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The Deazidoalkoxylation: Sequential Nucleophilic Substitutions with Diazidated Diethyl Malonate

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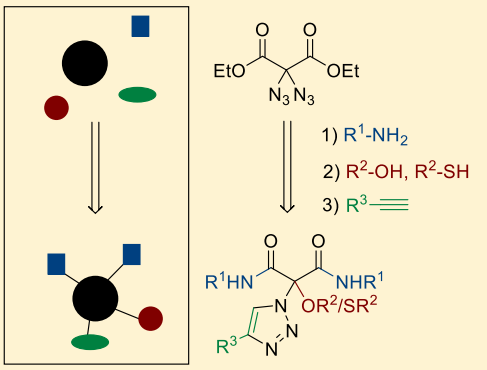
Supporting Information

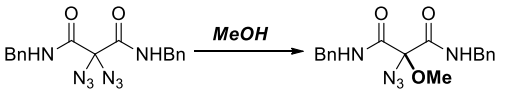
ABSTRACT: Diazidated malonamides derived from amines and diazidated diethyl malonate react with lithiated alcohols through nucleophilic substitution reactions where azide acts as an unconventional leaving group. This deazidoalkoxylation leads to the formal construction of *N*,*O*-acetals, and the remaining azide functionality is a useful entry point for further functionalizations through, for example, standard cycloaddition chemistry. Thus, the presented chemistry provides an easy route toward densely functionalized molecules: Amines, alcohols, and alkynes can be attached onto the small malonate core unit in a sequential manner.



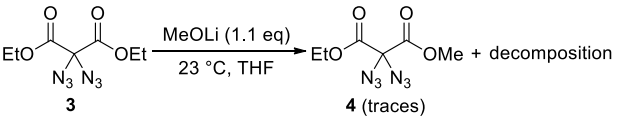
Organic azides have a rich reactivity with a plethora of chemical applications.[1,2] The current playground mainly consists of using azides in cycloaddition reactions, a field that has rapidly evolved over the last decades.[3,4] The pseudohalogenic character of azide, though known for a long period of time,[5] has found markedly less uses in organic reaction development: While the azides are naturally employed as excellent nucleophiles in all kinds of nucleophilic substitutions,[1,6] their value as potential leaving groups is somewhat unrecognized. As an exception, acyl azides are widely used as effective acylating agents, particularly in the acylation of amines.[7] The azide anion is the leaving group in this type of substitution proceeding through an addition−elimination mechanism.[8] To our surprise, however, our literature search revealed only a singular example where the nucleophilic substitution with aliphatic azides was reported. In this specific reaction, 3-azidopropanoic acid was transformed into aza heterocycles, and the azide group was proposed to formally act as a leaving group in an intramolecular substitution.[9] We now report the first example of an intermolecular substitution at a tetrahedral carbon that is based on azide acting as the leaving group.

We recently launched a research program aimed at the synthesis[10] and reactivity[11] of small molecules having a geminal diazido unit. When we investigated the reaction of geminal diazides with nucleophilic amines, we realized that the diazido moiety was capable to trigger a range of uncommon reactions including fragmentations with concomitant acyl transfer, most of which did not proceed with related oxygen nucleophiles.[12] However, it was observed that diazidated malonamides (such as **1a**) were smoothly transformed into *N*,*O*-acetal **2a** by simply adding an excess of *n*-butyllithium to a solution of **1a** in methanol (Scheme 1). The newly formed *N*,*O*-acetal

Scheme 1. Substitution of Geminal Diazides 1a and 3



conditions:		
	n-BuLi (4 eq), MeOH, 23 °C	73%
	n-BuLi (1.1 eq), MeOH (1.1 eq), THF, 23 °C	**83%**
	NaH (4.0 eq), MeOH, 23 °C	44%
	K_2CO_3 (4.0 eq), MeOH, 23 °C	80%



corresponds to the product of a nucleophilic substitution where methanol is the formal external nucleophile and azide acts as the leaving group. After careful optimization, excellent yields of **2a** were achieved using 1.1 equiv of *n*-butyllithium and 1.1 equiv of methanol in THF at room temperature. We point out that the lithium alkoxide (i.e., LiOMe) is the actual nucleophilic species under the conditions. The reaction with sodium methoxide (derived from NaH and methanol) proved to have a diminished efficacy, resulting in **2a** in 44% yield, and the experimental procedure was slightly more demanding. We note that the use of amine bases (as NEt_3) did not result in product formation. The use of the inorganic salt K_2CO_3, on the other hand, was successful and gave the product of substitution in 80% yield. When subjecting lithium methoxide to diazido diethyl malonate **3**, the substitution of the azide was not

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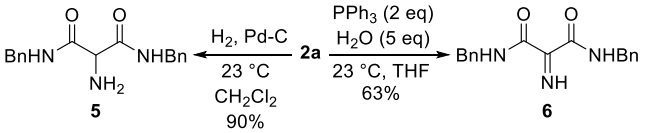
observed; instead, transesterification led to the traces of the mixed ester **4**, accompanied by a range of unidentified decomposition products. We conclude that the amide moiety is of primary importance to make the substitution possible. However, we currently cannot clarify whether the amide moieties are mandatory for simply stabilizing the starting diazide **1a**, or whether the amide NH has an active effect on the substitution; diazidated malonamides derived from secondary amines were not accessible to us for testings, despite heavy experimentations.

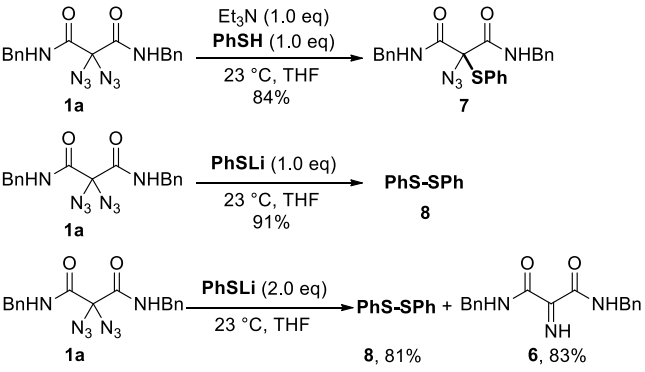
Preliminary experiments showed that the unique *N*,*O*-acetals containing azide groups are capable of allowing new reactions: for example, azide **2a** provides the primary amine **5** upon standard hydrogenation conditions with H_2 over palladium on charcoal (Scheme 2).[13] When using PPh_3 under aqueous conditions,[14] the imine **6** was formed, demonstrating that the degree of reduction is easily controlled by the choice of reaction conditions.

Scheme 2. Controlled Reduction of 2a



Sulfur nucleophiles were also briefly studied regarding their tendency to trigger an azide substitution with malonamide **1a**. As summarized in Scheme 3, it was found that, for example,

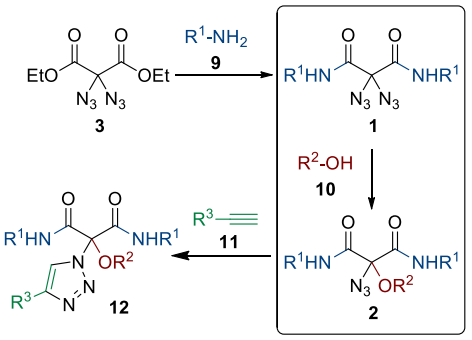
Scheme 3. Substitution with *S*- and *N*-Nucleophiles



thiophenol leads to the substitution product **7** in an excellent yield of 84%, when triethylamine was the base additive. In striking contrast, the use of *n*-BuLi resulted in the exclusive formation of disulfide **8**.[15] We also observed the disulfide **8** in 81% yield when using not more than 50 mol % of the diazide **1a**. In this reaction, the fate of the diazidated malonamide was unequivocally determined since imine **6** was isolated in 83% yield. We therefore assumed that **6** was obtained via the initially formed *N*,*S*-acetal **7** that may undergo substitution with an excess of PhSH to give **8** and **6**, accompanied by a loss of nitrogen. This assumption was supported by the smooth transformation of **7** into **8**, through simple treatment of **7** with PhSH.

We then applied this azide substitution to the sequential modification of diazidated diethyl malonate **3** (Scheme 4), a compound that was the ideal starting point for the synthesis of a range of malonamides **1** through the direct transamidation

Scheme 4. Sequential Substitutions with Diazido Malonate 3



with primary amines **9**.[16] The diazidated malonamides are then prone to the new deazidoalkoxylation with alcohol **10**, thus leading to the installation of the building block **2**. Of importance, this key reaction leaves one azide moiety untouched. The smooth introduction of additional functionalities via alkyne **11** and classical cycloaddition chemistry is now possible, i.e., the Cu(I)-catalyzed azide-alkyne cycloaddition (CuAAC).[17] The overall sequence consists of the sequential connection of (i) nucleophilic amines, (ii) nucleophilic alcohols, and (iii) alkynes to the central malonate unit, and the coupling of three functional modules is accomplished through formation of the final assembly **12**.

To this end, we began to study how to convert best the diethyl malonate **3** into the corresponding amides **1** using primary amines **9**. Typically, the direct reactions of malonic acid esters with amines require harsh conditions with temperatures > 100 °C.[18] Those temperatures appeared not applicable to malonate **3** since the diazide compound may suffer from thermal decomposition. Gratifyingly, it was found that milder conditions at lowered temperatures are possible for the conversion of diazide **3**: As summarized in Table 1, a broad range of amides **1** were formed with aliphatic and benzylic amines **9** at room temperature in THF; typically, no additional reagents were employed. Only in a few cases, NEt_3 was added to expedite the reaction. Anilines did not react under the conditions. Of primary importance, we did not observe any side products or decomposition in the course of the amidation reactions. The reactions with sufficiently nucleophilic amines were usually high-yielding after 12 h (entries 1–9, 11–13). Sterically more demanding amines led to reduced yields after 12 h, mostly due to incomplete conversion (entries 10 + 14).

