). ^b**6v** (0.2 mmol), Togni reagent (II) (0.6 mmol), DIPEA (0.2 mmol), K_2CO_3 (1.5 equiv.) in EtOAc (2 mL) at 35°C for 48 h under CO (40 bar). All yields are isolated yields.

We anticipate that heterocycles will undergo remote migration more rapidly than benzene rings. Under condition B, substrate **6a** containing benzothiazole and phenyl groups was employed for the preliminary test. The results showed that benzothiazole had an absolute advantage in undergoing remote migration, and the target product **7a** was successfully obtained, which was consistent with our expectations. To facilitate the full conversion of raw materials, appropriate modifications were made to migration condition B. The solvent was changed from MeCN to EtOAc, and the reaction temperature was raised to 35°C . Subsequently, we investigated the influence of modifying the phenyl group on the homoallylic alcohol substrate. The experimental results show that benzothiazole is the only object to be migrated, not the benzene ring (**7a–7n**). In addition, there are neither lactone products nor ketone products generated from the homolytic aromatic substitution of acyl radicals. Other heterocycles, including benzoxazole, thiazole, oxazole, and pyridine, have been demonstrated to undergo the same type of selective migration (**7o–7v**). The transfer of the heterocyclic ring to the acyl carbon always has an absolute advantage. This provides evidence that acyl radicals are the most efficient reactive acyl intermediates in the presence of DIPEA. As the migrated groups expand from aromatic to heteroaromatic groups, the applicability of this emerging DIPEA-promoted carbonylation migration platform is further confirmed.

To probe the possible radical mechanism, we added radical inhibitor TEMPO (2,2,6,6-tetramethyl-1-piperidinyloxy) to standard conditions A and B, respectively. As predicted, both the lactonization and migration processes were completely inhibited; no **2a** and **3a** were detected, and the raw material **1a** was completely recovered (Fig. 6a). We also designed and synthesized but-3-ene-1,1-diylbenzene **8** as a radical receptor and attempted to capture the acyl intermediate produced by carbonylation. Indeed, product **9** provides evidence for the existence of an acyl radical intermediate in condition B (Fig. 6b)⁵⁷. To explore our mechanistic hypothesis and quantitatively assess the role of the donor in promoting lactonization or migration, we examined the yield distributions of **2a** and **3a** over a range of D1/D4 donor mixtures. An initial experiment using 1:1 mixture of D1/D4 as donor

demonstrated that can give an approximate yield of **2a** and **3a** (1:1:1 lactonization/migration). Obviously, mixtures of D1/D4 demonstrated lower chemoselectivity compared to D1 or D4 alone when employed as donors. Lowering the ratio of D1/D4 to 1:3 increased production of **3a** (43%) and decreased the yield **2a** (28%), enhancing the ratio of D1/D4 to 3:1 increased production of **2a** (58%) and decreased the yield **3a** (26%). The ratio of lactonization products to migration products was positively correlated with the dosage of D1 and D4, which showed that D1 was beneficial to the lactonization process, while D4 was beneficial to the migration process. We can infer that lactonization and migration are two independent processes that do not interfere with each other, and the selectivity is mainly regulated by the amine as an electron donor (Fig. 6c).

To further illustrate how different electron donors regulate the reaction process, we performed cyclic voltammetry tests on four amines D1–D4. D1 (quinuclidine) showed an oxidation potential peak at $E_p = 1.33$ V vs. Ag/AgCl (blue line; Fig. 2d), which is higher than the oxidation potential of D4 (DIPEA, $E_p = 1.12$ V vs. Ag/AgCl (orange line; Fig. 2d)). The higher oxidation potential of D1 means that its cation radical has a stronger oxidizing ability. The lactonization process may go through an acyl carbon cation intermediate, which is obtained by the oxidation of the acyl radical by the amine cation radical. Although all amines D1–D4 have redox potentials of 1.12–1.39 V (vs. Ag/AgCl), it seems that they are capable of oxidizing acyl radicals to acyl cations^{58–63}. We speculate that, compared with other amines, the relatively constrained cyclic geometric structure of the quinuclidine radical cation allows it to easily immediately undergo single-electron transfer. Its unique structure determines that quinuclidine is the only electron donor that exhibits excellent intramolecular esterification selectivity.

