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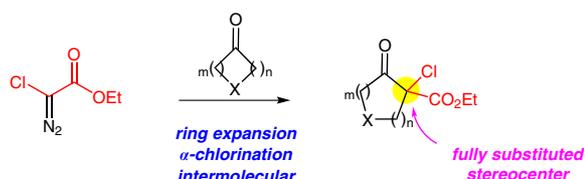
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Tiffeneau–Demjanov Rearrangement by Using α -Chloro- α -diazoacetate: A Direct Access to α -Chlorinated Medium-Size-Ring Ketones via Ring Enlargement

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Abstract α -Chloro(diazo)acetate can be readily used in an intermolecular ring expansion catalyzed by a boron Lewis acid to construct α -chlorinated medium-size cyclic ketones. This intermolecular Tiffeneau–Demjanov reaction proceeds in good yield from easily prepared or commercially available starting materials and allows the concomitant formation of a tetrasubstituted stereocenter.

Key words tetrasubstituted stereocenter, α -halogenation, ring expansion, chloro(diazo)acetate, cyclic ketones

Halogenated compounds are widely distributed in nature¹ and have attracted growing attention because of their interesting biological and pharmacological activities.² Drug designers frequently use chlorine or fluorine in the construction of potential medicines. As a matter of fact, the halogen atom can have a range of dramatic effects on the molecules. Selectivity, enzymatic stability, and/or affinity of pharmaceutically active compounds can indeed be modulated. Key examples include: Nasonex®, a glucocorticosteroid used topically to reduce inflammation in the airways (marketed by Schering), ranked in the top 200 brand-name drugs by retail dollars in 2012, and cyfluthrin, a synthetic pyrethroid insecticide that is a component of common household pesticides such as Temprid® (commercialized by Bayer) (Figure 1). From a synthetic point of view, halogenated derivatives can also serve as an entry point for further manipulations (carbon–carbon bond formation or selective introduction of a range of functional groups).³

On the other hand, halo(diazo)acetate **1** has recently been recognized as a potential halogen atom provider.⁴ Hansen and co-workers have described a mild procedure to reach this kind of building block and observed the quantita-

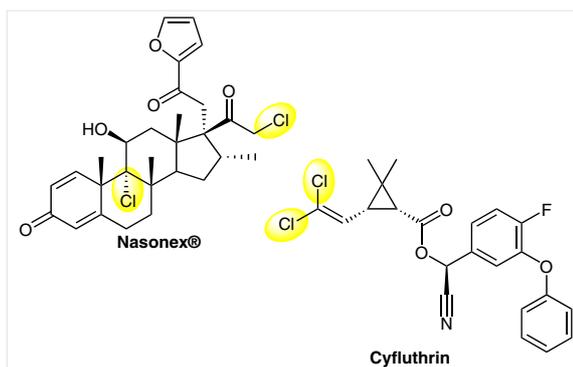
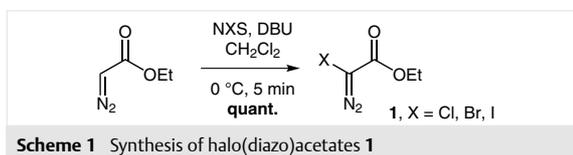


Figure 1 Chlorinated bioactive molecules

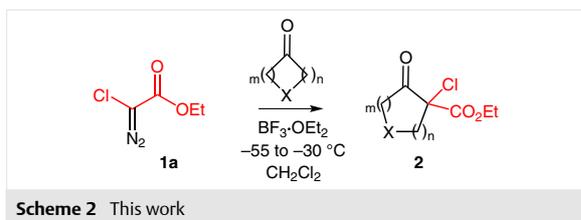
tive conversion of the commercially available ethyl(diazo)acetate in the presence of *N*-halosuccinimide (NXS) and DBU in dichloromethane in 5 minutes only (Scheme 1).^{4,5} They have afterwards demonstrated the synthetic utility of **1** in cyclopropanation^{4,5a,c,6} and C–H and Si–H insertion^{4,5b} reactions.