The ease of forming malonamides **1** from malonic diester **3** with simple primary amines was evidence for the capability of the diazido moiety to activate the adjacent ester groups for a nucleophilic attack.[16] The succeeding step of our planned series of substitutions, the deazidoalkoxylation of **1**, was again based on the enhanced electrophilicity induced by the azide groups: This time, the carbonyl remained untouched since the newly formed amide carbonyl was deactivated toward oxygen nucleophiles, and alcohol nucleophiles were aimed at replacing one azide of the tetrahedral carbon center.

To test the general use of the deazidoalkoxylation, we began with the substitution of selected diazides (i.e., **1a**, **1d**, **1f**, **1g**, **1i**, and **1j**), following the exact conditions illustrated in Scheme 1. As summarized in Scheme 5, methanol was successfully introduced in all examples with yields ranging from 69% to 95%, leaving a single unreacted azide in place. Most importantly, this small survey did not identify any structural limitations with regard to the newly formed amide moieties.

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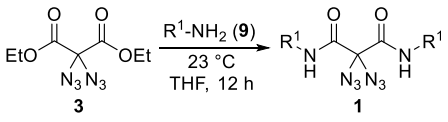
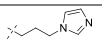
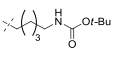
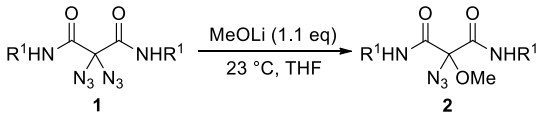
Table 1. Reactions of Malonate 3 with Amines[a]



entry	#	R^1	yield [%][b]	entry	#	R^1	yield [%][b]
1	**1a**		92	8	**1h**		97
2	**1b**		94	9	**1i**		91[c]
3	**1c**		75	10	**1j**		41[c]
4	**1d**		74[c]	11	**1k**		69
5	**1e**		93	12	**1l**		92
6	**1f**		91	13	**1m**		81
7	**1g**		94	14	**1n**		39

[a]Conditions: **3**, **9** (2.5 equiv), room temperature, THF. [b]Isolated yields after 12 h. [c]Conditions: **3**, **9** (3.0 equiv), NEt_3 (3.0 equiv), room temperature, THF.

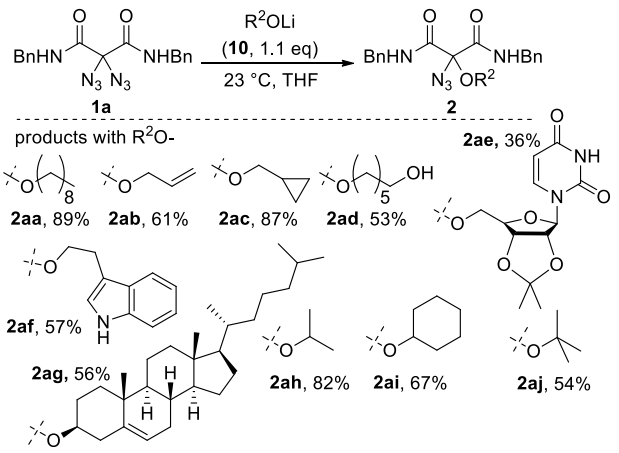
Scheme 5. Scope of the Substitutions with Methanol



1a → 2a	83%	**1g → 2g**	95%
1d → 2d	82%	**1i → 2i**	82%
1f → 2f	87%	**1j → 2j**	70%

Scheme 6 shows a broad variety of alcohols **10a–j** that were successfully coupled to the malonate core through deazidoalkoxylation. The reaction with the alcohols proceeded smoothly: when 1.1 equiv of the given alcohol and of *n*-BuLi were employed to treat the diazide **1a** in THF at room temperature, the monosubstituted products **2** were formed in yields ranging from 36% to 89%, leaving a single unreacted azide in place. Reactions of diazide **1a** with a selection of secondary and tertiary alcohols proceeded equally reliably, albeit with somewhat lowered yields, providing the desired *N*,*O*-acetals. We note that phenols, and derivatives thereof, do not react under the conditions.

Scheme 6. Reactions of 1a with Alcohols



With the goal of creating additional linkages to functional units through click chemistry,[3a,17] we next investigated the reaction of a selection of the monoazides **2** with alkynes **11** (Scheme 7). Using catalytic amounts of $CuSO_4$ and sodium ascorbate at room temperature in aqueous *t*BuOH or DMF, the monoazides underwent clean cycloaddition, leading to the formation of the triazoles **12**. As one would expect for this classical reaction, a range of linkages with complex alkynes could be easily installed, and the nature of the substituents R^1 and R^2 had only minor influence on the late-stage functionalization with R^3.

In summary, the diazidated diethyl malonate **3** is an excellent tool for providing a linkage between a nucleophilic amine and a nucleophilic alcohol. Our few experiments show an order of reactivity of **3** toward nucleophiles where the carbonyls react more easily than the tetrahedral carbon. Through sequential substitutions, amines are attached first to the connector molecule, followed by alcohols through subsequent deazidoalkoxylation under basic conditions. The remaining azide functionality is a simple handle for an additional linkage to alkynes using click chemistry. The overall concept adds synthetic value to diethyl 2,2-diazidomalonate **3** because the reagent is a versatile hub for creating multiple links between (nucleophilic) molecules, and the rapid and simple connection of functional molecules is of ongoing importance, from biology to materials applications.[19] We also demonstrated that the somewhat unique substitution of an azide attached to a tetrahedral carbon is not limited to alcohol nucleophiles: sulfur nucleophiles were also used in a successful manner, albeit with lower efficacy. We therefore conclude that the substitution of azides at saturated carbons may become a general mode of reaction, and studies with other classes of nucleophiles are currently ongoing.

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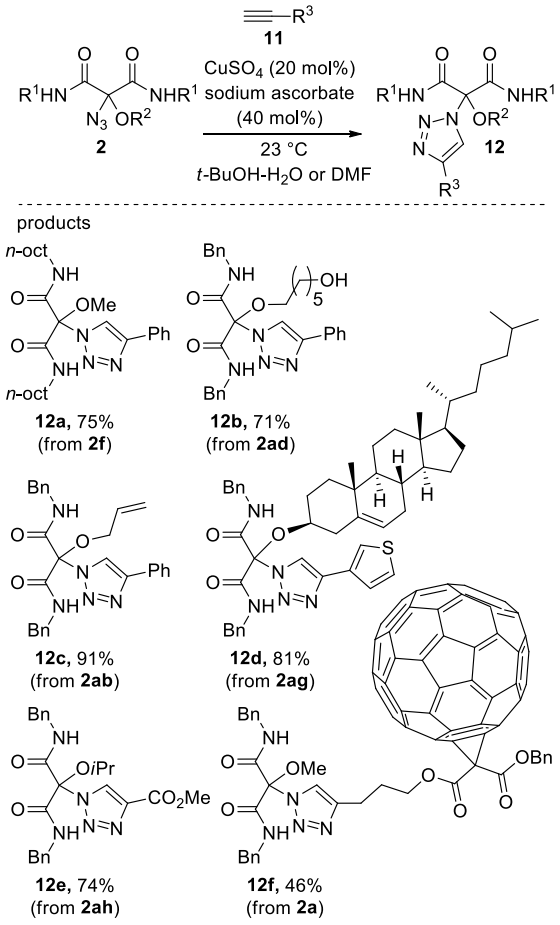
Scheme 7. Modifications of Monoazides with Alkynes



EXPERIMENTAL SECTION

General Remarks. All reactions, where it is not explicitly mentioned, were operated under air and no measures were taken to exclude water. The commercially available compounds and solvents were used as received. TLC was conducted with aluminum sheets (TLC silica gel 60 F_{254}) and visualized by exposure to UV light (254 nm), stained with ceric ammonium molybdate (CAM) or basic potassium permanganate ($KMnO_4$) and subsequent heating. Flash column chromatography was performed on silica gel (40−60 μm); the eluent used is reported in the particular experiments. IR spectra were measured using the ATR technique in the range of 400−4000 cm^{-1}. ^1H NMR spectra were recorded at 400 or 600 MHz spectrometers, ^{13}C NMR at 101 or 151 MHz. Chemical shifts are reported as δ values in ppm, coupling constants J in Hz. Multiplicities were defined by standard abbreviations. Low-resolution mass spectra (LRMS) were recorded using a LC/MS-combination (ESI). High-resolution mass spectra (HRMS) were obtained using ESI ionization methods on a MicroTOF.

Caution! *Geminal diazides are potentially hazardous and should be handled with care.*

General Procedures. *General Procedure A for the Synthesis of 2,2-Diazido Malonamides **1**.* Diethyl 2,2-diazidomalonate (1.0 equiv) (**3**) was dissolved in THF (1.00 M), and the amine **9** (2.5 equiv) was added. The reaction mixture was stirred overnight at room temperature, and the solvent was then concentrated under reduced pressure. Column chromatographic purification afforded the corresponding 2,2-diazido malonamides **1**.

*General Procedure B for the Synthesis of 2,2-Diazido Malonamides **1**.* Diethyl 2,2-diazidomalonate (1.0 equiv) (**3**) was dissolved in THF (0.50−1.00 M); the amine **9** (3.0 equiv) and triethylamine (3.0 equiv) were sequentially added. The reaction mixture was stirred overnight at room temperature, and the solvent was then concentrated under reduced pressure. Column chromatographic purification afforded the corresponding 2,2-diazido malonamides **1**.

*General Procedure C for the Substitution Reaction of 2,2-Diazido Malonamides **1** with Alcoholates **10**.* *n*-Butyllithium (2.5 M in hexane, 1.1 equiv) was added to a solution containing the corresponding alcohol (1.1 equiv) **10** in dry THF (0.15 M) under a nitrogen atmosphere at room temperature. After stirring for 10 min at this temperature, the 2,2-diazido malonamide (1.0 equiv) **1** was added, and the reaction mixture was allowed to stir overnight. The crude mixture was diluted with ethyl acetate (10 mL) and washed with water (2 × 5 mL). The aqueous phase was extracted with ethyl acetate (3 × 10 mL). The combined organic layer was washed with brine (10 mL), dried over Na_2SO_4, filtered, and evaporated under reduced pressure. Column chromatographic purification afforded the substituted azides **2**.

