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Traceless Isoprenylation

Traceless Isoprenylation of Aldehydes via *N*-Boc-*N*-(1,1-dimethylallyl)hydrazones

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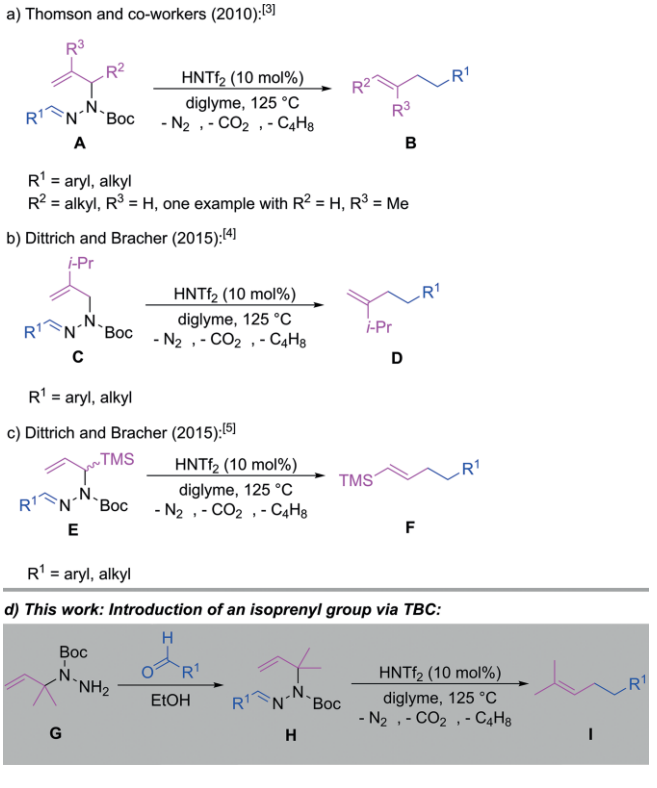
Abstract: A short isoprenylation protocol starting from non-conjugated *N*-Boc-*N*-(1,1-dimethylallyl)hydrazones was developed utilising Thomson's traceless bond construction. This type of [3,3]-sigmatropic rearrangement is catalysed by the Brønsted acid triflimide and liberates only gaseous by-products. The required *N*-Boc-*N*-allylhydrazine precursor is available in three steps starting from a known diazene using biocatalytic aldol addition and Tebbe olefination as key steps. Allylhydrazones are prepared via condensation with appropriate aldehydes. Scope and limitations of the [3,3]-sigmatropic rearrangements are analysed.

Introduction

The [3,3]-sigmatropic rearrangement is a common but impressive tool for the formation of new C–C-bonds in synthetic chemistry.[1] In 1973 Stevens showed that *N*-allylhydrazones undergo such a rearrangement under release of N_2 as well, but due to very harsh reaction conditions (300 °C) and low yields, this reaction was limited in its applicability.[2] For several decades, synthetic chemists did not see any real benefit of this unique rearrangement, until 2010, when Thomson and co-workers published the traceless bond construction (TBC), an improved variant of Stevens' [3,3]-sigmatropic rearrangement, working with *N*-Boc-*N*-allylhydrazones (**A**, Scheme 1a) and catalytic amounts of the Brønsted superacid triflimide ($HNTf_2$).[3] It was now possible to lower the temperature of the rearrangement to 125 °C and the yields of the products could be increased. This pioneering work of Thomson allowed the synthesis of various 1,2-disubstituted olefins (**B**) and one 1,1-disubstituted olefin (Scheme 1a). Mono-substituted olefins could not be obtained by this way. Later our group extended the scope to the synthesis of 1,1-disubstituted olefins (**D**, Scheme 1b), bearing an isopropyl group in 1-position, which resulted in a methylene branched end, a motif which is found in the side chains of steroidal natural products, e.g. episterol.[4] In the same year we reported the synthesis of terminal vinylsilanes (**F**, Scheme 1c) using TBC, which opened a new route to diversely substituted olefins.[5]



Scheme 1. a) Original TBC by Thomson and co-workers.[3] b) Extension of the TBC to the synthesis of 1,1-disubstituted olefins bearing an isopropyl group.[4] c) TBC yielding terminal vinylsilanes.[5] d) Introduction of an isoprenyl group via TBC developed in this work.

In this work we present a protocol for the introduction of an isopentenyl (isoprenyl) residue to aldehydes (Scheme 1d). The isoprenyl function is a common structural element in terpenoid

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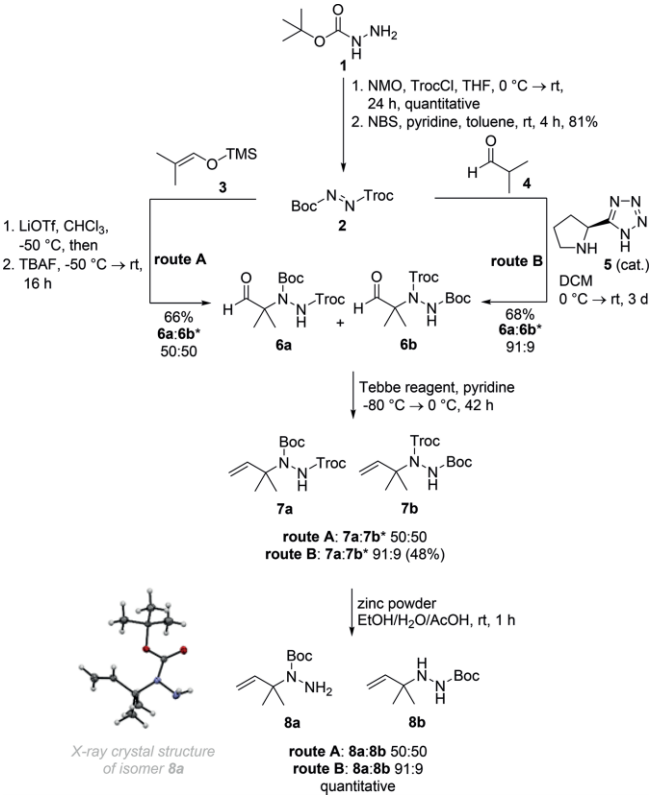
biomolecules and natural secondary metabolites.[6] The natural isoprene building block in terpenoid biosynthesis is dimethylallyl pyrophosphate (DMAPP).[7,8] Steroids like cholesterol as a membrane component,[9] pigments like β-carotene,[10] or cortisone or progesterone to name a few hormones,[11] are naturally occurring terpenoid derivatives, derived from DMAPP.

At the biological level, protein prenyltransferases attach terpenoid residues like farnesyl (C_{15}) or geranylgeranyl (C_{20}) groups to cysteinyl residues of proteins in posttranslational modifications. Due to the introduction of this hydrophobic group, the proteins can anchor in biomembranes resulting in altered biological activities.[12] In synthetic chemistry, organometallic building blocks like 3-methyl-2-butenylmagnesium chloride are commonly used for the introduction of an isoprenyl group.[13] Utilising inverse reactivities, 3,3-dimethylallyl bromide can be applied as an electrophilic isoprenyl building block,[14] as exemplified by the total syntheses of natural products, e.g. (±)-eldanolide[15] and (±)-fumagillin.[16] Besides direct isoprenylation, eliminations can lead to the isoprenyl function by forming the thermodynamically most stable double bond, e.g. from tertiary alcohols by dehydration.[17] An intramolecular isoprenylation, in which the group is constructed during a rearrangement, is to the best of our knowledge, not described in literature yet.

A further centrepiece of this work is the synthesis of the required, hitherto unknown, *N*-Boc-*N*-(1,1-dimethylallyl)hydrazine building block (**G**, Scheme 1d), bearing two geminal methyl groups in α-position to the hydrazine moiety to receive the desired isoprenylated products (**I**, Scheme 1d) via *N*-Boc-*N*-allylhydrazones (**H**, Scheme 1d). In our previous investigations leading to 1,1-disubstituted olefins,[4] undesired subsequent acid-catalysed isomerisations of the formed olefinic double bond were observed,[18] which led occasionally to isomeric mixtures of product alkenes. In the present case this is not expected to happen, since the resulting trisubstituted olefin should be the thermodynamically most stable isomer. An additional benefit of the two geminal methyl groups in precursor **G** is on the one hand that product **I** cannot be formed as mixture of *E*/*Z* isomers and on the other hand it is expected to facilitate the rearrangement due to the Thorpe-Ingold effect (gem-dimethyl effect).[19] As a result, less drastic reaction temperatures and shortened reaction times may be employable.[20]

Results and Discussion

The synthesis of the required *N*-Boc-*N*-(1,1-dimethylallyl)hydrazine building block **8a** (Scheme 2; **G** in Scheme 1d) started with the two-step synthesis of known *N*-Troc-*N*-Boc-protected diazene **2**.[21] Conversion into aldehyde **6a** was performed on two different routes. Route A used commercially available silyl enol ether **3**, which was activated by LiOTf and TBAF. The idea was to achieve a controlled O-Si-bond cleavage in **3** by slow addition of the fluoride source. Simultaneously, the presence of significant amounts of lithium ions should lead to an immediate formation of the lithium enolate. However, the addition of **3** to **2** did not proceed in a regioselective manner, and a 50:50 mixture of the isomeric aldehydes **6a** and its regioisomer **6b** was obtained. It is noteworthy, that the regioselectivity of this reaction could not be measured in this step, hence, it was determined retrospectively after conversion into **8a**/**8b** after the last step. Both isomers showed identical chromatographic behaviour and no distinct signals enabling quantification of the ratio of regioisomers could be observed by NMR spectroscopy until reaching **8a**/**8b**. Because of the lack of regioselectivity, an alternative approach to intermediate **6a** utilising organocatalysis[22,23] was worked out (route B). For this Aldol-type reaction with isobutyraldehyde (**4**), three catalysts were explored: L-proline,[24] L-phenylalanine,[25] and Ley's (*S*)-5-(pyrrolidin-2-yl)-1*H*-tetrazole (**5**).[21,26] Tetrazole catalyst **5** gave the best result with 68 % yield and the isomeric ratio could be improved to 91:9 (determined retrospectively by ^{1}H NMR spectroscopy) of the desired aldehyde **6a** and its regioisomer **6b**. Methylenation of the aldehyde function of **6a**/**6b** gave the olefins **7a** and **7b**. Different methods like Wittig,[27] Nysted-Takai[28] and Tebbe[29] olefination were tested, whereby the first two methods did not result in any product. Under Tebbe conditions the desired terminal olefin **7a** and its regioisomer **7b** were obtained in an acceptable yield of 48 % as an inseparable mixture.



