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 utilizing 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 N₂ 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 (HNTf₂).[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]

a) Thomson and co-workers (2010)\[3\]

\[
\begin{align*}
\text{A} \xrightarrow{\text{HNTf}_2 (10 \text{ mol})} \text{B} \\
\text{R}^1 = \text{aryl, alkyl} \\
\text{R}^2 = \text{aryl, R}^3 = \text{H} \text{, one example with R}^2 = \text{H}, \text{R}^3 = \text{Me} \\
\end{align*}
\]

b) Dittrich and Bracher (2015)\[4\]

\[
\begin{align*}
\text{C} \xrightarrow{\text{HNTf}_2 (10 \text{ mol})} \text{D} \\
\text{R}^1 = \text{aryl, alkyl} \\
\text{R}^2 = \text{aryl} \\
\end{align*}
\]

c) Dittrich and Bracher (2015)\[5\]

\[
\begin{align*}
\text{E} \xrightarrow{\text{HNTf}_2 (10 \text{ mol})} \text{F} \\
\text{R}^1 = \text{aryl, alkyl} \\
\end{align*}
\]

d) This work: Introduction of an isoprenyl group via TBC:

\[
\begin{align*}
\text{G} \xrightarrow{\text{HNTf}_2 (10 \text{ mol})} \text{I} \\
\text{H} \xrightarrow{\text{HNTf}_2 (10 \text{ mol})} \text{I} \\
\text{R}^1 = \text{aryl, alkyl} \\
\end{align*}
\]

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

At the biological level, protein prenyltransferrases attach terpenoid residues like farnesyl (C15) or geranylgeranyl (C20) 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. In synthetic chemistry, organo-metallic building blocks like 3-methyl-2-butenylmagnesium bromide can be applied as an electrophilic isoprenyl building block as exemplified by the total synthesis of an isoprenylated protein.

Utilising inverse reactivities, 3,3-dimethylallyl chloride are commonly used for the introduction of an isoprenyl group. Utilising inverse reactivities, 3,3-dimethylallyl chloride can be applied as an electrophilic isoprenyl building block as exemplified by the total synthesis of an isoprenylated protein. Moreover, isoprene building block, e.g. from tertiary alcohols by dehydration. 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)hydrazone building block, bearing two geminal methyl groups in α-position to the hydrazone moiety to receive the desired isoprenylated products. In our previous investigations leading to 1,1-disubstituted olefins undesired subsequent acid-catalysed isomerisations of the formed olefinic double bond were observed, 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 is on the one hand that product 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).

As a result, less drastic reaction temperatures and shortened reaction times may be employable.

### Results and Discussion

The synthesis of the required N-Boc-N-(1,1-dimethylallyl)hydrazone building block was started with the two-step synthesis of known N-Troc-N-Boc-protected di-azene. Conversion into aldehyde was performed on two different routes. Route A used commercially available silyl enol ether, which was activated by LiOTf and TBAF. The idea was to achieve a controlled O-Si-bond cleavage in 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 and its regioisomer 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 starting from aldehyde . The ratios of the isomers were determined retrospectively by NMR spectroscopy of the desired aldehyde and its regioisomer . Methylation of the aldehyde function of gave the olefins and . Different methods like Wittig, Nysted-Takai and Tebbe olefination were tested, whereby the first two methods did not result in any product. Under Tebbe conditions the desired terminal olefin and its regioisomer were obtained in an acceptable yield of 48% as an inseparable mixture.

![Scheme 2](image-url)

Scheme 2. Route A leading to an equimolar mixture of starting from silyl enol ether. Route B provides starting from aldehyde . The ratios of the isomers were determined retrospectively by NMR spectroscopy of the product . The X-ray crystal structure of the desired isomer is shown on the left. Diazene was synthesised according to literature.

