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Cascade Cleavage of Three-Membered Rings in the Reaction of D–A Cyclopropanes with 4,5-Diazaspiro[2.4]hept-4-enes: A Route to Highly Functionalized Pyrazolines

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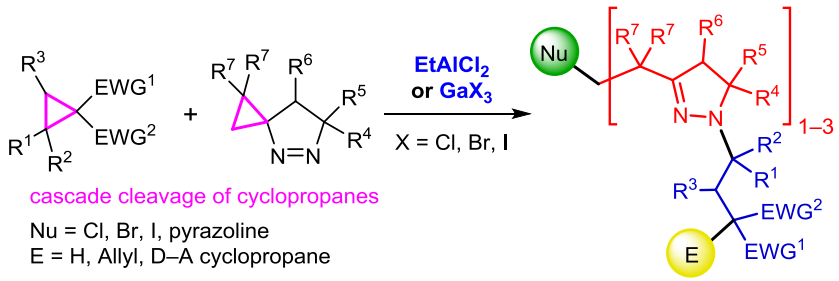
Supporting Information



ABSTRACT: A new cascade process for reactions of donor–acceptor cyclopropanes (DACs) with spiro[cyclopropanepyrazolines] in the presence of $EtAlCl_2$ or Ga halides is reported. The action of a Lewis acid results in DAC activation and addition of the carbocationic intermediate to the azocyclopropane system of the pyrazoline with opening of the second three-membered ring and addition of a halide anion from the Lewis acid. A specific feature of this process is that one activated cyclopropane ring activates another one, and depending on the component ratio, the process can involve two DAC molecules and one pyrazoline molecule, or one DAC molecule and two pyrazoline molecules. The process is tolerant to various functional groups and occurs with a wide range of substrates to give polyfunctionalized structures based on a 2-pyrazoline moiety.

■ INTRODUCTION

Donor-acceptor cyclopropanes (DACs)[1,2] are versatile building blocks in organic synthesis due to a combination of the reactive three-membered ring with various functional groups.[3] DACs are most commonly used for generation of 1,3-[3,4] and 1,2-zwitterions[5] followed by the utilization of these ions in cycloaddition and annulation reactions, in cascade processes and in reactions of other types.[6] The addition of various nucleophiles with opening of the three-membered ring (Scheme 1) is one of the simplest but important DAC reactions.[7–9] A wide range of substrates, including amines,[8a,b] azides,[8c] thiols,[8d] phenols,[8e] carboxylic acids,[8f] etc., are used as nucleophiles. Reactions where nitrogen-containing heterocycles,[9] such as indoles, imidazoles, triazoles, pyrazolines,[10] etc. are used as nucleophiles are very interesting and important. Using these reactions, it is possible to create complex heterocyclic systems that find use as biologically active compounds and in full syntheses of natural compounds.[7]

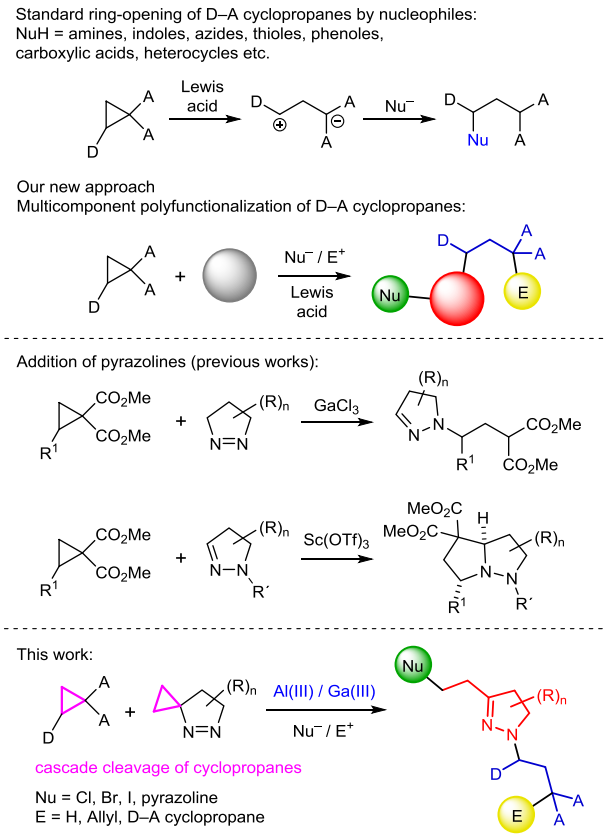
In this study our scientific team has suggested a new class of processes for DAC, namely, an extended multi-component version for nucleophilic addition based on introduction of additional linker between framework from DAC and nucleophile (Scheme 1). As a linker we have used interesting pyrazoline representatives, *viz.*, 4,5-diazaspiro[2.4]hept-4-enes,[11] that contain not only an N=N double bond but also a spiro-fused cyclopropane ring. Chloride, bromide, iodide, and other pyrazolines were used as nucleophiles.

Recently, our scientific team studied the nucleophilic opening of DACs with 1- and 2-pyrazolines to give *N*-functionalized 2-pyrazolines and diazabicyclo[3.3.0]-octanes (Scheme 1),[10a] as well as reactions that occur by other pathways.[10b] In continuation of studies on the reactions of DACs with nitrogen-containing heterocycles, we now studied the reactions of DACs with 4,5-

diazaspiro[2.4]hept-4-enes. The overall idea of this study was to perform a sequential opening of cyclopropane rings in both substrates in order to assemble complex polyfunctionalized pyrazolines.

Creation of new methods for the synthesis of pyrazolines with various functional groups is an important task in organic synthesis. Pyrazolines are popular building blocks[12] and as scaffold in bioactive molecules.[13] For example, the N–N bond in these compounds can be easily reduced to give diamine structures that can be functionalized further.[14,15] A series of total syntheses of natural compounds can be performed on the basis of pyrazolines.[15] Furthermore, the process appears very interesting from a mechanistic point of view since it involves targeted activation and opening of two different cyclopropane rings at once, which is a new synthetic concept in organic chemistry.

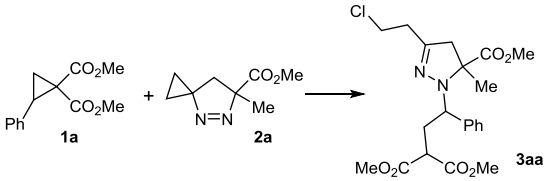
Scheme 1. Ring-opening reactions of D–A cyclopropanes with nucleophiles and pyrazolines, and novel multi-component process.



■ RESULTS AND DISCUSSION

A specific feature of this process is that the target product includes a halogen atom from a Lewis acid. This atom adds to the unsaturated carbon atom of the cyclopropane ring in the spiro[cyclopropanepyrazoline] molecule. This feature imposes a limitation on Lewis acids. In fact, an optimization performed on model substrates **1a** and **2a** (Table 1) has shown that the use of classic Lewis acids containing no halogen atoms, *e.g.*, $Sc(OTf)_3$, $Yb(OTf)_3$, $In(OTf)_3$, $Sn(OTf)_2$ or $Ni(ClO)_4$, failed. $EtAlCl_2$ showed the best result. $AlCl_3$ and Et_2AlCl gave rather poor yields of the product. $GaCl_3$ worked well, but sometimes it caused a considerable resinification of the reaction mixture, so it is more expedient to use it with less reactive substrates. Oddly enough, both $SnCl_4$ and $TiCl_4$ were found to be inferior Lewis acids in this process as they decomposed the starting cyclopropane **1a** to a large extent. Other metal chlorides worked very poorly. So, $ZnCl_2$ and YCl_3 gave traces of the product, while when using of $InCl_3$, $LaCl_3$ and $YbCl_3$ the reaction did not proceed at all. It should also be noted that the starting pyrazoline **2a** does not react with these Lewis acids ($GaCl_3$, $EtAlCl_2$, $SnCl_4$) and the three-membered ring is not opened.

Table 1. Optimization of the reaction conditions.



Entry [a]	Lewis acid (LA)	**1a**/**2a**/LA (equiv.)	T (°C)	*t* (min)	**3aa** Yield (%) [b]	diast. ratio [k]
1	$GaCl_3$	1 / 1.4 / 1	25	10	25–30 [c]	1.4/1
2	$GaCl_3$	1.3 / 1 / 1	10–15	30	20–30 [c]	1.3/1
3	$GaCl_3$	1.3 / 1 / 1	0–5	10	30–40 [c]	1.2/1
4	$GaCl_3$	1.3 / 1 / 1.3	0–5	15	55–60 [c]	1.2/1
5	$AlCl_3$	1.2 / 1 / 1.5	0–5	15	56	1/1
6	$EtAlCl_2$ [d]	1 / 1 / 1	25	5	40–50 [c]	1.1/1
7	$EtAlCl_2$ [e]	1.3 / 1 / 1.3	0–5	15	80–90 [c]	1.1/1
8	$EtAlCl_2$ [e]	1.3 / 1 / 2	0–5	15	~65 [c]	~1/1
9	$EtAlCl_2$ [e]	2 / 1 / 2	0–5	15	~70 [c]	~1/1
10	$EtAlCl_2$ [e]	1 / 2 / 1.5	0–5	15	~55 [c]	~1/1
11	$EtAlCl_2$ [e]	1.3 / 1 / 1.5	0–5	15	92 (86 [f])	1/1
12	Et_2AlCl	1.2 / 1 / 1	0–5	15	14	~1/1
13	Et_2AlCl	1.2 / 1 / 2	0–5	15	24	~1/1
14	$SnCl_4$	1.2 / 1 / 1.5	0–5	15	37	1/1
15	$TiCl_4$	1.2 / 1 / 1.5	0–5	15	30	1/1
16	$ZnCl_2$	1.2 / 1 / 1.5	25	60	8 [g]	1/1
17	$InCl_3$	1.2 / 1 / 1.5	25	60	0 [h]	
18	YCl_3	1.2 / 1 / 1.5	25	60	7 [i]	~1/1
19	$LaCl_3$	1.2 / 1 / 1.5	25	60	0 [h]	–
20	$YbCl_3$	1.2 / 1 / 1.5	25	60	0 [h]	–
21	$Yb(OTf)_3$	1 / 1.4 / 0.1	25	24 h	0 [j]	–
22	$Sc(OTf)_3$	1.2 / 1 / 0.1	25	24 h	0 [j]	–

[a] CH_2Cl_2 was used as a solvent (50–100 mM). [b] NMR Yield; they were determined by ^1H spectra using 1,4-dinitrobenzene as internal standard. [c] Data were collected based on several experiments. [d] $EtAlCl_2$ (1.0 M in toluene). [e] $EtAlCl_2$ (1.0 M in hexane). [f] Isolated yield. [g] Conversion ~10%. [h] No reaction, conversion <5%. [i] Conversion ~15%. [j] Complex mixture. [k] Diastereomer ratio was determined by ^1H NMR spectra.

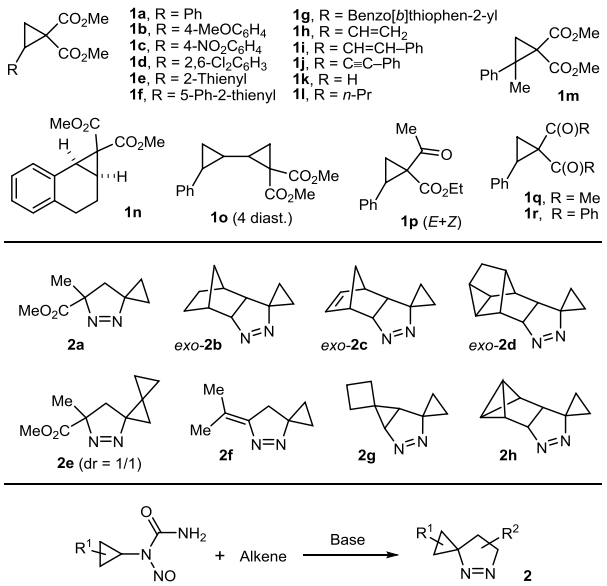
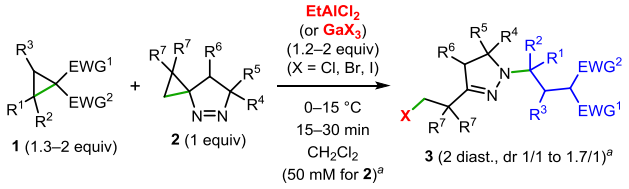
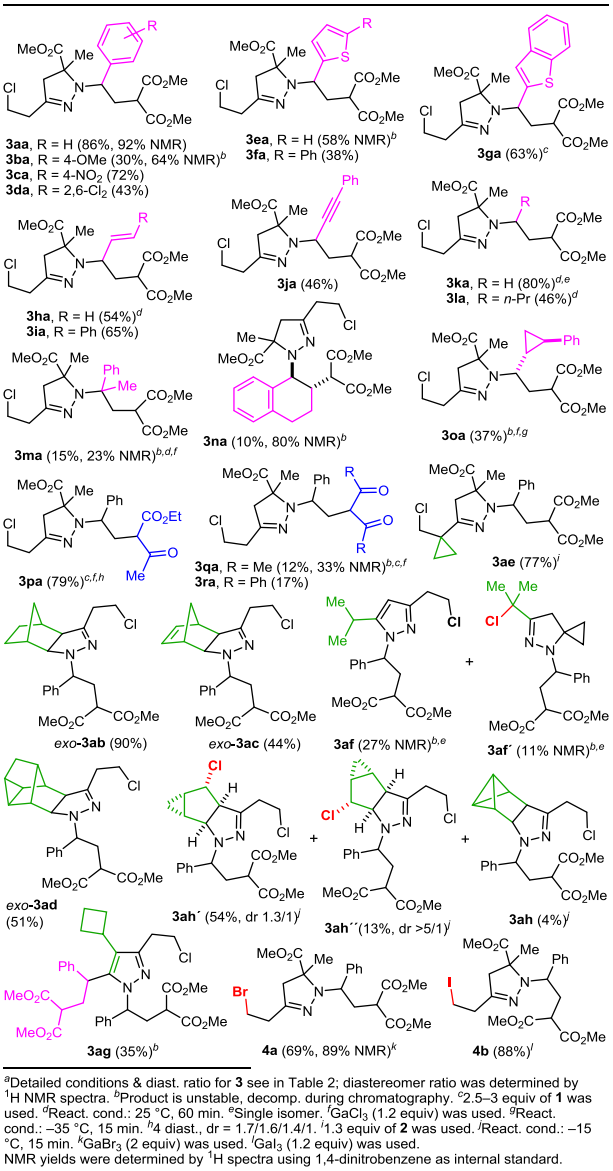


Figure 1. DACs 1 and spiropyrazolines 2 used in this study.

The reaction has general nature and occurs with a broad range of DACs **1** and diazaspiro[2.4]hept-4-enes **2** (Scheme 2). Cyclopropanedicarboxylates[2] with electron-donating and electron-withdrawing aryl and heteroaromatic substituents, vinyl, acetylenic, alkyl groups, non-substituted cyclopropanedicarboxylate **1j**, disubstituted DACs **1p** and **1q**, as well as bicyclopropyldicarboxylate **1o** readily enter this reaction.[16] DACs with one or more keto groups as electron-withdrawing substituents instead of ester groups can be used. Spiro[cyclopropanepyrazolines] **2a–h**, despite their rather exotic structure, are readily obtained by addition of diazo cyclopropane to methyl methacrylate, norbornene, norbornadiene, deltacyclene, dimethylallene, benzvalene and spiro[2.3]hexene, as well as by addition of diazo spiropentane to methyl methacrylate (Figure 1).[11] Opening of the cyclopropane ring in them was previously described only by the example of the acylation reaction.[17]

Scheme 2. Scope of the reaction.





[a]Detailed conditions & diast. ratio for **3** see in Table 2; diastereomer ratio was determined by ^{1}H NMR spectra. [b]Product is unstable, decomp. during chromatography. [c]2.5–3 equiv of **1** was used. [d]React. cond.: 25 °C, 60 min. [e]Single isomer. [f]$GaCl_3$ (1.2 equiv) was used. [g]React. cond.: –35 °C, 15 min. [h]4 diast., dr = 1.7/1.6/1.4/1. [i]1.3 equiv of **2** was used. [j]React. cond.: –15 °C, 15 min. [k]$GaBr_3$ (2 equiv) was used. [l]GaI_3 (1.2 equiv) was used.
NMR yields were determined by ^{1}H NMR spectra using 1,4-dinitrobenzene as internal standard.

Practically in all cases, using a (1.3–2)-fold excess of DAC and the same excess of $EtAlCl_2$ or $GaCl_3$ gave polyfunctional pyrazolines **3** as the main products (Scheme 2), *i.e.*, a molecule of DAC **1** alkylates a spiro[cyclopropanepyrazoline] **2** in the course of the reaction, with opening of a three-membered ring in it and addition of a chloride anion from the Lewis acid. Bromide or iodide anions can be added instead of chloride by using $GaBr_3$ or GaI_3, respectively. These reactions readily give bromo- or iodopyrazolines **4a** or **4b**. Pyrazolines **3** and **4** containing two or more stereocenters are formed as mixtures of two diastereomers the ratio of which depends on the nature of the substrates used. In the case of spiro[cyclopropanepyrazolines] **2f–h**, more complex processes also occur, such as opening of additional cyclopropane rings (**3ah´** and **3ah´´**), isomerization (**3af**), and addition of a second DAC molecule (**3ag**). Pyrazoline **2f** also undergoes an alternative process of chloride addition to the double bond (**3af´**) (Scheme 2). Detailed reaction conditions are given in Table 2. Overall, pyrazolines **3** are rather stable compounds and are easily isolated from reaction mixtures. Still, some representatives have low stability due to the presence of many functional groups in the molecule and are

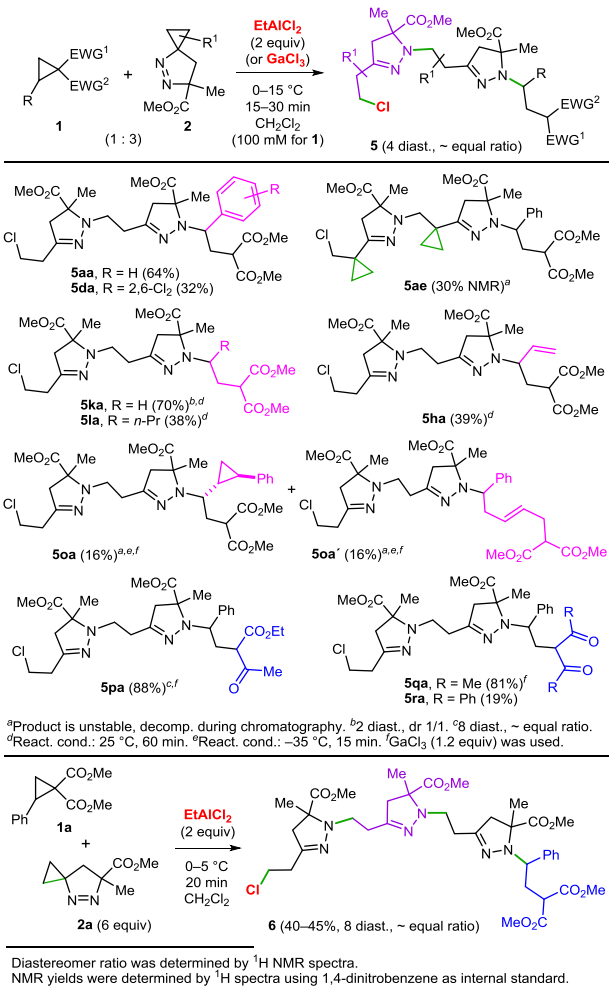
decomposed almost completely, *e.g.*, during chromatography on SiO_2.

Table 2. Summarized reaction conditions for general scope.