*General Procedure D for CuAAc of Azides **2** with Alkynes **11**.* The azide (1.0 equiv) **2** and the alkyne (1.1 equiv) **11** were dissolved in H_2O/*t*-BuOH (1:1, 0.15 M) or DMF (0.15 M). Sodium ascorbate (0.4 equiv) and copper(II) sulfate pentahydrate (0.2 equiv) were added. The reaction mixture was stirred overnight at room temperature. The crude mixture was diluted with ethyl acetate (10 mL) and washed with saturated aqueous EDTA-solution (15 mL) and water (2 × 5 mL). The aqueous phase was extracted with ethyl acetate (3 × 10 mL). The combined organic layer was washed with brine (10 mL), dried over Na_2SO_4, filtered, and evaporated under reduced pressure. Column chromatographic purification afforded the corresponding triazoles **12**.

*Synthesis of Geminal Diazide **3**.* The synthesis of geminal diazide **3** was published recently.[10d]

*2,2-Diazido-N^1,N^3-dibenzylmalonamide (**1a**).* According to general procedure A using (100 mg, 0.41 mmol) diethyl 2,2-diazidomalonate (**3**), 2,2-diazido-N^1,N^3-dibenzylmalonamide (**1a**) was obtained as a colorless solid after purification by column chromatography (EA:PE 15:85). Yield: 139 mg, 0.38 mmol, 92%. TLC: R_f = 0.51 (EA:PE 2:8) [Cl_2]. IR (ATR): 3308, 2118, 1689, 1516, 1240, 1062, 693 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.44−7.30 (m, 8 H), 7.30−7.24 (m, 4 H), 4.50 (d, J = 5.8 Hz, 4 H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 163.5, 136.7, 129.0, 128.0, 127.7, 81.8, 44.3 ppm. LRMS (ESI) m/z: 365.1 (100) $[M + H]^+$, 387.1 (12) $[M + Na]^+$. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{17}H_{16}N_8O_2Na_1^+$ 387.1288; Found 387.1272.

*2,2-Diazido-N^1,N^3-bis(4-methoxybenzyl)malonamide (**1b**).* According to general procedure A using (70 mg, 0.29 mmol) diethyl 2,2-diazidomalonate (**3**), 2,2-diazido-N^1,N^3-bis(4-methoxybenzyl)-malonamide (**1b**) was obtained as a colorless solid after purification by column chromatography (EA:PE 1:9 → 1:1). Yield: 115 mg, 0.27 mmol, 94%. TLC: R_f = 0.43 (EA:PE 2:8) [Cl_2]. IR (ATR): 3288, 2112, 1678, 1511, 1225, 1032 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$): δ 7.26 (br. s., 2 H), 7.20−7.12 (m, J = 9.0 Hz, 4 H), 6.90−6.80 (m, 4 H), 4.40 (d, J = 6.0 Hz, 4 H), 3.79 (s, 6 H) ppm. $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 163.4, 159.5, 129.2, 128.8, 114.4, 81.6, 55.4, 43.9 ppm. LRMS (ESI) m/z: 425.2 (100) $[M + H]^+$, 447.2 (9) $[M + Na]^+$. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{19}H_{20}N_8O_4Na_1^+$ 447.1500; Found 447.1500.

*2,2-Diazido-N^1,N^3-bis(4-(trifluoromethyl)benzyl)malonamide (**1c**).* According to general procedure A using (70 mg, 0.29 mmol) diethyl 2,2-diazidomalonate (**3**), 2,2-diazido-N^1,N^3-bis(4-(trifluoro-methyl)benzyl)malonamide (**1c**) was obtained as a colorless solid after purification by column chromatography (EA:PE 1:9 → 25:75). Yield: 108 mg, 0.22 mmol, 75%. TLC: R_f = 0.58 (EA:PE 2:8) [Cl_2]. IR (ATR): 3301, 2132, 1690, 1521, 1323, 1257, 1111, 1065 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.64−7.54 (m, 4 H), 7.51−7.39 (m, 2 H), 7.39−7.30 (m, 4 H), 4.53 (d, J = 6.1 Hz, 4 H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 163.7, 140.7, 130.4 (q, J = 32.9 Hz), 127.9, 126.0 (q, J = 3.7 Hz), 124.1 (q, J = 271.5 Hz), 82.1, 43.8 ppm. LRMS (ESI) m/z: 501.1 (55) $[M + H]^+$, 523.1 (11) $[M + Na]^+$. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{19}H_{14}F_6N_8O_2Na_1^+$ 523.1036; Found 523.1022.

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*2,2-Diazido-N^1,N^3-bis(4-iodobenzyl)malonamide (**1d**).* According to general procedure B using (250 mg, 1.03 mmol) diethyl 2,2-diazidomalonate (**3**), 2,2-diazido-N^1,N^3-bis(4-iodobenzyl)-malonamide (**1d**) was obtained as a colorless solid after purification by column chromatography (EA:PE 3:7). Yield: 468 mg, 0.76 mmol, 74%. TLC: R_f = 0.61 (EA:PE 3:7) [CAM]. IR (ATR): 3301, 2113, 1682, 1670, 1509, 1240, 807 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.71−7.62 (m, 4 H), 7.30 (br. s., 2 H), 7.01−6.95 (m, 4 H), 4.41 (d, J = 6.1 Hz, 4 H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 163.5, 138.2, 136.4, 129.7, 93.6, 81.7, 43.9 ppm. LRMS (ESI) m/z: 617.0 (46) $[M + H]^+$. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{17}H_{14}I_2N_8O_2Na_1^+$ 638.9221; Found 638.9226.

*2,2-Diazido-N^1,N^3-diphenethylmalonamide (**1e**).* According to general procedure A using (70 mg, 0.29 mmol) diethyl 2,2-diazidomalonate (**3**), 2,2-diazido-N^1,N^3-diphenethylmalonamide (**1e**) was obtained as a colorless solid after purification by column chromatography (EA:PE 1:9 → 2:8). Yield: 106 mg, 0.27 mmol, 93%. TLC: R_f = 0.86 (EA:PE 2:8) [Cl_2]. IR (ATR): 3318, 2114, 1673, 1520, 1211, 644 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.39−7.31 (m, 4 H), 7.31−7.24 (m, 2 H), 7.24−7.18 (m, 4 H), 7.02 (br. s., 2 H), 3.66−3.46 (m, 4 H), 2.85 (t, J = 7.1 Hz, 4 H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 163.5, 138.1, 128.8, 128.8, 126.9, 81.3, 41.6, 35.5 ppm. LRMS (ESI) m/z: 393.2 (33) $[M + H]^+$, 415.2 (21) $[M + Na]^+$. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{19}H_{20}N_8O_2Na_1^+$ 415.1601; Found 415.1585.

*2,2-Diazido-N^1,N^3-dioctylmalonamide (**1f**).* According to general procedure A (2.1 eq. amine) using (70 mg, 0.29 mmol) diethyl 2,2-diazidomalonate (**3**), 2,2-diazido-N^1,N^3-dioctylmalonamide (**1f**) was obtained as a colorless solid after purification by column chromatography (EA:PE 5:95 → 2:8). Yield: 107 mg, 0.26 mmol, 91%. TLC: R_f = 0.45 (EA:PE 1:9) [Cl_2]. IR (ATR): 3308, 2918, 2850, 2127, 1685, 1521, 1246 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.00 (br. s., 2 H), 3.38−3.18 (m, 4 H), 1.52 (quin, J = 7.1 Hz, 4 H), 1.37−1.22 (m, 20 H), 0.90−0.84 (m, 6 H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 163.6, 81.5, 40.5, 31.9, 29.3, 29.3, 26.9, 22.7, 14.2 ppm. LRMS (ESI) m/z: 409.3 (100) $[M + H]^+$. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{19}H_{36}N_8O_2Na_1^+$ 431.2853; Found 431.2841.

*2,2-Diazido-N^1,N^3-bis(3,3-diethoxypropyl)malonamide (**1g**).* According to general procedure A using (100 mg, 0.41 mmol) diethyl 2,2-diazidomalonate (**3**), 2,2-diazido-N^1,N^3-bis(3,3-diethoxypropyl)-malonamide (**1g**) was obtained as a yellow oil after purification by column chromatography (EA:PE 15:85 → 4:6). Yield: 172 mg, 0.39 mmol, 94%. TLC: R_f = 0.24 (EA:PE 2:8) [Cl_2]. IR (ATR): 3350, 2976, 2880, 2131, 2111, 1698, 1510, 1054 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.62 (br. s., 2 H), 4.56 (t, J = 5.1 Hz, 2 H), 3.68 (qd, J = 7.2, 9.1 Hz, 4 H), 3.51 (qd, J = 7.1, 9.1 Hz, 4 H), 3.44−3.36 (m, 4 H), 1.91−1.79 (m, 4 H), 1.23 (t, J = 7.1 Hz, 12 H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 163.2, 102.4, 81.6, 62.4, 36.4, 32.7, 15.4 ppm. LRMS (ESI) m/z: 354.2 (14) $[M - 2(C_2H_5O)^-]^+$, 399.2 (63) $[M - (C_2H_5O)^-]^+$. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{17}H_{32}N_8O_6Na_1^+$ 467.2337; Found 467.2337.