Density functional theory (DFT) calculations were conducted to gain deeper insights into the reaction mechanism and the origins of selectivity (Fig. 6e, and see Supplementary Fig. 3 for more details). Based on the analysis of the aforementioned results, DFT calculations, and related studies, the plausible reaction mechanisms are summarized in Fig. 6f. CF_3 radical and tertiary amine radical cation were

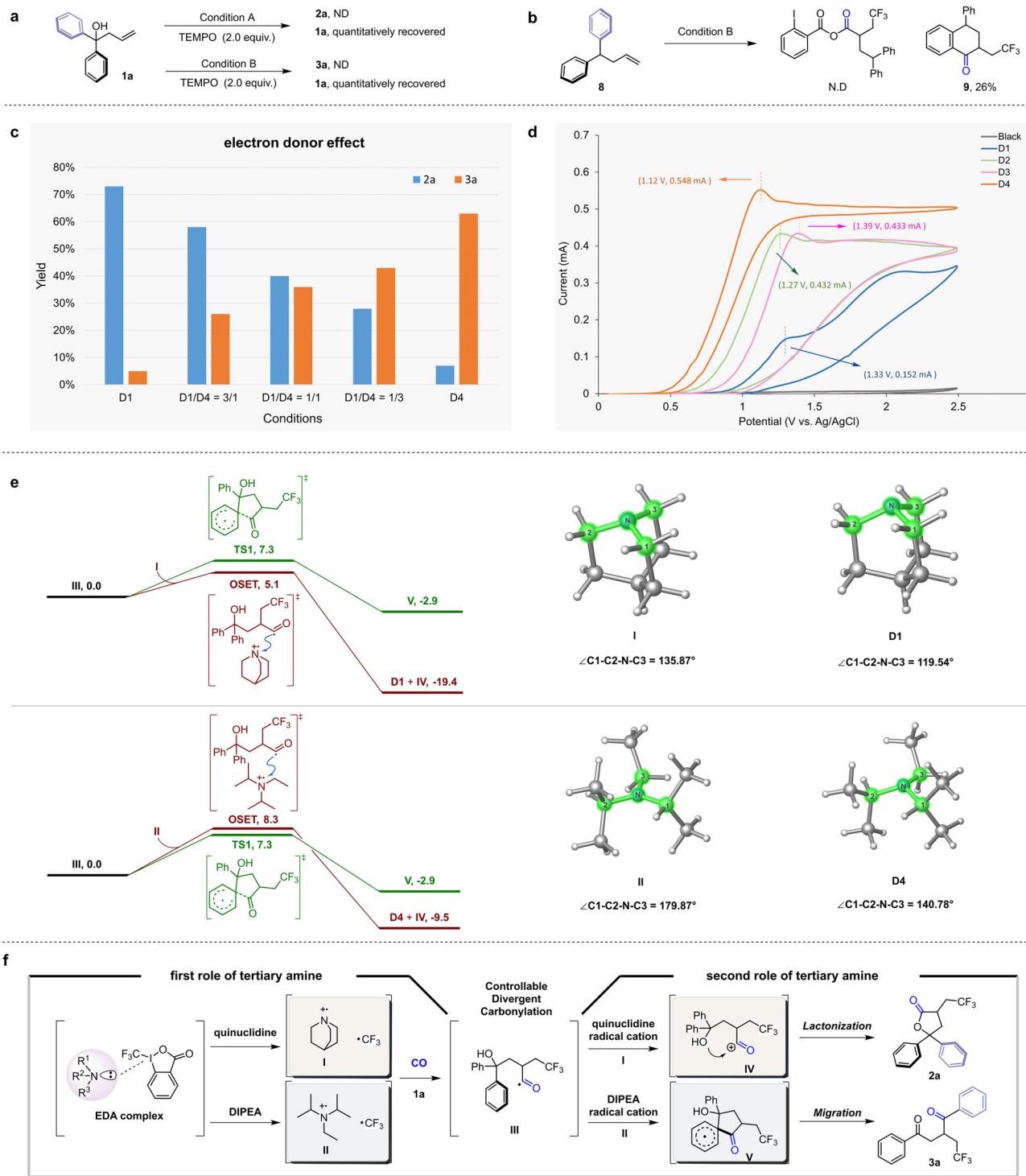


Fig. 6 | Mechanistic studies of controllable divergent carbonylation via distinct electron donor for the synthesis of 1,4-diones and γ -lactones. a Radical inhibition experiment. **b** Exploration of acyl intermediates. **c** Electron donor effect on

lactonization and migration selectivity. **d** Systematic evaluation of the redox potentials of electron donors (D1–D4) by cyclic voltammetry in acetonitrile. **e** DFT calculations. **f** Possible mechanism.

generated from an EDA complex of Togni's reagent **II** with tertiary amine, and then CF_3 radical added to olefin (**1a**) to produce a secondary carbon radical (Fig. 2f). In the CO atmosphere, carbon radicals capture CO to produce acyl radical intermediate **III** (Fig. 2f). The radical attack on the aryl ring occurs via transition state **TS1**, with an energy barrier of 7.3 kcal/mol. This step leads to the formation of the dearomatized radical intermediate **V**, from which migration of the aryl

group affords product **3a**. Alternatively, the acyl radical intermediate **III** can undergo an outer-sphere single-electron transfer (OSET) with the tertiary amine radical cation to generate the neutral tertiary amine and the acyl cation **IV**. The latter subsequently undergoes facile intramolecular lactonization to yield the cyclized product **2a**. According to Marcus theory, the OSET involving quinuclidine radical cation **I** requires an energy barrier of 5.1 kcal/mol, which is 2.2 kcal/mol

lower than that of the radical attack transition state **TS1**, consistent with experimental observations that the cyclized product **2a** should be observed with **D1**. However, the energy barrier for the OSET with DIPEA radical cation **II** was calculated to be 8.3 kcal/mol, which is 1.0 kcal/mol higher than that of **TS1**. Therefore, the computations clearly reproduce the observed selectivity switch upon changing the tertiary amine.