Entry	Ratio **1**:**2**:$EtAlCl_2$	T (°C)	*t* (min)	Product	Yield (%) [a]	*dr* (ratio) [g]
1	1.3:1:1.5	5	15	**3aa**	86 (92)	1:1
2	1.3:1:1.5	5	15	**3ba**	64	1.1:1
3	2:1:2	5	15	**3ca**	72	1:1
4	2:1:2	5	30	**3da**	43	1.3:1
5	2:1:2	0	15	**3ea** [b]	(58)	1.3:1
6	2:1:2	5	15	**3fa**	38	1.2:1
7	2.5:1:2	5	15	**3ga**	63	1.2:1
8	2:1:2	25	60	**3ha**	54	1.5:1
9	2:1:2	5	15	**3ia**	65	1.2:1
10	2:1:2	0	30	**3ja**	46	1.2:1
11	2:1:2	5	60	**3ka**	80	–
12	2:1:2	25	60	**3la**	46	1:1
13	2:1:1.2 [c]	25	60	**3ma** [b]	15 (25)	1:1
14	1.3:1:1.5	5	15	**3na** [b]	10 (80)	1.2:1 [d]
15	2:1:1.2 [c]	–35	15	**3oa** [b]	37	1.5:1 [d]
16	3:1:1.2 [c]	5	15	**3pa**	79	1.7:1.6:1.4:1
17	3:1:1.2 [c]	5	15	**3qa**	12 (33)	1.5:1
18	2:1:2 [c]	25	15	**3ra**	17	1:1
19	1.3:1:2	5	15	**3ab**	90	1:1
20	2:1:2	5	15	**3ac**	45	1:1
21	2:1:2	5	15	**3ad**	51	1.7:1
22	1:1.3:2	5	15	**3ae**	77	1.4:1
23	1.3:1:2	–15	15	**3af**	(27)	–
				3af´	(11)	–
24	2:1:2	5	20	**3ag**	35	1:1
25	1.3:1:2	5	45	**3ah**	4	~1:1
				3ah´	54	1.3:1
				3ah´´	13	>5:1
26	1.3:1:2 [e]	5	15	**4a**	69 (89)	1.1:1
27	1.3:1:1.2 [f]	5	15	**4b**	88	1.1:1

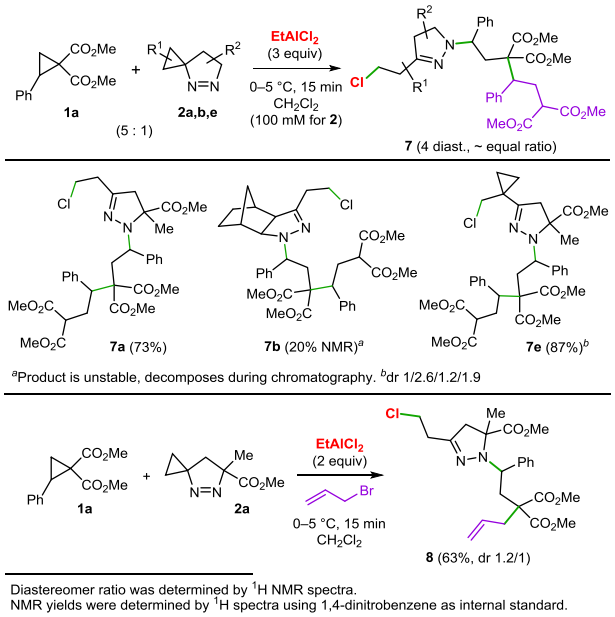
[a]In parants NMR Yield; they were determined by ^1H spectra using 1,4-dinitrobenzene as internal standard. [b]Product is unstable. [c]$GaCl_3$ was used. [d]The arrangement of the substituents in the carbocycle has an exclusively *trans*-configuration. [e]$GaBr_3$ was used. [f]GaI_3 was used. [g]Diastereomer ratio was determined by ^1H NMR spectra.

Scheme 3. Double and triple addition of spiro[cyclopropanepyrazolines] 2 initiated by DAC and Lewis acid.



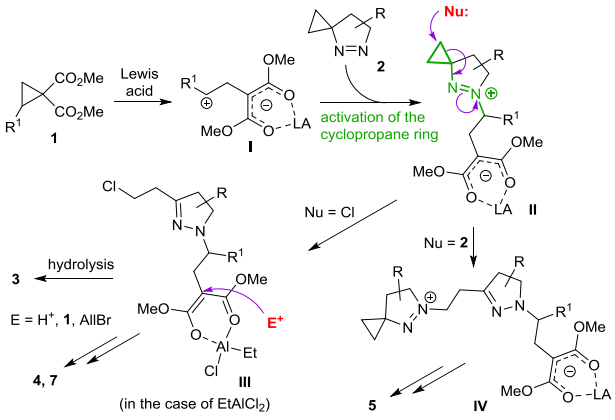
More complex cascade processes based on two DAC or spiro[cyclopropanepyrazoline] molecules can also be performed. In these cases, sequential opening of all three cyclopropane rings occurs. The process is controlled quite easily by the reagent ratio and by increasing the reagent concentrations in the reaction mixture. If two molecules of **2** and one molecule of **1** are assembled, the second molecule of spiro[cyclopropanepyrazoline] **2** adds as a nucleophile followed by opening of its own three-membered ring and chloride anion addition thereto. As a result, complex polyfunctional structures **5** containing two pyrazoline moieties in the molecule are formed. Compounds **5** are formed particularly well from cyclopropanedicarboxylates **1a,k** and acetyl-containing DACs **1p,q** (Scheme 3). Using a 6-fold excess of pyrazoline **2a** in the reaction with DAC **1a**, we succeeded in assembling compound **6** with participation of three pyrazoline molecules (Scheme 3), but this process occurred with great difficulty. (for details see Supp. Inf., Scheme S3 and S4). It is much more difficult to assemble structures based on two DAC molecules. Just an excess of the cyclopropane is usually insufficient; however, we succeeded in choosing conditions for the formation of long-chain *N*-substituted 2-pyrazolines **7** (Scheme 4). With an excess of DAC and $EtAlCl_2$ the second DAC molecule has time to add the nucleophilic malonyl moiety of the intermediate 1:1 adduct formed. Allyl bromide can also be used as an electrophile that also adds to the malonyl moiety giving compound **8** (Scheme 4).

Scheme 4. Double addition of DAC 1a with spiropyrazolines 2 and addition of allyl bromide.



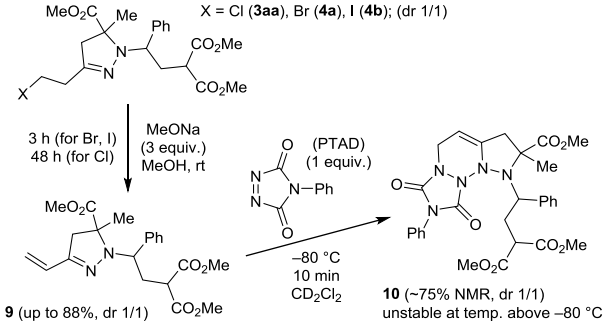
It is interesting to consider the mechanism of the cascade activation of both cyclopropane rings. In fact, the DAC molecule is activated in a standard way followed by opening to give 1,3-zwitterion **I**.[3] The activation of the cyclopropane ring in spiro[cyclopropanepyrazolines] **2** is more interesting. Simple addition of Lewis acids does not make compounds **2** react: in fact, they do not react even with strong Lewis acids. The situation changes in the presence of a DAC. In this case, the electrophilic moiety of the 1,3-zwitterion **I** that is generated attacks a nitrogen atom in pyrazoline **2**,[10] causing strong electron density displacement from the cyclopropane ring (**II**). This results in its opening with addition of a halide ion (**III**) or another spiro[cyclopropanepyrazoline] molecule (**IV**). Furthermore, depending on the conditions, structures **3–7** are assembled from intermediate **II** (Scheme 5). It occurs only after DAC addition, *i.e.*, one activated cyclopropane ring activates another one.

Scheme 5. Proposed mechanism for activation of 1 and 2.



The target structures **3–7** were designed on the basis of 2-pyrazoline moieties and contain many additional functional groups, including aryl and heteroaryl substituents, multiple bonds, cyclopropane rings, ester and carbonyl groups and halogen atoms. This opens rich opportunities for further modifications of the compounds obtained and their application as building blocks in subsequent syntheses. Development of methods for modification of these structures was not the goal of this study, however, an example of such reactions is presented in Scheme 6. In particular, rather simple procedures allow one to assemble complex polycyclic nitrogen-containing heterocycle **10**. So, the detachment of HX from **3aa** and **4a,b** gives a heterodyne system in compound 9. The addition of phenyltriazolindione (PTAD) to it at –80 °C using a Diels-Alder reaction leads to an interesting pentaazatriclic system **10** with four nitrogens in one row. This core is very reactive and rapidly decomposes at temperatures above –80 °C with polymerization. The structure was established using 2D NMR spectroscopy methods when the reaction has been carried out directly in a NMR spectrometer at –80 °C.

Scheme 6. Example of further transformations.



In conclusion, we have developed a new cascade process for reactions of DACs with 4,5-diazaspiro[2.4]hept-4-enes occurring in the presence of $EtAlCl_2$ or gallium halides, involving successive opening of two cyclopropane rings in both substrates and addition of a halide ion from a Lewis acid. As a result, polyfunctional structures are assembled on the basis of one or two 2-pyrazoline fragments, as well as one or two DAC molecules. The process is tolerant to various functional groups in the original substrates and allows for their further modification.

■ EXPERIMANTAL SECTION

General experimental details. All reagents and solvents were used commercial grade chemicals without additional purification. Starting D–A cyclopropanes **1a–r** were synthesized by known methods.[18] Starting pyrazolines **2a–h** were synthesized from the corresponding olefins.[11,19] All operations with $EtAlCl_2$, $GaCl_3$, $GaBr_3$ and GaI_3 were carried out under dry argon atmosphere. ^1H and ^{13}C NMR spectra were recorded on a 400 MHz (400.1 and 100.6 MHz, respectively) and 300 MHz (300.1 and 75.5 MHz, respectively) spectrometers in $CDCl_3$ and CD_2Cl_2 containing 0.05% Me_4Si as the internal standard. Determinations of structures and stereochemistry of obtained compounds and assignments of ^1H and ^{13}C signals were made with the aid of 1D and 2D gradient/non-gradient DEPT-135, CHCORR, COSY, NOESY, HSQC, HMBC and DOSY-LED spectra. IR spectra were obtained on a FT-IR spectrometer in KBr plates (thin layer). Mass spectra were recorded using electron impact ionization (EI, 70 eV, direct inlet probe). High resolution mass spectra were obtained using simultaneous electrospray (ESI-TOF).

General synthetic procedure for 4,5-dihydro-1*H*-pyrazol-1-yl-2-phenylethylmalonates 3,4. All operations were performed under dry argon atmosphere. The reagents ratio can be seen in Table 2. A Lewis acid ($EtAlCl_2$ (1.0 M in hexane) or a solid $GaCl_3$) was added to a solution of DACs **1a–r** and the pyrazolines **2a–h** in dry DCM (conc. 50 mM for **2**) and the mixture was stirring at conditions from Table S3. Then an aqueous solution of HCl (5%) was added at room temperature until pH 3 was achieved and the reaction mixture was extracted with CH_2Cl_2 (3×10 mL). The organic layer was dried over $MgSO_4$ and the solvent was removed in vacuo. The residue was purified by flash chromatography (benzene–EtOAc (30:1) to benzene–EtOAc (10:1)) on silica gel to afford the pure products. The resulting compounds can be additionally purified on a Silufol chromatographic plate (20×20 cm) using hexane–acetone (5:1) eluent. A mixture of 2 diastereomers is usually formed during the reaction. Diastereomers are practically inseparable in most cases using standard column chromatography on SiO_2 or PTLC, because their R_f are usually very close. In several cases the diastereomers were separated quite easily; this is specifically indicated in each case (see also the copies of spectra in Supp. Inf.). In many cases it is possible to separately describe the ^1H and ^{13}C NMR spectra of each of the diastereomers without any problems even for inseparable mixtures using of a set of 2D correlation NMR experiments.

*Dimethyl 2-(2-(3-(2-chloroethyl)-5-(methoxycarbonyl)-5-methyl-4,5-dihydro-1H-pyrazol-1-yl)-2-phenylethyl)malonate **(3aa)***. Compound **3aa** was prepared from **1a** and **2a** in yield 86% (224 mg, *dr* = 1/1). Light yellow oil. IR (KBr) $\tilde{\nu}$ 3082, 3059, 3024, 2999, 2955, 2847, 1733 br. (C=O), 1603, 1495, 1451, 1433 cm^{-1}. ^1H NMR (300.1 MHz, $CDCl_3$): δ 0.92 (s, 3H, Me_{mj}), 1.41 (s, 3H, Me_{mn}), 2.24–2.42 (m, 2H, $H_{mj\ and\ mn}(2')$), 2.47 (d, 1H, $H_{mj}(4)$, ^2J = 16.9 Hz), 2.59 (d, 1H, $H_{mn}(4)$, ^2J = 16.6 Hz), 2.60–2.79 (m, 6H, $H_{mj\ and\ mn}(2')$ and $H_{mj\ and\ mn}(1'')$), 2.90 (s, 3H, CO_2Me_{mn}), 3.18 (d, 1H, $H_{mn}(4)$, ^2J = 16.6 Hz), 3.27 (d, 1H, $H_{mj}(4)$, ^2J = 16.9 Hz), 3.53 (dd, 1H, $H_{mn}(3')$, ^3J = 8.8 Hz, ^3J = 6.3 Hz), 3.70 (s, 3H, CO_2Me_{mj}), 3.72 (s, 3H, CO_2Me_{mn}), 3.73 (s, 3H, CO_2Me_{mn}), 3.76 (s, 3H, CO_2Me_{mj}), 3.77 (s, 3H, CO_2Me_{mj}), 3.69–3.82 (m, 5H, $H_{mj}(3')$ and $H_{mj\ and\ mn}(2'')$), 4.09 (dd, 1H, $H_{mn}(1')$, ^3J = 8.8 Hz, ^3J = 6.3 Hz), 4.27 (dd, 1H, $H_{mj}(1')$, ^3J = 10.3 Hz, ^3J = 4.9 Hz), 7.17–7.29 (m, 6H, $H_{Ar\ mj\ and\ mn}$), 7.33 (dd, 2H, $H_{Ar\ mn}$, ^3J = 8.2 Hz, ^4J = 1.6 Hz), 7.45 (dd, 2H, $H_{Ar\ mj}$, ^3J = 7.9 Hz, ^4J = 1.6 Hz) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 20.8 and 22.0 (2 Me), 33.3, 33.4, 36.3, 36.4, 41.3, 41.4, 47.4 and 47.5 (6 CH_2), 49.0 and 49.1 (C(3′)), 51.3, 52.3, 52.4 and 52.5 (6 OMe), 59.3 and 60.2 (C(1′)), 69.1 and 71.1 (C(5)), 127.0, 127.3, 127.6, 128.0, 128.1 and 128.2 (10 CH_{Ar}), 140.5 and 145.8 (C(3)), 143.7 and 144.0 (C(*i*)), 169.7, 169.8, 169.9, 170.2, 172.4 and 172.5 (6 COO). MS (*m/z* for ^{35}Cl, %): 438 (15, M^+). HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{21}H_{27}N_2O_6Cl$ (for ^{35}Cl) 461.1455; Found 461.1450.

*Dimethyl 2-(2-(3-(2-chloroethyl)-5-(methoxycarbonyl)-5-methyl-4,5-dihydro-1H-pyrazol-1-yl)-2-(4-methoxyphenyl)-ethyl)malonate **(3ba)***. Compound **3ba** was prepared from **1b** and **2a** in yield 64% (178 mg, *dr* =1.1/1). The 2nd diastereomer decomposed on silica gel. Light yellow oil. IR (KBr) $\tilde{\nu}$ 3001, 2955, 2842, 1734 br. (C=O), 1609, 1512, 1437, 1347 cm^{-1}. 1st diastereomer: ^1H NMR (300.1 MHz, $CDCl_3$): δ 0.98 (s, 3H, Me), 2.31 (ddd, 1H, H(2′), ^2J = 13.7 Hz, ^3J = 8.6 Hz, ^3J = 5.2 Hz), 2.49 (d, 1H, H(4), ^2J = 16.8 Hz), 2.63–2.84 (m, 3H, H(2′) and 2×H(1′′)), 3.27 (d, 1H, H(4), ^2J = 16.8 Hz), 3.54–3.84 (m, 15H, 3×CO_2Me, OMe, 2×H(2′′) and H(3′)), 4.26 (dd, 1H, H(1′), ^3J = 9.9 Hz, ^3J = 5.2 Hz), 6.80 (d, 2H, H(3′′) and H(5′′), ^3J = 8.6 Hz), 7.38 (d, 2H, H(2′′) and H(6′′), ^3J = 8.6 Hz) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 21.8 (Me), 33.4 (C(1′′)), 36.4 (C(2′)), 41.4 (C(2′′)), 47.5 (C(4)), 49.0 (C(3′)), 52.3, 52.4 and 52.5 (3×CO_2Me), 55.1 (OMe), 59.8 (C(1′)), 71.3 (C(5)), 113.5 (C(3′′) and C(5′′)), 128.9 (C(2′′) and C(6′′)), 135.6 (C(1′′)), 144.4 (C(3)), 158.6 (C(4′′)), 169.8, 170.1 and 173.5 (3 COO). MS (*m/z* for ^{35}Cl, %): 468 (10, M^+). HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{22}H_{29}N_2O_7Cl$ (for ^{35}Cl) 491.1556; Found 491.1538.

*Dimethyl 2-(2-(3-(2-chloroethyl)-5-(methoxycarbonyl)-5-methyl-4,5-dihydro-1H-pyrazol-1-yl)-2-(4-nitrophenyl)ethyl)-malonate **(3ca)***. Compound **3ca** was prepared from **1c** and **2a** in yield 72% (207 mg, *dr* = 1/1). Yellow oil. IR (KBr) $\tilde{\nu}$ 3079, 2999, 2955, 2848, 1734 br. (C=O), 1605, 1523 (NO_2), 1436, 1348 (NO_2) cm^{-1}. ^1H NMR (300.1 MHz, $CDCl_3$): δ 0.92 (s, 3H, Me), 1.45 (s, 3H, Me), 2.22–2.37 (m, 2H, 2×H(2′)), 2.51 (d, 1H, H(4), ^2J = 17.0 Hz), 2.58–2.88 (m, 7H, H(4), 2×H(2′) and 4×H(1′′)), 2.94 (s, 3H, CO_2Me), 3.22 (d, 1H, H(4), ^2J = 17.0 Hz), 3.28 (d, 1H, H(4), ^2J = 16.8 Hz), 3.58 (dd, 1H, H(3′), ^3J = 9.2 Hz, ^3J = 5.6 Hz), 3.69–3.82 (m, 20H, 5×CO_2Me, 4×H(2′′) and H(3′)), 4.27 (dd, 1H, H(1′), ^3J = 9.2 Hz, ^3J = 5.6 Hz), 4.44 (dd, 1H, H(1′), ^3J = 10.7 Hz, ^3J = 4.2 Hz), 7.57 (d, 2H, H_{Ar}, ^3J = 8.7 Hz), 7.70 (d, 2H, H_{Ar}, ^3J = 8.7 Hz), 8.12 (d, 4H, H_{Ar}, ^3J = 8.7 Hz) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 21.3 and 22.1 (Me), 33.2 and 33.3 (C(1′′)), 35.9 and 36.0 (C(2′)), 41.1 and 41.2 (C(2′′)), 46.9 and 47.1 (C(4)), 48.6 and 48.8 (C(3′)), 51.3, 52.4, 52.5 and 52.6 (6×OMe), 58.2 and 59.4 (C(1′)), 69.0 and 71.0 (C(5)), 123.1 and 123.5 (2 C(2′′) and C(6′′)), 128.5 and 128.8 (2 C(3′′) and C(5′′)), 144.7 and 146.5 (C(3)), 147.0 and 147.1 (C(4′′)), 148.9 and 151.9 (C(1′′)), 169.4, 169.5, 169.6, 169.8, 171.8 and 173.1 (6 COO). MS (*m/z* for ^{35}Cl, %): 483 (15, M^+). HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{21}H_{26}N_3O_8Cl$ (for ^{35}Cl) 506.1301; Found 506.1302.