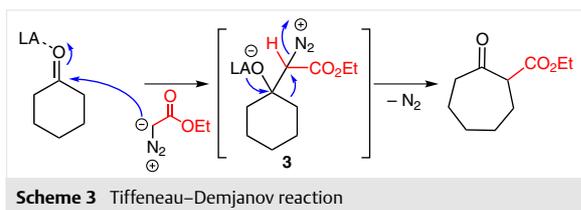
Scheme 1 Synthesis of halo(diazo)acetates **1**

In an effort to answer the increasing demand for halogenated precursors in organic synthesis, we envisioned that the halo(diazo)acetate moiety **1** could be a useful synthetic tool for the α -halogenation of cyclic ketones. As part of our continued interest in the area of medium-size-ring construction with concomitant formation of a tetrasubstituted

stereocenter,⁷ herein, we describe the behavior of the chloro(diazo)acetate derivative **1a** (X = Cl) in the Tiffeneau–Demjanov ring expansion reaction (Scheme 2).



Lewis acid catalyzed ring expansion reactions in the presence of α -diazoacetates have been known for decades.⁸ This kind of strategy quickly generates molecular complexity in a single operation. The nucleophilic addition of the α -diazoacetate to the Lewis acid activated ketone leads to the formation of intermediate **3** (Scheme 3). Following this, a skeletal rearrangement occurs and then the migration of the alkyl group is facilitated and accompanied by concurrent departure of the dinitrogen leaving group.

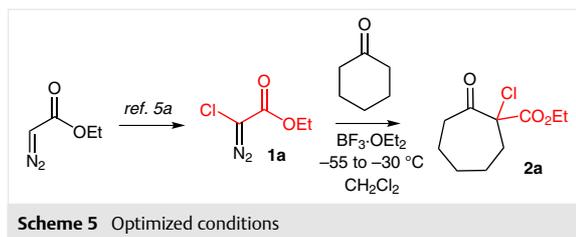


More recently several groups have shown that the Tiffeneau–Demjanov reaction is compatible with α -substituted- α -diazoacetates, therefore leading to the selective introduction of a tetrasubstituted stereocenter α to the ketone.⁹ Zhu and co-workers also reported¹⁰ a strategy to reach α -halo-tetrasubstituted ketone **5**; however, they started from an elaborate α -diazo tertiary alcohol **4**, and the approach was therefore an intramolecular one (Scheme 4).

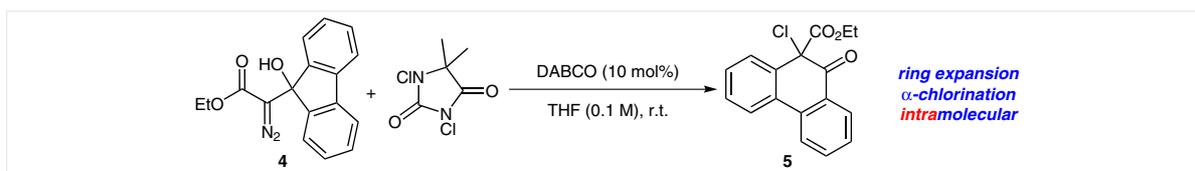
Owing to the importance of halogenated compounds as both building blocks and active pharmaceutical ingredients, we set out to develop a convergent α -halogenation of cyclic ketones by means of the chloro(diazo)acetate derivative **1a** in a carbon homologation type reaction (Scheme 2). There is definitely potential for the development of strate-

gies that would allow for generating both molecular complexity and stereochemical information. Accordingly, (a) medium-size-ring formation, (b) installation of a tetrasubstituted stereocenter, and (c) installation of a halogen atom are added value to such an approach.

Cyclohexanone was selected as the model substrate to evaluate the title reaction, and our initial screening revealed the boron trifluoride–diethyl ether complex to be the best Lewis acid for the Tiffeneau–Demjanov ring expansion in the presence of chloro(diazo)acetate (**1a**) (Scheme 5). Other Lewis acids [AlCl₃, AlMe₃, Yb(OTf)₃, Sc(OTf)₃, Cu(OTf)₂] were found to either decompose the diazo derivative **1a** or did not promote the reaction at all. Either way, they failed to deliver the expected product **2a**. In fact, the main difficulty we had to face, at that time, was handling the unstable chloro(diazo)acetate derivative **1a**. The latter decomposed in only a few hours at room temperature, it could not be stored, and therefore it required to be freshly prepared and to be quickly used in the next step. However, its utilization at temperatures below 0 °C in solution proved to circumvent this problem.