Scheme 2. Route A leading to an equimolar mixture of **8a**/**8b** starting from silyl enolether **3**. Route B provides **8a**, contaminated with 9 % of isomer **6b** starting from aldehyde **4**. *The ratios of the isomers were determined retrospectively by NMR spectroscopy of the product **8a**/**8b**. The X-ray crystal structure of the desired isomer **8a** is shown on the left. Diazene **2** was synthesised according to literature.[21]

Chemoselective reductive Troc cleavage with zinc powder gave a still inseparable mixture of the desired olefin **8a** and its constitutional isomer **8b** in excellent yield. However, at this stage NMR spectroscopy enabled determination of the ratio of

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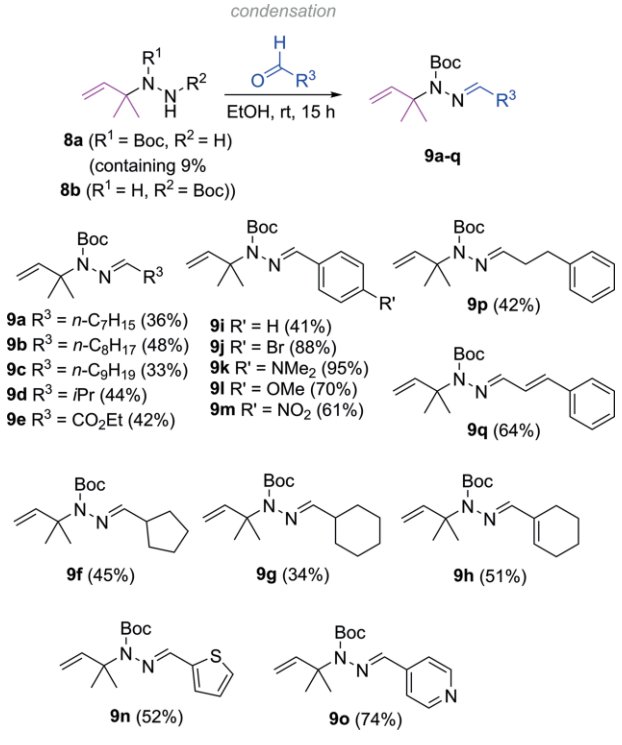
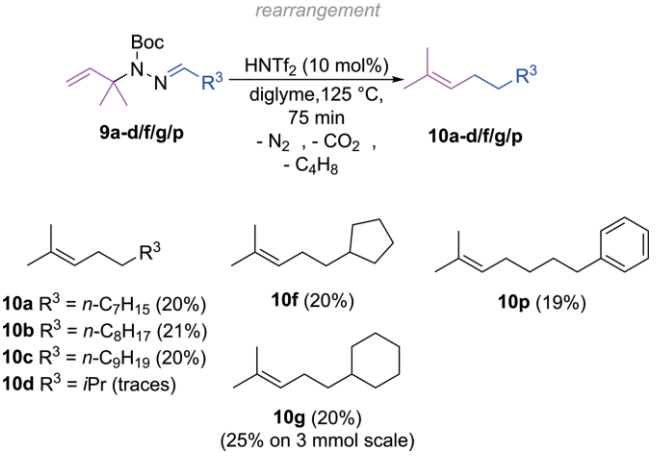
isomers (route A 50:50, route B 91:9). The structure of the desired *N*-Boc-*N*-allylhydrazine **8a** was unambiguously confirmed by X-ray crystal structure analysis (see Supporting Information). The enriched isomeric mixture of building block **8a** and **8b** could be used for the next step without further purification, since exclusively **8a** undergoes condensation with the employed aldehydes to give the *N*-Boc-*N*-allylhydrazones **9**, whereas the isomer **8b** remains unreacted. Scheme 3 shows the prepared allylhydrazones **9a**–**q**. Aliphatic (**9a**-**d**, **9f**, **9g**, **9p**), allylic (**9h**, **9q**) and aromatic (**9i**–**9o**) and ester-bearing (**9e**) allylhydrazones were synthesised by reacting the appropriate aldehydes with building block mixture **8a**/**b** in ethanol (yields 33–95 %). Especially non-conjugated allylhydrazones slowly decomposed during the purification process, which is reflected in the yields. Before we studied the capability of our *N*-Boc-*N*-allylhydrazine building block **8a**, we identified the optimum reaction conditions for the rearrangement utilising cyclohexanecarboxaldehyde-derived hydrazone **9g** as a model compound. Overall, 33 test reactions were performed with variations of temperature (23 to 125 °C), time (15 to 75 min) and solvents (THF and diglyme) (see Supporting Information). Significant rearrangement was only accomplished at temperatures of 75 °C and above. Besides $HNTf_2$ (pK_a –12.0, measured in DCE),[30] triflic acid (TfOH, pK_a –11.3, measured in DCE)[30] and trifluoroacetic acid (TFA, pK_a 0.23)[31] were tested. All in all, the hitherto used conditions of Thomson[3] ($HNTf_2$, diglyme, 125 °C) gave the best results for this conversion, closely followed by the rearrangement with triflic acid in diglyme at 125 °C, which would be a rewarding alternative to $HNTf_2$, which decomposes immediately in air and requires extremely dry reaction conditions. As the main side product, and even right at the beginning of the reaction, the corresponding Boc-deprotected allylhydrazone was observed, a compound which does not undergo the rearrangement. This is in accordance with the observations of Thomson and could not be prevented.[3] This prompted us to further investigate an alternative carbamate residue, which might be less prone to premature acidic cleavage. We prepared the ethyl carbamate analogue **S5a** of **8a** starting from ethyl carbazate on a route analogous to route B shown in Scheme 2 (for details, see Supporting Information). Two *N*-Boc-*N*-allylhydrazones **S6g** and **S6i** derived thereof were subjected to the previously determined best reaction conditions for rearrangement ($HNTf_2$, diglyme, 125 °C), but though the starting materials were fully consumed, none of the expected rearrangement products could be identified by GC/MS analysis. Consequently, the Boc group cannot be replaced in this protocol by the smaller ethoxycarbonyl group.

Scheme 4 shows the following rearrangement of substrates **9**. The allylhydrazones **9a**–**c** derived from *n*-alkanals underwent sigmatropic rearrangement providing the appropriate olefins **10a**–**c** in 20–21 % isolated yields. The poor yields are in part due to the high volatility of the olefinic products, as demonstrated by an increased yield (25 %) of **10g** on a larger scale (3 mmol). The rearrangement product **10d** of isobutyraldehyde-derived *N*-allylhydrazone **9d** could be detected by GC/MS, but could not be isolated due to its very high volatility (b.p. 135–136 °C[32]). Ester **9e** did not undergo rearrangement to the corresponding olefin and only the Boc-deprotected allylhydrazone was found.



Scheme 3. *N*-Boc-*N*-allylhydrazones **9a–q** prepared via condensation reaction between *N*-Boc-*N*-allylhydrazine **8a** and appropriate aldehydes. The yields refer to the content of *N*-Boc-*N*-allylhydrazine **8a** in the applied **8a**/**8b** mixture.



Scheme 4. Successful rearrangements of *N*-Boc-*N*-allyhydrazones using the standard conditions of the TBC. The reactions were performed at least in a 0.5 mmol scale. Isolated yields are given.

N-Allylhydrazones derived from cycloalkane carboxaldehydes (**9f**, **9g**) underwent rearrangement to olefins **10f** and **10g** with a yield of 20 % for both compounds (Scheme 4). In contrast, allylhydrazone **9h** derived from an α,β-unsaturated aldehyde did not undergo rearrangement and again only Boc-deprotected allylhydrazone was isolated. The attempted rearrangements of variously substituted arylidene hydrazones failed as well (**9i**–**m**). During the purification process of the attempted rearrangements of **9i** and **9j** crystalline solids were obtained,

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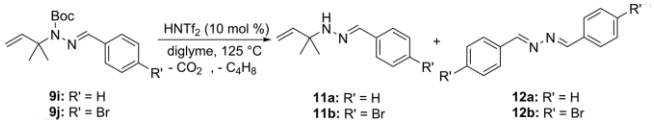
which were identified as the symmetric bis-hydrazones **12a**/**b** (Scheme 5).