*Dimethyl 2-(2-(3-(2-chloroethyl)-5-(methoxycarbonyl)-5-methyl-4,5-dihydro-1H-pyrazol-1-yl)-2-(2,6-dichlorophenyl)-ethyl)malonate **(3da)***. Compound **3da** was prepared from **1d** and **2a** in yield 43% (130 mg, *dr* = 1.3/1). Colorless oil. IR (KBr) $\tilde{\nu}$ 3078, 2998, 2954, 2845, 1733 br. (C=O), 1579, 1562, 1436 cm^{-1}. ^1H NMR (300.1 MHz, $CDCl_3$): δ 1.14 (s, 3H, Me_{mj}), 1.42 (s, 3H, Me_{mn}), 2.49–2.67 (m, 4H, $H(2')_{mj}$, $H(2')_{mn}$, $H(4)_{mj}$ and $H(4)_{mn}$), 2.69–2.84 (m, 4H, 2×$H(1'')_{mj}$ and 2×$H(1'')_{mn}$), 3.06 (d, 1H, $H(4)_{mj}$, ^2J = 16.5 Hz), 3.09–3.30 (m, 5H, $H(2')_{mj}$, $H(2')_{mn}$ and CO_2Me), 3.35 (d, 1H, $H(4)_{mn}$, ^2J = 16.4 Hz), 3.52–3.65 (m, 2H, $H(3')_{mj}$ and $H(3')_{mn}$), 3.67–3.88 (m, 19H, 2×$H(2'')_{mj}$, 2×$H(2'')_{mn}$ and 5×CO_2Me), 5.12–5.25 (m, 2H, $H(1')_{mj}$ and $H(1')_{mn}$), 7.06–7.15 (m, 2H, $H(4'')_{mj}$ and $H(4'')_{mn}$), 7.24–7.32 (m, 4H, $H(3'')_{mj\ and\ mn}$ and $H(5'')_{mj\ and\ mn}$) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 18.5 and 21.0 (Me), 31.0 and 31.4 (C(2′)), 33.3 and 33.4 (C(1′′)), 41.5 ($C(2'')_{mj\ and\ mn}$), 48.9 and 49.0 (C(4)), 49.4 and 49.8 (C(3′)), 51.8, 52.3, 52.4, 52.5 and 52.6 (6×CO_2Me), 55.9 and 57.4 (C(1′)), 70.5 and 71.4 (C(5)), 128.1 and 128.3 (C(3′′) or C(5′′)), 128.6 and 128.7 (C(4′′)), 130.5 and 130.6 (C(3′′) or C(5′′)), 135.1, 135.4 and 136.5 (C(2′′) and C(6′′)), 136.0 and 137.3 (C(1′′)), 142.5 and 142.8 (C(3)), 169.3, 169.6, 169.7, 169.8, 172.9 and 174.1 (6 COO). MS (*m/z* for ^{35}Cl, %): 506 (21, M^+). HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{21}H_{25}N_2O_6Cl_3$ (for ^{35}Cl) 529.0670; Found 529.0668.

*Dimethyl 2-(2-(3-(2-chloroethyl)-5-(methoxycarbonyl)-5-methyl-4,5-dihydro-1H-pyrazol-1-yl)-2-(5-phenylthiophen-2-yl)-ethyl)malonate **(3fa)***. Compound **3fa** was prepared from **1f** and **2a** in yield 38% (118 mg, *dr* = 1.2/1). Red oil. IR (KBr) $\tilde{\nu}$ 3065, 3000, 2953, 2846, 1735 br. (C=O), 1599, 1498, 1436 cm^{-1}. ^1H NMR (300.1 MHz, $CDCl_3$): δ 1.14 (s, 3H, Me_{mj}), 1.50 (s, 3H, Me_{mn}), 2.38–2.47 (m, 2H, $H(2')_{mj\ and\ mn}$), 2.52 (d, 1H, $H(4)_{mj}$, ^2J = 16.9 Hz), 2.65 (d, 1H, $H(4)_{mn}$, ^2J = 16.5 Hz), 2.69–2.86 (m, 6H, $H(2')_{mj\ and\ mn}$ and 4×$H(1'')_{mj\ and\ mn}$), 3.14 (s, 3H, CO_2Me_{mn}), 3.18 (d, 1H, $H(4)_{mn}$, ^2J = 16.5 Hz), 3.33 (d, 1H, $H(4)_{mj}$, ^2J = 16.9 Hz), 3.56–3.67 (m, 2H, $H(3')_{mj\ and\ mn}$), 3.68–3.93 (m, 19H, 5×CO_2Me, 4×$H(2'')_{mj\ and\ mn}$), 4.47 (dd, 1H, $H(1')_{mn}$, ^3J = 9.5 Hz, ^3J = 6.1 Hz), 4.73 (dd, 1H, $H(1')_{mj}$, ^3J = 10.1 Hz, ^3J = 5.0 Hz), 6.79 (d, 1H, $H(3'')_{mj}$, ^3J = 3.7 Hz), 6.93 (d, 1H, $H(3'')_{mn}$, ^3J = 3.7 Hz), 7.09 (d, 1H, $H(4'')_{mn}$, ^3J = 3.7 Hz), 7.12 (d, 1H, $H(4'')_{mj}$, ^3J = 3.7 Hz), 7.19–7.43 (m, 6H, H_{Ar}), 7.52–7.63 (m, 4H, H_{Ar}) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 20.9 and 21.6 (Me), 33.5 and 33.6 (C(1′′)), 37.5 and 37.7

(C(2′)), 41.2 and 41.4 (C(2′′)), 47.1 and 47.3 (C(4)), 48.8 and 48.9 (C(3′)), 51.4, 52.4 and 52.5 (6×OMe), 55.6 and 56.6 (C(1′)), 69.0 and 71.5 (C(5)), 121.4 and 121.9 (C(4′′)), 125.5 and 125.6 (3 $C_{Ar\ mj}$), 126.2 and 127.4 (C(3′′)), 127.2 and 127.3 (3 $C_{Ar\ mn}$), 128.3 (2 $C_{Ar\ mn}$), 128.8 (2 $C_{Ar\ mj}$), 134.5 (C(*i*)$_{mj}$), 142.2 (C(2′′)$_{mn}$), 143.6 (C(*i*)$_{mn}$), 144.2 (C(5′′)$_{mj\ and\ mn}$), 145.5 (C(2′′)$_{mj}$), 146.5 and 148.4 (C(3)), 169.6, 169.7, 170.0, 172.0 and 173.3 (6 COO). MS (*m/z* for ^{35}Cl, %): 520 (9, M^+). HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{25}H_{29}N_2O_6SCl$ (for ^{35}Cl) 543.1327; Found 543.1320.

*Dimethyl 2-(2-(benzo[b]thiophen-2-yl)-2-(3-(2-chloroethyl)-5-(methoxycarbonyl)-5-methyl-4,5-dihydro-1H-pyrazol-1-yl)-ethyl)malonate **(3ga)***. Compound **3ga** was prepared from **1g** and **2a** in yield 63% (185 mg, *dr* = 1.2/1). Orange oil. IR (KBr) $\tilde{\nu}$ 3056, 3002, 2954, 2844, 1734 br. (C=O), 1457, 1436 cm^{-1}. ^{1}H NMR (300.1 MHz, $CDCl_3$): δ 1.13 (s, 3H, Me$_{mj}$), 1.52 (s, 3H, Me$_{mn}$), 2.38–2.57 (m, 3H, H(2′)$_{mj\ and\ mn}$ and H(4)$_{mj}$), 2.66 (d, 1H, H(4)$_{mn}$, ^2J = 16.7 Hz), 2.70–2.88 (m, 6H, H(2′)$_{mj\ and\ mn}$ and 4×H(1′′′)$_{mj\ and\ mn}$), 2.94 (s, 3H, CO_2Me_{mn}), 3.20 (d, 1H, H(4)$_{mn}$, ^2J = 16.7 Hz), 3.34 (d, 1H, H(4)$_{mj}$, ^2J = 16.9 Hz), 3.63 (dd, 1H, H(3′)$_{mn}$, ^3J = 9.0 Hz, ^3J = 6.2 Hz), 3.68–3.93 (m, 20H, 5×CO_2Me, 4×H(2′′′)$_{mj\ and\ mn}$ and H(3′)$_{mj}$), 4.59 (dd, 1H, H(1′)$_{mn}$, ^3J = 9.0 Hz, ^3J = 6.2 Hz), 4.83 (dd, 1H, H(1′)$_{mj}$, ^3J = 10.1 Hz, ^3J = 5.0 Hz), 7.07 (s, 1H, H(3′′)$_{mn}$), 7.24 (s, 1H, H(3′′)$_{mj}$), 7.25–7.41 (m, 4H, H_{Ar}), 7.63–7.87 (m, 4H, H_{Ar}) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 20.9 and 21.7 (Me), 33.5 and 33.6 (C(1′′′)), 37.0 and 37.3 (C(2′)), 41.2 and 41.3 (C(2′′′)), 47.1 and 47.4 (C(4)), 48.8 and 48.9 (C(3′)), 51.2, 52.4 and 52.5 (6×OMe), 55.8 and 56.8 (C(1′)), 69.0 and 71.4 (C(5)), 121.7, 122.1, 122.2, 123.1, 123.2, 123.8, 123.9 and 124.0 (10 CH_{Ar}), 138.6, 139.0, 140.1 and 140.2 (C(3a′′)$_{mj\ and\ mn}$ and C(7a′′)$_{mj\ and\ mn}$), 143.9 (C(2′′)$_{mn}$), 146.4 (C(3)$_{mj}$), 147.3 (C(2′′)$_{mj}$), 148.1 (C(3)$_{mn}$), 169.5, 169.7, 169.9, 172.0 and 173.2 (6 COO). MS (*m/z* for ^{35}Cl, %): 494 (85, M^+). HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{23}H_{27}N_2O_6SCl$ (for ^{35}Cl) 517.1171; Found 517.1169.

*Dimethyl 2-(2-(3-(2-chloroethyl)-5-(methoxycarbonyl)-5-methyl-4,5-dihydro-1H-pyrazol-1-yl)but-3-en-1-yl)malonate **(3ha)***. Compound **3ha** was prepared from **1h** and **2a** in yield 54% (125 mg, *dr* = 1.5/1). Colorless oil. IR (KBr) $\tilde{\nu}$ 3075, 2955, 2846, 1735 br. (C=O), 1637, 1617, 1436 cm^{-1}. ^{1}H NMR (300.1 MHz, $CDCl_3$): δ 1.27 (s, 3H, Me$_{mn}$), 1.41 (s, 3H, Me$_{mj}$), 2.09–2.23 (m, 2H, H(2′)$_{mj}$ and H(2′)$_{mn}$), 2.34–2.49 (m, 2H, H(2′)$_{mj}$ and H(2′)$_{mn}$), 2.53 (d, 1H, H(4)$_{mn}$, ^2J = 17.0 Hz), 2.60 (d, 1H, H(4)$_{mj}$, ^2J = 16.6 Hz), 2.74 (br.t, 4H, 2×H(1′′′)$_{mj}$ and 2×H(1′′′)$_{mn}$, ^3J = 7.1 Hz), 3.18 (d, 1H, H(4)$_{mj}$, ^2J = 16.6 Hz), 3.27 (d, 1H, H(4)$_{mn}$, ^2J = 17.0 Hz), 3.46–3.67 (m, 5H, H(1′)$_{mj}$, H(1′)$_{mn}$ and CO_2Me), 3.68–3.80 (m, 21H, H(3′)$_{mj}$, H(3′)$_{mn}$, 2×H(2′′′)$_{mj}$, 2×H(2′′′)$_{mn}$ and 5×CO_2Me), 4.96–5.21 (m, 4H, 2×H(2′′)$_{mj}$ and 2×H(2′′)$_{mn}$), 5.78 (ddd, 1H, H(1′′)$_{mj}$, ^3J = 17.5 Hz, ^3J = 10.4 Hz, ^3J = 8.4 Hz), 5.97–6.13 (m, 1H, H(1′′)$_{mn}$) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 20.8 and 21.2 (Me), 33.3 and 33.5 (C(1′′′)), 34.3 and 34.8 (C(2′)), 41.2 and 41.4 (C(2′′′)), 47.3 (C(4)$_{mj\ and\ mn}$), 48.6 and 48.8 (C(3′)), 51.8, 52.2, 52.3 and 52.4 (6×CO_2Me), 58.4 and 59.1 (C(1′)), 69.3 and 71.5 (C(5)), 116.1 and 116.6 (C(2′′)), 137.0 and 139.9 (C(1′′)), 145.8 and 147.6 (C(3)), 169.8, 169.9, 170.1, 172.9 and 173.3 (6 COO). MS (*m/z* for ^{35}Cl, %): 388 (33, M^+). HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{17}H_{25}N_2O_6Cl$ (for ^{35}Cl) 411.1293; Found 411.1290.

*Dimethyl (E)-2-(2-(3-(2-chloroethyl)-5-(methoxycarbonyl)-5-methyl-4,5-dihydro-1H-pyrazol-1-yl)-4-phenylbut-3-en-1-yl)-malonate **(3ia)***. Compound **3ia** was prepared from **1i** and **2a** in yield 65% (180 mg, *dr* = 1.2/1). Diastereomers were partially separated using column chromatography on SiO_2. IR (KBr) $\tilde{\nu}$ 3082, 3058, 3027, 2999, 2954, 2907, 2845, 1731 br. (C=O), 1600, 1495, 1436 cm^{-1}. MS (*m/z* for ^{35}Cl, %): 464 (100, M^+). HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{23}H_{29}N_2O_6Cl$ (for ^{35}Cl) 487.1606; Found 487.1603. 1st diastereomer. Orange oil. ^{1}H NMR (300.1 MHz, $CDCl_3$): δ 1.45 (s, 3H, Me), 2.19–2.33 (m, 1H, H(2′)), 2.48–2.58 (m, 1H, H(2′)), 2.68 (d, 1H, H(4), ^2J = 16.6 Hz), 2.78 (t, 2H, H(1′′′), ^3J = 7.0 Hz), 3.17 (d, 1H, H(4), ^2J = 16.6 Hz), 3.37 (s, 3H, CO_2Me), 3.62–3.88 (m, 10H, H(1′), H(3′), 2×H(2′′′) and 2×CO_2Me), 6.17 (dd, 1H, H(1′′), ^3J = 16.1 Hz, ^3J = 8.5 Hz), 6.36 (d, 1H, H(2′′), ^3J = 16.1 Hz), 7.18–7.39 (m, 5H, H_{Ar}) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 21.2 (Me), 33.5 (C(1′′′)), 34.7 (C(2′)), 41.3 (C(2′′′)), 47.3 (C(4)), 48.8 (C(3′)), 52.0, 52.4 and 52.5 (3×OMe), 58.1 (C(1′)), 69.3 (C(5)), 126.3 (2×C(*o*)), 127.5 (C(*p*)), 128.0 (C(1′′)), 128.5 (2×C(*m*)), 132.0 (C(2′′)), 136.6 (C(*i*)), 148.3 (C(3)), 169.8, 169.9 and 172.7 (3 COO). 2nd diastereomer. Orange oil. ^{1}H NMR (300.1 MHz, $CDCl_3$): δ 1.28 (s, 3H, Me), 2.25 (ddd, 1H, H(2′), ^2J = 14.0 Hz, ^3J = 9.0 Hz, ^3J = 5.3 Hz), 2.43–2.57 (m, 2H, H(2′) and H(4)), 2.77 (td, 2H, H(1′′′), ^3J = 6.7 Hz, ^2J = 4.3 Hz), 3.29 (d, 1H, H(4), ^2J = 16.8 Hz), 3.60–3.86 (m, 12H, H(3′), 2×H(2′′′) and 3×CO_2Me), 3.93 (ddd, 1H, H(1′), ^3J = 9.7 Hz, ^3J = 6.9 Hz, ^3J = 5.3 Hz), 3.60–3.86 (m, 2H, H(1′′) and H(2′′)), 7.17–7.45 (m, 5H, H_{Ar}) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 21.1 (Me), 33.3 (C(1′′′)), 35.1 (C(2′)), 41.4 (C(2′′′)), 47.3 (C(4)), 48.6 (C(3′)), 52.3, 52.4 and 52.5 (3×OMe), 58.8 (C(1′)), 71.5 (C(5)), 126.2 (2×C(*o*)), 127.4 (C(*p*)), 128.5 (2×C(*m*)), 131.1 and 131.2 (C(1′′) and C(2′′)), 137.0 (C(*i*)), 146.1 (C(3)), 169.9, 170.1 and 172.3 (3 COO).

*Dimethyl 2-(2-(3-(2-chloroethyl)-5-(methoxycarbonyl)-5-methyl-4,5-dihydro-1H-pyrazol-1-yl)-4-phenylbut-3-yn-1-yl)-malonate **(3ja)***. Compound **3ja** was prepared from **1j** and **2a** in yield 46% (126 mg, *dr* = 1.2/1). Diastereomers were partially separated using column chromatography on SiO_2. IR (KBr) $\tilde{\nu}$ 3080, 2997, 2953, 2845, 2231 (C≡C), 1731 br. (C=O), 1628, 1598, 1573, 1491, 1435, 1350, 1272 cm^{-1}. MS (*m/z* for ^{35}Cl, %): 462 (12, M^+). HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{23}H_{27}N_2O_6Cl$ (for ^{35}Cl) 485.1450; Found 485.1446. 1st diastereomer. Colorless oil. ^{1}H NMR (300.1 MHz, $CDCl_3$): δ 1.50 (s, 3H, Me), 2.49–2.75 (m, 3H, 2×H(2′) and H(4)), 2.80 (t, 2H, H(1′′′), ^3J = 7.0 Hz), 3.31 (d, 1H, H(4), ^2J = 16.3 Hz), 3.65 (s, 3H, CO_2Me), 3.67–3.79 (m, 7H, 2×H(2′′′) and 2×CO_2Me), 3.84 (t, 1H, H(3′), ^3J = 7.0 Hz), 4.19 (dd, 1H, H(1′), ^3J = 8.6 Hz, ^3J = 6.2 Hz), 7.16–7.46 (m, 5H, H_{Ar}) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 21.0 (Me), 33.6 (C(1′′′)), 34.3 (C(2′)), 41.2 (C(2′′′)), 46.9 (C(4)), 48.5 and 48.6 (C(1′) and C(3′)), 52.3, 52.4 and 52.5 (3×OMe), 69.9 (C(5)), 84.6 and 86.9 (C(1′′) and C(2′′)), 122.8 (C(*i*)), 128.0 (C(*p*)), 128.1 (2×C(*m*)), 131.6 (2×C(*o*)), 150.6 (C(3)), 169.6, 169.7 and 172.1 (3 COO). 2nd diastereomer. Colorless oil. ^{1}H NMR (300.1 MHz, $CDCl_3$): δ 1.54 (s, 3H, Me), 2.47–2.94 (m, 5H, 2×H(1′′′), 2×H(2′) and H(4)), 3.32 (d, 1H, H(4), ^2J = 16.8 Hz), 3.73–3.79 (m, 11H, 2×H(2′′′) and 3×CO_2Me), 3.87 (dd, 1H, H(3′), ^3J = 8.8 Hz, ^3J = 5.8 Hz), 4.30 (dd, 1H, H(1′), ^3J = 8.8 Hz, ^3J = 5.8 Hz), 7.24–7.34 (m, 3H, H_{Ar}), 7.39 (dd, 2H, H_{Ar}, ^3J = 6.5 Hz, ^4J = 3.1 Hz) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 20.2 (Me), 33.3 (C(1′′′)), 34.6 (C(2′)), 41.5 (C(2′′′)), 47.0 (C(4)), 48.5 and 48.8 (C(1′) and C(3′)), 52.4 and 52.5 (3×OMe), 71.6 (C(5)), 84.7 and 89.1 (C(1′′) and C(2′′)), 123.1 (C(*i*)), 128.0 (C(*p*)), 128.1 (2×C(*m*)), 131.5 (2×C(*o*)), 148.7 (C(3)), 169.6, 169.8 and 173.1 (3 COO).