*N^1,N^3-Bis(3-(1H-imidazol-1-yl)propyl)-2,2-diazidomalonamide (**1h**).* According to general procedure A using (70 mg, 0.29 mmol) diethyl 2,2-diazidomalonate (**3**), N^1,N^3-bis(3-(1*H*-imidazol-1-yl)-propyl)-2,2-diazidomalonamide (**1h**) was obtained as a yellow oil after purification by column chromatography (DCM:MeOH 9:1 → 8:2). Yield: 112 mg, 0.28 mmol, 97%. TLC: R_f = 0.10 (DCM:MeOH 8:2) [Cl_2]. IR (ATR): 2938, 2113, 1676, 1505, 1228 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.84 (s, 2 H), 7.47 (s, 2 H), 7.01 (s, 2 H), 6.90 (s, 2 H), 3.95 (t, J = 6.8 Hz, 4 H), 3.26 (q, J = 6.6 Hz, 4 H), 2.00 (quin, J = 6.8 Hz, 4 H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 164.0, 137.2, 129.5, 119.0, 81.8, 44.2, 37.4, 30.6 ppm. LRMS (ESI) m/z: 401.2 (100) $[M + H]^+$. HRMS (ESI-TOF) m/z: $[M]^+$ Calcd for $C_{15}H_{21}N_{12}O_2^+$ 401.1905; Found 401.1905.

*N^1,N^3-Bis(2-(1H-indol-3-yl)ethyl)-2,2-diazidomalonamide (**1i**).* According to general procedure B using (300 mg, 1.24 mmol) diethyl 2,2-diazidomalonate (**3**), N^1,N^3-bis(2-(1*H*-indol-3-yl)ethyl)-2,2-diazidomalonamide (**1i**) was obtained as a pale brown solid after purification by column chromatography (EA:PE 1:1). Yield: 532 mg, 1.13 mmol, 91%. TLC: R_f = 0.67 (EA:PE 1:1) [CAM]. IR (ATR): 3367, 2112, 1619, 1509, 1226, 740 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.15 (br. s., 2 H), 7.60 (d, J = 7.8 Hz, 2 H), 7.35 (d, J = 8.1 Hz, 2 H), 7.22 (dt, J = 1.3, 7.6 Hz, 2 H), 7.19−7.12 (m, 2 H), 7.04 (t, J = 5.4 Hz, 2 H), 6.96 (d, J = 2.3 Hz, 2 H), 3.59 (q, J = 6.7 Hz, 4 H), 2.97 (t, J = 6.7 Hz, 4 H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 163.5, 136.5, 127.1, 122.4, 122.3, 119.6, 118.6, 112.0, 111.5, 81.2, 40.6, 25.1 ppm. LRMS (ESI) m/z: 471.2 (100) $[M + H]^+$, 493.2 (14) $[M + Na]^+$. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{23}H_{22}N_{10}O_2Na_1^+$ 493.1819; Found 493.1824.

*2,2-Diazido-N^1,N^3-bis((R)-1-(naphthalen-2-yl)ethyl)malonamide (**1j**).* According to general procedure B using (300 mg, 1.24 mmol) diethyl 2,2-diazidomalonate (**3**), 2,2-diazido-N^1,N^3-bis((*R*)-1-(naphthalen-2-yl)ethyl)malonamide (**1j**) was obtained as a colorless solid after purification by column chromatography (EA:PE 1:9). Yield: 248 mg, 0.50 mmol, 41%. TLC: R_f = 0.27 (EA:PE 1:9) [CAM]. IR (ATR): 3372, 2117, 1688, 1517, 1215, 745 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.77−7.62 (m, 8 H), 7.48−7.41 (m, 4 H), 7.35 (d, J = 7.8 Hz, 2 H), 7.30−7.24 (m, 2 H), 5.23 (quin, J = 7.1 Hz, 2 H), 1.62 (d, J = 6.8 Hz, 6 H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 162.9, 139.2, 133.4, 133.0, 128.9, 128.1, 127.8, 126.6, 126.2, 124.7, 124.1, 81.3, 50.4, 21.9 ppm. LRMS (ESI) m/z: 493.2 (31) $[M + H]^+$, 515.2 (3) $[M + Na]^+$. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{27}H_{24}N_8O_2Na_1^+$ 515.1914; Found 515.1919.

*2,2-Diazido-N^1,N^3-di(prop-2-yn-1-yl)malonamide (**1k**).* According to general procedure A using (70 mg, 0.29 mmol) diethyl 2,2-diazidomalonate (**3**), 2,2-diazido-N^1,N^3-di(prop-2-yn-1-yl)-malonamide (**1k**) was obtained as a colorless solid after purification by column chromatography (EA:PE 15:85 → 3:7). Yield: 59 mg, 0.20 mmol, 69%. TLC: R_f = 0.29 (EA:PE 2:8) [Cl_2]. IR (ATR): 3292, 2151, 2135, 1689, 1505, 1258 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.20 (br. s., 2 H), 4.08 (dd, J = 2.5, 5.3 Hz, 4 H), 2.29 (t, J = 2.5 Hz, 2 H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 163.2, 81.0, 77.8, 73.0, 30.2 ppm. LRMS (ESI) m/z: 283.1 (100) $[M + Na]^+$. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_9H_8N_8O_2Na_1^+$ 283.0662; Found 283.0662.

*2,2-Diazido-N^1,N^3-diisobutylmalonamide (**1l**).* According to general procedure A using (100 mg, 0.41 mmol) diethyl 2,2-diazidomalonate (**3**), 2,2-diazido-N^1,N^3-diisobutylmalonamide (**1l**) was obtained as a colorless solid after purification by column chromatography (EA:PE 15:85 → 2:8). Yield: 112 mg, 0.38 mmol, 92%. TLC: R_f = 0.73 (EA:PE 2:8) [Cl_2]. IR (ATR): 3326, 2960, 2112, 1682, 1522, 1157 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$): δ 7.05 (br. s., 2 H), 3.12 (t, J = 6.6 Hz, 4 H), 1.90−1.76 (m, 2 H), 0.90 (d, J = 6.8 Hz, 12 H) ppm. $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 163.7, 81.8, 47.6, 28.5, 20.0 ppm. LRMS (ESI) m/z: 297.2 (100) $[M + H]^+$, 319.2 (82) $[M + Na]^+$. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{11}H_{20}N_8O_2Na_1^+$ 319.1601; Found 319.1604.

*Di-tert-butyl (((2,2-Diazidomalonyl)bis(azanediyl))bis(pentane-5,1-diyl))dicarbamate (**1m**).* According to general procedure A using (86 mg, 0.36 mmol) diethyl 2,2-diazidomalonate (**3**), di-*tert*-butyl (((2,2-diazidomalonyl)bis(azanediyl))bis(pentane-5,1-diyl))-dicarbamate (**1m**) was obtained as a colorless solid after purification by column chromatography (EA:PE 3:7 → 1:1). Yield: 160 mg, 0.29 mmol, 81%. TLC: R_f = 0.68 (EA:PE 1:1) [Cl_2]. IR (ATR): 3319, 2130, 1682, 1535, 1251, 1172 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$): δ 7.03 (br. s., 2 H), 4.59 (br. s., 2 H), 3.32−3.23 (m, 4 H), 3.15−3.03 (m, 4 H), 1.55 (quin, J = 7.4 Hz, 4 H), 1.49 (quin, J = 7.3 Hz, 4 H), 1.43 (s, 18 H), 1.36−1.29 (m, 4 H) ppm. $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 163.6, 156.2, 81.6, 79.2, 40.4, 40.3, 29.7, 29.0, 28.6, 24.0 ppm. LRMS (ESI) m/z: 577.0 (100) $[M + Na]^+$. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{23}H_{42}N_{10}O_6Na_1^+$ 577.3181; Found 577.3182.

*2,2-Diazido-N^1,N^3-bis(1-hydroxy-2-methylpropan-2-yl)-malonamide (**1n**).* According to general procedure A using (70 mg, 0.29 mmol) diethyl 2,2-diazidomalonate (**3**), 2,2-diazido-N^1,N^3-bis(1-hydroxy-2-methylpropan-2-yl)malonamide (**1n**) was obtained as a colorless oil after purification by column chromatography (EA:PE 85:15 → 9:1). Yield: 37 mg, 0.11 mmol, 39%. TLC: R_f = 0.47 (EA:PE 9:1) [Cl_2]. IR (ATR): 3368, 2114, 1698, 1510, 1217 cm^{-1}. ^1H NMR

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(400 MHz, $CDCl_3$): δ 6.91 (br. s., 2 H), 3.61 (s, 4 H), 3.38 (br. s., 2 H), 1.33 (s, 12 H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 163.7, 81.8, 47.7, 28.5, 20.0 ppm. LRMS (ESI) m/z: 329.2 (100) $[M + H]^+$, 351.2 (7) $[M + Na]^+$. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{11}H_{20}N_8O_4Na_1^+$ 351.1500; Found 351.1499.

*2-Azido-N^1,N^3-dibenzyl-2-methoxymalonamide (**2a**).* According to general procedure C using (150 mg, 0.41 mmol) 2,2-diazido-N^1,N^3-dibenzylmalonamide (**1a**), 2-azido-N^1,N^3-dibenzyl-2-methoxymalonamide (**2a**) was obtained as a colorless solid after purification by column chromatography (EA:PE 3:7). Yield: 120 mg, 0.34 mmol, 83%. TLC: R_f = 0.42 (EA:PE 3:7) [CAM]. IR (ATR): 3324, 2923, 2128, 1685, 1517, 694 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.37−7.26 (m, 10 H), 7.16 (br. s., 2 H), 4.50 (d, J = 5.8 Hz, 4 H), 3.47 (s, 3 H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 164.2, 137.2, 129.0, 127.9, 127.8, 94.3, 53.4, 44.1 ppm. LRMS (ESI) m/z: 354.0 (100) $[M + H]^+$, 377.0 (24) $[M + Na]^+$. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{18}H_{19}N_5O_3Na_1^+$ 376.1380; Found 376.1382.