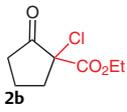
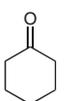
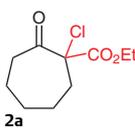
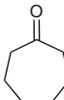
Further optimizations were carried out to enhance the yield of ring expansion product **2a** (Scheme 5). Initially, the Lewis acid was added neat to a solution of chloro(diazo)acetate **1a** (1 equivalent) and cyclohexanone (2 equivalents) in dichloromethane at -55 °C. An excess of ketone relative to the chloro(diazo)acetate **1a** was used in order to prevent the diazo dimerization side reaction. The product **2a** was delivered in 41% yield over two steps [starting from ethyl(diazo)acetate] together with 10% of the dimer. Ultimately, we chose to premix the boron trifluoride reagent and the cyclohexanone in dichloromethane and to add the chloro(diazo)acetate (**1a**) to that solution at -55 °C. In addition, we also decided to perform a slow addition via syringe pump of the diazoacetate derivative **1a** in solution, to prevent its dimerization with itself. Gratifyingly, in those opti-



mized conditions the corresponding cycloheptanone **2a** was isolated in 67% yield over two steps, namely in 82% yield per step. To summarize, the optimized set of conditions to obtain the desired cycloheptanone derivative **2a** requires a slow addition of the chloro(diazo)acetate derivative **1a** (1 equivalent freshly prepared) to a cold ($-55\text{ }^{\circ}\text{C}$) solution of cyclohexanone (2 equivalents) and a catalytic amount of the boron trifluoride–diethyl ether complex (40 mol%) in dichloromethane (Scheme 5).

Next we explored the scope of this catalytic system with various ketones. As shown in Table 1, the course of cyclization is influenced by the ring size of the starting ketone. Cyclobutanone delivered the corresponding five-membered ring **2b** in 56% average yield per step (entry 1). However, the cyclopentanone did not lead to the desired ring expansion product (entry 2). This is not really surprising, since cyclopentanone is known to undergo nucleophilic addition much slower than cyclobutanone (entry 1) or cyclohexanone (entry 3). Such a lack of reactivity can be rationalized by angle strain in the transition state. Accordingly, in a five-membered ring system, converting an sp^2 atom into an sp^3 one increases the numbers of eclipsing interactions.¹¹ Finally, a limit was reached when cycloheptanone was used as starting ketone in this ring expansion reaction (entry 4).

Table 1 Influence of the Size and the Nature of the Ring^a

Entry	Ketone	Product	Yield (%)	Average yield per step (%)
1			31	56
2		–	–	–
3			67	82
4		–	–	–

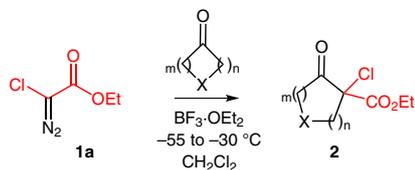
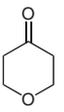
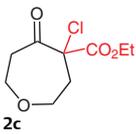
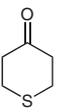
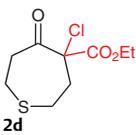
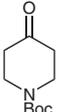
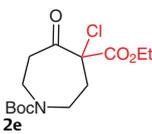
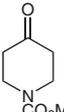
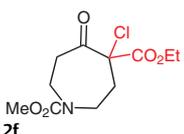
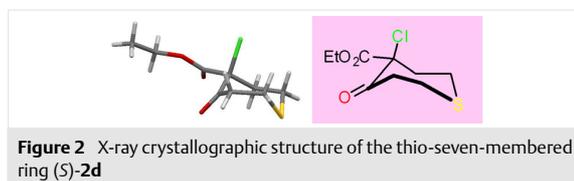


Table (continued)

Entry	Ketone	Product	Yield (%)	Average yield per step (%)
5			34	58
6			55	74
7			10 + 3 (side product 6)	32
8			36	60

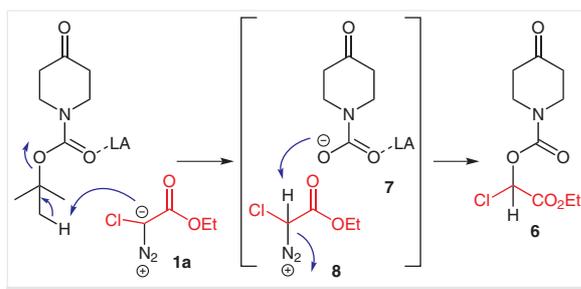
^a Reaction conditions: cycloalkanone (4 mmol), **1a** (2 mmol), $\text{BF}_3\cdot\text{OEt}_2$ (0.8 mmol), CH_2Cl_2 (15 mL), -55 to $-30\text{ }^{\circ}\text{C}$.