Marcus theory indicates that the energy barrier of the OSET is sensitive to the energy difference between the tertiary amine radical cation and the neutral tertiary amine. Specifically, the OSET leading to the formation of quinuclidine **D1** is exergonic by -19.4 kcal/mol, whereas it is only -9.5 kcal/mol for the formation of DIPEA **D4**, making the OSET with **II** lower in energy than with **II**. The optimized geometries reveal that the DIPEA radical cation **II** adopts a nearly ideal planar geometry for the radical species (179.87°), whereas quinuclidine radical cation **I** adopts a nearly tetrahedral geometry due to its constrained cyclic structure (135.87°). These geometric features render quinuclidine radical cation **I** relatively less stable compared to **II**. Furthermore, quinuclidine **D1** adopts a geometry closer to tetrahedral than that of DIPEA **D4**, likely due to the steric effects of the bulkier substituents in **D4**, making **D1** relatively more stable than **D4**. The combination of the relatively unstable **I** and the more stable **D1** results in the thermodynamics of the OSET with **I** being 5.1 kcal/mol more favorable than with **II**, thereby enabling the experimentally observed selectivity switch. Experimentally, a mixture of products **2a** and **3a** was observed when tertiary amines **D2** and **D3** were used. The energies of the OSET processes involving these tertiary amine radical cations were calculated to be 7.5 and 7.2 kcal/mol, being very close to the energy of **TS1**, which aligns well with experimental observations (see Supplementary Fig. 4 for details). This can be attributed to the fact that compared to **D4**, the substituents in **D2** and **D3** are relatively smaller, rendering **D2** and **D3** more stable than **D4**, which leads to a relatively easier OSET process.

Discussion

The selective synthesis of γ -lactones and 1,4-diones starting from the same materials confirms the feasibility of the strategy for regulating switchable carbonylation by electron donors. Further extension of the synthetic scope to γ -spironolactones and heteroaryl-substituted diketones demonstrates the excellent compatibility of this system. We have pioneered the discovery of another important function of tertiary amine in the EDA complex besides being an electron donor, which is to act as a tuner to control the chemoselectivity of the carbonylative reaction. Mechanistic studies show that amine electron donors with different structural properties are the key to controlling the acyl intermediates in the form of electrophilic acyl cations or nucleophilic acyl radicals. Controllable carbonylation enables the diversification of the transformation of homoallylic alcohols, showing the unique appeal of CO activation and utilization. Considering the potential of EDA systems in organic transformations, the protocol we developed to use dual functions of electron donors will serve as a launchpad for exploring new EDA complex platforms to achieve chemoselective control.

Methods

General procedure for the carbonylation-triggered lactonization or migration. A 4 mL screw-cap vial was charged with homoallylic alcohols (0.2 mmol), Togni's reagent (**II**) (0.4–0.6 mmol) or other radical precursors (0.4–0.6 mmol), electron donor amine (50 mol%), K_2CO_3 (0.1–0.3 mmol), and an oven-dried stirring bar. The vial was closed with a Teflon septum and cap and connected to the atmosphere via a needle. Then solvent (2 mL) was added with a syringe under N_2 atmosphere. The closed autoclave was flushed two times with nitrogen (-5 bar), and a pressure of 40 bar CO was charged. The autoclave was then placed on a magnetic stirrer. The reaction mixture was stirred at

30 – 35 $^\circ$ C for 24–36 h. After the reaction, the mixture was concentrated under vacuum. The crude product was purified by column chromatography (PE/EA = 50/1–2/1) on silica gel to afford the corresponding products. Note: Because of the high toxicity of carbon monoxide, all the reactions should be performed in an autoclave. The laboratory should be well-equipped with a CO detector and alarm system.

Data availability

The data supporting the findings of this study are available within the paper and its Supplementary Information or from the authors upon request.

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Author contributions

Y.W. designed and carried out most of the reactions and analyzed the data. Y.X. performed the DFT calculations under the supervision of G.H. X.-F.W. designed and supervised the project. Y.W., X.Q., L.-C.W. and C.X. provided raw material support. X.-F.W., G.H. and Y.W. wrote and revised the manuscript.

Competing interests

The authors declare no competing interests.

Additional information

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Correspondence and requests for materials should be addressed to Genping Huang or Xiao-Feng Wu.

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