Chemoselective reductive Troc cleavage with zinc powder gave a still inseparable mixture of the desired olefin and its constitutional isomer in excellent yield. However, at this stage NMR spectroscopy enabled determination of the ratio of...
isomers (route A 50:50, route B 91:9). The structure of the desired N-Boc-N-allyldrazine 8a was unambiguously confirmed by X-ray crystal structure analysis (see Supporting Information). The enriched isomeric mixture of building block mixture 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-allyldrazones 9, whereas the isomer 8b remains unreacted. Scheme 3 shows the prepared allyldrazones 9a–q. Aliphatic (9a–d, 9f, 9g, 9p), aliphatic (9h, 9q) and aromatic (9i–9o) and ester-bearing (9e) are allyldrazones were synthesised by reacting the appropriate aldehydes with building block mixture 8a/b in ethanol (yields 33–95 %). Especially non-conjugated allyldrazones slowly decomposed during the purification process, which is reflected in the yields. Before we studied the capability of our N-Boc-N-allyldrazine building block 8a, we identified the optimum reaction conditions for the rearrangement utilising cyclohexanecarboxaldehyde-derived hydrazine 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 (TFA, 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$_2$, 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 allyldrazones 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-allyldrazine 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 allyldrazylhydrazine was found.
which were identified as the symmetric bis-hydrazones 12a/b (Scheme 5).

\[\text{Scheme 5. Attempted rearrangements of allylhydrazones 9i and 9j leading to deprotected allylhydrazones 11a/b and bis-hydrazones 12a/b.}\]

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 9i) 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-allylhydrazones 9p derived from phenylpropanol showed a successful rearrangement with 19% yield, whereas its cinnamaldehyde-derived congener 9q did not give the desired alkene 10q and only Boc-deprotected allylhydrazones 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 methylation. 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 x 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\(^{\text{TM}}\) Prodigy. Chemical shifts \(\delta\) are reported as \(\delta\) values in ppm relative to the deuterated solvent peak. The chemical shifts are reported in parts per million [ppm] and refer to the \(\delta\) scale. 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, Flawil, 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 Workstast 6.9 SP1 software (Darmstadt, Germany). A Varian VF-5ms 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 \(m/z\) SO–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\(_\alpha\) rotating-anode X-ray tube (\(\lambda = 0.71073\) 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 CHCl₃ (20 mL) was cooled to -50 °C.

A solution of diazene 2 (1.70 g, 5.56 mmol, 1.5 equiv.) in CHCl₃ (10 mL), 2-methyl-1-(trimethylsiloxyl)-propene (3) (533 mg, 3.70 mmol, 1.0 equiv.) in CHCl₃ (10 mL) was added, followed by TBAF (1M 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. NaHSO₃ solution (10 mL) and the layers were separated. The organic layer was washed with aq. sat. NaHCO₃ solution (10 mL) and dried with MgSO₄, filtered and the solvent was removed in vacuo. Purification by flash column chromatography. Isolated yields are correlated to the amount of material.

The mixture of 91:9 (determined retrospectively via 1H NMR): δ ppm = 9.49 (s, 1H), 6.70 (s, 1H), 4.93–4.51 (m, 2H), 1.44 (s, 9H), 1.33 (s, 6H); 13C NMR δ ppm = 198.1, 155.4, 154.3, 94.9, 84.3, 75.2, 67.4, 28.2, 20.5; IR (ATR) ν = /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 C₁₂H₁₈Cl₃N₂O₅ [M–H] – 375.0287, found 375.0287.

**tert-Butyl 1-(2-Methylbut-3-yl)hydrazine-1-carboxylate (8a)** and **tert-Butyl 2-(2-Methylbut-3-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 (2 × 3 mL) and the residue was extracted. The combined organic layers were washed with saturated aqueous NaHCO₃ solution (5 mL) and the organic layer was dried with MgSO₄, filtered and the solvent was removed in vacuo. The product was used without purification.