Scheme 5. Attempted rearrangements of allylhydrazones **9i** and **9j** leading to deprotected allylhydrazons **11a/b** and bis-hydrazones **12a/b**.

Obviously, acid-mediated removal of both the Boc and the dimethylallyl residue took place in these experiments. Next to those, once again Boc-deprotected allylhydrazones **11a**/**b** were formed. Introduction of both electron-donating (methoxy compound **9l**) and electron-withdrawing groups (nitro compound **9m**) did not lead to successful rearrangements, and the same holds for hydrazones derived from heteroaromatic aldehydes (thiophene **9n** and pyridine **9o**). After these experiments it became evident which type of allylhydrazones would undergo the attempted acid-catalysed rearrangement. Non-conjugated allylhydrazones, like aliphatic systems **9a**-**d**, **9f**, and **9g** form the corresponding olefins, in contrast to allylhydrazones conjugated with aryl or ester groups, which do not show any rearrangement. The following experiments supported this assumption: Non-conjugated *N*-allylhydrazone **9p** derived from phenylpropanal showed a successful rearrangement with 19 % yield, whereas its cinnamaldehyde-derived congener **9q** did not give the desired alkene **10q** and only Boc-deprotected allylhydrazone was obtained. Thomson also reported on problems during the development of methods for hydrazone rearrangements, but with aliphatic systems,[3,33] which resulted in unidentified decomposition products. However, the rearrangement of aryl-substituted allylhydrazones worked well in his setup. Boc-deprotected allylhydrazones were observed in every reaction as by-products by GC/MS analysis, but no rearrangement takes place with these deprotected forms under our conditions. The deprotection reaction outcompetes the rearrangement and is a possible reason for the observed yields. This finding validates computational studies towards the mechanism of the triflimide-catalysed [3,3]-sigmatropic rearrangement by Gutierrez et al. indicating that conversion of deprotected allylhydrazones does not proceed well or not at all.[34]

Conclusion

In summary, we present a unique method for traceless isoprenylation of aliphatic aldehydes via triflimide-catalysed [3,3]-sigmatropic rearrangement of *N*-Boc-*N*-allylhydrazones. The central *N*-Boc-*N*-allylhydrazine building block **8a** is available in four steps utilising organocatalysis and Tebbe methylenation. This method opens a new route to isoprenyl compounds. This novel protocol is compromised by poor yields in the final step and its limitation to non-conjugated systems. Nevertheless, it broadens the scope of Stevens-type traceless bond constructions and represents the first example of a TBC for the introduction of an isoprenyl group into readily available aliphatic aldehydes. Therefore, this work extends the repertoire of methods for the total synthesis of isoprenoid natural products.

Experimental Section

General Information: All reactions were carried out in oven-dried Schlenk flasks equipped with a septum and a magnetic stirring bar which were evacuated and back filled with dry nitrogen. Solvents were dried according to standard methods by distillation over drying agents. Thin layer chromatography (TLC) was performed using polyester sheets polygram SIL G/UV254 covered with SiO_2 (layer thickness 0.2 mm, 40 × 80 mm) from Macherey-Nagel. Spots were visualized with a CAM (ceric ammonium molybdate) solution followed by heating. Flash column chromatography was performed using SiO_2 60 (0.040–0.063 mm, 230–400 mesh ASTM) from Merck. For chromatography distilled solvents were used. NMR spectra were recorded on JNM-Eclipse 400 (400 MHz), JNM-Eclipse 500 (500 MHz), Avance III HD 400 MHz Bruker Biospin (400 MHz) and Avance III HD 500 MHz Bruker Biospin (500 MHz) with CryoProbe™ Prodigy. Chemical shifts δ are reported as δ values in ppm relative to the deuterated solvent peak. The chemical shifts are reported in parts per million [ppm] and refer to the δ scala. Coupling constants *J* are indicated in Hertz [Hz]. For the characterization of the observed signal multiplicities the following abbreviations were applied: s (singlet), d (doublet), dd (doublet of doublet), dt (doublet of triplet), t (triplet), q (quartet), quint (quintet), m (multiplet), br (broad). Infrared spectra were recorded from 4000–650 cm^{-1} on a PERKIN ELMER Spectrum BX-59343 FT-IR instrument. For detection a Smiths Detection DuraSamp IR II Diamond ATR sensor was used. The absorption bands are reported in wave numbers (cm^{-1}). High resolution mass spectra (HRMS) were recorded on a Jeol Mstation 700 (Fa. Jeol, Peabody, USA) or JMS GCmate II Jeol instrument for electron impact ionisation (EI) equipped with a quadrupole doublet based lens system. Thermo Finnigan LTQ FT (Fa. Thermo Electron Corporation, Bremen, Germany) was used for electrospray ionization (ESI) equipped with an ion trap. Melting points were measured with a Büchi apparatus B-540 (Büchi, Flawill, Switzerland) and are reported in °C and are not corrected. Gas chromatography (GC) was performed on a Varian 3800 gas chromatograph coupled to a Saturn 2200 ion trap from Varian (Darmstadt, Germany). The autosampler was from CTC Analytics (Zwingen, Switzerland) and the split/splitless injector was a Varian 1177 (Darmstadt, Germany). Instrument control and data analysis were carried out with Varian Workstation 6.9 SP1 software (Darmstadt, Germany). A Varian VF-5-ms capillary column of 30 m length, 0.25 mm i.d. and 0.25 µm film thickness (Darmstadt, Germany) was used at a constant flow rate of 1.4 mL/min. Carrier gas was helium 99.999 % from Air Liquide (Düsseldorf, Germany). The inlet temperature was kept at 300 °C and injection volume was 1 µL with splitless time 1.0 min. The initial column temperature was 50 °C and was held for 1.0 min. Then the temperature was ramped up to 250 °C with 50 °C/min. Then the products were eluted at a rate of 5 °C/min until 310 °C (hold time 3 min). Total run time was 20 min. Transfer line temperature was 300 °C and the ion trap temperature was 150 °C. The ion trap was operated with electron ionization (EI) at 70 eV in scan mode (*m*/*z* 50–650) with a solvent delay of 6.3 min.

Crystallography: All X-ray intensity data were measured on a Bruker D8 Venture TXS system equipped with a multilayer mirror optics monochromator and a Mo K_α rotating-anode X-ray tube (λ = 0.71073 Å). The data collections were performed at 103 K. The frames were integrated with the Bruker SAINT Software package.[35] Data were corrected for absorption effects using the Multi-Scan method (SADABS).[36] The structures were solved and refined using the Bruker SHELXTL Software Package.[37] All C-bound hydrogen atoms were calculated in positions having ideal geometry riding on their parent atoms.

Deposition Number(s) 1907495 (for **8a**) contain(s) the supplementary crystallographic data for this paper. These data are provided free of charge by the joint Cambridge Crystallographic Data Centre and Fachinformationszentrum Karlsruhe Access Structures service www.ccdc.cam.ac.uk/structures.

Synthesis of Compounds

Diazene **2** was synthesised according to a literature protocol[21] in two steps and a total yield of 81 %.

1-(*tert*-Butyl) 2-(2,2,2-Trichloroethyl) 1-(2-Methyl-1-oxopropan-2-yl)hydrazine-1,2-dicarboxylate (6a) and 2-(*tert*-Butyl) 1-(2,2,2-Trichloroethyl) 1-(2-Methyl-1-oxopropan-2-yl)hydrazine-1,2-dicarboxylate (6b): *Route A*: A suspension of LiOTf (875 mg, 5.61 mmol, 1.52 equiv.) in dry $CHCl_3$ (20 mL) was cooled to - 50 °C. A solution of diazene **2** (1.70 g, 5.56 mmol, 1.5 equiv.) in $CHCl_3$ (10 mL), 2-methyl-1-(trimethylsilyloxy)-1-propene (**3**) (533 mg, 3.70 mmol, 1.0 equiv.) in $CHCl_3$ (10 mL) was added, followed by TBAF (1 M in THF, 3.7 mL, 3.7 mmol, 1.0 equiv.). The resulting reaction mixture was warmed to room temperature and stirred for 16 h. The reaction was stopped with aq. sat. NH_4Cl solution (10 mL) and the layers were separated. The organic layer was washed with aq. sat. $NaHCO_3$ solution (10 mL), dried with $MgSO_4$, filtered and the solvent was removed in vacuo. The title compound was purified by flash column chromatography (hexanes/EtOAc, 8:1). An inseparable mixture of aldehydes **6a**/**6b** (911 mg, 2.43 mmol, 66 %) were obtained as a colourless solid in an isomeric mixture of 50:50 (determined retrospectively via ^{1}H NMR). *Route B*: Diazene **2** (690 mg, 2.26 mmol, 1.0 equiv.) and (*S*)-5-(pyrrolidin-2-yl)-1*H*-tetrazole (**5**) (31.4 mg, 0.226 mmol, 10 mol-%) were dissolved in dry dichloromethane (15 mL) and the solution was cooled to 0 °C. Isobutyraldehyde (**4**) (0.25 mL, 2.71 mmol, 1.2 equiv.) was added slowly and the reaction mixture was warmed to room temperature. After completion of the reaction, the solvent was removed in vacuo and the product was purified by flash column chromatography (hexanes/EtOAc, 8:1). An inseparable mixture of aldehydes **6a**/**6b** (580 mg, 1.53 mmol, 68 %) were obtained as a colourless solid in an isomeric mixture of 91:9 (determined retrospectively via ^{1}H NMR): R_f = 0.17 (hexanes/EtOAc, 8:1); m.p. 128–129 °C; ^{1}H NMR (500 MHz, [D]chloroform) δ/ppm = 9.49 (s, 1H), 6.70 (s, 1H), 4.93–4.51 (m, 2H), 1.44 (s, 9H), 1.36 (s, 3H), 1.29 (s, 3H); ^{13}C NMR (101 MHz, [D]chloroform δ/ppm = 198.1, 155.4, 154.3, 94.9, 84.3, 75.2, 67.4, 28.2, 20.5; IR (ATR) $\tilde{\nu}$ = /cm^{-1} = 3255, 3013, 2980, 2936, 1771, 1723, 1694, 1528, 1457, 1391, 1380, 1365, 1358, 1287, 1254, 1220, 1161, 1108, 1054, 992, 945, 916, 882, 858, 834, 817, 799, 763, 750, 724, 709, 658; HRMS (ESI): *m/z* calcd. for $C_{12}H_{18}Cl_3N_2O_5$ $[M - H]^-$ 375.0287, found 375.0287.