Encouraged by these results, we next surveyed various heterocyclic six-membered rings and studied the course of the ring expansion reaction with the chloro(diazo)acetate **1a**. To our delight, the desired compound (Table 1, entries 5–8) was delivered in each case. The reaction was compatible with the use of tetrahydro-4*H*-pyran-4-one or tetrahydrothiopyranone and gave the corresponding seven-membered rings **2c** and **2d** in 34 and 55% yield, respectively (over 2 steps). Interestingly, the thio-seven-membered ring **2d** turned out to be a solid and this chiral compound crystallized as conglomerates (Figure 2).¹²



On the other hand, when the reaction was performed with the *N*-Boc-pyridinone, the desired product **2e** was isolated in low yield (10% over 2 steps) (Table 1, entry 7) and was accompanied by 3% of side product **6** (Scheme 6). The following mechanism was postulated to explain the formation of the undesired compound **6**. Deprotonation of the Lewis acid activated carbamate by the halo(diazo)acetate

1a could lead to the formation of intermediate **7** (Scheme 6). Following that, a nucleophilic substitution of the carboxylate onto diazonium **8** could deliver the observed carbamate **6**.



Scheme 6 Hypothetical mechanism for the formation of **6**

To circumvent the formation of product **6**, the *N*-Boc protecting group was simply replaced by an *N*-CO₂Me one. And it actually did the trick, since the corresponding nitrogenated seven-membered ring **2f** was isolated in 60% yield per step (Table 1, entry 8). No side product was observed, thus supporting the suggested mechanism.

This side reaction is quite remarkable (Scheme 6), since solely the partial deprotection of the carbamate was observed (see intermediate **7**) and alkylation of the carboxylate part was therefore feasible. Theoretically, this could not be obtained by employing classical transesterification conditions. Further investigations into this unprecedented direct formal transesterification of *tert*-butyl carbamates with diazo derivatives are ongoing in our laboratory and will be reported in due course.

To summarize, this ring expansion method in the presence of chloro(diazo)acetate (**1a**) leads to various α -halo- α -tetrasubstituted medium-size-ring ketones **2a** and **2c-f** and a five-membered-ring ketone **2b**. Compared to the existing strategy involving halogenation/semipinacol rearrangement of a diazo compound,¹⁰ this approach neither requires the prior installation of a tertiary alcohol nor the synthesis of an elaborated diazo derivative (see Scheme 4).

In one single intermolecular operation we were not only able to bring about molecular complexity (medium-size-ring formation, installation of a tetrasubstituted center, α -chlorination of a ketone), but we also managed to generate stereochemical information (creation of a stereocenter starting from achiral easily available starting materials). As stated earlier, α -chlorinated- β -keto esters could be useful intermediates for the preparation of various molecules via S_N2 displacement of the tertiary chloride, for instance.¹³

In conclusion, we have successfully carried out the α -chlorination of cyclic ketones with a concomitant ring expansion, thus demonstrating the synthetic potential of chloro(diazo)acetate (**1a**). This method proves sufficiently general to provide various medium-size cyclic α -chlorinat-

ed- β -keto esters, which could serve as useful building blocks for further manipulations. An unprecedented reactivity of carbamate derivatives has been highlighted and the scope of this new chemical reaction is under investigation.

¹H and ¹³C NMR spectra were recorded on a Bruker AC400 (400 MHz) and a Bruker AC300 (75 MHz) spectrometer, respectively. IR spectra were recorded on a Bruker VERTEX70 FT-IR spectrometer fitted with a single reflection diamond ATR Bruker A222 accessory. High-resolution mass spectra were obtained on a QStar Elite (Applied Biosystems SCIEX) spectrometer equipped with an atmospheric pressure ionization (API) source. Analytical TLC was carried out on Merck Kieselgel 60 F254 plates and visualized under 254 nm UV light, after treatment with a KMnO₄ solution. Flash column chromatography was carried out on Merck Kieselgel 60 (230–400 mesh) silica gel. Anhydrous THF, CH₂Cl₂, toluene, and Et₂O were obtained from a MBraun SPS-800 solvent purification system. All experiments were performed under anhydrous conditions and an inert atmosphere of argon and, except where stated, by using dried apparatus and employing standard techniques for handling air-sensitive materials.