*2-Amino-N^1,N^3-dibenzylmalonamide (**5**).* Azide **2a** (67 mg, 0.19 mmol, 1.0 equiv) was dissolved in 1.26 mL of DCM (0.15 m). Palladium on activated charcoal (30 mg, 0.03 mmol, 15 mol %) was added, and the reaction mixture was stirred for 1 h at room temperature in an autoclave with a hydrogen pressure of 100 psi. Filtration over Celite with ethyl acetate as eluent and concentration under reduced pressure furnished the primary amine **5** as a colorless solid in 90% (51 mg, 0.17 mmol) yield. TLC: R_f = 0.17 (EA:PE 1:1) [Ninhydrin]. ^1H NMR (400 MHz, $CDCl_3$): δ 8.21 (br. s., 2 H), 7.39−7.20 (m, 10 H), 4.55−4.37 (m, 4 H), 4.11 (s, 1 H), 2.20 (br. s., 2 H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 169.6, 137.9, 128.8, 127.7, 127.6, 57.0, 43.8 ppm. The analytical data are in agreement with previously reported ones.[13]

*N^1,N^3-Dibenzyl-2-iminomalonamide (**6**).* Azide **2a** (100 mg, 0.28 mmol, 1.0 equiv) was dissolved in 1.77 mL of THF (0.16 m). Triphenylphosphine (148 mg, 0.57 mmol, 2.0 equiv) and water (25 μL, 25 mg, 1.41 mmol, 5.0 equiv) were added, and the reaction mixture was stirred for 48 h at room temperature. Concentration under reduced pressure and column chromatography (EA:PE 3:7) furnished the imine **6** as a pale yellow solid in 63% (53 mg, 0.18 mmol) yield. TLC: R_f = 0.80 (EA:PE 1:1) [Ninhydrin]. ^1H NMR (600 MHz, $CDCl_3$): δ 12.18 (s, 1 H), 9.91 (br. s., 1 H), 8.11 (br. s., 1 H), 7.38−7.28 (m, 10 H), 4.57 (d, J = 6.0 Hz, 2 H), 4.51 (d, J = 6.0 Hz, 2 H) ppm. $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 163.6, 158.9, 158.0, 137.2, 136.9, 129.0, 129.0, 128.1, 128.0, 127.9, 127.9, 44.3, 43.7 ppm. The analytical data are in agreement with previously reported ones.[13]

*2-Azido-N^1,N^3-dibenzyl-2-(phenylthio)malonamide (**7**).* Thiophenol (42 μL, 45 mg, 0.41 mmol, 1.00 equiv) and triethylamine (57 μL, 42 mg, 0.41 mmol, 1.00 equiv) were dissolved in dry tetrahydrofuran (6 mL). 2,2-Diazido-N^1,N^3-dibenzylmalonamide (**1a**) (150 mg, 0.41 mmol, 1.00 equiv) was added, and the mixture was stirred for 24 h at ambient temperature. The reaction was terminated with 1 M NaOH, the aqueous phase was extracted with ethyl acetate, and the combined organic phase was washed with brine, dried over Na_2SO_4, and concentrated *in vacuo*. After purification by flash chromatography (PE:EA 70:30), 83% (149 mg, 0.35 mmol) of a yellow oil was obtained. TLC: R_f = 0.68 (EA:PE 3:7) [UV, $KMnO_4$]. IR (ATR): 3394, 2124, 1691, 1507, 1246, 691 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.67−7.53 (m, 4 H), 7.49−7.40 (m, 1 H), 7.38−7.25 (m, 8 H), 7.17−7.08 (m, 4 H), 4.43−4.24 (m, 4 H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 165.2, 137.0, 136.9, 130.6, 129.4, 128.8, 128.5, 127.8, 127.8, 77.4, 44.4 ppm. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{23}H_{21}N_5O_2S_1Na_1^+$ 454.1310; Found 454.1308.

*1,2-Diphenyldisulfane (**8**).* Thiophenol (23 μL, 25 mg, 0.23 mmol, 1.10 equiv) was dissolved in dry tetrahydrofuran (1.5 mL). A 2.5 M solution of *n*-buthyllithium in hexane (91 μL, 63 mg, 0.23 mmol, 1.10 equiv) was added, and the resulting mixture was stirred for 5 min at ambient temperature. 2,2-Diazido-*N*,*N*′-dibenzylmalonamide (**1a**) (75 mg, 0.21 mmol, 1.00 equiv) was added, and the reaction mixture was stirred for 12 h at ambient temperature. The reaction was terminated with 1 M NaOH, the aqueous phase was extracted with ethyl acetate, and the combined organic phase was washed with brine, dried over Na_2SO_4, and concentrated *in vacuo*. After purification by flash chromatography, (PE:EA 70:30), 23 mg (0.11 mmol, 91%) of a colorless solid was obtained. TLC: R_f = 0.88 (EA:PE 3:7) [UV, $KMnO_4$]. ^1H NMR (600 MHz, $CDCl_3$): δ 7.53−7.48 (m, 4 H), 7.33−7.28 (m, 4 H), 7.25−7.21 (m, 2 H) ppm. $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 137.2, 129.2, 127.7, 127.3 ppm. The analytical data are in agreement with previously reported ones.[20]

*2-Azido-N^1,N^3-bis(4-iodobenzyl)-2-methoxymalonamide (**2d**).* According to general procedure C using (300 mg, 0.49 mmol) 2,2-diazido-N^1,N^3-bis(4-iodobenzyl)malonamide (**1d**), 2-azido-N^1,N^3-bis-(4-iodobenzyl)-2-methoxymalonamide (**2d**) was obtained as a colorless solid after purification by column chromatography (EA:PE 4:6 → 6:4). Yield: 241 mg, 0.40 mmol, 82%. TLC: R_f = 0.45 (EA:PE 4:6) [CAM]. IR (ATR): 3319, 2128, 1687, 1512, 1270, 1005 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$): δ 7.69−7.60 (m, 4 H), 7.15 (t, J = 5.1 Hz, 2 H), 7.03−6.97 (m, 4 H), 4.42 (d, J = 6.0 Hz, 4 H), 3.45 (s, 3 H) ppm. $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 164.3, 138.1, 136.9, 129.6, 94.3, 93.4, 53.5, 43.5 ppm. LRMS (ESI) m/z: 606.0 (100) $[M + H]^+$. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{18}H_{17}I_2N_5O_3Na_1^+$ 627.9313; Found 627.9314.

*2-Azido-2-methoxy-N^1,N^3-dioctylmalonamide (**2f**).* According to general procedure C using (150 mg, 0.37 mmol) 2,2-diazido-N^1,N^3-dioctylmalonamide (**1f**), 2-azido-2-methoxy-N^1,N^3-dioctylmalonamide (**2f**) was obtained as a colorless solid after purification by column chromatography (EA:PE 2:8). Yield: 128 mg, 0.32 mmol, 87%. TLC: R_f = 0.29 (EA:PE 2:8) [CAM]. IR (ATR): 3324, 2954, 2126, 1681, 1518, 1158 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 6.79 (br. s., 2 H), 3.44 (s, 3 H), 3.33−3.17 (m, 4 H), 1.51 (quin, J = 7.1 Hz, 4 H), 1.32−1.23 (m, 20 H), 0.92−0.78 (m, 6 H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 164.2, 94.3, 53.3, 40.1, 31.9, 29.4, 29.3, 26.9, 22.7, 14.2 ppm. LRMS (ESI) m/z: 398.3 (69) $[M + H]^+$. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{20}H_{39}N_5O_3Na_1^+$ 420.2945; Found 420.2946.

*2-Azido-N^1,N^3-bis(3,3-diethoxypropyl)-2-methoxymalonamide (**2g**).* According to general procedure C using (150 mg, 0.34 mmol) 2,2-diazido-N^1,N^3-bis(3,3-diethoxypropyl)malonamide (**1g**), 2-azido-N^1,N^3-bis(3,3-diethoxypropyl)-2-methoxymalonamide (**2g**) was obtained as a colorless solid after purification by column chromatography (EA:PE 8:2). Yield: 140 mg, 0.32 mmol, 95%. TLC: R_f = 0.54 (EA:PE 8:2) [CAM]. IR (ATR): 3330, 2972, 2129, 1701, 1519, 1058 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.41 (br. s., 2 H), 4.55 (t, J = 5.2 Hz, 2 H), 3.73−3.61 (m, 4 H), 3.57−3.45 (m, 4 H), 3.42 (s, 3 H), 3.41−3.35 (m, 4 H), 1.88−1.79 (m, 4 H), 1.26−1.18 (m, 12 H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 164.0, 102.4, 94.1, 62.2, 62.2, 53.2, 36.1, 32.8, 15.4 ppm. LRMS (ESI) m/z: 388.2 (33) $[M - (EtO)^-]^+$. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{18}H_{35}N_5O_7Na_1^+$ 456.2458; Found 456.2430.

*N^1,N^3-Bis(2-(1H-indol-3-yl)ethyl)-2-azido-2-methoxymalonamide (**2i**).* According to general procedure C using (100 mg, 0.21 mmol) N^1,N^3-bis(2-(1*H*-indol-3-yl)ethyl)-2,2-diazidomalonamide (**1i**), N^1,N^3-bis(2-(1*H*-indol-3-yl)ethyl)-2-azido-2-methoxymalonamide (**2i**) was obtained as a colorless solid after purification by column chromatography (EA:PE 6:4). Yield: 80 mg, 0.17 mmol, 82%. TLC: R_f = 0.61 (EA:PE 6:4) [CAM]. IR (ATR): 3325, 2122, 1671, 1512, 1228, 740 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$): δ 8.11 (br. s., 2 H), 7.61 (d, J = 7.9 Hz, 2 H), 7.35 (d, J = 7.9 Hz, 2 H), 7.21 (dt, J = 1.1, 7.5 Hz, 2 H), 7.16−7.11 (m, 2 H), 7.02 (d, J = 2.3 Hz, 2 H), 6.90 (t, J = 5.8 Hz, 2 H), 3.69−3.55 (m, 4 H), 3.31 (s, 3 H), 2.98 (dt, J = 1.9, 6.8 Hz, 4 H) ppm. $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 164.3, 136.5, 127.3, 122.5, 122.4, 119.6, 118.8, 112.6, 111.4, 94.0, 53.2, 40.3, 25.3 ppm. LRMS (ESI) m/z: 460.2 (100) $[M + H]^+$, 482.2 (12) $[M + Na]^+$. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{24}H_{25}N_7O_3Na_1^+$ 482.1911; Found 482.1909.