1-(*tert*-Butyl) 2-(2,2,2-Trichloroethyl) 1-(2-Methylbut-3-en-2-yl)hydrazine-1,2-di-carboxylate (7a) and 2-(*tert*-Butyl) 1-(2,2,2-Trichloroethyl) 1-(2-Methylbut-3-en-2-yl)hydrazine-1,2-dicarboxylate (7b): The isomeric mixture of aldehydes **6a**/**6b** (569 mg, 1.51 mmol, 1.0 equiv.) and pyridine (0.22 mL, 2.7 mmol, 1.8 equiv.) were added to a flame dried flask and the mixture was blended to a gel via ultrasound bath. The suspension was cooled to –80 °C and Tebbe reagent (0.5 M in toluene, 3.92 mL, 1.96 mmol, 1.3 equiv.) was added carefully by adding it along the flask. The reaction mixture was warmed to 0 °C and stirred 48 h. The reaction was quenched with a saturated aqueous $NaHCO_3$ solution (6 mL) at –80 °C and extracted with dichloromethane (3 × 10 mL). The combined organic layers were dried with $MgSO_4$, filtered and the solvent was removed in vacuo. Purification by flash column chromatography (hexanes/EtOAc, 9:1) gave an inseparable mixture of olefins **7a**/**7b** (270 mg, 0.719 mmol, 48 %) as a colourless solid in an isomeric mixture of 91:9 (determined retrospectively via ^{1}H NMR): R_f = 0.29 (hexanes/EtOAc, 9:1); m.p. 103–104 °C; ^{1}H NMR (500 MHz, [D]chloroform) δ/ppm = 6.68 (s, 1H), 6.10 (dd, $^3J_{H,H}$ = 17.4, 11.0 Hz, 1H), 5.08 (d, $^3J_{H,H}$ = 17.1 Hz, 1H), 5.00 (d, $^3J_{H,H}$ = 10.9 Hz, 1H), 4.87 (d, $^2J_{H,H}$ = 11.5 Hz, 1H), 4.68 (d, $^2J_{H,H}$ = 11.8 Hz, 1H), 1.50 (s, 3H), 1.44 (s, 9H), 1.42 (s, 3H); ^{13}C NMR (126 MHz, [D]chloroform) δ/ppm = 155.4, 154.5, 144.6, 111.2, 95.2, 82.1, 75.1, 62.9, 28.4, 26.6, 26.4; IR (ATR) $\tilde{\nu}$ = /cm^{-1} = 3323, 2924, 2854, 1733, 1706, 1644, 1522, 1456, 1414, 1386, 1359, 1274, 1253, 1233, 1156, 1101, 1078, 1044, 1011, 990, 967, 922, 907, 851, 815, 759, 741, 724, 688; HRMS (ESI): *m/z* calcd. for $C_{13}H_{20}O_4N_2Cl_3$ $[M - H]^-$ 373.0494, found 373.0499.

***tert*-Butyl 1-(2-Methylbut-3-en-2-yl)hydrazine-1-carboxylate (8a) and *tert*-Butyl 2-(2-Methylbut-3-en-2-yl)hydrazine-1-carboxylate (8b)**: The mixture of olefins **7a**/**7b** (95.6 mg, 0.254 mmol, 1.0 equiv.) was dissolved in a mixture of ethanol (0.3 mL), water (0.3 mL) and acetic acid (0.3 mL). Zinc powder (582 mg, 8.91 mmol, 35.0 equiv.) was added and the reaction mixture was stirred for 10 minutes at room temperature. After filtration of the reaction mixture, the filtrate was extracted with dichloromethane (3 × 3 mL) and the residue was extracted. The combined organic layers were washed was saturated aqueous $NaHCO_3$ solution (5 mL) and the organic layer was dried with $MgSO_4$, filtered and the solvent was removed in vacuo. The product was used without purification. **8a**/**8b** (57 mg, 0.28 mmol, quantitative) was obtained as a colourless oil in an isomeric mixture of 91:9: R_f = 0.15 (hexanes/EtOAc, 8:2); ^{1}H NMR (**8a**) (400 MHz, [D$_6$]DMSO) δ/ppm = 6.00 (dd, $^3J_{H,H}$ = 17.5, 10.7 Hz, 1H), 4.87 (dd, $^3J_{H,H}$ = 17.5, 10.8, 2H), 4.24 (s, 2H), 1.38 (s, 9H), 1.33 (s, 6H); ^{13}C NMR (**8a**) (126 MHz, [D$_6$]DMSO) δ/ppm = 156.4, 146.2, 108.8, 79.3, 60.6, 28.1, 26.5; ^{1}H NMR (**8b**) (500 MHz, [D$_6$]DMSO) δ/ppm = 7.95 (s, 1H), 5.81 (dd, $^3J_{H,H}$ = 17.6, 10.8 Hz, 1H), 5.08–4.92 (m, 2H), 4.07 (s, 1H), 1.38 (s, 9H), 1.03 (s, 6H); ^{13}C NMR (**8b**) (126 MHz, [D$_6$]DMSO) δ/ppm = 155.6, 145.0, 112.2, 78.1, 57.8, 28.2, 24.8; IR (ATR) $\tilde{\nu}$ = /cm^{-1} = 3334, 2977, 2932, 1679, 1477, 1455, 1412, 1365, 1249, 1163, 1101, 1005, 994, 948, 907, 868, 766, 724, 687; HRMS (ESI): *m/z* calcd. for $C_{10}H_{21}N_2O_2$ $[M + H]^+$ 201.1597, found 201.1597.

General Procedure 1 (GP1) for the Synthesis of *N*-Boc-*N*-(1,1-Dimethylallyl)hydrazones 9a–q: The mixture of *N*-(1,1-dimethylallyl)hydrazines **8a**/**8b** (1.0 equiv.) was dissolved in absolute EtOH and the appropriate aldehyde (1.0 equiv.) was added. The reaction mixture was stirred at room temperature for 15 h, then the solvent was removed in vacuo and the crude product was purified by flash column chromatography. Isolated yields are correlated to the amount of **8a** in the isomeric mixture **8a**/**8b**.

***tert*-Butyl 1-(2-methylbut-3-en-2-yl)-2-octylidenehydrazine-1-carboxylate (9a):** Mixture of allylhydrazines **8a**/**8b** (250 mg, 1.75 mmol ≙ 1.59 mmol of isomer **8a**) and octanal (0.298 mL, 1.75 mmol) gave *N*-Boc-*N*-allylhydrazone **9a** (178 mg, 0.576 mmol, 36 % referred to isomer **8a**) as colourless oil via GP1: R_f = 0.58 (hexanes/EtOAc, 9:1); ^{1}H NMR (400 MHz, [D]chloroform) δ/ppm = 7.71 (t, $^3J_{H,H}$ = 5.6 Hz, 1H), 6.11 (dd, $^3J_{H,H}$ = 17.5, 10.8 Hz, 1H), 5.07–4.86 (m, 2H), 2.35 (td, $^3J_{H,H}$ = 5.6 Hz, 2H), 1.59–1.50 (m, 2H), 1.42 (s, 9H), 1.39 (s, 6H), 1.34–1.24 (m, 8H), 0.87 (m, 3H); ^{13}C NMR (101 MHz, [D]chloroform) δ/ppm = 169.5, 154.3, 146.3, 109.4, 80.9, 61.7, 33.0, 31.9, 29.5, 29.2, 28.6, 26.7, 26.2, 22.8, 14.3; IR (ATR) $\tilde{\nu}$ = /cm^{-1} = 3084, 3004, 2972, 2958, 2927, 2857, 1698, 1641, 1455, 1412, 1391, 1366, 1302, 1244, 1157, 1101, 1003, 991, 901, 855, 757, 724, 686; HRMS (ESI): *m/z* calcd. for $C_{18}H_{35}N_2O_2$ $[M + H]^+$ 311.2693, found 311.2694.