Cyclic Ketones **2** by Tiffeneau–Demjanov Ring Expansion; General Procedure

To a cooled (–55 °C) solution of cycloalkanone (4 mmol, 2 equiv) and BF₃·OEt₂ (0.1 mL, 0.8 mmol, 0.4 equiv) in CH₂Cl₂ (10 mL) was slowly added (30 mL per hour), via syringe pump, a solution of crude chloro(diazo)acetate (**1a**; 2 mmol, 1 equiv) in CH₂Cl₂ (5 mL). The reaction mixture was allowed to warm up to –30 °C. The reaction was monitored by TLC until complete disappearance of **1a**. The reaction mixture was then washed with an aqueous saturated solution of NaHCO₃. The aqueous layer was extracted twice with CH₂Cl₂. The combined organic layers were washed with brine, dried over Na₂SO₄, filtered and concentrated in vacuo. The residue was finally purified by flash chromatography over silica gel.

Ethyl 1-Chloro-2-oxocyclopentanecarboxylate (**2b**)

The resulting crude material was purified by flash chromatography (silica gel, PE–EtOAc, 90:10). Fractions that contained the desired product were collected and concentrated under reduced pressure to give five-membered ring **2b**.

Yield: 118 mg (31%) (2 steps); *R*_f = 0.21 (PE–EtOAc, 90:10).

¹H NMR (400 MHz, CDCl₃): δ = 4.28 (q, *J* = 7.0 Hz, 2 H, H6), 2.79–2.71 (m, 1 H, H5a), 2.61–2.52 (m, 1 H, H3a), 2.44–2.35 (m, 2 H, H5b, H3b), 2.20–2.09 (m, 2 H, H4), 1.30 (t, *J* = 7.0 Hz, 3 H, H7).

¹³C NMR (100 MHz, CDCl₃): δ = 206.3 (C_q, C2), 167.4 (C_q, C8), 69.8 (C_q, C1), 63.3 (CH₂, C6), 38.5 (CH₂, C5), 35.5 (CH₂, C3), 19.3 (CH₂, C4), 14.1 (CH₃, C7).

HRMS (ESI): *m/z* [M + Na]⁺ calcd for C₈H₁₁ClO₃Na: 213.0289; found: 213.0286.

Ethyl 1-Chloro-2-oxocycloheptanecarboxylate (**2a**)

The resulting crude material was purified by flash chromatography (silica gel, PE–EtOAc, 90:10). Fractions that contained the desired product were collected and concentrated under reduced pressure to give seven-membered ring **2a**.

Yield: 293 mg (67%) (2 steps); *R*_f = 0.23 (PE–EtOAc, 90:10).

IR (neat): 2986, 2935, 2862, 1730, 1452, 1391, 1367, 1321, 1296, 1254, 1227, 1196, 1159, 1130, 1095, 1061, 1024, 970, 937, 858, 804, 735, 687, 581, 509 cm⁻¹.

¹H NMR (400 MHz, CDCl₃): δ = 4.29 (q, *J* = 7.3 Hz, 2 H, 2 × H8), 2.85–2.79 (m, 1 H, H7a), 2.70–2.64 (m, 1 H, H7b), 2.48–2.41 (m, 1 H, H3a), 2.33–2.27 (m, 1 H, H3b), 1.90–1.66 (m, 5 H, 2 × H6, H5a, 2 × H4), 1.59–1.49 (m, 1 H, H5b), 1.31 (t, *J* = 7.3 Hz, 3 H, 3 × H9).

¹³C NMR (100 MHz, CDCl₃): δ = 205.5 (C_q, C2), 168.2 (C_q, C10), 76.3 (C_q, C1), 63.0 (CH₂, C8), 40.8 (CH₂, C7), 37.8 (CH₂, C3), 29.2 (CH₂, C5), 25.4 (CH₂, C4 or C6), 24.8 (CH₂, C4 or C6), 14.0 (CH₃, C9).

HRMS (ESI): *m/z* [M + H]⁺ calcd for C₁₀H₁₆ClO₃: 219.0782; found: 219.0781.