*2-Azido-2-methoxy-N^1,N^3-bis((R)-1-(naphthalen-2-yl)ethyl)-malonamide (**2j**).* According to general procedure C using (150 mg, 0.31 mmol) 2,2-diazido-N^1,N^3-bis((*R*)-1-(naphthalen-2-yl)ethyl)-malonamide (**1j**), 2-azido-2-methoxy-N^1,N^3-bis((*R*)-1-(naphthalen-2-yl)ethyl)malonamide (**2j**) was obtained as a colorless solid after purification by column chromatography (EA:PE 3:7 → 1:1). Yield: 102 mg, 0.21 mmol, 70%. TLC: R_f = 0.40 (EA:PE 3:7) [CAM]. IR

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(ATR): 3379, 2128, 1683, 1504, 745 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$) δ [ppm] 7.77−7.70 (m, 6 H), 7.68 (t, J = 9.0 Hz, 2 H), 7.48−7.39 (m, 4 H), 7.36−7.31 (m, 2 H), 7.14 (dd, J = 7.9, 17.7 Hz, 2 H), 5.25 (quin, J = 7.2 Hz, 2 H), 3.45 (s, 3 H), 1.62 (d, J = 7.2 Hz, 3 H), 1.61 (d, J = 7.2 Hz, 3 H) ppm. $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 163.6, 163.5, 139.8, 139.6, 133.4, 132.9, 132.9, 128.7, 128.7, 128.1, 128.1, 127.7, 126.3, 126.3, 126.1, 124.7, 124.6, 124.5, 124.4, 94.1, 53.4, 49.8, 49.8, 21.8, 21.7 ppm. LRMS (ESI) m/z: 482.2 (84) $[M + H]^+$, 504.2 (2) $[M + Na]^+$. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{28}H_{27}N_5O_3Na_1^+$ 504.2006; Found 504.2009.

*2-Azido-N^1,N^3-dibenzyl-2-(decyloxy)malonamide (**2aa**).* According to general procedure C using (150 mg, 0.41 mmol) 2,2-diazido-N^1,N^3-dibenzylmalonamide (**1a**), 2-azido-N^1,N^3-dibenzyl-2-(decyloxy)malonamide (**2aa**) was obtained as a colorless solid after purification by column chromatography (EA:DCM 2:8). Yield: 175 mg, 0.37 mmol, 89%. TLC: R_f = 0.85 (EA:PE 2:8) [CAM]. IR (ATR): 3341, 3032, 2123, 1684, 1514, 1161, 697 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.39−7.24 (m, 10H), 7.15 (t, J = 5.6 Hz, 2H), 4.50 (d, J = 6.0 Hz, 4H), 3.63 (t, J = 6.7 Hz, 2H), 1.71−1.59 (m, 2H), 1.35−1.24 (m, 14H), 0.88 (t, J = 6.9 Hz, 3H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 164.6, 137.3, 129.0, 127.8, 127.7, 94.0, 66.6, 44.0, 32.0, 29.6, 29.6, 29.4, 29.4, 26.1, 22.8, 14.2 ppm. LRMS (ESI) m/z: 480.3 (65) $[M + H]^+$. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{27}H_{37}N_5O_3Na_1^+$ 502.2789; Found 502.2777.

*2-(Allyloxy)-2-azido-N^1,N^3-dibenzylmalonamide (**2ab**).* According to general procedure C using (150 mg, 0.41 mmol) 2,2-diazido-N^1,N^3-dibenzylmalonamide (**1a**), 2-(allyloxy)-2-azido-N^1,N^3-dibenzylmalonamide (**2ab**) was obtained as a colorless solid after purification by column chromatography (EA:PE 2:8). Yield: 96 mg, 0.25 mmol, 61%. TLC: R_f = 0.54 (EA:PE 3:7) [CAM]. IR (ATR): 3333, 2924, 2127, 1685, 1512, 1154, 695 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$): δ 7.38−7.32 (m, 4 H), 7.31−7.26 (m, 6 H), 7.16 (br. s., 2 H), 5.99−5.91 (m, 1 H), 5.33−5.29 (m, 1 H), 5.25−5.22 (m, 1 H), 4.50 (d, J = 6.0 Hz, 4 H), 4.18 (td, J = 1.3, 6.0 Hz, 2 H) ppm. $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 164.4, 137.2, 129.0, 128.9, 127.9, 127.8, 118.8, 94.0, 67.6, 44.1 ppm. LRMS (ESI) m/z: 380.1 (84) $[M + H]^+$, 402.1 (8) $[M + Na]^+$. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{20}H_{21}N_5O_3Na_1^+$ 402.1537; Found 402.1534.

*2-Azido-N^1,N^3-dibenzyl-2-(cyclopropylmethoxy)malonamide (**2ac**).* According to general procedure C using (150 mg, 0.41 mmol) 2,2-diazido-N^1,N^3-dibenzylmalonamide (**1a**), 2-azido-N^1,N^3-dibenzyl-2-(cyclopropylmethoxy)malonamide (**2ac**) was obtained as a colorless solid after purification by column chromatography (EA:PE 3:7). Yield: 140 mg, 0.36 mmol, 87%. TLC: R_f = 0.50 (EA:PE 3:7) [CAM]. IR (ATR): 3347, 2129, 1682, 1513, 1160, 700 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$): δ 7.37−7.25 (m, 10 H), 7.18 (br. s., 2 H), 4.50 (d, J = 6.0 Hz, 4 H), 3.48 (d, J = 7.2 Hz, 2 H), 1.18−1.07 (m, 1 H), 0.63−0.52 (m, 2 H), 0.32−0.21 (m, 2 H) ppm. $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 164.6, 137.3, 129.0, 127.8, 127.7, 93.8, 71.6, 44.0, 10.6, 3.5 ppm. LRMS (ESI) m/z: 394.1 (100) $[M + H]^+$. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{21}H_{23}N_5O_3Na_1^+$ 416.1704; Found 416.1705.

*2-Azido-N^1,N^3-dibenzyl-2-((6-hydroxyhexyl)oxy)malonamide (**2ad**).* According to general procedure C using (80 mg, 0.22 mmol) 2,2-diazido-N^1,N^3-dibenzylmalonamide (**1a**), 2-azido-N^1,N^3-dibenzyl-2-((6-hydroxyhexyl)oxy)malonamide (**2ad**) was obtained as a colorless solid after purification by column chromatography (EA:PE 4:6 → 9:1). Yield: 52 mg, 0.12 mmol, 53%. TLC: R_f = 0.50 (EA:PE 8:2) [CAM]. IR (ATR): 3323, 3033, 2126, 1683, 1514, 1158, 698 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.39−7.34 (m, 4 H), 7.34−7.27 (m, 6 H), 7.21 (t, J = 5.6 Hz, 2 H), 4.52 (d, J = 6.0 Hz, 4 H), 3.67 (t, J = 6.4 Hz, 2 H), 3.63 (t, J = 6.4 Hz, 2 H), 1.73−1.67 (m, 2 H), 1.63−1.52 (m, 3 H), 1.45−1.38 (m, 4 H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 164.5, 137.3, 129.0, 127.9, 127.7, 94.0, 66.3, 62.8, 44.0, 32.6, 29.4, 25.7, 25.4 ppm. LRMS (ESI) m/z: 440.2 (100) $[M + H]^+$. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{23}H_{29}N_5O_4Na_1^+$ 462.2112; Found 462.2111.

*2-Azido-N^1,N^3-dibenzyl-2-(((3aR,4R,6R,6aR)-6-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-2,2-dimethyltetrahydrofuro[3,4-d][1,3]-dioxol-4-yl)methoxy)malonamide (**2ae**).* According to general procedure C using (150 mg, 0.41 mmol) 2,2-diazido-N^1,N^3-dibenzylmalonamide (**1a**), 2-Azido-N^1,N^3-dibenzyl-2-(((3a*R*,4*R*,6*R*,-6a*R*)-6-(2,4-dioxo-3,4-dihydropyrimidin-1(2*H*)-yl)-2,2-dimethyltetrahydrofuro[3,4-*d*][1,3]dioxol-4-yl)methoxy)malonamide (**2ae**) was obtained as a yellow oil after purification by column chromatography (EA:DCM 8:2). Yield: 91 mg, 0.15 mmol, 36%. TLC: R_f = 0.63 (EA:PE 8:2) [Cl_2]. IR (ATR): 3337, 2126, 1674, 1514, 1155, 1068, 697 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.61 (s, 1 H), 7.52 (t, J = 5.8 Hz, 1 H), 7.40 (t, J = 5.8 Hz, 1 H), 7.36−7.30 (m, 6 H), 7.27 (d, J = 2.0 Hz, 4 H), 7.13 (d, J = 8.1 Hz, 1 H), 5.58 (dd, J = 2.0, 8.1 Hz, 1 H), 5.38 (d, J = 2.0 Hz, 1 H), 5.08 (dd, J = 5.1, 6.3 Hz, 1 H), 4.98 (dd, J = 2.0, 6.6 Hz, 1 H), 4.59 (dd, J = 6.3, 14.9 Hz, 2 H), 4.45−4.35 (m, 2 H), 4.21−4.16 (m, 1 H), 3.96−3.86 (m, 2 H), 1.53 (s, 3 H), 1.33 (s, 3 H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 164.3, 162.8, 149.8, 143.1, 137.5, 137.4, 128.9, 128.0, 127.9, 127.9, 127.8, 114.8, 102.7, 95.8, 93.1, 85.1, 83.9, 79.9, 64.9, 44.0, 27.4, 25.5 ppm. LRMS (ESI) m/z: 606.2 (100) $[M + H]^+$. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{29}H_{31}N_7O_8Na_1^+$ 628.2126; Found 628.2130.