*Dimethyl 2-(2-(3-(2-chloroethyl)-5-(methoxycarbonyl)-5-methyl-4,5-dihydro-1H-pyrazol-1-yl)ethyl)malonate **(3ka)***. Compound **3ka** was prepared from **1k** and **2a** in yield 80% (173 mg). Colorless oil. IR (KBr) $\tilde{\nu}$ 3000, 2955, 2920, 2915, 2844, 1736 br. (C=O), 1698, 1601, 1497, 1450, 1370 cm^{-1}. ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 1.31 (s, 3H, Me), 2.22–2.35 (m, 2H, H(2′)), 2.57 (d, 1H, H(4), ^2J = 16.5 Hz), 2.73 (t, 2H, H(1′′), ^3J = 6.6 Hz), 2.89–3.03 (m, 2H, H(1′)), 3.20 (d, 2H, H(4), ^2J = 16.5 Hz), 3.67–3.78 (m, 3H, H(3′) and 2 H(2′′)), 3.71 (s, 3H, CO_2Me), 3.72 (s, 3H, CO_2Me), 3.74 (s, 3H, CO_2Me) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 18.8 (Me), 28.2 (C(2′)), 33.4 (C(1′′)), 41.3 (C(2′′)), 46.4 (C(1′)), 47.2 (C(4)), 48.9 (C(3′)), 52.1 and 52.3 (3 OMe), 71.2 (C(5)), 148.6 (C(3)), 169.9, 170.0 and 173.1 (3 COO). MS (*m/z* for ^{35}Cl, %): 362 (12, M^+). HRMS

(ESI-TOF) *m/z*: [M + Na]$^+$ Calcd for $C_{15}H_{23}N_2O_6Cl$ (for ^{35}Cl) 385.1142; Found 385.1140.

*Dimethyl 2-(2-(3-(2-chloroethyl)-5-(methoxycarbonyl)-5-methyl-4,5-dihydro-1H-pyrazol-1-yl)pentyl)malonate **(3la)***. Compound **3la** was prepared from **1l** and **2a** in yield 46% (111 mg, *dr* = 1/1). Diastereomers were partially separated using column chromatography on SiO_2. IR (KBr) $\tilde{\nu}$ 2957, 2875, 1732 br. (C=O), 1436, 1380 cm^{-1}. MS (*m/z* for ^{35}Cl, %): 404 (20, M$^+$). HRMS (ESI-TOF) *m/z*: [M + Na]$^+$ Calcd for $C_{18}H_{29}N_2O_6Cl$ (for ^{35}Cl) 427.1606; Found 427.1605. 1st diastereomer. Colorless oil. ^{1}H NMR (300.1 MHz, $CDCl_3$): δ 0.88 (t, 3H, H(3´´), ^3J = 6.9 Hz), 1.17–1.56 (m, 7H, Me, H(1´´) and H(2´´)), 2.07–2.32 (m, 2H, H(2´)), 2.55 (d, 1H, H(4), ^2J = 16.5 Hz), 2.74 (t, 2H, H(1´´´), ^3J = 7.2 Hz), 2.98 (dt, 1H, H(1´), ^3J = 8.3 Hz, ^3J = 4.3 Hz), 3.30 (d, 1H, H(4), ^2J = 16.5 Hz), 3.65 (dd, 1H, H(3´), ^3J = 8.8 Hz, ^3J = 5.8 Hz), 3.68–3.87 (m, 11H, 2×H(2´´´) and 3×CO_2Me) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 14.0 (C(3´´)), 19.9 (C(2´´)), 21.6 (Me), 33.1 (C(2´)), 33.5 (C(1´´´)), 35.1 (C(1´´)), 41.3 (C(2´´´)), 46.5 (C(4)), 49.2 (C(3´)), 52.0, 52.3 and 52.4 (3×OMe), 54.9 (C(1´)), 69.6 (C(5)), 146.5 (C(3)), 169.9, 170.1 and 173.0 (3 COO). 2nd diastereomer. Colorless oil. ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 0.90 (t, 3H, H(3´´), ^3J = 7.0 Hz), 1.19–1.59 (m, 7H, Me, H(1´´) and H(2´´)), 2.08 (ddd, 1H, H(2´), ^2J = 13.3 Hz, ^3J = 9.7 Hz, ^3J = 3.4 Hz), 2.22 (ddd, 1H, H(2´), ^2J = 13.3 Hz, ^3J = 9.7 Hz, ^3J = 3.4 Hz), 2.52 (d, 1H, H(4), ^2J = 16.7 Hz), 2.62–2.78 (m, 2H, H(1´´´)), 2.91–3.01 (m, 1H, H(1´)), 3.26 (d, 1H, H(4), ^2J = 16.7 Hz), 3.61–3.82 (m, 12H, 2×H(2´´´), H(3´) and 3×CO_2Me) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 14.1 (C(3´´)), 20.0 (C(2´´)), 20.2 (Me), 33.3 (C(2´)), 33.4 (C(1´´´)), 36.9 (C(1´´)), 41.6 (C(2´´´)), 47.0 (C(4)), 48.8 (C(3´)), 52.2, 52.3 and 52.4 (3×OMe), 55.7 (C(1´)), 71.0 (C(5)), 144.5 (C(3)), 170.0, 170.5 and 173.4 (3 COO).

*Dimethyl 2-(2-(3-(2-chloroethyl)-5-(methoxycarbonyl)-5-methyl-4,5-dihydro-1H-pyrazol-1-yl)-2-phenylpropyl)malonate **(3ma)***. Compound **3ma** was prepared from **1m** and **2a** in yield 15% (40 mg, *dr* = 1/1). The second diastereomer decomposed on silica gel. Colorless oil. IR (KBr) $\tilde{\nu}$ 3039, 3009, 2956, 2847, 1734 br. (C=O), 1448, 1437, 1269, 1235 cm^{-1}. ^{1}H NMR (300.1 MHz, $CDCl_3$): δ 0.84 (s, 3H, Me), 1.48 (s, 3H, Me), 2.41–2.59 (m, 2H, H(2´) and H(4)), 2.75 (dd, 2H, H(1´´), ^3J = 12.9 Hz, ^3J = 6.8 Hz), 3.07 (dd, 1H, H(2´), ^2J = 14.4 Hz, ^3J = 3.8 Hz), 3.17 (d, 1H, H(4), ^2J = 16.4 Hz), 3.59–3.93 (m, 11H, 2×H(2´´) and 3×CO_2Me), 7.17–7.35 (m, 3H, H_{Ar}), 7.57 (dd, 2H, H_{Ar}, ^3J = 8.1 Hz, ^4J = 1.5 Hz) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 21.0 and 21.3 (2 Me), 33.2 (C(1´´)), 41.4 (C(2´´)), 42.8 (C(2´)), 48.1 (C(4)), 51.3 (C(3´)), 52.3, 52.4 and 52.7 (3 OMe), 62.6 (C(1´)), 69.4 (C(5)), 126.4 (2 C(*o*)), 126.9 (C(*p*)), 127.8 (2 C(*m*)), 140.6 (C(*i*)), 146.4 (C(3)), 170.3, 170.8 and 176.4 (3 COO). MS (*m/z* for ^{35}Cl, %): 450 (11, M$^+$). HRMS (ESI-TOF) *m/z*: [M + Na]$^+$ Calcd for $C_{22}H_{29}N_2O_6Cl$ (for ^{35}Cl) 475.1606; Found 475.1605.

*Dimethyl 2-(1-(3-(2-chloroethyl)-5-(methoxycarbonyl)-5-methyl-4,5-dihydro-1H-pyrazol-1-yl)-1,2,3,4-tetrahydronaphthalen-2-yl)malonate **(3na)***. Compound **3na** was prepared from **1n** and **2a** in yield 10% (28 mg, *dr* = 1.2/1). The 2nd diastereomer decomposed on silica gel. 1st diastereomer: Colorless oil. IR (KBr) $\tilde{\nu}$ 3009, 2997, 2953, 2849, 1735 br. (C=O), 1491, 1435 cm^{-1}. ^{1}H NMR (300.1 MHz, CD_2Cl_2): δ 1.39 (s, 3H, Me), 1.50–1.64 (m, 1H, H(3´)), 2.22–2.45 (m, 1H, H(3´)), 2.61 (d, 1H, H(4), ^2J = 16.8 Hz), 2.65–2.94 (m, 5H, H(2´), 2×H(4´) and 2×H(1´´)), 3.26 (d, 1H, H(4), ^2J = 16.8 Hz), 3.48 (d, 1H, H(1´´´), ^3J = 8.5 Hz), 3.56 (s, 3H, CO_2Me), 3.63–3.85 (m, 8H, 2×H(2´´) and 2×CO_2Me), 4.46 (d, 1H, H(1´), ^3J = 5.5 Hz), 7.05–7.23 (m, 4H, H_{Ar}) ppm. ^{13}C NMR (75.5 MHz, CD_2Cl_2): δ 21.0 (Me), 21.8 (C(3´)), 25.9 (C(4´)), 33.2 (C(1´´)), 38.4 (C(2´)), 41.9 (C(2´´)), 48.0 (C(4)), 52.4, 52.5 and 52.8 (3 OMe and C(1´´´)), 57.9 (C(1´)), 70.5 (C(5)), 125.5, 127.1, 128.5 and 129.5 (4 CH_{Ar}), 136.0 and 137.7 (C(4a´) and C(8a´)), 144.0 (C(3)), 169.0, 169.5 and 173.9 (3 COO). MS (*m/z* for ^{35}Cl, %): 464 (34, M$^+$). HRMS (ESI-TOF) *m/z*: [M + Na]$^+$ Calcd for $C_{23}H_{29}N_2O_6Cl$ (for ^{35}Cl) 487.1606; Found 487.1605.

*Dimethyl 2-(2-(3-(2-chloroethyl)-5-(methoxycarbonyl)-5-methyl-4,5-dihydro-1H-pyrazol-1-yl)-2-(2-phenylcyclopropyl)ethyl)malonate **(3oa)***. Compound **3oa** was prepared from **1o** and **2a** in yield 37% (105 mg, *dr* = 1.5/1). Diastereomers were partially separated using column chromatography on SiO_2. IR (KBr) $\tilde{\nu}$ 3061, 3028, 3003, 2954, 2847, 1752 and 1736 br. (C=O), 1604, 1498, 1458, 1438 cm^{-1}. MS (*m/z* for ^{35}Cl, %): 478 (11, M$^+$). HRMS (ESI-TOF) *m/z*: [M + Na]$^+$ Calcd for $C_{24}H_{31}N_2O_6Cl$ (for ^{35}Cl) 501.1763; Found 501.1753. 1st diastereomer. Colorless oil. ^{1}H NMR (300.1 MHz, $CDCl_3$): δ 0.93 (ddd, 2H, H(3´´), ^2J = 10.4 Hz, ^3J = 8.5 Hz, ^3J = 5.1 Hz), 1.31–1.47 (m, 4H, Me and H(1´´)), 1.74–1.84 (m, 1H, H(2´´)), 2.25–2.48 (m, 2H, H(2´)), 2.62 (d, 1H, H(4), ^2J = 16.6 Hz), 2.69–2.82 (m, 3H, 2×H(1´´´) and H(1´)), 3.32 (d, 1H, H(4), ^2J = 16.6 Hz), 3.58–3.89 (m, 12H, H(3´), 2×H(2´´´) and 3×CO_2Me), 7.02–7.42 (m, 5H, H_{Ar}) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 15.1 (C(3´´)), 20.6 (Me), 22.3 (C(2´´)), 27.3 (C(1´´)), 33.5 (C(1´´´)), 33.7 (C(2´)), 41.3 (C(2´´´)), 47.3 (C(4)), 49.0 (C(3´)), 52.4 (3×OMe), 58.7 (C(1´)), 70.5 (C(5)), 125.5 (C(*p*)), 125.6 (2×C(*o*)), 128.3 (2×C(*m*)), 142.5 (C(*i*)), 145.6 (C(3)), 169.9, 170.0 and 173.7 (3 COO). 2nd diastereomer. Colorless oil. ^{1}H NMR (300.1 MHz, $CDCl_3$): δ 0.85–1.09 (m, 2H, H(3´´)), 1.29–1.48 (m, 4H, Me and H(1´´)), 1.88–1.99 (m, 1H, H(2´´)), 2.22–2.48 (m, 2H, H(2´)), 2.60 (d, 1H, H(4), ^2J = 16.7 Hz), 2.71–2.83 (m, 3H, 2×H(1´´´) and H(1´)), 3.34 (d, 1H, H(4), ^2J = 16.7 Hz), 3.63–3.86 (m, 12H, H(3´), 2×H(2´´´) and 3×CO_2Me), 7.00–7.46 (m, 5H, H_{Ar}) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 17.6 (C(3´´)), 22.6 (Me), 22.7 (C(2´´)), 26.8 (C(1´´)), 33.4 (C(1´´´)), 33.9 (C(2´)), 41.5 (C(2´´´)), 47.5 (C(4)), 48.6 (C(3´)), 52.2, 52.3 and 52.4 (3×OMe), 59.6 (C(1´)), 70.2 (C(5)), 125.5 (C(*p*)), 125.8 (2×C(*o*)), 128.2 (2×C(*m*)), 142.7 (C(*i*)), 144.4 (C(3)), 169.1, 170.4 and 173.3 (3 COO).

*Methyl 3-(2-chloroethyl)-1-(3-(ethoxycarbonyl)-4-oxo-1-phenylpentyl)-5-methyl-4,5-dihydro-1H-pyrazole-5-carboxylate **(3pa)***. Compound **3pa** was prepared from **1p** and **2a** in yield 79% (205 mg, *dr* = 1.7/1.6/1.4/1). Light yellow oil. IR (KBr) $\tilde{\nu}$ 3085, 3062, 3026, 2981, 2954, 2909, 2845, 1736 and 1716 br. (C=O), 1644, 1493, 1454, 1435, 1360, 1283, 1249 cm^{-1}. ^{1}H NMR (300.1 MHz, $CDCl_3$): δ 0.94 (s, 3H, Me), 0.96 (s, 3H, Me), 1.15–1.37 (m, 12H, Me_{CO2Et}), 1.42 (s, 3H, Me), 1.44 (s, 3H, Me), 2.09–2.83 (m, 28H, 8×H(1´´), 8×H(2´), 4×COMe and 4×H(4)), 2.90 (s, 3H, CO_2Me), 3.00 (s, 3H, CO_2Me), 3.12–3.36 (m, 4H, 4×H(4)), 3.39–3.91 (m, 18H, 8×H(2´´), 4×H(3´), 2×CO_2Me), 3.99–4.35 (m, 12H, 4×$CH_{2\ CO2Et}$ and 4×H(1´)), 7.13–7.52 (m, 20H, H_{Ar}) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 14.1 (4×Me_{CO2Et}), 20.6, 21.0, 21.9 and 22.1 (4×Me), 28.7, 28.8, 29.0 and 29.3 (4×COMe), 33.3, 33.4, 33.5 and 33.6 (4×C(1´´)), 35.4, 35.6 and 35.7 (4×C(2´)), 41.2, 41.3, 41.4 and 41.4 (4×C(2´´)), 47.4, 47.5, 47.6 and 47.7 (4×C(4)), 51.3, 51.4 and 52.4 (4×OMe), 56.6, 57.0, 57.1 and 57.5 (4×C(3´)), 59.3, 59.6, 60.1 and 60.5 (4×C(1´)), 61.0, 61.1, 61.2 and 61.3 (4×$CH_{2\ CO2Et}$), 68.9, 69.5, 71.1 and 71.3 (4×C(5)), 127.0–128.6 (20 CH_{Ar}), 140.6, 141.1, 143.7, 143.9, 144.2 and 144.3 (4×C(*i*) and 4× C(3)), 169.6, 169.7, 169.9, 172.2, 172.5, 173.5 and 173.6 (8×COO), 202.8, 203.0, 203.4 and 203.8 (4×CO). MS (*m/z* for ^{35}Cl, %): 436 (25, M$^+$). HRMS (ESI-TOF) *m/z*: [M + Na]$^+$ Calcd for $C_{22}H_{29}N_2O_5Cl$ (for ^{35}Cl) 459.1657; Found 459.1646.

*Methyl 1-(3-acetyl-4-oxo-1-phenylpentyl)-3-(2-chloroethyl)-5-methyl-4,5-dihydro-1H-pyrazole-5-carboxylate **(3qa)***. Compound **3qa** was prepared from **1q** and **2a** in yield 12% (29 mg, *dr* = 1.5/1; ketone : enol = 2.5/1). The 2nd diastereomer decomposed on silica gel. 1st diastereomer (ketone form): Light yellow oil. IR (KBr) $\tilde{\nu}$ 3063, 3031, 3002, 2954, 2928, 2866, 1736 br. (C=O), 1672, 1602 br., 1495, 1453, 1435, 1385, 1362, 1299, 1266, 1225 cm^{-1}. ^{1}H NMR (300.1 MHz, CD_2Cl_2): δ 0.95 (s, 3H, Me), 2.22 (s, 6H, 2×COMe), 2.54 (d, 1H, H(4), ^2J = 17.0

Hz), 2.81 (t, 2H, H(1´´), ^3J = 6.4 Hz), 2.91–3.03 (m, 1H, H(2´)), 3.29 (d, 1H, H(4), ^2J = 17.0 Hz), 3.36–3.48 (m, 1H, H(2´)), 3.84 (t, 2H, H(2´´), ^3J = 6.4 Hz), 3.88 (s, 3H, CO_2Me), 4.08–4.19 (m, 1H, H(1´)), 5.63 (dd, 1H, H(3´), ^3J = 10.7 Hz, ^3J = 8.3 Hz), 7.21–7.57 (m, 5H, H_{Ar}) ppm. ^{13}C NMR (75.5 MHz, CD_2Cl_2): δ 21.9 (Me), 29.2 (2×COMe), 33.3 (C(1´´)), 38.8 (C(2′)), 41.6 (C(2´´)), 47.4 (C(4)), 53.5 (OMe), 60.4 (C(1′)), 71.1 (C(5)), 83.0 (C(3′)), 125.6, 128.0 and 128.6 (5 CH_{Ar}), 141.6 (C(*i*)), 144.7 (C(3)), 166.9 (COO), 193.8 (2 CO). MS (*m/z* for ^{35}Cl, %): 406 (9, M^+). HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{21}H_{27}N_2O_4Cl$ (for ^{35}Cl) 429.1552; Found 429.1552. 1st diastereomer (enol form): ^1H NMR (300.1 MHz, CD_2Cl_2) (key signals): δ 2.23 (s, 3H, Me), 17.05 (s, 1H, OH).

Methyl 1-(3-benzoyl-4-oxo-1,4-diphenylbutyl)-3-(2-chloroethyl)-5-methyl-4,5-dihydro-1H-pyrazole-5-carboxylate ***(3ra)***. Compound **3ra** was prepared from **1r** and **2a** in yield 17% (54 mg, *dr* = 1/1). Light yellow oil. IR (KBr) $\tilde{\nu}$ 3085, 3062, 3030, 3003, 2954, 2932, 2873, 1732, 1695 and 1673 br. (C=O), 1597, 1580, 1493, 1449, 1347, 1268, 1239 cm^{-1}. ^1H NMR (300.1 MHz, $CDCl_3$): δ 0.98 (s, 3H, Me), 2.43–2.84 (m, 3H, 2×H(2′) and H(4)), 2.91 (t, 2H, H(1´´), ^3J = 6.8 Hz), 3.23 (s, 3H, CO_2Me), 3.41 (d, 1H, H(4), ^2J = 17.0 Hz), 3.88 (t, 2H, H(2´´), ^3J = 6.8 Hz), 4.45 (dd, 1H, H(1′), ^3J = 10.4 Hz, ^3J = 3.5 Hz), 5.81 (dd, 1H, H(3′), ^3J = 10.4 Hz, ^3J = 3.5 Hz), 6.98–7.70 (m, 11H, H_{Ar}), 7.92 (d, 2H, H_{Ar}, ^3J = 8.4 Hz, ^4J = 1.3 Hz), 8.13–8.24 (m, 2H, H_{Ar}) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 22.2 (Me), 33.5 (C(1´´)), 36.7 (C(2′)), 41.4 (C(2´´)), 47.7 (C(4)), 52.2 (OMe), 53.4 (C(3′)), 60.6 (C(1′)), 71.3 (C(5)), 127.4–129.2 (15 CH_{Ar}), 135.4, 136.7 and 144.7 (3 C(*i*)), 143.8 (C(3)), 173.7 (COO), 196.0 and 197.5 (2 CO). MS (*m/z* for ^{35}Cl, %): 530 (12, M^+). HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{31}H_{31}N_2O_4Cl$ (for ^{35}Cl) 553.1865; Found 553.1870.