Ethyl 4-Chloro-5-oxooxepane-4-carboxylate (2c)

The resulting crude material was purified by flash chromatography (silica gel, PE–EtOAc, 90:10). Fractions that contained the desired product were collected and concentrated under reduced pressure to give seven-membered ring **2c**.

Yield: 150 mg (34%) (2 steps); *R*_f = 0.32 (PE–EtOAc, 80:20).

¹H NMR (400 MHz, CDCl₃): δ = 4.30 (q, *J* = 7.0 Hz, 2 H, H9), 4.02–3.97 (m, 1 H, H7a), 3.93–3.87 (m, 3 H, H7b, H2), 3.10–3.03 (m, 1 H, H3a), 2.97–2.90 (m, 1 H, H3b), 2.71–2.64 (m, 1 H, H6a), 2.27–2.21 (m, 1 H, H6b), 1.32 (t, *J* = 7.0 Hz, 3 H, H10).

¹³C NMR (100 MHz, CDCl₃): δ = 199.7 (C_q, C5), 167.5 (C_q, C8), 74.9 (C_q, C1), 68.2 (CH₂, C7), 66.2 (CH₂, C2), 63.3 (CH₂, C9), 44.2 (CH₂, C3), 38.9 (CH₂, C6), 14.0 (CH₃, C10).

HRMS (ESI): *m/z* [M + H]⁺ calcd for C₉H₁₄ClO₄: 221.0575; found: 221.0576.

Ethyl 4-Chloro-5-oxothiepane-4-carboxylate (2d)

The resulting crude material was purified by flash chromatography (silica gel, PE–EtOAc, 90:10). Fractions that contained the desired product were collected and concentrated under reduced pressure to give seven-membered ring **2d**.

Yield: 260 mg (55%) (2 steps); *R*_f = 0.50 (PE–EtOAc, 80:20).

IR (neat): 2984, 2930, 1743, 1713, 1468, 1423, 1367, 1298, 1246, 1202, 1178, 1126, 1092, 1030, 1001, 945, 854, 735, 702, 652, 579, 546, 505, 455, 407 cm⁻¹.

¹H NMR (400 MHz, CDCl₃): δ = 4.28 (q, *J* = 7.2 Hz, 2 H, H8), 3.49–3.43 (m, 1 H, H3a), 3.15–3.04 (m, 1 H, H2a), 3.01–2.97 (m, 1 H, H4a), 2.92–2.77 (m, 3 H, H4b, H2b and H3b), 2.58–2.44 (m, 2 H, H5), 1.30 (t, *J* = 7.2 Hz, 3 H, H9).

¹³C NMR (100 MHz, CDCl₃): δ = 201.7 (C_q, C6), 167.6 (C_q, C7), 76.0 (C_q, C1), 63.0 (CH₂, C8), 44.3 (CH₂, C3), 39.7 (CH₂, C5) 29.6 (CH₂, C4), 25.3 (CH₂, C2), 14.0 (CH₃, C9).

HRMS (ESI): *m/z* [M + H]⁺ calcd for C₉H₁₄ClO₃S: 237.0347; found: 237.0348.

1-tert-Butyl 4-Ethyl 4-Chloro-5-oxoazepane-1,4-dicarboxylate (2e)

The resulting crude material was purified by flash chromatography (silica gel, PE–EtOAc, 90:10) and furnished seven membered ring **2e** and side product **6**.

Yield (**2e**): 64 mg (10%) (2 steps); yield (**6**): 15.5 mg (3%); *R*_f = 0.55 (PE–EtOAc, 70:30).

IR (neat): 2976, 2928, 1747, 1695, 1470, 1410, 1367, 1338, 1300, 1238, 1165, 1117, 1095, 1030, 970, 941, 889, 856, 773, 689, 631, 542, 461, 420 cm⁻¹.

¹H NMR (600 MHz, CDCl₃, T = 360 K): δ = 4.30–4.24 (m, 2 H, H8), 4.03–3.87 (m, 1 H, H5a), 3.89–3.75 (m, 1 H, H4a), 3.58–3.86 (m, 1 H, H4b), 3.42–3.33 (m, 1 H, H5b), 3.17–3.13 (m, 1 H, H6a), 2.98–2.86 (m, 1 H, H6b), 2.54–2.41 (m, 1 H, H3a), 2.15–2.10 (m, 1 H, H3b), 1.42–1.41 (m, 9 H, H12), 1.29 (t, *J* = 7.1 Hz, 3 H, H9).