***tert*-Butyl 1-(2-Methylbut-3-en-2-yl)-2-nonylidenehydrazine-1-carboxylate (9b):** Mixture of allylhydrazines **8a**/**8b** (404 mg, 2.02 mmol ≙ 1.83 mmol of isomer **8a**) and nonanal (0.346 mL, 2.02 mmol) gave *N*-Boc-*N*-allylhydrazone **9b** (284 mg, 0.877 mmol, 48 % referred to isomer **8a**) as colourless oil via GP1: R_f = 0.58

(hexanes/EtOAc, 9:1); ^{1}H NMR (500 MHz, [D]chloroform) δ/ppm = 7.71 (t, $^3J_{H,H}$ = 5.6 Hz, 1H), 6.11 (dd, $^3J_{H,H}$ = 17.5, 10.8 Hz, 1H), 5.05–4.89 (m, 2H), 2.34 (td, $^3J_{H,H}$ = 5.6 Hz, 2H), 1.55 (m, 2H), 1.42 (s, 9H), 1.39 (s, 6H), 1.36–1.21 (m, 10H), 0.89–0.85 (m, 3H); ^{13}C NMR (101 MHz, [D]chloroform) δ/ppm = 169.4, 154.3, 146.3, 109.4, 80.9, 61.7, 33.0, 31.9, 29.5, 29.4, 29.3, 28.5, 26.7, 26.2, 22.8, 14.2; IR (ATR) $\tilde{\nu}$ = /cm^{-1} = 3086, 2972, 2956, 2926, 2856, 1698, 1640, 1455, 1412, 1390, 1366, 1302, 1244, 1157, 1100, 1003, 992, 900, 874, 857, 783, 756, 723, 687, 599; HRMS (ESI): *m/z* calcd. for $C_{19}H_{37}N_2O_2$ [M + H]$^+$ 325.2849, found 325.2849.

***tert*-Butyl 2-Decylidene-1-(2-methylbut-3-en-2-yl)hydrazine-1-carboxylate (9c):** Mixture of allylhydrazines **8a**/**8b** (115 mg, 0.574 mmol ≙ 0.522 mmol of isomer **8a**) and decanal (0.108 mL, 0.574 mmol) gave *N*-Boc-*N*-allylhydrazone **9c** (56 mg, 0.17 mmol, 33 % referred to isomer **8a**) as colourless oil via GP1: R_f = 0.56 (hexanes/EtOAc, 9:1). ^{1}H NMR (500 MHz, [D]chloroform) δ/ppm = 7.71 (t, $^3J_{H,H}$ = 5.6 Hz, 1H), 6.11 (dd, $^3J_{H,H}$ = 17.5, 10.8 Hz, 1H), 5.01 (dd, $^3J_{H,H}$ = 17.5, $^2J_{H,H}$ = 0.7 Hz, 1H), 4.92 (dd, *J* $^3J_{H,H}$ = 10.8, $^2J_{H,H}$ = 0.7 Hz, 1H), 2.35 (td, $^3J_{H,H}$ = 5.6 Hz, 2H), 1.57–1.54 (m, 2H), 1.42 (s, 9H), 1.39 (s, 6H), 1.26 (m, 12H), 0.89–0.86 (m, 3H). ^{13}C NMR (126 MHz, [D]chloroform) δ/ppm = 169.5, 154.3, 146.3, 109.4, 80.9, 61.7, 33.0, 32.0, 29.6, 29.5, 29.5, 29.4, 28.6, 26.7, 26.2, 22.8, 14.3. IR (ATR) $\tilde{\nu}$ = /cm^{-1} = 2924, 2853, 1696, 1458, 1407, 1368, 1310, 1245, 1158, 1101, 990, 903, 852, 754, 719, 665. HRMS (ESI): *m/z* calcd. for $C_{20}H_{39}N_2O_2$ [M + H]$^+$ 339.3006, found 339.3011.

***tert*-Butyl 1-(2-Methylbut-3-en-2-yl)-2-(2-methylpropylidene)-hydrazine-1-carboxylate (9d):** Mixture of olefins **8a**/**8b** (519 mg, 2.59 mmol ≙ 2.36 mmol of isomer **8a**) and isobutyraldehyde (**4**) (0.237 mL, 2.59 mmol) gave *N*-Boc-*N*-allylhydrazone **9d** (262 mg, 1.03 mmol, 44 % referred to isomer **8a**) as colourless oil via GP1: R_f = 0.55 (hexanes/EtOAc, 9:1); ^{1}H NMR (400 MHz, [D]chloroform) δ/ppm = 7.61 (d, $^3J_{H,H}$ = 5.9 Hz, 1H), 6.11 (dd, $^3J_{H,H}$ = 17.6, 10.8 Hz, 1H), 5.03–4.90 (m, 2H), 2.66–2.56 (m, 1H), 1.42 (s, 9H), 1.39 (s, 6H), 1.13 (s, 3H), 1.12 (s, 3H). ^{13}C NMR (101 MHz, [D]chloroform) δ/ppm = 173.2, 154.1, 146.3, 109.4, 80.9, 61.9, 32.2, 28.6, 26.6, 19.6. IR (ATR) $\tilde{\nu}$ = /cm^{-1} = 3086, 3008, 2973, 2930, 2872, 1698, 1641, 1456, 1412, 1390, 1366, 1304, 1289, 1244, 1156, 1092, 1058, 992, 970, 902, 879, 856, 756, 686, 599, 588. HRMS (ESI): *m/z* calcd. for $C_{14}H_{27}N_2O_2$ [M + H]$^+$ 255.2067, found 255.2066.

***tert*-Butyl 2-(2-Ethoxy-2-oxoethylidene)-1-(2-methylbut-3-en-2-yl)hydrazine-1-carboxylate (9e):** Mixture of olefins **8a**/**8b** (200 mg, 0.990 mmol, ≙ 0.901 mmol of isomer **8a**) and ethyl glyoxalate solution (ca. 50 % in toluene, 0.198 mL, 0.990 mmol) gave *N*-Boc-*N*-allylhydrazone **9e** (108 mg, 0.380 mmol, 42 % referred to isomer **8a**) as colourless oil via GP1: R_f = 0.44 (hexanes/EtOAc, 9:1); ^{1}H NMR (400 MHz, [D]chloroform) δ/ppm = 8.41 (s, 1H), 6.05 (dd, $^3J_{H,H}$ = 17.5, 10.8 Hz, 1H), 5.07–4.93 (m, 2H), 4.26 (q, $^3J_{H,H}$ = 7.1 Hz, 2H), 1.52 (s, 6H), 1.48 (s, 9H), 1.31 (t, $^3J_{H,H}$ = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, [D]chloroform) δ/ppm = 164.9, 151.9, 145.5, 135.7, 110.6, 83.6, 65.9, 60.9, 28.3, 27.7, 14.4; IR (ATR) $\tilde{\nu}$ = /cm^{-1} = 1742, 1708, 1585, 1477, 1456, 1369, 1339, 1288, 1242, 1206, 1181, 1148, 1113, 1093, 1044, 911, 848, 798, 759, 744, 576; HRMS (EI): *m/z* calcd. for $C_9H_{16}N_2O_2$ [M – Boc]$^+$ 184.1206, found 184.1205.

***tert*-Butyl 2-(Cyclopentylmethylene)-1-(2-methylbut-3-en-2-yl)-hydrazine-1-carboxylate (9f):** Mixture of olefins **8a**/**8b.** (430 mg, 2.15 mmol ≙ 1.96 mmol of isomer **8a**) and cyclopentane carboxaldehyde (0.229 mL, 2.15 mmol) gave *N*-Boc-*N*-allylhydrazone **9f** (245 mg, 0.874 mmol, 45 % referred to isomer **8a**) as colourless oil via GP1: R_f = 0.57 (hexanes/EtOAc, 9:1); ^{1}H NMR (400 MHz, [D]chloroform) δ/ppm = 7.62 (d, $^3J_{H,H}$ = 6.8 Hz, 1H), 6.11 (dd, $^3J_{H,H}$ = 17.5, 10.8 Hz, 1H), 5.08–4.82 (m, 2H), 2.87–2.71 (m, 1H), 1.95–1.79 (m, 2H), 1.73–1.54 (m, 6H), 1.42 (s, 9H), 1.38 (s, 6H); ^{13}C NMR (101 MHz, [D]chloroform) δ/ppm = 172.6, 154.2, 146.2, 109.4, 80.8, 61.8, 42.9, 30.3, 28.6, 28.5, 26.6, 25.7; IR (ATR) $\tilde{\nu}$ = /cm^{-1} = 3084, 2968, 2956, 2869, 1697, 1639, 1476, 1454, 1412, 1390, 1366, 1304, 1244, 1156, 1101, 1061, 1003, 992, 900, 877, 856, 783, 757, 687; HRMS (ESI): *m/z* calcd. for $C_{16}H_{29}N_2O_2$ [M + H]$^+$ 281.2224, found 281.2225.