**General Procedure 1 (GP1) for the Synthesis of N-Benzyl-(1,1-Dimethylyl)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-yl)hydrazine-1-carboxylate (9a):** Mixture of aldehydes 8a/8b (250 mg, 1.75 mmol) was dissolved in EtOH (1.59 mmol of isomer 8a) and octanal (0.298 mL, 1.75 mmol) gave N-Boc-N-allylhydrazine 9a (178 mg, 0.576 mmol, 36 % referred to isomer 8a) as colourless oil via GP1: Rf = 0.58 (hexanes/EtOAc, 9:1); 1H NMR (500 MHz, [D]chloroform) δ/ppm = 6.68 (s, 1H), 6.10 (dd, J = 17.4, 11.0 Hz, 1H), 5.08 (dd, J = 11.5, 10.9 Hz, 1H), 4.87 (dd, J = 11.5, 10.9 Hz, 1H), 4.68 (dd, J = 11.8 Hz, 1H, 1.50 (s, 3H), 1.44 (s, 9H), 1.42 (s, 3H); 13C 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, 24.4; IR (ATR) ν = /cm–1 = 3323, 2924, 2854, 1733, 1706, 1642, 1542, 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 C₁₉H₂₄NO₇ [M + H] + 373.0494, found 373.0499.
(hexanes/EtOAc, 9:1); 1H NMR (500 MHz, [D]chloroform) δ/ppm = 7.71 (t, J=4.2 Hz, 1H), 6.11 (dd, J=4.2, 17.5 Hz, 1H), 5.05–4.89 (m, 2H), 2.34 (td, J=4.2, 17.5 Hz, 2H), 1.55 (m, 2H), 1.42 (s, 9H), 1.39 (s, 9H), 1.36–1.21 (m, 10H), 0.89–0.85 (m, 3H); 13C NMR (101 MHz, [D]chloroform) δ/ppm = 176.2, 154.2, 146.2, 109.4, 80.8, 61.8, 42.9, 30.3, 28.6, 28.5, 26.6, 25.7; IR (ATR) ν = cm⁻¹ = 3084, 2968, 2956, 2869, 1697, 1639, 1476, 1454, 1412, 1390, 1366, 1304, 1244, 1156, 1101, 1003, 992, 900, 877, 856, 783, 757, 687; HRMS (ESI): m/z calcd. for C₁₉H₂₀N₂O₂ [M + H⁺] = 325.2849, found 325.2849.

tert-Butyl 2-Decylidene-1-(2-methylbut-3-en-2-yl)hydrazine-1-carboxylate (9c): Mixture of olefins 8a/8b (115 mg, 0.57 mmol) gave N-Boc-N'-allylhydrazine 9c (56 mg, 0.17 mmol, 33 % referred to isomer 8a) as colourless oil via GP1: R₁ = 0.56 (hexanes/EtOAc, 9:1); 1H NMR (500 MHz, [D]chloroform) δ/ppm = 7.71 (t, J=4.2 Hz, 1H), 6.11 (dd, J=4.2, 17.5 Hz, 1H), 5.01 (dd, J=4.2, 17.5 Hz, 0.7 Hz, 1H). 4.92 (dd, J=4.2, 17.5 Hz, 0.7 Hz, 1H), 2.35 (td, J=4.2, 17.5 Hz, 2H), 1.57–1.54 (m, 2H), 1.42 (s, 9H), 1.39 (s, 9H), 1.26 (m, 12H), 0.89–0.85 (m, 3H); 13C NMR (126 MHz, [D]chloroform) δ/ppm = 169.5, 159.4, 146.3, 109.4, 80.9, 61.7, 33.0, 32.0, 29.5, 29.4, 29.3, 28.5, 26.7, 26.2, 22.8, 14.2; IR (ATR) ν = cm⁻¹ = 3084, 2972, 2956, 2926, 2856, 1698, 1640, 1455, 1412, 1390, 1366, 1304, 1224, 1157, 1100, 1003, 992, 900, 877, 856, 753, 687, 599; HRMS (ESI): m/z calcd. for C₂₀H₃₉N₂O₂ [M + H⁺] = 339.3006, found 339.3011.