*2-(2-(1H-Indol-3-yl)ethoxy)-2-azido-N^1,N^3-dibenzylmalonamide (**2af**).* According to general procedure C using (150 mg, 0.41 mmol) 2,2-diazido-N^1,N^3-dibenzylmalonamide (**1a**), 2-(2-(1*H*-indol-3-yl)-ethoxy)-2-azido-N^1,N^3-dibenzylmalonamide (**2af**) was obtained as an orange oil after purification by column chromatography (EA:PE 1:1). Yield: 113 mg, 0.23 mmol, 57%. TLC: R_f = 0.64 (EA:PE 1:1) [CAM]. IR (ATR): 3357, 2123, 1678, 1511, 1230, 731, 697 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.99 (br. s., 1 H), 7.62−7.55 (m, 1 H), 7.35−7.28 (m, 7 H), 7.23−7.14 (m, 5 H), 7.09−6.98 (m, 4 H), 4.48−4.33 (m, 4 H), 3.94 (t, J = 6.8 Hz, 2 H), 3.13 (t, J = 6.7 Hz, 2 H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 164.6, 137.3, 136.3, 128.9, 127.8, 127.7, 127.6, 122.29, 122.26, 119.7, 118.6, 112.2, 111.4, 93.5, 66.7, 43.9, 25.6 ppm. LRMS (ESI) m/z: 483.2 (100) $[M + H]^+$. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{27}H_{26}N_6O_3Na_1^+$ 505.1959; Found 505.1949.

*2-Azido-N^1,N^3-dibenzyl-2-(((3S,8S,9S,10R,13R,14S,17R)-10,13-dimethyl-17-((R)-6-methylheptan-2-yl)-2,3,4,7,8,9,10,11,12,13,14,15,-16,17-tetradecahydro-1H-cyclopenta[a]phenanthren-3-yl)oxy)-malonamide (**2ag**).* According to general procedure C using (150 mg, 0.41 mmol) 2,2-diazido-N^1,N^3-dibenzylmalonamide (**1a**), 2-azido-N^1,N^3-dibenzyl-2-(((3*S*,8*S*,9*S*,10*R*,13*R*,14*S*,17*R*)-10,13-dimethyl-17-((*R*)-6-methylheptan-2-yl)-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1*H*-cyclopenta[*a*]phenanthren-3-yl)oxy)malonamide (**2ag**) was obtained as a colorless solid after purification by column chromatography (EA:DCM 3:7). Yield: 164 mg, 0.23 mmol, 56%. TLC: R_f = 0.28 (EA:PE 2:8) [CAM]. IR (ATR): 3329, 3030, 2125, 1694, 1536, 1161, 698 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.41−7.23 (m, 10 H), 7.23−7.15 (m, 2 H), 5.41−5.30 (m, 1 H), 4.59−4.43 (m, 4 H), 3.62−3.49 (m, 1 H), 2.45−2.34 (m, 2 H), 2.07−1.90 (m, 3 H), 1.89−1.78 (m, 2 H), 1.61−1.02 (m, 21 H), 1.00 (s, 3 H), 0.92 (d, J = 6.6 Hz, 3 H), 0.88 (d, J = 1.8 Hz, 3 H), 0.86 (d, J = 1.8 Hz, 3 H), 0.68 (s, 3 H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 164.9, 164.9, 140.1, 137.4, 137.4, 128.9, 127.8, 127.8, 127.7, 122.7, 94.2, 78.4, 56.9, 56.3, 50.3, 44.0, 42.5, 40.1, 39.9, 39.7, 37.3, 36.6, 36.3, 35.9, 32.1, 32.1, 32.0, 29.7, 28.4, 28.2, 24.4, 24.0, 23.0, 22.7, 21.2, 19.4, 18.9, 12.0 ppm. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{44}H_{61}N_5O_3Na_1^+$ 730.4667; Found 730.4666.

*2-Azido-N^1,N^3-dibenzyl-2-isopropoxymalonamide (**2ah**).* According to general procedure C using (150 mg, 0.41 mmol) 2,2-diazido-N^1,N^3-dibenzylmalonamide (**1a**), 2-azido-N^1,N^3-dibenzyl-2-isopropoxymalonamide (**2ah**) was obtained as a colorless solid after purification by column chromatography (EA:PE 3:7). Yield: 129 mg, 0.34 mmol, 82%. TLC: R_f = 0.53 (EA:PE 2:8) [CAM]. IR (ATR): 3379, 2119, 1689, 1526, 1505, 1267, 1138, 702 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.38−7.26 (m, 10 H), 7.17 (br. s., 2 H), 4.50 (d, J = 5.8 Hz, 4 H), 4.00 (spt, J = 6.1 Hz, 1 H), 1.29 (d, J = 6.1 Hz, 6 H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 164.9, 137.4, 129.0, 127.8, 127.7, 94.5, 71.8, 44.0, 23.8 ppm. LRMS (ESI) m/z: 382.2 (47) $[M + H]^+$, 404.1 (5) $[M + Na]^+$. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{20}H_{23}N_5O_3Na_1^+$ 404.1693; Found 404.1687.

*2-Azido-N^1,N^3-dibenzyl-2-(cyclohexyloxy)malonamide (**2ai**).* According to general procedure C using (100 mg, 0.27 mmol) 2,2-

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diazido-N^1,N^3-dibenzylmalonamide (**1a**), 2-azido-N^1,N^3-dibenzyl-2-(cyclohexyloxy)malonamide (**2ai**) was obtained as a colorless solid after purification by column chromatography (EA:DCM 1:9). Yield: 78 mg, 0.19 mmol, 67%. TLC: R_f = 0.57 (EA:PE 2:8) [CAM]. IR (ATR): 3340, 2943, 2126, 1682, 1511, 1144, 696 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$): δ 7.38−7.32 (m, 4 H), 7.31−7.26 (m, 6 H), 7.20 (t, J = 5.1 Hz, 2 H), 4.59−4.43 (m, 4 H), 3.73−3.58 (m, 1 H), 2.03−1.91 (m, 2 H), 1.80−1.68 (m, 2 H), 1.57−1.49 (m, 1 H), 1.49−1.39 (m, 2 H), 1.31−1.12 (m, 3 H) ppm. $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 165.0, 137.4, 128.9, 127.8, 127.7, 94.3, 77.3, 44.0, 33.7, 25.4, 24.4 ppm. LRMS (ESI) m/z: 422.3 (75) $[M + H]^+$, 444.2 (20) $[M + Na]^+$. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{23}H_{27}N_5O_3Na_1^+$ 444.2006; Found 444.2007.

*2-Azido-N^1,N^3-dibenzyl-2-(tert-butoxy)malonamide (**2aj**).* According to general procedure C using (100 mg, 0.27 mmol) 2,2-diazido-N^1,N^3-dibenzylmalonamide (**1a**), 2-azido-N^1,N^3-dibenzyl-2-(*tert*-butoxy)malonamide (**2aj**) was obtained as a colorless solid after purification by column chromatography (EA:PE 2:8). Yield: 59 mg, 0.15 mmol, 54%. TLC: R_f = 0.65 (EA:PE 2:8) [CAM]. IR (ATR): 3358, 2120, 1681, 1531, 1497, 1135, 693 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.37−7.26 (m, 10 H), 7.14 (br. s., 2 H), 4.48 (d, J = 6.1 Hz, 4 H), 1.38 (s, 9 H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 166.1, 137.4, 128.9, 127.7, 92.7, 80.5, 44.1, 29.6 ppm. LRMS (ESI) m/z: 396.2 (15) $[M + H]^+$, 418.2 (13) $[M + Na]^+$. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{21}H_{25}N_5O_3Na_1^+$ 418.1850; Found 418.1836.

*2-Methoxy-N^1,N^3-dioctyl-2-(4-phenyl-1H-1,2,3-triazol-1-yl)-malonamide (**12a**).* According to general procedure D (H_2O/*t*-BuOH) using (100 mg, 0.25 mmol) 2-azido-2-methoxy-N^1,N^3-dioctylmalonamide (**2f**), 2-methoxy-N^1,N^3-dioctyl-2-(4-phenyl-1*H*-1,2,3-triazol-1-yl)malonamide (**12a**) was obtained as a colorless solid after purification by column chromatography (EA:PE 2:8). Yield: 94 mg, 0.19 mmol, 75%. TLC: R_f = 0.74 (EA:PE 3:7) [CAM]. IR (ATR): 3313, 2924, 2854, 1698, 1538, 1518, 693 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$): δ 7.96 (s, 1 H), 7.86−7.83 (m, 2 H), 7.46−7.41 (m, 2 H), 7.37−7.31 (m, 3 H), 3.41 (s, 3 H), 3.39−3.34 (m, 4 H), 1.58 (quin, J = 7.2 Hz, 4 H), 1.36−1.25 (m, 20 H), 0.87 (t, J = 7.2 Hz, 6 H) ppm. $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 163.8, 147.7, 130.0, 129.0, 128.7, 126.0, 121.0, 90.5, 54.6, 40.5, 31.9, 29.3, 29.3, 27.0, 22.8, 14.2 ppm. LRMS (ESI) m/z: 500.3 (100) $[M + H]^+$. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{28}H_{45}N_5O_3Na_1^+$ 522.3415; Found 522.3416.