Dimethyl 2-(2-(3-(2-chloroethyl)-3a,4,5,6,7,7a-hexahydro-1H-4,7-methanoindazol-1-yl)-2-phenylethyl)malonate ***(3ab)***. Compound **3ab** was prepared from **1a** and **2b** in yield 90% (240 mg, *dr* = 1/1). Diastereomers were partially separated using column chromatography on SiO_2. IR (KBr) $\tilde{\nu}$ 3035, 2955, 2938, 2923, 2910, 2843, 1739 br. (C=O), 1610, 1505, 1450, 1333 cm^{-1}. MS (*m/z* for ^{35}Cl, %): 432 (27, M^+). HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{23}H_{29}N_2O_4Cl$ (for ^{35}Cl) 455.1714; Found 455.1720. 1st diastereomer. Light yellow oil. ^1H NMR (400.1 MHz, $CDCl_3$): δ 0.91–1.16 (m, 3H, H(5), H(6) and H(8)), 1.42 (ddd, 3H, H(5), H(6) and H(8), ^2J = 13.0 Hz, ^3J = 10.3 Hz, ^3J = 5.2 Hz), 2.16 (br.d, 1H, H(7), ^3J = 3.4 Hz), 2.25 (br.d, 1H, H(4), ^3J = 2.7 Hz), 2.38 (ddd, 1H, H(2′), ^2J = 13.9 Hz, ^3J = 9.9 Hz, ^3J = 5.7 Hz), 2.51–2.61 (m, 2H, H(3a) and H(1´´)), 2.62–2.80 (m, 2H, H(2′) and H(1´´)), 3.09 (d, 1H, H(7a), ^3J = 9.7 Hz), 3.70–3.76 (m, 2H, H(2´´)), 3.72 (s, 3H, CO_2Me), 3.74 (s, 3H, CO_2Me), 3.83 (dd, 1H, H(3′), ^3J = 9.9 Hz, ^3J = 5.7 Hz), 3.93 (dd, 1H, H(1′), ^3J = 9.9 Hz, ^3J = 5.7 Hz), 7.20–7.32 (m, 5H, H_{Ar}) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 23.9 (C(5)), 28.4 (C(6)), 32.5 (C(1´´)), 33.6 (C(2′)), 33.7 (C(8)), 39.6 (C(4)), 41.3 (C(2´´)), 42.2 (C(7)), 49.1 (C(3′)), 52.2 and 52.3 (2 OMe), 57.9 (C(3a)), 63.4 (C(1′)), 69.3 (C(7a)), 127.3, 128.1 and 128.5 (5 CH_{Ar}), 140.1 (C(*i*)), 150.1 (C(3)), 169.9 and 170.2 (2 COO). 2nd diastereomer. Light yellow oil. ^1H NMR (400.1 MHz, $CDCl_3$): δ 0.83–0.94 (m, 1H, H(5)), 1.02–1.11 (m, 2H, H(6) and H(8)), 1.19 (br.d, 1H, H(7), ^3J = 4.4 Hz), 1.22–1.49 (m, 3H, H(5), H(6) and H(8)), 2.23 (br.d, 1H, H(4), ^3J = 3.8 Hz), 2.44 (ddd, 1H, H(2′), ^2J = 14.2 Hz, ^3J = 8.3 Hz, ^3J = 6.5 Hz), 2.50–2.74 (m, 4H, H(3a), H(2′) and 2×H(1´´)), 3.07 (d, 1H, H(7a), ^3J = 9.4 Hz), 3.64 (dd, 1H, H(3′), ^3J = 8.3 Hz, ^3J = 6.5 Hz), 3.68–3.75 (m, 8H, 2×CO_2Me and 2×H(2´´)), 4.16 (dd, 1H, H(1′), ^3J = 8.3 Hz, ^3J = 6.5 Hz), 7.21–7.34 (m, 5H, H_{Ar}) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 24.3 (C(5)), 28.3 (C(6)), 32.4 (C(1´´)), 32.6 (C(2′)), 33.3 (C(8)), 39.1 (C(4)), 41.1 (C(2´´)), 43.4 (C(7)), 49.2 (C(3′)), 52.4 and 52.5 (2 OMe), 58.5 (C(3a)), 65.2 (C(1′)), 68.9 (C(7a)), 127.5, 128.1 and 128.4 (5 CH_{Ar}), 139.3 (C(*i*)), 151.4 (C(3)), 169.8 and 170.1 (2 COO).

Dimethyl 2-(2-(3-(2-chloroethyl)-3a,4,7,7a-tetrahydro-1H-4,7-methanoindazol-1-yl)-2-phenylethyl)malonate ***(3ac)***. Compound **3ac** was prepared from **1a** and **2c** in yield 44% (118 mg, *dr* = 1/1). Diastereomers were partially separated using column chromatography on SiO_2. IR (KBr) $\tilde{\nu}$ 3061, 3027, 2970, 2953, 2845, 1751 and 1734 br. (C=O), 1493, 1454, 1436 cm^{-1}. MS (*m/z* for ^{35}Cl, %): 430 (4, M^+). HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{23}H_{27}N_2O_4Cl$ (for ^{35}Cl) 453.1552; Found 453.1549. 1st diastereomer. Light yellow oil. ^1H NMR (300.1 MHz, $CDCl_3$): δ 1.52–1.64 (m, 2H, H(8)), 2.40 (ddd, 1H, H(2′), ^2J = 13.9 Hz, ^3J = 9.9 Hz, ^3J = 5.6 Hz), 2.52–2.85 (m, 4H, H(2′), 2×H(1´´) and H(4)), 2.86–2.94 (m, 2H, H(3a) and H(7)), 3.49 (d, 1H, H(7a), ^3J = 9.5 Hz), 3.70–3.81 (m, 8H, 2×CO_2Me and 2×H(2´´)), 3.85 (dd, 1H, H(3′), ^3J = 9.9 Hz, ^3J = 5.6 Hz), 4.01 (dd, 1H, H(1′), ^3J = 9.9 Hz, ^3J = 5.7 Hz), 5.94 (dd, 1H, H(5), ^3J = 5.8 Hz, ^3J = 3.0 Hz), 6.10 (dd, 1H, H(6), ^3J = 5.8 Hz, ^3J = 3.0 Hz), 7.21–7.36 (m, 5H, H_{Ar}) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 32.5 (C(1´´)), 33.4 (C(2′)), 41.2 (C(2´´)), 44.2 (C(8)), 45.4 (C(7)), 48.8 (C(3′)), 49.1 (C(4)), 52.2 and 52.4 (2×OMe), 58.4 (C(3a)), 63.6 (C(1′)), 71.0 (C(7a)), 127.3 (C(*p*)), 128.1 (C(*o*)), 128.4 (C(*m*)), 135.9 (C(5)), 139.6 (C(6)), 139.8 (C(*i*)), 148.7 (C(3)), 170.0 and 170.2 (2 COO). 2nd diastereomer. Light yellow oil. ^1H NMR (400.1 MHz, $CDCl_3$): δ 1.42–1.50 (m, 1H, H(8)), 1.54 (br.d, 1H, H(8), ^3J = 8.9 Hz), 2.54 (ddd, 1H, H(2′), ^2J = 14.2 Hz, ^3J = 7.9 Hz, ^3J = 6.5 Hz), 250–2.79 (m, 4H, H(2′), 2×H(1´´) and H(4)), 2.85 (br.d, 1H, H(7)), 2.89 (d, 1H, H(3a), ^3J = 9.2 Hz), 3.43 (d, 1H, H(7a), ^3J = 9.2 Hz), 3.63 (dd, 1H, H(3′), ^3J = 7.9 Hz, ^3J = 6.5 Hz), 3.65–3.75 (m, 8H, 2×CO_2Me and 2×H(2´´)), 4.16 (dd, 1H, H(1′), ^3J = 7.9 Hz, ^3J = 6.5 Hz), 5.84 (dd, 1H, H(5), ^3J = 5.8 Hz, ^3J = 3.0 Hz), 6.06 (dd, 1H, H(6), ^3J = 5.8 Hz, ^3J = 3.0 Hz), 7.22–7.34 (m, 5H, H_{Ar}) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 32.4 and 32.7 (C(2′) and C(1´´)), 41.0 (C(2´´)), 43.9 (C(8)), 44.9 (C(7)), 49.1 (C(3′)), 49.9 (C(4)), 52.4 and 52.5 (2×OMe), 58.7 (C(3a)), 65.2 (C(1′)), 70.4 (C(7a)), 127.5 (C(*p*)), 128.1 (C(*o*)), 128.4 (C(*m*)), 136.2 (C(5)), 139.3 (C(6) and C(*i*)), 150.0 (C(3)), 169.8 and 170.1 (2 COO).

Dimethyl 2-(2-(3-(2-chloroethyl)-3a,4,4a,5,6,7,7a,7b-octahydro-1H-4,6,7-(epimethanetriyl)pentaleno[1,2-c]pyrazol-1-yl)-2-phenylethyl)malonate ***(3ad)***. Compound **3ad** was prepared from **1a** and **2d** in yield 51% (125 mg, *dr* = 1.7/1). Diastereomers were partially separated using column chromatography on SiO_2. IR (KBr) $\tilde{\nu}$ 3060, 3028, 2933, 2865, 1783, 1752, 1736 br. (C=O), 1601, 1493, 1450, 1438 cm^{-1}. MS (*m/z* for ^{35}Cl, %): 456 (24, M^+). HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{25}H_{29}N_2O_4Cl$ (for ^{35}Cl) 479.1708; Found 479.1708. 1st diastereomer. Colorless oil. ^1H NMR (300.1 MHz, $CDCl_3$): δ 0.77 (br.t, 1H, H(8), ^3J = 5.6 Hz), 0.89 (br.t, 1H, H(4a), ^3J = 5.6 Hz), 1.22 (br.t, 1H, H(5), ^3J = 5.6 Hz), 1.57 (s, 2H, H(6)), 1.86 (s, 1H, H(7)), 1.97–2.05 (m, 2H, H(4) and H(7a)), 2.41 (ddd, 1H, H(2′), ^2J = 13.9 Hz, ^3J = 9.9 Hz, ^3J = 5.8 Hz), 2.51–2.86 (m, 3H, 2×H(1´´) and H(2′)), 3.03 (d, 1H, H(3a), ^3J = 9.6 Hz), 3.54 (d, 1H, H(7b), ^3J = 9.6 Hz), 3.71–3.79 (m, 8H, 2×CO_2Me and 2×H(2´´)), 3.80–3.89 (m, 1H, H(3′)), 3.94 (dd, 1H, H(1′), ^3J = 9.9 Hz, ^3J = 5.8 Hz), 7.09–7.57 (m, 5H, H_{Ar}) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 12.5 (C(8)), 15.8 (C(5)), 16.0 (C(4a)), 31.2 (C(6)), 32.6 (C(1´´)), 33.6 (C(2′)), 37.9 (C(7)), 41.3 (C(2´´)), 45.9 and 49.4 (C(4) and C(7a)), 49.1 (C(3′)), 52.2 and 52.4 (2×OMe), 56.3 (C(3a)), 63.3 (C(1′)), 68.8 (C(7b)), 127.3 (C(*p*)), 128.1 (C(*o*)), 128.5 (C(*m*)), 139.7 (C(*i*)), 150.5 (C(3)), 170.0 and 170.2 (2 COO). 2nd diastereomer. Colorless oil. ^1H NMR (300.1 MHz, $CDCl_3$): δ 0.70 (br.t, 1H, H(8), ^3J = 5.9 Hz), 0.90 (br.t, 1H, H(4a), ^3J = 5.9 Hz), 1.17 (br.t, 1H, H(5), ^3J = 5.9 Hz), 1.52 (s, 2H, H(6)), 1.80 (s, 1H, H(7)), 1.84 (s, 1H, H(4)), 2.01–2.03 (m, 1H, H(7a)), 2.40–2.80 (m, 4H, 2×H(1´´) and 2×H(2′)), 3.11 (d, 1H, H(3a), ^3J = 9.3 Hz), 3.55 (d, 1H, H(7b), ^3J = 9.3 Hz), 3.64 (dd, 1H, H(3′), ^3J = 7.9 Hz, ^3J = 7.0 Hz), 3.68–3.80 (m, 8H, 2×CO_2Me and 2×H(2´´)), 4.15 (dd, 1H, H(1′), ^3J = 7.9 Hz, ^3J = 7.0 Hz), 7.22–7.38 (m, 5H, H_{Ar}) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 12.9 (C(8)), 15.6 (C(5)),

15.8 (C(4a)), 31.1 (C(6)), 32.4 (C(1′′)), 32.6 (C(2′)), 37.5 (C(7)), 41.1 (C(2′′)), 46.6 and 50.5 (C(4) and C(7a)), 49.1 (C(3′)), 52.4 and 52.5 (2×OMe), 57.0 (C(3a)), 65.3 (C(1′)), 68.2 (C(7b)), 127.4 (C(*p*)), 128.1 (C(*o*)), 128.5 (C(*m*)), 139.2 (C(*i*)), 152.0 (C(3)), 169.8 and 170.0 (2 COO).

Dimethyl 2-(2-(3-(1-(chloromethyl)cyclopropyl)-5-(methoxycarbonyl)-5-methyl-4,5-dihydro-1H-pyrazol-1-yl)-2-phenylethyl)malonate ***(3ae)***. Compound **3ae** was prepared from **1a** and **2e** in yield 77% (142 mg, *dr* = 1.4/1). Light yellow oil. IR (KBr) $\tilde{\nu}$ 3063, 3035, 3000, 2954, 2929, 2920, 2845, 1736 br. (C=O), 1600, 1493, 1450, 1380 cm^{-1}. ^1H NMR (400.1 MHz, $CDCl_3$): δ 0.88–0.99 (m, 6H, Me_{mn} and H_{cyclp}), 1.02–1.21 (m, 5H, H_{cyclp}), 1.41 (s, 3H, Me_{mj}), 2.26–2.37 (m, 2H, $H_{mn}(2')$), 2.39 (d, 1H, $H_{mn}(4)$, ^2J = 16.5 Hz), 2.53 (d, 1H, $H_{mj}(4)$, ^2J = 16.2 Hz), 2.66–2.82 (m, 2H, $H_{mj}(2')$), 2.91 (s, 3H, CO_2Me_{mj}), 3.07 (d, 1H, $H_{mj}(4)$, ^2J = 16.2 Hz), 3.18 (d, 1H, $H_{mn}(4)$, ^2J = 16.5 Hz), 3.57 (dd, 1H, $H_{mj}(3')$, ^3J = 8.6 Hz, ^3J = 6.2 Hz), 3.60 (d, 1H, $H_{mn}(4'')$, ^2J = 11.4 Hz), 3.69 (s, 3H, CO_2Me_{mn}), 3.71 (s, 3H, CO_2Me_{mj}), 3.72 (d, 1H, $H_{mj}(4'')$, ^2J = 11.0 Hz), 3.72 (s, 3H, CO_2Me_{mj}), 3.74 (s, 3H, CO_2Me_{mn}), 3.77 (s, 3H, CO_2Me_{mn}), 3.68–3.80 (m, 1H, $H_{mn}(3')$), 3.81 (d, 1H, $H_{mj}(4'')$, ^2J = 11.0 Hz), 3.92 (d, 1H, $H_{mn}(4'')$, ^2J = 11.4 Hz), 4.08 (dd, 1H, $H_{mj}(1')$, ^3J = 8.8 Hz, ^3J = 6.2 Hz), 4.27 (dd, 1H, $H_{mn}(1')$, ^3J = 10.2 Hz, ^3J = 4.9 Hz), 7.13–7.29 (m, 6H, $H_{Ar\ mj\ and\ mn}$), 7.30–7.37 (m, 2H, $H_{Ar\ mj}$), 7.44–7.52 (m, 2H, $H_{Ar\ mn}$) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 13.7, 13.8, 14.1 and 14.2 (2×C(2′′) and 2×C(3′′)), 20.7 and 21.9 (2×Me), 23.6 and 23.7 (C(1′′)), 36.5 (2×C(2′)), 45.0 and 45.2 (C(4)), 49.2 and 49.4 (2×C(3′)), 50.7 and 50.8 (C(4′′)), 51.4, 52.3, 52.4 (6×OMe), 59.6 and 60.5 (2×C(1′)), 69.7 and 71.3 (2 C(5)), 127.1, 127.3, 127.9, 128.0, 128.2 and 128.3 (10×CH_{Ar}), 140.8 and 149.0 (C(3)), 144.1 and 146.8 (2×C(*i*)), 169.9, 170.0, 170.3, 172.5 (6 COO). MS (*m/z* for ^{35}Cl, %): 464 (13, M^+). HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{23}H_{29}N_2O_6Cl$ (for ^{35}Cl) 487.1612; Found 487.1605.

Tetramethyl 2,2'-((3-(2-chloroethyl)-4-cyclobutyl-1H-pyrazole-1,5-diyl)bis(2-phenylethane-2,1-diyl))dimalonate ***(3ag)***. Compound **3ag** was prepared from **1a** and **2g** in yield 35% (154 mg, *dr* = 1/1). This compound decomposes rapidly in the $CDCl_3$ and CD_2Cl_2 solutions, so the satisfactory ^{13}C NMR specta were failed to obtain. Yellow oil. ^1H NMR (400.1 MHz, $CDCl_3$): δ 1.69–2.69 (m, 24H, 4×H(2′), 4×H(1′′), 4×H(2′′′), 4×H(2′′′′), 4×H(3′′′′) and 4×H(4′′′′)), 2.91–3.15 (m, 4H, 2×H(1′′′) and 2×H(1′′′′)), 3.29 (s, 3H, CO_2Me), 3.50 (s, 3H, CO_2Me), 3.51 (s, 3H, CO_2Me), 3.59–3.89 (m, 23H, 5×CO_2Me, 4×H(2′′), 2×H(3′) and 2×H(3′′′)), 5.04–5.15 (m, 2H, 2×H(1′)), 6.82–7.47 (m, 10H, H_{Ar}) ppm. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{35}H_{41}N_2O_8Cl$ (for ^{35}Cl) 675.2449; Found 675.2457.

Dimethyl 2-(2-(3-(2-chloroethyl)-4,5,6,6a-tetrahydro-4,5,6-(epimethanetriyl)cyclopenta[c]pyrazol-1(3aH)-yl)-2-phenylethyl)malonate ***(3ah)***. Compound **3ah** was prepared from **1a** and **2h** in yield 4% (11 mg, *dr* = 1/1). HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{22}H_{25}N_2O_4Cl$ (for ^{35}Cl) 439.1401; Found 439.1393. 1st diastereomer. Light yellow oil. ^1H NMR (400.1 MHz, $CDCl_3$): δ 1.97 (br.s, 2H, H(5) and H(7)), 2.17 (ddd, 1H, H(6), ^3J = 4.8 Hz, ^3J = 3.0 Hz, ^3J = 1.6 Hz), 2.24 (ddd, 1H, H(4), ^3J = 4.8 Hz, ^3J = 3.0 Hz, ^3J = 1.6 Hz), 2.40 (ddd, 1H, H(2′), ^2J = 14.0 Hz, ^3J = 8.4 Hz, ^3J = 6.6 Hz), 2.51–2.64 (m, 2H, H(1′′) and H(3a)), 2.65–2.74 (m, 1H, H(1′′)), 2.82 (ddd, 1H, H(2′), ^2J = 14.0 Hz, ^3J = 8.4 Hz, ^3J = 6.6 Hz), 3.65–3.76 (m, 10H, 2×CO_2Me, 2×H(2′′), H(6a) and H(3′)), 3.99 (dd, 1H, H(1′), ^3J = 8.4 Hz, ^3J = 6.6 Hz), 7.03–7.43 (m, 5H, H_{Ar}) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 1.6 (C(5)), 6.9 (C(7)), 33.1 (C(2′)), 33.7 (C(1′′)), 36.9 (C(4)), 39.1 (C(6)), 41.2 (C(2′′)), 49.1 (C(3′)), 52.3 and 52.4 (2 OMe), 57.3 (C(3a)), 64.3 (C(1′)), 70.4 (C(6a)), 127.5, 128.2 and 128.5 (5 CH_{Ar}), 139.8 (C(*i*)), 150.5 (C(3)), 170.1 and 170.2 (2 COO). 2nd diastereomer. Light yellow oil. ^1H NMR (400.1 MHz, $CDCl_3$): δ 1.91–1.95 (m, 2H, H(5) and H(7)), 2.02 (ddd, 1H, H(6), ^3J = 5.6 Hz, ^3J = 3.0 Hz, ^3J = 1.5 Hz), 2.23 (ddd, 1H, H(4), ^3J = 5.6 Hz, ^3J = 3.0 Hz, ^3J = 1.5 Hz), 2.43 (ddd, 1H, H(2′), ^2J = 14.2 Hz, ^3J = 7.8 Hz, ^3J = 6.8 Hz), 2.52–2.85 (m, 4H, 2×H(1′′), H(2′) and H(3a)), 3.56–3.87 (m, 10H, 2×CO_2Me, 2×H(2′′), H(6a) and H(3′)), 4.03 (dd, 1H, H(1′), ^3J = 7.8 Hz, ^3J = 6.8 Hz), 6.98–7.42 (m, 5H, H_{Ar}) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 1.5 (C(5)), 7.3 (C(7)), 33.0 (C(2′)), 33.5 (C(1′′)), 36.7 (C(4)), 40.3 (C(6)), 41.1 (C(2′′)), 49.3 (C(3′)), 52.5 and 52.6 (2 OMe), 57.6 (C(3a)), 65.6 (C(1′)), 70.8 (C(6a)), 128.0, 128.3 and 128.6 (5 CH_{Ar}), 140.0 (C(*i*)), 152.1 (C(3)), 169.9 and 172.3 (2 COO).