tert-Butyl 1-(2-Methylthio-3-phenyl-1-naphthalenyl)-1-phenylhydrazine-1-carboxylate (9d): Mixture of olefins 8a/8b (196 mg, 0.99 mmol) gave N-Cbz-N'-allylhydrazine 9d (62 mg, 0.13 mmol, 103 mmol % referred to isomer 8a) as colourless oil via GP1: R₁ = 0.55 (hexanes/EtOAc, 9:1); 1H NMR (400 MHz, [D]chloroform) δ/ppm = 7.61 (t, J=4.2 Hz, 1H), 6.01 (dd, J=4.2, 17.5 Hz, 1H), 5.03–4.90 (m, 2H), 2.67–2.56 (m, 2H), 1.42 (s, 9H), 1.39 (s, 9H), 1.27 (s, 3H), 1.13 (s, 6H); 13C NMR (101 MHz, [D]chloroform) δ/ppm = 173.2, 151.4, 146.3, 109.4, 80.9, 61.9, 32.2, 16.6, 26.1, 19.6; IR (ATR) ν = cm⁻¹ = 3086, 2908, 2932, 2930, 2872, 1698, 1641, 1456, 1346, 1390, 1366, 1304, 1289, 1244, 1156, 1092, 958, 992, 970, 892, 856, 756, 686, 599, 588; HRMS (ESI): m/z calcd. for C₁₉H₂₀N₂O₂ [M + H⁺] = 339.3006, found 339.2993.

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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 \( \pm \) 0.454 mmol of isomer 8a) and 4-dimethylaminobenzaldehyde (74.5 mg, 0.499 mmol) gave N-Boc-N-allylhydrazine 9 (143 mg, 0.431 mmol, 95 % referred to isomer 8a) as white crystalline solid via GP1: \( R_1 = 0.35 \) (hexanes/\( \text{EtOAc} \), 9:1); m.p. 73–75 °C; \( \nu \text{cm}^{-1} = 2975, 2922, 1742, 1708, 1585, 1369, 1282, 1150, 1094, 886, 833, 722; \) HRMS (ESI): m/z calc’d for \( \text{C}_{19}\text{H}_{30}\text{N}_3\text{O}_2 [M + H]^+ \) 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 \( \pm \) 1.07 mmol of isomer 8a) and 3-phenylpropionaldehyde (0.157 mmol, 1.18 mmol) gave N-Boc-N-allylhydrazine 9 (141 mg, 0.446 mmol, 42 % referred to isomer 8a) as colourless oil via GP1: \( R_1 = 0.46 \) (hexanes/\( \text{EtOAc} \), 9:1); \( \nu \text{cm}^{-1} = 2977, 2933, 1698, 1590, 1367, 1287, 1246, 1147, 989, 853, 815, 755, 731; \) HRMS (ESI): m/z calc’d for \( \text{C}_{19}\text{H}_{26}\text{N}_2\text{O}_2 [M + H]^+ \) 292.1222, found 292.1222.
(19 mg, 0.10 mmol, 21 %) as colourless oil via GP2: \( R_t = 0.88 \) (pentane/toluene, 9:1); \( ^1H \) NMR (400 MHz, [D]chloroform) \( \delta/\text{ppm} = 5.12 \) (ddt, \( 3J_{CH} = 7.2, 1.5 \text{ Hz}, 1J_{CH} = 1.96 \) (q, \( 3J_{CH} = 6.8 \text{ Hz}, 2H), 1.69 \) (d, \( 3J_{CH} = 1.4 \text{ Hz}, 3H), 1.60 \) (d, \( 3J_{CH} = 1.3 \text{ Hz}, 3H), 1.26 \) (16H), 0.93–0.83 \( (3J_{CH} = 1.3 \text{ Hz}, 3H), 0.92–0.83 \) (m, 2H); \( ^13C \) NMR (126 MHz, [D]chloroform) \( \delta/\text{ppm} = 131.3, 125.1, 32.1, 30.1, 29.8, 29.8, 29.9, 29.5, 28.2, 25.9, 22.9, 17.8, 14.3; IR (ATR) \( \nu = 1311, 1231, 1436, 1376, 1246, 1270, 1109, 1042, 984, 886, 832, 721, 593, 556; \) HRMS (EI): \( m/z \) calcd. for \( C_{14}H_{28} \text{[M]+} 210.2185, \) found 210.2183.