¹³C NMR (75 MHz, CDCl₃): δ = 201.3 (C_q, C2), 167.3 (C_q, C7), 154.3 (C_q, C10), 80.7 (C_q, C1), 75.6 (C_q, C11), 63.1 (CH₂, C8), 44.4 (CH₂, C5), 41.9 (CH₂, C4), 41.5 (CH₂, C6), 37.6 (CH₂, C3), 28.4 (CH₃, 3 × C12), 14.0 (CH₃, C9).

HRMS (ESI): *m/z* [M + H]⁺ calcd for C₁₄H₂₃ClNO₅: 320.1259; found: 320.1261.

4-Ethyl 1-Methyl 4-Chloro-5-oxoazepane-1,4-dicarboxylate (2f)

The resulting crude material was purified by flash chromatography (silica gel, PE–EtOAc, 80:20). Fractions that contained the desired product were collected and concentrated under reduced pressure to give seven-membered ring **2f**.

Yield: 200 mg (36%) (2 steps); *R*_f = 0.20 (PE–EtOAc, 70:30).

IR (neat): 2954, 1743, 1699, 1477, 1440, 1405, 1297, 1232, 1211, 1116, 1035, 1010, 912, 889, 771, 730 cm⁻¹.

¹H NMR (500 MHz, CDCl₃): δ = 4.27–4.21 (m, 2 H, H8), 4.04–3.88 (m, 1 H, H5a), 3.90–3.74 (m, 1 H, H4a), 3.64–3.63 (m, 3 H, H11), 3.61–3.50 (m, 1 H, H4b), 3.45–3.38 (m, 1 H, H5b), 3.13–3.07 (m, 1 H, H6a), 2.94–2.81 (m, 1 H, H6b), 2.52–2.41 (m, 1 H, H3a), 2.13–2.00 (1 H, 1 H, H3b), 1.29 (t, *J* = 7.2 Hz, 3 H, H9).

¹³C NMR (125 MHz, CDCl₃): δ = 201.5 (C_q, C2), 167.1 (C_q, C7), 155.6 (C_q, C10), 75.5 (C_q, C1), 63.2 (CH₂, C8), 53.2 (CH₃, C11), 44.4 (CH₂, C5), 41.8 (CH₂, C4), 41.3 (CH₂, C6), 37.2 (CH₂, C3), 13.9 (CH₃, C9).

HRMS (ESI): *m/z* [M + H]⁺ calcd for C₁₁H₁₇ClNO₅: 278.0790; found: 278.0794.

Compound 6

*R*_f = 0.35 (PE–EtOAc, 60:40).

IR (neat): 3446, 2958, 2920, 2850, 2360, 2341, 1757, 1712, 1465, 1435, 1371, 1344, 1273, 1228, 1215, 1188, 1108, 1026, 983, 958, 871, 798, 756, 721, 673, 595, 497 cm⁻¹.

¹H NMR (400 MHz, CDCl₃): δ = 6.65 (s, 1 H, H2), 4.36 (q, *J* = 7.2 Hz, 2 H, OEt), 3.89 (dt, 4 H, *J* = 18 and 6.4 Hz, H5), 2.54 (t, *J* = 6.4 Hz, 4 H, H4), 1.37 (t, *J* = 7.2 Hz, 3 H, OEt).

¹³C NMR (150 MHz, CDCl₃): δ = 206.2 (C_q, C6), 164.9 (C_q, C1), 151.8 (C_q, C3), 77.8 (CH, C2), 63.2 (CH₂, OEt), 43.6 (CH₂, C5a or C5b), 43.4 (CH₂, C5a or C5b), 41.0 (CH₂, C4a or C4b), 40.7 (CH₂, C4a or C4b), 14.1 (CH₃, OEt).

HRMS (ESI): *m/z* [M + H]⁺ calcd for C₁₀H₁₅ClNO₅: 264.0633; found: 264.0632.

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- (12) About 10% only of racemic chiral compounds crystallize as conglomerate. CCDC 1410693 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.
- (13) For instance, Shibatomi and co-workers have used sodium azide alkylthiols or cesium fluoride as nucleophiles to displace the chloride atom. See: Shibatomi, K.; Soga, Y.; Narayama, A.; Fujisawa, I.; Iwasa, S. *J. Am. Chem. Soc.* **2012**, *134*, 9836.