*N^1,N^3-Dibenzyl-2-((6-hydroxyhexyl)oxy)-2-(4-phenyl-1H-1,2,3-triazol-1-yl)malonamide (**12b**).* According to general procedure D (DMF) using (180 mg, 0.41 mmol) 2-azido-N^1,N^3-dibenzyl-2-((6-hydroxyhexyl)oxy)malonamide (**2ad**), N^1,N^3-dibenzyl-2-((6-hydroxyhexyl)oxy)-2-(4-phenyl-1*H*-1,2,3-triazol-1-yl)malonamide (**12b**) was obtained as a pale yellow resin after purification by column chromatography (EA:PE 1:1 → 6:4). Yield: 157 mg, 0.29 mmol, 71%. TLC: R_f = 0.23 (EA:PE 1:1) [CAM]. IR (ATR): 3229, 2932, 2858, 1699, 1512, 1156, 693 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.94 (s, 1 H), 7.86−7.78 (m, 2 H), 7.75 (t, J = 5.8 Hz, 2 H), 7.48−7.39 (m, 2 H), 7.39−7.28 (m, 11 H), 4.65−4.52 (m, 4 H), 3.59 (t, J = 6.6 Hz, 2 H), 3.52 (t, J = 6.4 Hz, 2 H), 1.58−1.50 (m, 3 H), 1.50−1.41 (m, 2 H), 1.33−1.21 (m, 4 H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 164.1, 147.7, 137.1, 129.8, 129.0, 129.0, 128.7, 127.9, 127.8, 126.0, 121.0, 90.5, 67.4, 62.6, 44.3, 32.5, 29.3, 25.4, 25.2 ppm. LRMS (ESI) m/z: 542.2 (100) $[M + H]^+$. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{31}H_{35}N_5O_4Na_1^+$ 564.2581; Found 564.2582.

*2-(Allyloxy)-N^1,N^3-dibenzyl-2-(4-phenyl-1H-1,2,3-triazol-1-yl)-malonamide (**12c**).* According to general procedure D (DMF) using (80 mg, 0.21 mmol) 2-(allyloxy)-2-azido-N^1,N^3-dibenzylmalonamide (**2ab**), N^1,N^3-dibenzyl-2-(cyclopropylmethoxy)-2-(4-phenyl-1*H*-1,2,3-triazol-1-yl)malonamide (**12c**) was obtained as a colorless solid after purification by column chromatography (EA:DCM 4:6). Yield: 92 mg, 0.19 mmol, 91%. TLC: R_f = 0.69 (EA:PE 4:6) [CAM]. IR (ATR): 3276, 1683, 1520, 1082, 690 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.91 (s, 1H), 7.83−7.78 (m, 2H), 7.72 (t, J = 5.9 Hz, 2H), 7.48−7.40 (m, 2H), 7.39−7.29 (m, 11H), 5.77 (ddt, J = 17.1, 10.3, 6.0 Hz, 1H), 5.18−5.07 (m, 2H), 4.65−4.52 (m, 4H), 4.19 (dt, J = 6.0, 1.3 Hz, 2H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 163.9, 147.8, 137.0, 132.7, 129.9, 129.0, 128.8, 128.0, 127.8, 126.0, 120.9, 118.8, 90.2, 68.9, 44.3 ppm. LRMS (ESI) m/z: 482.2 (100) $[M + H]^+$. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{28}H_{27}N_5O_3Na_1^+$ 504.2006; Found 504.2005.

*N^1,N^3-Dibenzyl-2-(((3S,8S,9S,10R,13R,14S,17R)-10,13-dimethyl-17-((R)-6-methylheptan-2-yl)-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1H-cyclopenta[a]phenanthren-3-yl)oxy)-2-(4-(thiophen-3-yl)-1H-1,2,3-triazol-1-yl)malonamide (**12d**).* According to general procedure D (H_2O/*t*-BuOH) using (30 mg, 0.04 mmol) 2-azido-N^1,N^3-dibenzyl-2-(((3*S*,8*S*,9*S*,10*R*,13*R*,14*S*,17*R*)-10,13-dimethyl-17-((*R*)-6-methylheptan-2-yl)-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1*H*-cyclopenta[*a*]phenanthren-3-yl)oxy)malonamide (**2ag**), N^1,N^3-dibenzyl-2-(((3*S*,8*S*,9*S*,10*R*,13*R*,14*S*,17*R*)-10,13-dimethyl-17-((*R*)-6-methylheptan-2-yl)-2,3,4,7,8,9,10,11,12,13,14,15,-16,17-tetradecahydro-1*H*-cyclopenta[*a*]phenanthren-3-yl)oxy)-2-(4-(thiophen-3-yl)-1*H*-1,2,3-triazol-1-yl)malonamide (**12d**) was obtained as a yellow solid after purification by column chromatography (EA:DCM 2:8). Yield: 28 mg, 0.03 mmol, 81%. TLC: R_f = 0.71 (EA:PE 2:8) [CAM]. IR (ATR): 3326, 2932, 1703, 1511, 1150, 1078, 1027, 779, 729, 696 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$): δ 7.80 (s, 1 H), 7.75−7.64 (m, 3 H), 7.46−7.27 (m, 12 H), 5.15 (d, J = 4.9 Hz, 1 H), 4.64−4.53 (m, 4 H), 4.01−3.87 (m, 1 H), 2.24−2.12 (m, 1 H), 2.01−1.93 (m, 1 H), 1.92−1.78 (m, 3 H), 1.70−1.62 (m, 1 H), 1.56−1.50 (m, 2 H), 1.46−1.28 (m, 10 H), 1.17−0.95 (m, 10 H), 0.91−0.88 (m, 6 H), 0.87 (d, J = 3.0 Hz, 3 H), 0.86 (d, J = 2.6 Hz, 3 H), 0.63 (s, 3 H) ppm. $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 164.5, 164.3, 143.9, 139.8, 137.2, 131.1, 129.0, 127.9, 127.9, 127.8, 126.6, 126.0, 122.8, 122.0, 121.0, 90.4, 79.0, 56.8, 56.3, 50.1, 44.3, 42.4, 39.9, 39.7, 39.7, 37.3, 36.5, 36.3, 35.9, 32.0, 32.0, 29.3, 28.4, 28.2, 24.4, 24.0, 23.0, 22.7, 21.1, 19.4, 18.9, 12.0 ppm. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{50}H_{65}N_5O_3S_1Na_1^+$ 838.4700; Found 838.4684.

*Methyl 1-(1,3-Bis(benzylamino)-2-isopropoxy-1,3-dioxopropan-2-yl)-1H-1,2,3-triazole-4-carboxylate (**12e**).* According to general procedure D (DMF) using (80 mg, 0.21 mmol) 2-azido-N^1,N^3-dibenzyl-2-isopropoxymalonamide (**2ah**), methyl 1-(1,3-bis(benzylamino)-2-isopropoxy-1,3-dioxopropan-2-yl)-1*H*-1,2,3-triazole-4-carboxylate (**12e**) was obtained as a colorless solid after purification by column chromatography (EA:PE 1:1). Yield: 79 mg, 0.17 mmol, 81%. TLC: R_f = 0.67 (EA:PE 1:1) [CAM]. IR (ATR): 3317, 1682, 1535, 1240 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$): δ 8.32 (s, 1 H), 7.47 (t, J = 5.8 Hz, 2 H), 7.39−7.26 (m, 10 H), 4.68−4.47 (m, 3 H), 4.45−4.30 (m, 1 H), 3.96 (s, 3 H), 0.93 (d, J = 6.1 Hz, 6 H) ppm. $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 163.9, 160.7, 139.9, 136.9, 129.7, 129.1, 128.0, 127.7, 90.7, 73.1, 52.5, 44.4, 23.3 ppm. LRMS (ESI) m/z: 466.2 (15) $[M + H]^+$. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{24}H_{27}N_5O_5Na_1^+$ 488.1904; Found 488.1910.

*1-Benzyl 1-(3-(1-(1,3-bis(benzylamino)-2-methoxy-1,3-dioxopropan-2-yl)-1H-1,2,3-triazol-4-yl)propyl)-3′H-cyclopropa[1,9][5,6]-fulleren-C_{60}-I_h-1,1-dicarboxylate (**12f**).* According to general procedure D (H_2O/DCM) using (19 mg, 0.05 mmol)), 2-azido-N^1,N^3-dibenzyl-2-methoxymalonamide (**2a**), 1-Benzyl 1-(3-(1-(1,3-bis(benzylamino)-2-methoxy-1,3-dioxopropan-2-yl)-1*H*-1,2,3-triazol-4-yl)propyl)-3′*H*-cyclopropa[1,9][5,6]fulleren-C_{60}-I_h-1,1-dicarboxylate (**12f**) was obtained as a dark purple solid after purification by column chromatography (EA:DCM 1:9). Yield: 33 mg, 0.03 mmol, 46%. TLC: R_f = 0.62 (EA:DCM 1:9) [CAM]. IR (ATR): 3307, 2921, 1740, 1699, 695 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.67 (t, J = 5.9 Hz, 2 H), 7.52 (s, 1 H), 7.51−7.48 (m, 2 H), 7.39−7.28 (m, 13 H), 5.52 (s, 2 H), 4.62−4.53 (m, 4 H), 4.53−4.46 (m, 2 H), 3.36 (s, 3 H), 2.83 (t, J = 7.5 Hz, 2 H), 2.22−2.09 (m, 2 H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 163.9, 163.6, 163.6, 146.6, 145.4, 145.3, 145.3, 145.2, 145.1, 144.9, 144.8, 144.8, 144.8, 144.7, 144.0, 144.0, 143.2, 143.2, 143.2, 143.2, 143.1, 142.4, 142.0, 142.0, 141.1, 141.1, 139.3, 139.1, 137.0, 134.7, 129.3, 129.2, 129.0, 128.9, 128.0, 127.8, 122.6, 90.5, 71.6, 69.2, 66.5, 54.6, 44.3, 28.0, 22.1 ppm. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{93}H_{33}N_5O_7Na_1^+$ 1355.2311; Found 1355.2312.

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■ ASSOCIATED CONTENT

Supporting Information

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^{1}H and ^{13}C NMR spectra of selected examples (PDF)

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Notes

The authors declare no competing financial interest.

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