2-Methyltetradec-2-ene (10c): Allylhydrazone \( \text{HC} \) (169 mg, 0.500 mmol) and HNTf₂ (14 mg, 0.050 mmol) gave olefin \( 10c \) (21 mg, 0.099 mmol, 20 %) as colourless oil via GP2: \( R_t = 0.95 \) (pentane); \( ^1H \) NMR (500 MHz, [D]chloroform) \( \delta/\text{ppm} = 1.17–1.73 \) (m, 2H), 1.69 \( (3J_{CH} = 1.4 \text{ Hz}, 3H), 1.60 \) (d, \( 3J_{CH} = 1.2 \text{ Hz}, 3H), 1.52–1.46 \) (m, 2H), 1.34–1.30 \( (3J_{CH} = 1.2 \text{ Hz}, 3H), 1.11–1.05 \) (m, 2H), 0.91–0.86 \( (3J_{CH} = 1.2 \text{ Hz}, 3H)\); \( ^13C \) NMR (126 MHz, [D]chloroform) \( \delta/\text{ppm} = 131.1, 125.2, 39.9, 36.2, 32.8, 27.4, 25.9, 17.8; IR (ATR) \( \nu = 2983, 2950, 2922, 2857, 1452, 1376, 1105, 985, 907, 830, 735, 650, 574, 560; \) HRMS (EI): \( m/z \) calcd. for \( C_{14}H_{20} \text{[M]+} 188.1565, \) found 188.1565.

2,6-Dimethyltetradec-2-ene (10d): Allylhydrazone \( \text{HC} \) (18 mg, 0.11 mmol) gave olefin \( 10d \) (19 mg, 0.099 mmol, 20 %) as colourless oil via GP2: \( R_t = 0.97 \) (pentane/toluene, 9:1); \( ^1H \) NMR (500 MHz, [D]chloroform) \( \delta/\text{ppm} = 1.18–1.73 \) (m, 2H), 2.01–1.95 \( (3J_{CH} = 1.4 \text{ Hz}, 3H), 1.69 \) (q, \( 3J_{CH} = 6.9 \text{ Hz}, 2H), 1.69 \) (s, 3H), 1.60 \( (3J_{CH} = 1.2 \text{ Hz}, 3H), 1.52–1.46 \) (m, 2H), 1.34–1.30 \( (3J_{CH} = 1.2 \text{ Hz}, 3H), 1.11–1.05 \) (m, 2H), 0.91–0.86 \( (3J_{CH} = 1.2 \text{ Hz}, 3H)\); \( ^13C \) NMR (126 MHz, [D]chloroform) \( \delta/\text{ppm} = 131.1, 125.2, 39.9, 36.2, 32.8, 27.4, 25.9, 17.8; IR (ATR) \( \nu = 2983, 2950, 2922, 2857, 1452, 1376, 1105, 985, 907, 830, 735, 650, 574, 560; \) HRMS (EI): \( m/z \) calcd. for \( C_{15}H_{30} \text{[M]+} 210.2342, \) found 210.2347.

2850, 1461, 1250, 1094, 984, 886, 832, 721, 593, 556; HRMS (EI): \( m/z \) calcd. for \( C_{15}H_{30} \text{[M]+} 188.1565, \) found 188.1565.

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

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