***tert*-Butyl 2-(Cyclohexylmethylene)-1-(2-methylbut-3-en-2-yl)-hydrazine-1-carboxylate (9g):** Mixture of olefins **8a**/**8b** (91.6 mg, 0.686 mmol ≙ 0.624 mmol of isomer **8a**) and cyclohexanecarboxaldehyde (55.4 µL, 0.686 mmol) gave *N*-Boc-*N*-allylhydrazone **9f** (63.3 mg, 0.215 mmol, 34 % referred to isomer **8a**) as colourless oil via GP1: R_f = 0.64 (hexanes/EtOAc, 9:1); ^{1}H NMR (500 MHz, [D]chloroform) δ/ppm = 7.58 (d, $^3J_{H,H}$ = 6.0 Hz, 1H), 6.11 (dd, $^3J_{H,H}$ = 17.5, 10.8 Hz, 1H), 5.01 (dd, $^3J_{H,H}$ = 17.5, $^2J_{H,H}$ = 0.9 Hz, 1H), 4.92 (dd, $^3J_{H,H}$ = 10.8, $^2J_{H,H}$ = 0.9 Hz, 1H), 2.42–2.25 (m, 1H), 1.89–1.80 (m, 2H), 1.80–1.73 (m, 2H), 1.70–1.64 (m, 1H), 1.41 (s, 9H), 1.39 (s, 6H), 1.35–1.28 (m, 4H), 1.27–1.18 (m, 1H). ^{13}C NMR (101 MHz, [D]chloroform) δ/ppm = 172.6, 154.3, 146.3, 109.4, 80.8, 61.8, 41.5, 29.9, 28.6, 26.7, 26.1, 25.5; IR (ATR) $\tilde{\nu}$ = /cm^{-1} = 2929, 2854, 1709, 1366, 1308, 1244, 1160; HRMS (ESI): *m/z* calcd. for $C_{17}H_{31}N_2O_2$: 295.2380 [M + H]$^+$, found 295.2385.

***tert*-Butyl 2-(Cyclohex-1-en-1-ylmethylene)-1-(2-methylbut-3-en-2-yl)hydrazine-1-carboxylate (9h):** Mixture of olefins **8a**/**8b** (200 mg, 0.999 mmol ≙ 0.909 mmol of isomer **8a**) and 1-cyclohexene-1-carboxaldehyde (0.114 mL, 0.990 mmol) gave *N*-Boc-*N*-allylhydrazone **9h** (135 mg, 0.460 mmol, 51 % referred to isomer **8a**) as colourless oil via GP1: R_f = 0.52 (hexanes/EtOAc, 9:1); ^{1}H NMR (400 MHz, [D]chloroform) δ/ppm = 7.99 (s, 1H), 6.18–6.05 (m, 2H), 5.05–4.85 (m, 2H), 2.37–2.12 (m, 4H), 1.70–1.61 (m, 4H), 1.43 (s, 9H), 1.41 (s, 6H); ^{13}C NMR (101 MHz, [D]chloroform) δ/ppm = 163.9, 153.9, 146.6, 138.2, 136.3, 109.1, 81.2, 62.7, 28.6, 26.9, 26.3, 23.4, 22.5, 22.1; IR (ATR) $\tilde{\nu}$ = /cm^{-1} = 2976, 2931, 2859, 1697, 1639, 1596, 1366, 1291, 1243, 1152, 1107, 902, 881, 754, 699; HRMS (ESI): *m/z* calcd. for $C_{17}H_{29}N_2O_2$ [M + H]$^+$ 293.2224, found 293.2223.

***tert*-Butyl 2-Benzylidene-1-(2-methylbut-3-en-2-yl)hydrazine-1-carboxylate (9i):** Mixture of olefins **8a**/**8b** (580 mg, 2.90 mmol ≙ 2.64 mmol of isomer **8a**) and benzaldehyde (0.294 mL, 2.90 mmol) gave *N*-Boc-*N*-allylhydrazone **9i** (312 mg, 1.08 mmol, 41 % referred to isomer **8a**) as colourless oil via GP1: R_f = 0.64 (hexanes/EtOAc, 9:1); ^{1}H NMR (400 MHz, [D]chloroform) δ/ppm = 8.65 (s, 1H), 7.74–7.68 (m, 2H), 7.43–7.34 (m, 3H), 6.17 (dd, $^3J_{H,H}$ = 17.5, 10.8 Hz, 1H), 5.11–4.90 (m, 2H), 1.52 (s, 6H), 1.47 (s, 9H); ^{13}C NMR (101 MHz, [D]chloroform) δ/ppm = 157.1, 153.6, 146.4, 135.4, 130.2, 128.7, 127.7, 109.4, 81.8, 63.6, 28.5, 27.2; IR (ATR) $\tilde{\nu}$ = /cm^{-1} = 3083, 3062, 2976, 2932, 1697, 1642, 1574, 1476, 1449, 1412, 1391, 1366, 1289, 1243, 1149, 1109, 1071, 992, 947, 898, 856, 784, 753, 692, 659, 563; HRMS (ESI): *m/z* calcd. for $C_{17}H_{25}N_2O_2$ [M + H]$^+$ 289.1910, found 289.1909.

***tert*-Butyl 2-(4-Bromobenzylidene)-1-(2-methylbut-3-en-2-yl)-hydrazine-1-carboxylate (9j):** Mixture of olefins **8a**/**8b** (243 mg, 1.21 mmol ≙ 1.10 mmol of isomer **8a**) and 4-bromobenzaldehyde (224 mg, 1.21 mmol) gave *N*-Boc-*N*-allylhydrazone **9j** (356 mg, 0.971 mmol, 88 % referred to isomer **8a**) as colourless oil via GP1: R_f = 0.64 (hexanes/EtOAc, 9:1); ^{1}H NMR (500 MHz, [D]chloroform) δ/ppm = 8.68 (s, 1H), 7.56 (d, $^3J_{H,H}$ = 8.4 Hz, 2H), 7.50 (d, $^3J_{H,H}$ = 8.3 Hz, 2H), 6.14 (dd, $^3J_{H,H}$ = 17.5, 10.8 Hz, 1H), 5.07–4.92 (m, 2H), 1.51 (s, 6H), 1.47 (s, 9H); ^{13}C NMR (126 MHz, [D]chloroform) δ/ppm = 153.9, 153.5, 146.3, 134.7, 131.9, 128.9, 124.1, 109.6, 82.1, 63.9, 28.5, 27.3; IR (ATR) $\tilde{\nu}$ = /cm^{-1} = 3086, 2979, 2932, 1696, 1643, 1591, 1564, 1487, 1455, 1412, 1392, 1367, 1289, 1244, 1148, 1115, 1098, 1069, 1044, 1009, 992, 953, 929, 901, 856, 819, 786, 752, 708, 691, 667; HRMS (ESI): *m/z* calcd. for $C_{17}H_{24}BrN_2O_2$ [M + H]$^+$ 367.1015, found 367.1026.

***tert*-Butyl 2-(4-(Dimethylamino)benzylidene)-1-(2-methylbut-3-en-2-yl)hydrazine-1-carboxylate (9k):** Mixture of olefins **8a**/**8b** (100 mg, 0.499 mmol ≙ 0.454 mmol of isomer **8a**) and 4-dimethylaminobenzaldehyde (74.5 mg, 0.499 mmol) gave *N*-Boc-*N*-allylhydrazone **9k** (143 mg, 0.431 mmol, 95 % referred to isomer **8a**) as white crystalline solid via GP1: R_f = 0.35 (hexanes/EtOAc, 9:1); m.p. 73–75 °C; ^{1}H NMR (400 MHz, [D]chloroform) δ/ppm = 8.30 (s, 1H), 7.61 (d, $^3J_{H,H}$ = 8.9 Hz, 2H), 6.69 (d, $^3J_{H,H}$ = 8.9 Hz, 2H), 6.19 (dd, $^3J_{H,H}$ = 17.5, 10.8 Hz, 1H), 5.08–4.90 (m, 2H), 3.01 (s, 6H), 1.47 (s, 6H), 1.44 (s, 9H); ^{13}C NMR (101 MHz, [D]chloroform) δ/ppm = 162.4, 154.2, 152.2, 146.6, 129.4, 122.4, 111.8, 109.2, 80.9, 62.6, 40.4, 28.6, 26.9; IR (ATR) $\tilde{\nu}$ = /cm^{-1} = 2976, 2930, 1693, 1616, 1601, 1528, 1477, 1455, 1363, 1300, 1237, 1155, 1100, 1060, 894, 859, 816, 755, 731; HRMS (ESI): *m/z* calcd. for $C_{19}H_{30}N_3O_2$ [M + H]$^+$ 332.2333, found 332.2333.

***tert*-Butyl 2-(4-Methoxybenzylidene)-1-(2-methylbut-3-en-2-yl)-hydrazine-1-carboxylate (9l):** Mixture of olefins **8a**/**8b** (150 mg, 0.749 mmol ≙ 0.682 mmol of isomer **8a**) and 4-anisaldehyde (102 mg, 91.1 µL, 0.749 mmol) gave *N*-Boc-*N*-allylhydrazone **9l** (151 mg, 0.475 mmol, 70 % referred to isomer **8a**) as colourless oil via GP1: R_f = 0.42 (hexanes/EtOAc, 9:1); ^{1}H NMR (400 MHz, [D]chloroform) δ/ppm = 8.48 (s, 1H), 7.66 (d, $^3J_{H,H}$ = 8.8 Hz, 2H), 6.91 (d, $^3J_{H,H}$ = 8.9 Hz, 2H), 6.17 (dd, $^3J_{H,H}$ = 17.5, 10.8 Hz, 1H), 5.08–4.92 (m, 2H), 3.84 (s, 3H), 1.49 (s, 6H), 1.45 (s, 9H); ^{13}C NMR (101 MHz, [D]chloroform) δ/ppm = 161.5, 159.0, 153.9, 146.5, 129.3, 127.8, 114.1, 109.3, 81.4, 63.1, 55.5, 28.6, 27.0; IR (ATR) $\tilde{\nu}$ = /cm^{-1} = 2975, 2932, 1693, 1606, 1512, 1456, 1366, 1293, 1245, 1150, 1104, 1031, 900, 859, 831, 75; HRMS (ESI): *m/z* calcd. for $C_{18}H_{27}N_2O_3$ [M + H]$^+$ 319.2016, found 319.2015.