Dimethyl 2-(2-(4-chloro-3-(2-chloroethyl)-3a,4,4a,5,5a,5b-hexahydro-1H-cyclopropa[4,5]cyclopenta[1,2-c]pyrazol-1-yl)-2-phenylethyl)malonate ***(3ah′)***. Compound **3ah′** was prepared from **1a** and **2h** in yield 54% (167 mg, *dr* = 1.3/1). IR (KBr) $\tilde{\nu}$ 3040, 3031, 2956, 2940, 2929, 2850, 1737 br. (C=O), 1594, 1495, 1450, 1346, 1283 cm^{-1}. MS (*m/z* for ^{35}Cl, %): 452 (2, M^+). HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{22}H_{26}N_2O_4Cl_2$ (for ^{35}Cl) 475.1162; Found 475.1133. 1st diastereomer. Light yellow oil. ^1H NMR (400.1 MHz, $CDCl_3$): δ 0.36 (dt, 1H, H(5), ^2J = 5.7 Hz, ^3J = 4.6 Hz), 0.79 (td, 1H, H(5), ^2J = 5.7 Hz, ^3J = 8.6 Hz), 1.69–1.76 (m, 1H, H(4a)), 1.94 (dt, 1H, H(5a), ^3J = 8.6 Hz, ^3J = 4.6 Hz), 2.46 (ddd, 1H, H(2′), ^2J = 14.0 Hz, ^3J = 9.1 Hz, ^3J = 6.0 Hz), 2.62–2.77 (m, 2H, H(1′′) and H(3a)), 2.79–2.89 (m, 2H, H(2′) and H(1′′)), 3.71 (s, 3H, CO_2Me), 3.73 (s, 3H, CO_2Me), 3.73–3.79 (m, 4H, 2×H(2′′), H(3′) and H(4)), 3.97 (dd, 1H, H(1′), ^3J = 9.1 Hz, ^3J = 6.0 Hz), 4.51 (dd, 1H, H(5b), ^3J = 6.7 Hz, ^3J = 4.6 Hz), 7.17–7.43 (m, 5H, H_{Ar}) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 9.3 (C(5)), 24.4 (C(4a)), 26.6 (C(5a)), 32.6 (C(1′′)), 33.4 (C(2′)), 40.9 (C(2′′)), 49.2 (C(3′)), 52.5 and 52.6 (2 OMe), 58.9 (C(3a)), 63.3 (C(1′)), 66.1 (C(5b)), 72.9 (C(4)), 128.1, 128.4 and 129.2 (5 CH_{Ar}), 137.4 (C(*i*)), 143.0 (C(3)), 169.9 and 170.0 (2 COO). 2nd diastereomer. Light yellow oil. ^1H NMR (400.1 MHz, $CDCl_3$): δ 0.28 (dt, 1H, H(5), ^2J = 5.9 Hz, ^3J = 5.3 Hz), 0.60 (td, 1H, H(5), ^2J = 5.9 Hz, ^3J = 8.2 Hz), 1.18 (ddd, 1H, H(4a), ^3J = 8.2 Hz, ^3J = 5.3 Hz, ^3J = 4.5 Hz), 1.49–1.64 (m, 1H, H(5a)), 1.76–1.91 (m, 1H, H(2′)), 2.46 (ddd, 1H, H(2′), ^2J = 14.2 Hz, ^3J = 8.0 Hz, ^3J = 6.9 Hz), 2.71–3.00 (m, 3H, 2×H(1′′) and H(3a)), 3.66 (s, 3H, CO_2Me), 3.72 (s, 3H, CO_2Me), 3.70–3.80 (m, 4H, 2×H(2′′), H(3′) and H(4)), 3.95 (dd, 1H, H(1′), ^3J = 8.0 Hz, ^3J = 6.9 Hz), 4.50 (dd, 1H, H(5b), ^3J = 6.5 Hz, ^3J = 5.0 Hz), 7.16–7.38 (m, 5H, H_{Ar}) ppm.

Dimethyl 2-(2-(5-chloro-3-(2-chloroethyl)-3a,3b,4,4a,5,5a-hexahydro-1H-cyclopropa[3,4]cyclopenta[1,2-c]pyrazol-1-yl)-2-phenylethyl)malonate ***(3ah′′)***. Compound **3ah′′** was prepared from **1a** and **2h** in yield 13% (40 mg, *dr* = 5/1). This compound decomposes rapidly in the $CDCl_3$ and CD_2Cl_2 solutions, so the satisfactory ^{13}C NMR specta were failed to obtain. ^1H NMR (400.1 MHz, $CDCl_3$): δ 0.34 (dd, 1H, H(4), ^3J = 9.6 Hz, ^3J = 4.3 Hz), 0.79 (td, 1H, H(4), ^3J = 8.2 Hz, ^3J = 5.5 Hz), 1.58 (ddd, 1H, H(4a), ^3J = 8.2 Hz, ^3J = 5.7 Hz, ^3J = 4.3 Hz), 1.65–1.76 (m, 1H, H(3b)), 2.45 (ddd, 1H, H(2′), ^2J = 14.2 Hz, ^3J = 9.0 Hz, ^3J = 5.7 Hz), 2.57–2.87 (m, 4H, H(2′), 2×H(1′′) and H(3a)), 3.39–3.53 (m, 2H, H(3′) and 3.59–3.88 (m, 8H, 2×H(2′′) and 2×CO_2Me), 4.26 (dd, 1H, H(1′), ^3J = 9.0 Hz, ^3J = 5.7 Hz), 4.36 (br.t, 1H, H(5a), ^3J = 4.6 Hz), 7.20–7.42 (m, 5H, H_{Ar}) ppm. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{22}H_{26}N_2O_4Cl_2$ (for ^{35}Cl) 475.1162; Found 475.1146.

Dimethyl 2-(2-(3-(2-bromoethyl)-5-(methoxycarbonyl)-5-methyl-4,5-dihydro-1H-pyrazol-1-yl)-2-phenylethyl)malonate ***(4a)***. Compound **4a** was prepared from **1a** and **2a** in yield 69% (198 mg, *dr* = 1.1/1). Light yellow oil. IR (KBr) $\tilde{\nu}$ 3085, 3061, 3027, 3002, 2953, 2845, 1734 br. (C=O), 1601, 1493, 1454, 1436 cm^{-1}. ^1H NMR (300.1 MHz, $CDCl_3$): δ 0.94 (s, 3H, Me), 1.41 (s, 3H, Me), 2.23–2.41 (m, 2H, 2×H(2′)), 2.46 (d, 1H, H(4), ^2J = 16.9 Hz), 2.58 (d, 1H, H(4), ^2J = 16.6 Hz), 2.62–2.95 (m, 9H, 2×H(2′), 4×H(1′′) and CO_2Me), 3.17 (d, 1H, H(4), ^2J = 16.6 Hz), 3.26 (d, 1H, H(4), ^2J = 16.9 Hz), 3.47–3.65 (m, 5H, H(3′) and 4×H(2′′)), 3.66–3.83 (m, 16H, H(3′) and 5×CO_2Me), 4.10 (dd, 1H, H(1′), ^3J = 9.2 Hz, ^3J = 6.2 Hz), 4.27 (dd, 1H,

H(1′), ^3J = 10.2 Hz, ^3J = 5.0 Hz), 7.14–7.36 (m, 8H, H_{Ar}), 7.45 (dd, 2H, H_{Ar}, ^3J = 7.9 Hz, ^4J = 1.4 Hz) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 20.9 and 22.0 (Me), 28.8 and 29.0 (C(2′′)), 33.4 and 33.6 (C(1′′)), 36.3 and 36.4 (C(2′)), 47.2 and 47.3 (C(4)), 49.0 and 49.1 (C(3′)), 51.3, 52.2, 52.3 and 52.4 (6 OMe), 59.2 and 60.2 (C(1′)), 69.0 and 71.2 (C(5)), 127.0 and 127.3 (C(*p*)), 127.6, 127.9, 128.1 and 128.2 (2 C(*o*) and 2 C(*m*)), 140.7 and 143.9 (C(*i*)), 144.3 and 146.1 (C(3)), 169.7, 169.8, 169.9, 170.1, 172.2 and 173.4 (6 COO). MS (*m/z*, %): 484 and 482 (15, M^+). HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{21}H_{27}N_2O_6Br$ 505.0945 and 507.0925; Found 505.0958 and 507.093.

*Dimethyl 2-(2-(3-(2-iodoethyl)-5-(methoxycarbonyl)-5-methyl-4,5-dihydro-1H-pyrazol-1-yl)-2-phenylethyl)malonate **(4b)***. Compound **4b** was prepared from **1a** and **2a** in yield 88% (278 mg, *dr* = 1.1/1). Light yellow oil. IR (KBr) $\tilde{\nu}$ 3085, 3061, 3027, 3004, 2953, 2844, 1734 br. (C=O), 1602, 1584, 1493, 1454, 1436 cm^{-1}. ^{1}H NMR (300.1 MHz, $CDCl_3$): δ 0.95 (s, 3H, Me), 1.42 (s, 3H, Me), 2.22–2.40 (m, 2H, 2×H(2′)), 2.46 (d, 1H, H(4), ^2J = 16.8 Hz), 2.57 (d, 1H, H(4), ^2J = 16.6 Hz), 2.63–2.82 (m, 2H, 2×H(2′)), 2.78–2.99 (m, 7H, 4×H(1′′) and CO_2Me), 3.17 (d, 1H, H(4), ^2J = 16.6 Hz), 3.25 (d, 1H, H(4), ^2J = 16.8 Hz), 3.30–3.42 (m, 4H, 4×H(2′′)), 3.55 (dd, 1H, H(3′), ^3J = 9.2 Hz, ^3J = 6.2 Hz), 3.64–3.84 (m, 16H, H(3′) and 5×CO_2Me), 4.11 (dd, 1H, H(1′), ^3J = 9.2 Hz, ^3J = 6.2 Hz), 4.28 (dd, 1H, H(1′), ^3J = 10.2 Hz, ^3J = 4.9 Hz), 7.12–7.37 (m, 8H, H_{Ar}), 7.47 (dd, 2H, H_{Ar}, ^3J = 7.7 Hz, ^4J = 1.2 Hz) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 0.4 and 0.8 (C(2′′)), 20.9 and 22.0 (Me), 34.2 and 34.4 (C(1′′)), 36.3 and 36.4 (C(2′)), 47.0 and 47.1 (C(4)), 48.9 and 49.1 (C(3′)), 51.3, 52.2, 52.3 and 52.4 (6 OMe), 59.2 and 60.1 (C(1′)), 69.0 and 71.1 (C(5)), 127.0 and 127.2 (C(*p*)), 127.7, 127.9, 128.1 and 128.2 (2 C(*o*) and 2 C(*m*)), 140.7 and 144.0 (C(*i*)), 145.4 and 147.1 (C(3)), 169.7, 169.8, 169.9, 170.1, 172.2 and 173.4 (6 COO). MS (*m/z*, %): 530 (30, M^+). HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{21}H_{27}N_2O_6I$ 553.0806; Found 553.0816.

General synthetic procedure and spectroscopic data for products of double addition of spiro[cyclopropane-pyrazoline] 2a,e with DAC 1a,d,h,l,k,o–r. All operations were performed under dry argon atmosphere. A Lewis acid ($EtAlCl_2$ (1.0 M in hexane) or a solid $GaCl_3$) was added to a solution of DACs **1a,d,h,l,k,o–r** (0.25 mmol) and pyrazoline **2a,e** (100 mg, 0.51 mmol) in dry DCM (4 mL) and the mixture was stirring at conditions from Table 2. Then an aqueous solution of HCl (5%) was added at room temperature until pH 3 was achieved and the reaction mixture was extracted with CH_2Cl_2 (3×10 mL). The organic layer was dried over $MgSO_4$ and the solvent was removed in vacuo. The residue was purified by flash chromatography (benzene–EtOAc (30:1) to EtOAc) on silica gel to afford the pure products.

*Dimethyl 2-(2-(3-(2-(3-(2-chloroethyl)-5-(methoxycarbonyl)-5-methyl-4,5-dihydro-1H-pyrazol-1-yl)ethyl)-5-(methoxycarbonyl)-5-methyl-4,5-dihydro-1H-pyrazol-1-yl)-2-phenylethyl)malonate **(5aa)***. Compound **5aa** was prepared from **1a** and **2a** in yield 64% (116 mg, *dr* = 1/1/1/1). All four diastereomers were partially separated using column chromatography on SiO_2. IR (KBr) $\tilde{\nu}$ 3069, 3021, 2955, 2834, 1731 br. (C=O), 1580, 1555, 1438, 1356 cm^{-1}. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{29}H_{39}N_4O_8Cl$ (for ^{35}Cl) 629.2354; Found 629.2341. 1st diastereomer. Yellow oil. ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 0.92 (s, 3H, Me), 1.39 (s, 3H, Me), 2.29 (ddd, 1H, H(2′′′), ^2J = 14.1 Hz, ^3J = 9.2 Hz, ^3J = 5.0 Hz), 2.47 (d, 1H, H(4), ^2J = 16.8 Hz), 2.57–2.79 (m, 5H, H(2′), 2×H(1′′), H(2′′′) and H(4)), 3.13–3.28 (m, 3H, H(2′) and 2×H(4)), 3.62–3.81 (m, 17H, 4×CO_2Me, 2×H(1′), 2×H(2′′) and H(3′′′)), 4.23 (d, 1H, H(1′′′), ^3J = 9.2 Hz, ^3J = 5.0 Hz), 7.16–7.28 (m, 4H, H_{Ar}), 7.45 (dd, 1H, H_{Ar}, ^3J = 8.0 Hz, ^4J = 1.5 Hz) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 19.3, and 22.0 (2×Me), 30.0 (C(2′′)), 33.6 (C(1′′)), 36.6 (C(2′)), 41.3 (C(2′′)), 47.0 and 47.4 (2×C(4)), 48.1 (C(3′′)), 49.1 (C(1′)), 52.3 (4×OMe), 60.4 (C(1′′′)), 70.9 and 71.6 (2×C(5)), 127.0, 127.9 and 128.1 (5 CH_{Ar}), 144.3 (C(*i*)), 146.2 (2×C(3)), 170.0, 170.3, 173.0 and 173.9 (4 COO). 2nd diastereomer. Yellow oil. ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 0.91 (s, 3H, Me), 1.38 (s, 3H, Me), 2.30 (ddd, 1H, H(2′′′), ^2J = 13.9 Hz, ^3J = 10.2 Hz, ^3J = 4.1 Hz), 2.47 (d, 1H, H(4), ^2J = 16.6 Hz), 2.56–3.01 (m, 5H, H(2′), 2×H(1′′), H(2′′′) and H(4)), 3.08–3.31 (m, 3H, H(2′) and 2×H(4)), 3.46 (br.t, 2H, 2×H(1′), ^3J = 6.0 Hz) 3.59–3.84 (m, 15H, 4×CO_2Me, 2×H(2′′) and H(3′′′)), 4.23 (d, 1H, H(1′′′), ^3J = 10.2 Hz, ^3J = 4.1 Hz), 6.94–7.36 (m, 4H, H_{Ar}), 7.45 (dd, 1H, H_{Ar}, ^3J = 8.0 Hz, ^4J = 1.5 Hz) ppm. 3rd & 4th diastereomers. Yellow oil. ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 1.37–1.42 (m, 12H, Me), 2.25–2.39 (m, 2H, 2×H(2′′)), 2.48 (d, 1H, H(4), ^2J = 16.5 Hz), 2.55–2.83 (m, 11H, 2×H(2′), 4×H(1′′), 2×H(2′′′) and 3×H(4)), 2.94 (s, 3H, CO_2Me), 2.96 (s, 3H, CO_2Me), 3.08–3.30 (m, 6H, 2×H(2′) and 4×H(4)), 3.48–3.51 (m, 2H, 2×H(1′)) 3.53–3.80 (m, 26H, 6×CO_2Me, 2×H(1′), 4×H(2′′) and 2×H(3′′′)), 4.08 (br.t, 1H, H(1′′′), ^3J = 7.5 Hz), 4.23 (d, 1H, H(1′′′), ^3J = 10.2 Hz, ^3J = 5.0 Hz), 7.15–7.29 (m, 7H, H_{Ar}), 7.30–7.34 (m, 2H, H_{Ar}), 7.45 (dd, 1H, H_{Ar}, ^3J = 7.9 Hz, ^4J = 1.3 Hz) ppm.

*Dimethyl 2-(2-(3-(2-(3-(2-chloroethyl)-5-(methoxycarbonyl)-5-methyl-4,5-dihydro-1H-pyrazol-1-yl)ethyl)-5-(methoxycarbonyl)-5-methyl-4,5-dihydro-1H-pyrazol-1-yl)-2-(2,6-dichlorophenyl)ethyl)malonate **(5da)***. Compound **5da** was prepared from **1d** and **2a** in yield 32% (54 mg, *dr* = 1/1/1/1). Yellow oil. IR (KBr) $\tilde{\nu}$ 3065, 3020, 2953, 2845, 1735 br. (C=O), 1579, 1561, 1437, 1376 cm^{-1}. ^{1}H NMR (300.1 MHz, $CDCl_3$): δ 1.12 (s, 3H, Me), 1.13 (s, 3H, Me), 1.30–1.51 (m, 18H, 6×Me), 2.45–2.87 (m, 28H, 4×H(2′), 8×H(1′′), 8×H(2′′′) and 8×H(4)), 2.92–3.40 (m, 24H, 4×CO_2Me, 4×H(2′) and 8×H(4)), 3.48–3.64 (m, 4H, 4×H(3′′′)), 3.66–3.86 (m, 44H, 12×CO_2Me and 8×H(2′′)), 5.03–5.24 (m, 12H, 8×H(1′) and 4×H(1′′′)), 7.04–7.14 (m, 4H, H_{Ar}), 7.23–7.33 (m, 8H, H_{Ar}) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 18.2, 18.3, 18.7, 18.9, 19.0, 19.2, 20.9 and 21.1 (8×Me), 29.9 (4×C(2′′′)), 31.0, 31.1, 31.6 and 31.7 (4×C(2′)), 33.5 (4×C(1′′)), 41.2 (4×C(2′′)), 46.9, 47.0, 47.2, 47.3, 47.4, 49.4 and 49.5 (8×C(4)), 49.6 and 50.1 (4×C(3′′′)), 51.2, 52.2, 52.3, 52.4 and 52.5 (16×OMe), 56.0 and 56.5 (4×C(1′′′)), 57.5 (4×C(1′)), 70.3, 70.4, 71.0, 71.1 and 71.5 (8×C(5)), 128.1, 128.3, 128.5, 128.6, 130.4 and 130.6 (12 CH_{Ar}), 135.2, 135.3, 135.4, 135.5 136.1, 136.2, 137.5, 137.6, 144.8, 144.9, 145.5 and 145.7 (4×C(1′′′′), 4×C(2′′′′) and 4×C(6′′′′)), 149.3, 149.4 and 149.6 (8×C(3)), 169.4, 169.6, 169.7, 169.8, 173.0, 173.4, 174.4 and 174.5 (16×COO). HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{29}H_{37}N_4O_8Cl_3$ (for ^{35}Cl) 697.1569; Found 697.1580.