***tert*-Butyl 1-(2-Methylbut-3-en-2-yl)-2-(4-nitrobenzylidene)-hydrazine-1-carboxylate (9m):** Mixture of olefins **8a**/**8b** (250 mg, 1.25 mmol ≙ 1.14 mmol of isomer **8a**) and 4-nitrobenzaldehyde (0.126 mL, 1.25 mmol) gave *N*-Boc-*N*-allylhydrazone **9m** (233 mg, 0.698 mmol, 61 % referred to isomer **8a**) as yellow solid via GP1: R_f = 0.51 (hexanes/EtOAc, 9:1); m.p. 67–69 °C; ^{1}H NMR (400 MHz, [D]chloroform) δ/ppm = 9.02 (s, 1H), 8.24–8.19 (m, 2H), 7.82–7.75 (m, 2H), 6.12 (dd, *J* = 17.5, 10.8 Hz, 1H), 5.10–4.93 (m, 2H), 1.56 (s, 6H), 1.50 (s, 9H); ^{13}C NMR (101 MHz, [D]chloroform) δ/ppm = 152.9, 148.1, 147.7, 145.9, 142.7, 127.6, 124.0, 110.1, 82.9, 65.0, 28.5, 27.6; IR (ATR) $\tilde{\nu}$ = /cm^{-1} = 1699, 1598, 1572, 1518, 1368, 1343, 1286, 1246, 1146, 1107, 907, 849, 832, 729, 692, 647; HRMS (EI): *m/z* calcd. for $C_{17}H_{23}N_3O_4$ [M]$^{\cdot+}$ 333.1683, found 333.1710.

***tert*-Butyl 1-(2-Methylbut-3-en-2-yl)-2-(thiophen-2-ylmethylene)hydrazine-1-carboxylate (9n):** Mixture of olefins **8a**/**8b** (150 mg, 0.749 mmol ≙ 0.681 mmol of isomer **8a**) and 2-thiophenecarboxaldehyde (70 µL, 0.749 mmol) gave *N*-Boc-*N*-allylhydrazone **9n** (104 mg, 0.352 mmol, 52 % referred to isomer **8a**) as light yellow oil via GP1: R_f = 0.60 (hexanes/EtOAc, 9:1); ^{1}H NMR (400 MHz, [D]chloroform) δ/ppm = 8.85–8.83 (m, 1H), 7.32 (dt, $^3J_{H,H}$ = 5.0, 1.0 Hz, 1H), 7.24 (dd, $^3J_{H,H}$ = 3.6, 1.2 Hz, 1H), 7.04 (dd, $^3J_{H,H}$ = 5.1, 3.6 Hz, 1H), 6.14 (dd, $^3J_{H,H}$ = 17.5, 10.8 Hz, 1H), 5.08–4.91 (m, 2H), 1.49 (s, 6H), 1.47 (s, 9H); ^{13}C NMR (101 MHz, [D]chloroform) δ/ppm = 153.6, 150.2, 146.3, 140.9, 129.7, 127.9, 127.4, 109.5, 81.9, 63.7, 28.5, 27.2; IR (ATR) $\tilde{\nu}$ = /cm^{-1} = 2985, 2938, 1742, 1708, 1585, 1369, 128, 1242, 1181, 1148, 1113, 1093, 1044, 911, 848, 759, 744, 576; HRMS (EI): *m/z* calcd. for $C_{15}H_{22}N_2O_2S$ [M]$^{\cdot+}$ 294.1396, found 294.1392.

***tert*-Butyl 1-(2-Methylbut-3-en-2-yl)-2-(pyridin-4-ylmethylene)-hydrazine-1-carboxylate (9o):** Mixture of olefins **8a**/**8b** (350 mg, 1.75 mmol ≙ 1.59 mmol of isomer **8a**) and 4-pyridinecarboxaldehyde (0.165 mL, 1.75 mmol) gave *N*-Boc-*N*-allylhydrazone **9o** (342 mg, 1.18 mmol, 74 % referred to isomer **8a**) as light yellow oil via GP1: R_f = 0.12 (hexanes/EtOAc, 9:1); ^{1}H NMR (400 MHz, [D]chloroform) δ/ppm = 8.90 (s, 1H), 8.65–8.55 (m, 2H), 7.50 (dd, $^3J_{H,H}$ = 6.1, 0.4 Hz, 2H), 6.11 (dd, $^3J_{H,H}$ = 17.5, 10.8 Hz, 1H), 5.11–4.90 (m, 2H), 1.54 (s, 6H), 1.49 (s, 9H); ^{13}C NMR (101 MHz, [D]chloroform) δ/ppm = 152.9, 150.3, 147.7, 146.0, 143.8, 121.1, 109.9, 82.8, 64.9, 28.5, 27.6; IR (ATR) $\tilde{\nu}$ = /cm^{-1} = 2977, 2933, 1698, 1590, 1367, 1287, 1246, 1147, 989, 903, 859, 814, 755, 732, 656; HRMS (ESI): *m/z* calcd. for $C_{16}H_{24}N_3O_2$ [M + H]$^+$ 290.1863, found 290.1862.

***tert*-Butyl 1-(2-Methylbut-3-en-2-yl)-2-(3-phenylpropylidene)-hydrazine-1-carboxylate (9p):** Mixture of olefins **8a**/**8b** (237 mg, 1.18 mmol ≙ 1.07 mmol of isomer **8a**) and 3-phenylpropionaldehyde (0.157 mL, 1.18 mmol) gave *N*-Boc-*N*-allylhydrazone **9p** (141 mg, 0.446 mmol, 42 % referred to isomer **8a**) as colourless oil via GP1: R_f = 0.46 (hexanes/EtOAc, 9:1); ^{1}H NMR (400 MHz, [D$_6$]DMSO) δ/ppm = 7.75 (t, $^3J_{H,H}$ = 5.3 Hz, 1H), 7.31–7.22 (m, 4H), 7.18 (m, 1H), 5.99 (dd, $^3J_{H,H}$ = 17.5, 10.8 Hz, 1H), 4.94 (dd, $^3J_{H,H}$ = 17.5, $^2J_{H,H}$ = 1.1 Hz, 1H), 4.86 (dd, $^3J_{H,H}$ = 10.8, $^2J_{H,H}$ = 1.1 Hz, 1H), 2.83 (t, $^3J_{H,H}$ = 7.3 Hz, 2H), 2.59 (ddd, $^3J_{H,H}$ = 7.3, 5.3 Hz, 2H),1.36 (s, 9H), 1.25 (s, 6H); ^{13}C NMR (101 MHz, [D$_6$]DMSO) δ/ppm = 166.7, 153.2, 145.7, 140.9, 128.3, 128.3, 125.9, 109.4, 80.1, 61.1, 33.9, 31.3, 27.9, 26.4; IR (ATR) $\tilde{\nu}$ = /cm^{-1} = 2979, 2929, 1693, 1639, 1455, 1264, 1303, 1241, 1155, 1101, 903, 870, 856, 748; HRMS (ESI): *m/z* calcd. for $C_{19}H_{29}N_2O_2$ [M + H]$^+$ 317.2224, found 317.2229.

***tert*-Butyl 1-(2-Methylbut-3-en-2-yl)-2-((*E*)-3-phenylallylidene)-hydrazine-1-carboxylate (9q):** Mixture of olefins **8a**/**8b** (250 mg, 1.25 mmol ≙ 1.13 mmol of isomer **8a**) and cinnamaldehyde (0.157 mL, 1.25 mmol) gave *N*-Boc-*N*-allylhydrazone **9q** (228 mg, 0.725 mmol, 64 % referred to isomer **8a**) as yellow oil via GP1: R_f = 0.56 (hexanes/EtOAc, 9:1); ^{1}H NMR (500 MHz, [D]chloroform) δ/ppm = 8.33 (dd, $^3J_{H,H}$ = 7.2, 1.5 Hz, 1H), 7.49–7.47 (m, 2H), 7.38–7.33 (m, 2H), 7.32–7.28 (m, 1H), 6.96–6.93 (m, 2H), 6.14 (dd, $^3J_{H,H}$ = 17.5, 10.8 Hz, 1H), 5.07–4.92 (m, 2H), 1.47 (s, 6H), 1.46 (s, 9H); ^{13}C NMR (101 MHz, [D]chloroform) δ/ppm = 161.7, 153.7, 146.2, 140.5, 136.2, 128.9, 128.9, 127.2, 126.0, 109.5, 81.6, 62.9, 28.5, 26.9; IR (ATR) $\tilde{\nu}$ = /cm^{-1} = 1694, 1449, 1366, 1289, 1243, 1148, 1109, 1051, 973, 906, 879, 850, 749, 689; HRMS (ESI): *m/z* calcd. for $C_{19}H_{27}N_2O_2$ [M + H]$^+$ 315.2067, found 315.2066.