*Dimethyl 2-(2-(3-(2-(3-(2-chloroethyl)-5-(methoxycarbonyl)-5-methyl-4,5-dihydro-1H-pyrazol-1-yl)ethyl)-5-(methoxycarbonyl)-5-methyl-4,5-dihydro-1H-pyrazol-1-yl)ethyl)malonate **(5ka)***. Compound **5ka** was prepared from **1k** and **2a** in yield 70% (93 mg, *dr* = 1.1/1).Yellow oil. IR (KBr) $\tilde{\nu}$ 3060, 3027, 2954, 2841, 1731 br. (C=O), 1694, 1602, 1495, 1453, 1369, 1289 cm^{-1}. ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 1.27 and 1.28 (s, 6H, $Me_{mj\ and\ mn}$), 1.37 (s, 6H, $Me_{mj\ and\ mn}$), 2.21–2.34 (m, 4H, $H_{mj\ and\ mn}$(2′′′)), 2.52–2.62 (m, 6H, H_{mn}(2′) and $H_{mj\ and\ mn}$(4′)), 2.64–2.71 (m, 2H, H_{mj}(2′)), 2.74 (t, 4H, $H_{mj\ and\ mn}$(1′′), ^3J = 6.9 Hz), 2.89–2.99 (m, 4H, $H_{mj\ and\ mn}$(1′′′)), 3.05–3.18 (m, 8H, $H_{mj\ and\ mn}$(1′) and $H_{mj\ and\ mn}$(4)), 3.22 (d, 2H, H_{mn}(4), ^2J = 16.4 Hz), 3.60–3.84 (m, 6H, $H_{mj\ and\ mn}$(3′) and $H_{mj\ and\ mn}$(2′′)), 3.71 (s, 6H, $CO_2Me_{mj\ and\ mn}$), 3.72 (s, 6H, $CO_2Me_{mj\ and\ mn}$), 3.73 (s, 6H, $CO_2Me_{mj\ and\ mn}$), 3.74 (s, 6H, $CO_2Me_{mj\ and\ mn}$) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 18.6, 18.7 and 19.0 (4 Me), 28.3 (2 C(2′′)), 30.2 and 30.3 (2 C(2′)), 33.5 (2 C(1′′)), 41.3 (2 C(2′′)), 41.4 (2 C(1′′′)), 46.8 and 46.9 (2 C(1′)), 47.3, 47.4 and 47.8 (4 C(4)), 48.9 (2 C(3′′′)), 52.1, 52.3 and 52.4 (6 OMe), 70.9, 71.0 and 71.4 (4 C(5)), 148.6 and 151.1 (4 C(3)), 170.0, 170.2, 173.2 and 173.5 (8 COO). MS (*m/z* for ^{35}Cl, %): 530 (1, M^+). HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{23}H_{35}N_4O_8Cl$ (for ^{35}Cl) 553.2041; Found 553.2050.

*Dimethyl 2-(2-(3-(2-(3-(2-chloroethyl)-5-(methoxycarbonyl)-5-methyl-4,5-dihydro-1H-pyrazol-1-yl)ethyl)-5-(methoxycarbonyl)-5-methyl-4,5-dihydro-1H-pyrazol-1-yl)but-3-en-1-yl)malonate **(5ha)***. Compound **5ha** was prepared from **1h** and **2a** in yield 39% (54 mg, *dr* = 1/1/1/1). Yellow oil. IR (KBr) $\tilde{\nu}$ 3074, 2955, 2847, 1732 br. (C=O), 1634, 1436, 1343 cm^{-1}. ^1H NMR (300.1 MHz, $CDCl_3$): δ 1.23 (s, 3H, Me), 1.24 (s, 3H, Me), 1.27 (s, 3H, Me), 1.36–1.43 (m, 15H, 5×Me), 2.08–2.23 (m, 4H, 4×H(2´´´)), 2.33–2.83 (m, 28H, 8×H(2´), 8×H(1´´), 4×H(2´´´) and 8×H(4)), 3.05–3.31 (m, 8H, 8×H(4)), 3.43–3.90 (m, 68H, 16×CO_2Me, 4×H(3´´´), 4×H(1´), 4×H(1´´´) and 8×H(2´´)), 4.92–5.25 (m, 8H, 8×H(2´´´´)), 5.71–5.87 (m, 2H, 2×H(1´´´´)), 5.97–6.16 (m, 2H, 2×H(1´´´´)) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 18.8, 18.9, 19.0, 19.1, 20.7, 20.9, 21.1 and 21.2 (8×Me), 30.0, 30.1 and 30.2 (4×C(2´´)), 33.3, 33.5, 34.3 and 34.9 (4×C(2´)), 33.4 (4×C(1´´)), 41.2 (4×C(2´´)), 46.7, 46.8, 46.9, 47.0, 47.3, 47.4, 47.8 and 47.9 (8×C(4)), 48.6, 48.7 and 48.8 (4×C(3´´´)), 52.2, 52.3, 52.4 and 52.5 (16×OMe), 58.4 and 58.6 (4×C(1´´´)), 59.1 (4×C(1´)), 69.1, 69.2, 69.4, 71.1, 71.2, 71.4 and 71.5 (8×C(5)), 115.8, 116.1, 116.5 and 116.6 (4×C(2´´´´)), 137.1, 137.3, 140.0 and 140.2 (4×C(1´´´´)), 147.6, 148.2, 148.3, 148.9, 149.1, 149.8 and 149.9 (8×C(3)), 169.1, 169.8, 169.9, 170.0, 170.2, 172.9, 173.1, 173.3 and 173.8 (16×COO). HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{25}H_{37}N_4O_8Cl$ (for ^{35}Cl) 579.2192; Found 579.2193.

*Dimethyl 2-(2-(3-(2-(3-(2-chloroethyl)-5-(methoxycarbonyl)-5-methyl-4,5-dihydro-1H-pyrazol-1-yl)ethyl)-5-(methoxycarbonyl)-5-methyl-4,5-dihydro-1H-pyrazol-1-yl)pentyl)malonate **(5la)***. Compound **5la** was prepared from **1l** and **2a** in yield 33% (56 mg, *dr* = 1/1/1/1). Dark yellow oil. IR (KBr) $\tilde{\nu}$ 2956, 2873, 2850, 1736 br. (C=O), 1436, 1376, 1344, 1284 cm^{-1}. ^1H NMR (300.1 MHz, $CDCl_3$): δ 0.85–0.94 (m, 12H, H(3´´´´)), 108–1.58 (m, 40H, 8×Me, 8×H(1´´´´) and 8×H(2´´´)), 1.96–2.38 (m, 8H, 8×H(2´´)), 2.47–2.82 (m, 24H, 8×H(2´), 8×H(1´´) and 8×H(4)), 2.86–3.06 (m, 4H, 4×H(1´´)), 3.10–3.31 (m, 16H, 8×H(4) and 8×H(1´)), 3.59–3.87 (m, 60H, 16×CO_2Me, 4×H(3´´´) and 8×H(2´´)) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 13.7, 14.1, 14.2 and 14.4 (4×C(3´´´´)), 18.9, 19.0, 21.4 and 21.6 (4×C(2´´´´)), 20.2, 20.1, 20.2 and 20.3 (8×Me), 29.6 and 30.2 (4×C(1´´)), 33.2, 33.3 and 33.5 (4×C(2´´´) and 4×C(2´)), 36.8 and 36.9 (4×C(1´´´´)), 41.3 and 41.6 (4×C(2´´)), 46.5, 46.8, 46.9, 47.0, 47.3, 47.4 and 47.5 (8×C(4) and 4×C(1´)), 48.8 and 49.3 (4×C(3´´´)), 51.9, 52.1, 52.2, 52.3, 52.4 and 52.7 (16×OMe), 54.8 and 55.7 (4×C(1´´´)), 71.0 and 71.3 (8×C(5)), 148.4 and 148.5 (8×C(3)), 169.9, 170.0, 170.1, 170.2, 170.5, 170.6 and 173.2 (16×COO). MS (*m/z* for ^{35}Cl, %): 541 (1, M^+ – OMe), 513 (100, $M^+ – CO_2$Me). HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{26}H_{41}N_4O_8Cl$ (for ^{35}Cl) 595.2505; Found 595.2512.

*Dimethyl 2-(2-(3-(2-(3-(2-chloroethyl)-5-(methoxycarbonyl)-5-methyl-4,5-dihydro-1H-pyrazol-1-yl)ethyl)-5-(methoxycarbonyl)-5-methyl-4,5-dihydro-1H-pyrazol-1-yl)-2-(2-phenylcyclopropyl)ethyl)malonate **(5oa)***. Compound **5oa** was prepared from **1o** and **2a** in yield 26% (42 mg, *dr* = 1/1/1/1). ^1H NMR (300.1 MHz, $CDCl_3$): δ 0.83–1.07 (m, 8H, 8×H(3´´´´)), 1.12–1.49 (m, 27H, 8×Me and 4×H(1´´´´)), 1.81–2.00 (m, 4H, 4×H(2´´´´)), 2.30–2.91 (m, 36H, 8×H(2´), 8×H(1´´), 4×H(1´´´), 8×H(2´´´) and 8×H(4)), 3.04–3.38 (m, 8H, 8×H(4)), 3.53–3.88 (m, 60H, 16×CO_2Me, 8×H(2´´) and 4×H(3´´´)), 4.96–5.90 (m, 8H, 8×H(1´)), 6.93–7.44 (m, 20H, H_{Ar}) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 13.7, 14.5 and 15.0 (4×C(3´´´´)), 17.8, 18.9 and 19.1 (8×Me), 20.4–21.0 (4×C(1´´´´)), 22.5–22.8 (4×C(2´´´´)), 30.1 (4×C(2´´´)), 33.5 (4×C(1´´) and 4×C(2´)), 41.3 (4×C(2´´)), 46.7–49.3 (8×C(4) and 4×C(3´´´)), 51.6–52.8 (16×OMe), 57.9, 58.3 and 58.6 (4×C(1´) and 4×C(1´´´)), 69.8–71.4 (8×C(5)), 125.3–133.0 (20 CH_{Ar}), 142.8 and 146.6 (4×C(*i*)), 149.0 (8×C(3)), 169.2–173.7 (16 COO).

*Dimethyl (E)-2-(5-(3-(2-(3-(2-chloroethyl)-5-(methoxycarbonyl)-5-methyl-4,5-dihydro-1H-pyrazol-1-yl)ethyl)-5-(methoxycarbonyl)-5-methyl-4,5-dihydro-1H-pyrazol-1-yl)-5-phenylpent-2-en-1-yl)malonate **(5oa´)***. Compound **5oa´** was prepared from **1o** and **2a** in yield 6% (10 mg, *dr* = 1/1/1/1). Yellow oil. IR (KBr) $\tilde{\nu}$ 3084, 3061, 3027, 3000, 2953, 2849, 1731 br. (C=O), 1634, 1604, 1496, 1435, 1284, 1199 cm^{-1}. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{32}H_{43}N_4O_8Cl$ (for ^{35}Cl) 669.2662; Found 669.2663. ^1H NMR (300.1 MHz, $CDCl_3$): δ 2.01–2.27 (m, 8H, 8×H(5´´´)), 3.43–3.52 (m, 8H, 8×H(2´´´)), 3.88–4.16 (m, 4H, 4×H(1´´´)), 4.96–5.90 (m, 8H, 4×H(3´´´) and 4×H(4´´´)) ppm.

*Methyl 3-(2-chloroethyl)-1-(2-(1-(3-(ethoxycarbonyl)-4-oxo-1-phenylpentyl)-5-(methoxycarbonyl)-5-methyl-4,5-dihydro-1H-pyrazol-3-yl)ethyl)-5-methyl-4,5-dihydro-1H-pyrazole-5-carboxylate **(5pa)***. Compound **5pa** was prepared from **1p** and **2a** in yield 88% (133 mg, *dr* = 1/1/1/1/1/1/1/1). Dark yellow oil. IR (KBr) $\tilde{\nu}$ 3062, 2980, 2953, 2850, 1735 br. (C=O), 1492, 1454, 1435, 1370, 1285 cm^{-1}. ^1H NMR (300.1 MHz, $CDCl_3$): δ 1.19–1.34 (m, 3H, Me_{CO2Et}), 1.33–1.46 (m, 6H, 2×Me), 2.16–2.25 (m, 3H, COMe) 2.27–2.82 (m, 8H, 2×H(2´), 2×H(1´´), 2×H(2´´´) and 2×H(4)), 3.10–3.34 (m, 2H, 2×H(4)), 3.63–3.88 (m, 9H, 2×CO_2Me, 2×H(2´´) and H(3´´´)), 3.99–4.09 (m, 1H, H(1´´´)), 4.10–4.26 (m, 3H, H(1´) and $CH_{2\ CO2Et}$), 7.12–7.53 (m, 5H, H_{Ar}) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 14.1 (Me_{CO2Et}), 18.9 and 19.0 (2×Me), 28.7 and 28.8 (2×COMe), 30.2 (C(2´´´)), 33.5 (C(1´´)), 35.7 (C(2´)), 41.3 (C(2´´)), 46.8 and 47.2 (2×C(4)), 52.2 and 52.3 (2×OMe and C(3´´´)), 59.6, 59.9 and 61.1 ($CH_{2\ CO2Et}$, C(1´) and C(1´´´)), 71.4 (2×C(5)), 127.6, 128.0 and 128.1 (5 CH_{Ar}), 141.3 (C(*i*)), 148.3 and 148.8 (2×C(3)), 169.7, 173.1 and 173.2 (3×COO), 203.2 (CO). MS (*m/z* for ^{35}Cl, %): 545 (100, $M^+ – CO_2$Me). HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{30}H_{41}N_4O_7Cl$ (for ^{35}Cl) 627.2556; Found 627.2551.

*Methyl 1-(3-acetyl-4-oxo-1-phenylpentyl)-3-(2-(3-(2-chloroethyl)-5-(methoxycarbonyl)-5-methyl-4,5-dihydro-1H-pyrazol-1-yl)ethyl)-5-methyl-4,5-dihydro-1H-pyrazole-5-carboxylate **(5qa)***. Compound **5qa** was prepared from **1q** and **2a** in yield 81% (116 mg, *dr* = 1/1/1/1; ketone : enol = 2.2/1). Dark oil. IR (KBr) $\tilde{\nu}$ 3061, 3025, 2953, 2850, 1731 br. (C=O), 1699, 1601, 1493, 1454, 1434, 1359, 1286 cm^{-1}. MS (*m/z* for ^{35}Cl, %): 515 (100, $M^+ – CO_2$Me). HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{29}H_{39}N_4O_6Cl$ (for ^{35}Cl) 597.2450; Found 597.2439. Ketone form: ^1H NMR (300.1 MHz, CD_2Cl_2): δ 1.02–1.46 (m, 24H, 8×Me), 2.02–2.35 (m, 28H, 8×COMe and 4×H(2´)), 2.45–2.90 (m, 28H, 4×H(2´), 8×H(1´´), 8×H(2´´´) and 8×H(4)), 3.10–3.34 (m, 8H, 8×H(4)), 3.66–3.89 (m, 36H, 8×CO_2Me, 8×H(2´´) and 4×H(3´´´)), 3.98 (dd, 4H, 4×H(1´´´), ^3J = 8.2 Hz, ^3J = 6.7 Hz), 4.03–4.18 (m, 4H, 4×H(1´)), 7.14–7.61 (m, 20H, H_{Ar}) ppm. ^{13}C NMR (75.5 MHz, CD_2Cl_2): δ 18.7 and 18.8 (8×Me), 28.7 and 29.5 (8×COMe), 30.1 (4×C(2´´´)), 33.4 (4×C(1´´)), 35.5 (4×C(2´)), 41.7 (4×C(2´´)), 46.7 and 47.1 (8×C(4)), 52.0, 52.1 and 52.3 (8×OMe and 4×C(3´´´)), 60.1 and 60.4 (4×C(1´) and 4×C(1´´´)), 71.3 (8×C(5)), 127.2, 127.6 and 127.9 (20 CH_{Ar}), 141.2 (4×C(*i*)), 148.7 and 148.8 (8×C(3)), 172.8 and 173.0 (8×COO), 204.2 and 204.4 (8 CO). Enol form (key signals): ^1H NMR (300.1 MHz, CD_2Cl_2): δ 1.02–1.46 (m, 24H, 8×Me), 17.03 (s, 2H, OH), 17.10 (s, 2H, OH).

*Methyl 1-(3-benzoyl-4-oxo-1,4-diphenylbutyl)-3-(2-(3-(2-chloroethyl)-5-(methoxycarbonyl)-5-methyl-4,5-dihydro-1H-pyrazol-1-yl)ethyl)-5-methyl-4,5-dihydro-1H-pyrazole-5-carboxylate **(5ra)***. Compound **5ra** was prepared from **1r** and **2a** in yield 19% (33 mg, *dr* = 1/1/1/1). Dark oil. IR (KBr) $\tilde{\nu}$ 3063, 3026, 2951, 2931, 2855, 1732 br. (C=O), 1695, 1672, 1597, 1495, 1449, 1434, 1351, 1282 cm^{-1}. ^1H NMR (300.1 MHz, $CDCl_3$): δ 0.94 (s, 6H, 2×Me), 1.27 (s, 6H, 2×Me), 1.36–1.46 (m, 12H, 4×Me), 2.50–3.01 (m, 38H, 2×CO_2Me, 8×H(2´), 8×H(1´´), 8×H(2´´´) and 8×H(4)), 3.14–3.46 (m, 14H, 2×CO_2Me and 8×H(4)), 3.69–3.82 (m, 24H, 4×CO_2Me, 8×H(2´´) and 4×H(3´´´)), 4.24–4.33 (m, 4H, 4×H(1´)), 4.37 (dd, 4H, 4×H(1´), ^3J = 10.9 Hz, ^3J = 4.0 Hz), 5.49–5.59 (m, 4H,

4×H(1´´´)), 4.37 (br.d, 4H, 4×H(1´´´), ^3J = 9.9 Hz), 7.17–7.67 (m, 44H, H_{Ar}), 7.78–7.96 (m, 8H, H_{Ar}), 8.01–8.25 (m, 8H, H_{Ar}) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 19.0, 19.1, 21.2 and 22.2 (8×Me), 29.6 and 30.3 (4×C(2´´´)), 33.4 and 33.5 (4×C(1´´)), 36.8 and 37.1 (4×C(2´)), 41.2 (4×C(2´´)), 46.9–48.3 (8×C(4)), 51.3–52.4 (8×OMe and 4×C(3´´´)), 53.5 and 53.8 (4×C(1´´´)), 59.5 and 60.7 (4×C(1´)), 70.9, 71.0, 71.4 and 71.5 (8×C(5)), 127.1–133.4 (60 CH_{Ar}), 135.3, 135.7, 136.4, 136.8, 141.7 and 141.8 (12×C(*i*)), 147.9, 148.0, 149.5 and 149.6 (8×C(3)), 172.6, 173.0, 173.1 and 174.2 (8×COO), 196.1, 196.2, 197.0 and 197.8 (8 CO). MS (*m/z* for ^{35}Cl, %): 661 (16, M^+ – HCl), 638 (54, M^+ – CO_2Me). HRMS (ESI-TOF) *m/z*: [M + Na]$^+$ Calcd for $C_{39}H_{43}N_4O_6Cl$ (for ^{35}Cl) 721.2763; Found 721.2760.

General synthetic procedure and spectroscopic data for products of double addition of DAC 1a with spiro[cyclopropanepyrazolines] 2a,b,e. All operations were performed under dry argon atmosphere. An $EtAlCl_2$ (1.5 mL, 1.53 mmol, 1.0 M in hexane) was added to a solution of DAC **1a** (603 mg, 2.57 mmol) and pyrazolines **2a,b,e** (0.51 mmol) in dry DCM (4 mL) and the mixture was stirring for 15 minutes at 0–5ºC. Then an aqueous solution of HCl (5%) was added at room temperature until pH 3 was achieved and the reaction mixture was extracted with CH_2Cl_2 (3×10 mL). The organic layer was dried over $MgSO_4$ and the solvent was removed in vacuo. The residue was purified by flash chromatography (benzene–EtOAc (30:1) to EtOAc) on silica gel to afford the pure products.

*Tetramethyl 6-(3-(2-chloroethyl)-5-(methoxycarbonyl)-5-methyl-4,5-dihydro-1H-pyrazol-1-yl)-3,6-diphenylhexane-1,1,4,4-tetracarboxylate **(7a)***. Compound **7a** was prepared from **1a** and **2a** in yield 73% (292 mg, *dr* = ~1/1/1/1). All four diastereomers were partially separated using column chromatography on SiO_2. IR (KBr) $\tilde{\nu}$ 3060, 3031, 2956, 2951, 2920, 2848, 1730 br. (C=O), 1599, 1489, 1351, 1289 cm^{-1}. HRMS (ESI-TOF) *m/z*: [M + Na]$^+$ Calcd for $C_{34}H_{41}N_2O_{10}Cl$ (for ^{35}Cl) 695.2347; Found 695.2358. 1st diastereomer. Light yellow oil. ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 1.51 (s, 3H, Me), 2.06 (dd, 1H, H(5), ^2J = 14.5 Hz, ^3J = 4.6 Hz), 2.26 (ddd, 1H, H(2), ^2J = 14.5 Hz, ^3J = 12.1 Hz, ^3J = 4.6 Hz), 2.52 (d, 1H, H(4´), ^2J = 16.4 Hz), 2.65–2.78 (m, 3H, H(2) and 2×H(1´´)), 2.82 (s, 3H, CO_2Me), 2.92–3.09 (m, 3H, H(3), H(5) and H(4´)), 3.37–3.57 (m, 7H, 2×CO_2Me and H(1)), 3.64–3.81 (m, 8H, 2×CO_2Me and 2×H(2´´)), 4.25 (dd, 1H, H(6), ^3J = 8.5 Hz, ^3J = 4.7 Hz), 7.03–7.37 (m, 10H, H_{Ar}) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 20.7 (Me), 32.6 (C(2)), 33.7 (C(1´´)), 40.8 (C(5)), 41.2 (C(2´´)), 47.1 (C(3)), 47.5 (C(4´)), 50.5 (C(1)), 51.2, 51.8, 52.0, 52.3 and 52.4 (5 OMe), 57.5 (C(6)), 59.4 (C(4)), 69.8 (C(5´)), 126.9, 127.5 and 128.7 (5 CH_{Ar}), 138.2 and 140.5 (2 C(*i*)), 146.4 (C(3´)), 169.5, 169.6, 170.6, 171.1 and 171.2 (5 COO). 2nd & 3rd diastereomers. Light yellow oil. ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 0.82 (s, 3H, Me), 1.44 (s, 3H, Me), 1.96 (dd, 1H, H(5), ^2J = 14.9 Hz, ^3J = 3.6 Hz), 2.06 (dd, 1H, H(5), ^2J = 14.7 Hz, ^3J = 3.7 Hz), 2.20–2.34 (m, 1H, H(2)), 2.42–2.57 (m, 3H, H(2) and 2×H(4´)), 2.66–2.81 (m, 9H, CO_2Me, 2×H(2) and 4×H(1´´)), 2.85–3.10 (m, 2H, 2×H(3)), 3.35 (d, 2H, 2×H(4´), ^2J = 16.9 Hz), 3.40–3.57 (m, 14H, 4×CO_2Me and 2×H(1)), 3.64–3.80 (m, 16H, 4×CO_2Me and 4×H(2´´)), 3.88 (m, 3H, CO_2Me), 4.37 (dd, 1H, H(6), ^3J = 9.3 Hz, ^3J = 3.6 Hz), 4.61 (dd, 1H, H(6), ^3J = 9.7 Hz, ^3J = 3.6 Hz), 7.03–7.38 (m, 20H, H_{Ar}) ppm. 4th diastereomer. Light yellow oil. ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 0.77 (s, 3H, Me), 1.89 (dd, 1H, H(5), ^2J = 14.5 Hz, ^3J = 2.2 Hz), 2.18–3.03 (m, 7H, 2×H(2), H(3), H(5), H(4´) and 2×H(1´´)), 3.35–3.93 (m, 19H, 5×CO_2Me, H(1), H(4´) and 2×H(2´´)), 4.75 (dd, 1H, H(6), ^3J = 10.1 Hz, ^3J = 2.1 Hz), 6.96–7.50 (m, 10H, H_{Ar}) ppm.

*Tetramethyl 6-(3-(2-chloroethyl)-3a,4,5,6,7,7a-hexahydro-1H-4,7-methanoindazol-1-yl)-3,6-diphenylhexane-1,1,4,4-tetracarboxylate **(7b)***. Compound **7b** was prepared from **1b** and **2a** in yield 10% (41 mg, *dr* = 2.8/1.5/1.4/1). Light yellow oil. IR (KBr) $\tilde{\nu}$ 3055, 3029, 2955, 2945, 2912, 2905, 2845, 1737 br. (C=O), 1602, 1491, 1355, 1298 cm^{-1}. ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 1.81–1.64 (m, 24H, 8×H(5´), 8×H(6´) and 8×H(8´)), 1.84–2.81 (m, 28H, 8×H(2), 4×H(5), 4×H(4´), 4×H(7´) and 8×H(1´´)), 2.98–3.19 (m, 12H, 4×H(3), 4×H(3a) and 4×H(5)), 3.23 (s, 3H, CO_2Me) 3.34–3.88 (m, 61H, 15×CO_2Me, 8×H(2´´), 4×H(7a´) and 4×H(1)), 3.93 (dd, 1H, H(6), ^3J = 10.4 Hz, ^3J = 5.7 Hz), 4.16 (dd, 1H, H(6), ^3J = 8.6 Hz, ^3J = 6.3 Hz), 4.34 (dd, 1H, H(6), ^3J = 6.2 Hz, ^3J = 5.5 Hz), 4.49 (dd, 1H, H(6), ^3J = 7.1 Hz, ^3J = 4.7 Hz), 6.95–7.42 (m, 40H, H_{Ar}) ppm. HRMS (ESI-TOF) *m/z*: [M + Na]$^+$ Calcd for $C_{36}H_{43}N_2O_8Cl$ (for ^{35}Cl) 689.2606; Found 689.2592.

*Tetramethyl 6-(3-(1-(chloromethyl)cyclopropyl)-5-(methoxycarbonyl)-5-methyl-4,5-dihydro-1H-pyrazol-1-yl)-3,6-diphenylhexane-1,1,4,4-tetracarboxylate **(7e)***. Compound **7e** was prepared from **1e** and **2a** in yield 87% (313 mg, *dr* = 2.6/1.9/1.2/1). All four diastereomers were partially separated using column chromatography on SiO_2. IR (KBr) $\tilde{\nu}$ 3040, 3035, 2955, 2940, 2923, 2857, 1731 br. (C=O), 1594, 1496, 1350, 1280 cm^{-1}. MS (*m/z* for ^{35}Cl, %): 698 (1, M^+), 639 (57, M^+ – CO_2Me). HRMS (ESI-TOF) *m/z*: [M + Na]$^+$ Calcd for $C_{36}H_{43}N_2O_{10}Cl$ (for ^{35}Cl) 721.2498; Found 721.2495. 1st diastereomer. Light yellow oil. ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 0.75 (s, 3H, Me), 0.84–1.58 (m, 4H, $H_{cycloprop}$), 1.87 (dd, 1H, H(5), ^2J = 13.0 Hz, ^3J = 2.2 Hz), 2.20 (d, 1H, H(4´), ^2J = 16.6 Hz), 2.32–2.43 (m, 1H, H(2)), 2.53–2.66 (m, 1H, H(5)), 2.82–3.02 (m, 1H, H(2)), 3.26–3.34 (m, 1H, H(3)), 3.29 (dd, 1H, H(1), ^3J = 13.0 Hz, ^3J = 2.2 Hz), 3.36 (d, 1H, H(4´), ^2J = 16.6 Hz), 3.51 (s, 3H, CO_2Me), 3.54 (s, 3H, CO_2Me), 3.61 (d, 1H, H(4´´), ^2J = 11.2 Hz), 3.73 (s, 3H, CO_2Me), 3.75 (s, 3H, CO_2Me), 3.85 (s, 3H, CO_2Me), 3.96 (d, 1H, H(4´´), ^2J = 11.2 Hz), 4.74 (dd, 1H, H(6), ^3J = 10.3 Hz, ^3J = 1.9 Hz), 6.99–7.05 (m, 2H, H_{Ar}), 7.09–7.37 (m, 6H, H_{Ar}), 7.44–7.50 (m, 2H, H_{Ar}) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 13.5 and 14.2 (C(2´´) and C(3´´)), 22.0 (Me), 23.9 (C(1´´)), 31.3 (C(2)), 42.2 (C(5)), 43.9 (C(4´)), 50.0 (C(4´´)), 50.4 (C(3)), 50.8 (C(1)), 51.6, 51.7, 52.4 and 52.6 (5 OMe), 59.3 (C(6)), 61.3 (C(4)), 72.2 (C(5´)), 126.6, 127.7, 127.9, 128.0, 128.4 (10 CH_{Ar}), 137.5 and 145.3 (2 C(*i*)), 147.5 (C(3´)), 169.5, 169.6, 170.4, 170.7, 171.6 (5 COO). 2nd diastereomer. Yellow oil. ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 0.74–1.53 (m, 7H, Me and $H_{cycloprop}$), 1.90 (dd, 1H, H(5), ^2J = 10.1 Hz, ^3J = 3.3 Hz), 2.18–2.26 (m, 2H, H(2) and H(4´)), 2.45–2.56 (m, 1H, H(2)), 2.84–3.17 (m, 2H, H(4´´) and H(5)), 3.28 (d, 1H, H(4´), ^2J = 14.7 Hz), 3.40–3.62 (m, 7H, 2×CO_2Me and H(3)), 3.63–3.83 (m, 5H, 2×CO_2Me and H(1)), 3.90 (s, 3H, CO_2Me), 3.96 (d, 1H, H(4´´), ^2J = 11.3 Hz), 4.60 (dd, 1H, H(6), ^3J = 10.1 Hz, ^3J = 3.3 Hz), 7.05–7.46 (m, 10H, H_{Ar}) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 14.4 and 14.5 (C(2´´) and C(3´´)), 22.0 (Me), 23.8 (C(1´´)), 32.2 (C(2)), 40.6 (C(5)), 43.8 (C(4´)), 46.8 (C(1)), 50.7 (C(4´´)), 51.7 (C(3)), 52.0, 52.2, 52.3 and 52.4 (5 OMe), 58.1 (C(6)), 59.7 (C(4)), 71.9 (C(5´)), 126.7, 127.5, 127.7, 128.0, 128.2 and 128.4 (10 CH_{Ar}), 138.5 and 144.3 (2 C(*i*)), 147.5 (C(3´)), 169.6, 169.7, 170.7, 171.3 and 172.2 (5 COO). 3rd diastereomer. Yellow oil. ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 0.74–1.61 (m, 7H, Me and $H_{cycloprop}$), 2.01 (dd, 1H, H(5), ^2J = 14.9 Hz, ^3J = 4.6 Hz), 2.24 (ddd, 1H, H(2), ^2J = 14.4 Hz, ^3J = 6.1 Hz, ^3J = 3.4 Hz), 2.51 (d, 1H, H(4´), ^2J = 16.0 Hz), 2.60–2.84 (m, 4H, CO_2Me and H(2)), 2.87–3.28 (m, 3H, H(4´), H(4´´) and H(5)), 3.39–3.57 (m, 7H, 2×CO_2Me and H(3)), 3.61–3.96 (m, 8H, 2×CO_2Me, H(4´´) and H(1)), 4.22 (dd, 1H, H(6), ^3J = 8.7 Hz, ^3J = 4.6 Hz), 7.02–7.50 (m, 10H, H_{Ar}) ppm. 4th diastereomer. Yellow oil. ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 0.73–1.63 (m, 7H, Me and $H_{cycloprop}$), 1.90 (dd, 1H, H(5), ^2J = 14.9 Hz, ^3J = 3.3 Hz), 2.16–2.60 (m, 3H, 2×H(2) and H(4´)), 2.63–3.36 (m, 6H, CO_2Me, H(4´), H(4´´) and H(5)), 3.38–3.99 (m, 15H, 4×CO_2Me, H(1), H(4´´) and H(3)), 4.34 (dd, 1H, H(6), ^3J = 9.4 Hz, ^3J = 3.3 Hz), 6.97–7.54 (m, 10H, H_{Ar}) ppm.

Transformations of Pyrazolines.

Dimethyl 2-allyl-2-(2-(3-(2-chloroethyl)-5-(methoxycarbonyl)-5-methyl-4,5-dihydro-1H-pyrazol-1-yl)-2-phenylethyl)malonate ***(8)***. All operations were performed under dry argon atmosphere. A solution of LDA (0.1 mL, 0.18 mmol, 2.0 M in THF/hexane/ethylbenzole) was added to a solution of pyrazoline **3aa** (80 mg, 0.18 mmol) in dry THF (2 mL) at –78ºC and the mixture was stirring at that tempereture for 1.5 hours. Then an allylbromide (29 mg, 0.02 mL, 0.24 mmol) was added at –78ºC and the mixture was warmed up to room temperature and stirred for 18 hours. After that an aqueous solution of NH_4Cl (10%) was diluted to the mixture at room temperature and the reaction mixture was extracted with CH_2Cl_2 (3×10 mL). The organic layer was washed by distilled water and the brine then it was dried over $MgSO_4$ and the solvent was removed in vacuo. The residue was purified by column chromatography (hexane–acetone (5:1)) on silica gel to afford the pure product **8** in yield 67% (58 mg, *dr* = 1/1). Light yellow oil. IR (KBr) $\tilde{\nu}$ 3074, 3024, 2999, 2973, 2954, 2872, 2843, 1733 br. (C=O), 1640, 1600, 1581, 1495, 1492, 1435, 1375, 1287 cm^{-1}. ^1H NMR (300.1 MHz, $CDCl_3$): δ 0.87 (s, 3H, Me_{mj}), 1.53 (s, 3H, Me_{mn}), 2.18–2.32 (m, 2H, $H_{mj\ and\ mn}(2')$), 2.36 (d, 1H, $H_{mj}(4)$, ^2J = 16.9 Hz), 2.57 (d, 1H, $H_{mn}(4)$, ^2J = 16.4 Hz), 2.70–2.92 (m, 11H, CO_2Me_{mn}, 4×$H_{mj\ and\ mn}(4')$ and 4×$H_{mj\ and\ mn}(1'')$), 3.01–3.14 (m, 3H, $H(4)_{mn}$ and $H_{mj\ and\ mn}(2')$), 3.42 (d, 1H, $H_{mj}(4)$, ^2J = 16.9 Hz), 3.56–3.63 (m, 12H, 4×CO_2Me), 3.70–3.85 (m, 4H, 4×$H_{mj\ and\ mn}(2'')$), 4.15 (dd, 1H, $H_{mn}(1')$, ^3J = 9.1 Hz, ^3J = 4.6 Hz), 4.48 (dd, 1H, $H_{mj}(1')$, ^3J = 9.9 Hz, ^3J = 3.8 Hz), 5.05–5.22 (m, 4H, $H(6')_{mj\ and\ mn}$), 5.60–5.76 (m, 2H, $H(5')_{mj\ and\ mn}$), 7.13–7.51 (m, 10H, H_{Ar}) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 20.9 and 22.0 (2 Me), 33.4 and 33.6 (C(4′)), 36.6 and 36.8 (C(1′′)), 39.0 and 39.1 (C(2′)), 41.2 and 41.3 (C(2′′)), 46.6 and 47.1 (C(4)), 51.1, 51.8, 51.9, 52.1 and 52.5 (6 OMe), 56.3 and 56.4 (C(3′)), 57.7 and 58.4 (C(1′)), 69.4 and 71.5 (C(5)), 118.7 and 118.9 (C(6′)), 126.9, 127.0, 127.2, 127.7, 127.9, 128.0, 128.3 and 128.5 (10 CH_{Ar}), 132.6 and 132.9 (C(5′)), 140.7 and 146.0 (C(3)), 144.4 and 144.6 (C(*i*)), 171.1, 171.3, 171.4, 172.1 and 172.2 (6 COO). MS (*m/z* for ^{35}Cl, %): 478 (6, M^+), 447 (23, M^+ – OMe), 419 (91, $M^+ – CO_2Me$). HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{24}H_{31}N_2O_6Cl$ (for ^{35}Cl) 501.1763; Found 501.1760.

Dimethyl 2-(2-(5-(methoxycarbonyl)-5-methyl-3-vinyl-4,5-dihydro-1H-pyrazol-1-yl)-2-phenylethyl)malonate ***(9)***. All operations were performed under dry argon atmosphere. A solution of Na (29 mg, 1.3 mmol) in dry MeOH (1 mL) was added to a solution of pyrazoline **3aa** (203 mg, 0.42 mmol) in dry MeOH (5 mL) and the mixture was stirring for 3 hours at 25ºC. Then the brine was added at room temperature and the reaction mixture was extracted with CH_2Cl_2 (3×10 mL). The organic layer was washed by distilled water and the brine then it was dried over $MgSO_4$ and the solvent was removed in vacuo to afford the pure product **9** in yield 66% (113 mg, *dr* = 1/1) without any purifications. Yellow oil. IR (KBr) $\tilde{\nu}$ 3088, 3062, 3027, 3001, 2954, 2846, 1735 br. (C=O), 1614, 1493, 1455, 1436, 1355, 1288, 1268 cm^{-1}. ^1H NMR (300.1 MHz, $CDCl_3$): δ 1.00 (s, 3H, Me), 1.47 (s, 3H, Me), 2.26–2.48 (m, 2H, 2×H(2′)), 2.58–2.82 (m, 4H, 2×H(4) and 2×H(2′)), 2.88 (s, 3H, CO_2Me), 3.34 (d, 1H, H(4), ^2J = 16.6 Hz), 3.36 (d, 1H, H(4), ^2J = 16.4 Hz), 3.52 (dd, 1H, H(3′), ^3J = 9.0 Hz, ^3J = 6.0 Hz), 3.69–3.82 (m, 16H, 5×CO_2Me and H(3′)), 4.23 (dd, 1H, H(1′), ^3J = 9.0 Hz, ^3J = 6.0 Hz), 4.40 (dd, 1H, H(1′), ^3J = 10.2 Hz, ^3J = 5.0 Hz), 5.12 (dd, 2H, H(2′′), ^2J = 9.4 Hz, ^3J = 17.6 Hz), 5.27 (dd, 2H, H(2′′), ^2J = 9.4 Hz, ^3J = 10.2 Hz), 6.69 (dd, 2H, H(1′′), ^3J = 17.6 Hz, ^3J = 10.2 Hz), 7.08–7.52 (m, 10H, H_{Ar}) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 21.6 and 22.8 (2 Me), 36.3 and 36.4 (C(2′)), 43.1 and 43.4 (C(4)), 48.9 and 49.2 (C(3′)), 51.4, 52.3, 51.4 and 52.5 (6 OMe), 58.9 and 60.1 (C(1′)), 68.9 and 71.2 (C(5)), 115.4 and 115.8 (C(2′′)), 127.1, 127.2, 127.3, 127.7, 128.0 and 128.3 (10 CH_{Ar}), 130.5 and 130.6 (C(1′′)), 141.0 and 144.1 (C(*i*)), 144.6 and 146.1 (C(3)), 169.6, 169.7, 169.8, 170.1, 172.0 and 173.5 (6 COO). MS (*m/z*, %): 402 (90, M^+), 371 (33, M^+ – OMe), 343 (100, $M^+ – CO_2Me$), 311 (14, $M^+ – CO_2Me$ – MeOH). HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{21}H_{26}N_2O_6$ 425.1683; Found 425.1697.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI:

^1H and ^{13}C NMR spectra for all pure products (PDF)

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Notes

The authors declare no competing financial interest.

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