General Procedure for the Synthesis of Olefins via [3,3]-Sigmatropic Rearrangement (GP2): In an oven dried two-necked Schlenk flask $HNTf_2$ (10 mol-%) was dissolved in dry diglyme (1 mL). A solution of the appropriate *N*-Boc-*N*-allylhydrazone **9** (1.0 equiv.) in dry diglyme (2 mL + 1 mL rinse) was added at room temperature. The reaction mixture was fitted with a N_2 flashed reflux condenser and immediately heated to 125 °C in a pre-heated oil bath. After completion of the rearrangement detected by TLC (75 min), the reaction was immediately cooled to room temperature via water bath and then quenched with a sat. aq. $NaHCO_3$ solution (4 mL). Pentane (10 mL) was added and the organic layer was washed with at least 100 mL water. The solvent was removed in vacuo (30 °C, max. 700 mbar) and the crude product was purified by flash column chromatography.

2-Methyldodec-2-ene (10a): Allylhydrazone **9a** (155 mg, 0.500 mmol) and $HNTf_2$ (14 mg, 0.050 mmol) gave olefin **10a** (18 mg, 0.099 mmol, 20 %) as colourless oil via GP2: R_f = 0.94 (pentane); ^{1}H NMR (400 MHz, [D]chloroform) δ/ppm = 5.15–5.08 (m, 1H), 1.96 (q, $^3J_{H,H}$ = 7.1 Hz, 2H), 1.69 (d, $^3J_{H,H}$ = 1.4 Hz, 3H), 1.60 (d, $^3J_{H,H}$ = 1.3 Hz, 3H), 1.26 (s, 14H), 0.88 (t, $^3J_{H,H}$ = 2.9 Hz, 3H). ^{13}C NMR (101 MHz, [D]chloroform) δ/ppm = 131.3, 125.1, 32.1, 30.1, 29.8, 29.8, 29.5, 29.5, 28.2, 25.9, 22.9, 17.8, 14.3. IR (ATR) $\tilde{\nu}$ = /cm^{-1} = 2956, 2922, 2853, 1462, 1376, 1094, 985, 886, 833, 722; HRMS (EI): *m/z* calcd. for $C_{13}H_{26}$ [M]$^{\cdot+}$ 182.2029, found 182.2027.

2-Methyltridec-2-ene (10b): Allylhydrazone **9b** (162 mg, 0.500 mmol) and $HNTf_2$ (14 mg, 0.050 mmol) gave olefin **10b**

(19 mg, 0.10 mmol, 21 %) as colourless oil via GP2: R_f = 0.88 (pentane/Et_2O, 9:1); ^{1}H NMR (400 MHz, [D]chloroform) δ/ppm = 5.12 (tdt, $^3J_{H,H}$ = 7.2, 1.5 Hz, 1H), 1.96 (q, $^3J_{H,H}$ = 6.8 Hz, 2H), 1.69 (d, $^3J_{H,H}$ = 1.4 Hz, 3H), 1.60 (d, $^3J_{H,H}$ = 1.3 Hz, 3H), 1.26 (s, 16H), 0.93–0.83 (m, 3H); ^{13}C NMR (101 MHz, [D]chloroform) δ/ppm = 131.3, 125.1, 32.1, 30.1, 29.8, 29.8, 29.8, 29.5, 29.5, 28.2, 25.9, 22.9, 17.8, 14.3; IR (ATR) $\tilde{\nu}$ = /cm^{-1} = 2955, 2922, 2853, 1456, 1376, 1094, 984, 886, 832, 721, 593, 556; HRMS (EI): *m/z* calcd. for $C_{14}H_{28}$ [M]$^{+}$ 196.2185, found 196.2183.

2-Methyltetradec-2-ene (10c): Allylhydrazone **9c** (169 mg, 0.500 mmol) and $HNTf_2$ (14 mg, 0.050 mmol) gave olefin **10c** (21 mg, 0.099 mmol, 20 %) as colourless oil via GP2: R_f = 0.98 (pentane); ^{1}H NMR (400 MHz, [D]chloroform) δ/ppm = 5.12 (ddt, $^3J_{H,H}$ = 7.1 Hz, 1H), 1.96 (q, $^3J_{H,H}$ = 6.9 Hz, 2H), 1.69 (s, 3H), 1.60 (s, 3H), 1.26 (br, 18H), 0.88 (t, $^3J_{H,H}$ = 6.8 Hz, 3H); ^{13}C NMR (101 MHz, [D]chloroform) δ/ppm = 131.3, 125.1, 34.3, 32.1, 30.1, 29.9, 29.8, 29.8, 29.5, 28.2, 25.9, 22.9, 22.5, 17.8, 14.3; IR (ATR) $\tilde{\nu}$ = /cm^{-1} = 2958, 2921, 2850, 1461, 1372, 1260, 1090, 1022, 881, 806, 723; HRMS (EI): *m/z* calcd. for $C_{15}H_{30}$ [M]$^{+}$ 210.2342, found 210.2347.

(4-Methylpent-3-en-1-yl)cyclopentane (10f): Allylhydrazone **9f** (140 mg, 0.500 mmol) and $HNTf_2$ (14 mg, 0.050 mmol) gave olefin **10f** (15 mg, 0.099 mmol, 20 %) as colourless oil via GP2: R_f = 0.95 (pentane); ^{1}H NMR (500 MHz, [D]chloroform) δ/ppm = 5.15–5.10 (m, 1H), 2.01–1.95 (m, 2H), 1.77–1.73 (m, 2H), 1.69 (d, $^3J_{H,H}$ = 1.4 Hz, 3H), 1.60 (d, $^3J_{H,H}$ = 1.2 Hz, 3H), 1.52–1.46 (m, 2H), 1.34–1.30 (m, 2H), 1.11–1.05 (m, 2H), 0.91–0.86 (m, 3H); ^{13}C NMR (126 MHz, [D]chloroform) δ/ppm = 131.1, 125.2, 39.9, 36.6, 32.8, 27.4, 25.9, 25.4, 17.8; IR (ATR) $\tilde{\nu}$ = /cm^{-1} = 2983, 2950, 2922, 2857, 1452, 1376, 1105, 985, 907, 830, 735, 650, 574, 560; HRMS (EI): *m/z* calcd. for $C_{11}H_{20}$ [M]$^{+}$ 152.1559, found 152.1558.

(4-Methylpent-3-en-1-yl)cyclohexane (10g): Allylhydrazone **9g** (147 mg, 0.500 mmol) and $HNTf_2$ (14 mg, 0.050 mmol) gave olefin **10g** (17 mg, 0.10 mmol, 20 %) as colourless oil via GP2. **(4-Methylpent-3-en-1-yl)cyclohexane (10g, 30 mol-% $HNTf_2$).** Allylhydrazone **9g** (127 mg, 0.433 mmol) and $HNTf_2$ (37 mg, 0.13 mmol) gave olefin **10g** (18 mg, 0.11 mmol, 22 %) as colourless oil via GP2. **(4-Methylpent-3-en-1-yl)cyclohexane (10g, 3.00 mmol scale).** Allylhydrazone **9g** (822 mg, 3.00 mmol) and $HNTf_2$ (84 mg, 0.30 mmol) gave olefin **10g** (129 mg, 0.759 mmol, 25 %) as colourless oil via GP2: R_f = 0.91 (pentane); ^{1}H NMR (500 MHz, [D]chloroform) δ/ppm = 5.15–5.00 (m, 1H), 2.03–1.91 (m, 2H), 1.75–1.57 (m, 11H), 1.25–1.15 (m, 6H), 0.92–0.83 (m, 2H); ^{13}C NMR (126 MHz, [D]chloroform) δ/ppm = 131.1, 125.3, 37.8, 37.5, 33.5, 26.9, 26.6, 25.9, 25.5, 17.8; IR (ATR) $\tilde{\nu}$ = /cm^{-1} = 2923, 2852, 1694, 1448, 1376; HRMS (EI): *m/z* calcd. for $C_{12}H_{22}$ [M]$^{+}$ 166.1722, found 166.1720.

(6-Methylhept-5-en-1-yl)benzene (10p): Allylhydrazone **9p** (217 mg, 0.686 mmol) and $HNTf_2$ (14 mg, 0.068 mmol) gave olefin **10p** (25 mg, 0.13 mmol, 19 %) as colourless oil via GP2: R_f = 0.48 (pentane); ^{1}H NMR (400 MHz, dichloromethane-d_2) δ/ppm = 7.29–7.23 (m, 2H), 7.20–7.13 (m, 3H), 5.12 (tdt, $^3J_{H,H}$ = 7.2, 1.5 Hz, 1H), 2.60 (t, $^3J_{H,H}$ = 7.7 Hz, 2H), 2.01 (q, $^3J_{H,H}$ = 7.3 Hz, 2H), 1.68 (d, $^3J_{H,H}$ = 1.4 Hz, 3H), 1.64–1.58 (m, 5H), 1.41–1.33 (m, 2H); ^{13}C NMR (101 MHz, dichloromethane-d_2) δ/ppm = 143.6, 131.8, 128.9, 128.7, 126.1, 125.2, 36.4, 31.8, 30.1, 28.4, 25.9, 17.9; IR (ATR) $\tilde{\nu}$ = /cm^{-1} = 3026, 2922, 2853, 1602, 1494, 1451, 1378, 1108, 1079, 1029, 741, 698, 571; HRMS (EI): *m/z* calcd. for $C_{14}H_{20}$ [M]$^{+}$ 188.1565, found 188.1565.

Keywords: Hydrazones · Isoprenylation · Sigmatropic rearrangement · Traceless bond construction · Triflimide

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