Tetrahedron: *Asymmetry* 24 (2013) 817–821

Contents lists available at SciVerse ScienceDirect

Tetrahedron: *Asymmetry*

journal homepage: www.elsevier.com/locate/tetasy

# Rearrangement of chiral 1-bromo-*N*-nitrobicyclo[2.2.1]heptan-2-imines

Oleksandr V. Grytsai [a], Marian V. Gorichko [a,*], Vladimir B. Golovko [b,*]

[a] *Department of Chemistry, Taras Shevchenko National University of Kyiv, 01601, Ukraine*
[b] *Department of Chemistry, University of Canterbury, P.B. 4800, Christchurch 8140, New Zealand*

ARTICLE INFO

*Article history:*
Received 15 April 2013
Accepted 13 June 2013

ABSTRACT

The regio- and diastereospecific Wagner-Meerwein-type rearrangements of the potassium cyanide adducts of camphor-derived substituted 1-bromo-*N*-nitrobicyclo[2.2.1]heptan-2-imines under acidic conditions have been investigated. The selective formation of bromonorbornene derivatives has been demonstrated in the case of rearrangements involving intermediate α-bromocarbocations containing vicinal hydrogen atoms. In all other cases, hydrolysis of the intermediates resulted in the formation of a carbonyl group. The simplicity of this transformation opens up a novel and straightforward synthetic pathway to enantiopure derivatives of bridgehead-substituted norbornane carboxamides in just three steps, starting from 1-bromonorbornanones.



## 1. Introduction

Nitroimines constitute a relatively unexplored class of compounds due to the carbon atom of the nitroimine group having high electrophilicity, which is significantly greater than that of the carbon atom of the carbonyl group. Such high electrophilicity leads to high reactivity of the nitroimine functional group. Hydrolysis to the parent carbonyl compounds is the simplest example of this phenomenon.[1a–e] Moreover, compounds containing a hydrogen atom at the α-position relative to the nitroimine functional group have a strong propensity to undergo a range of condensation reactions.

More than 100 years ago Angeli and Rimini reported on the preparation of 'pernitrosocamphor', probably the first example of a nitroimine described in the literature.[2] Impressively, it took 65 years to elucidate its structure as that of 1,7,7-trimethyl-*N*-nitrobicyclo[2.2.1]heptane-2-imine, another indirect indication of the very high reactivity of this class of compounds.[3] The vast majority of relatively stable nitroimines are stabilized either by the presence of nearby substituents with substantial steric demands leading to efficient shielding[4] or the influence of functional groups with pronounced positive mesomeric effects[5a,5b] capable of reducing the reactivity of the C=N-$NO_2$ group.

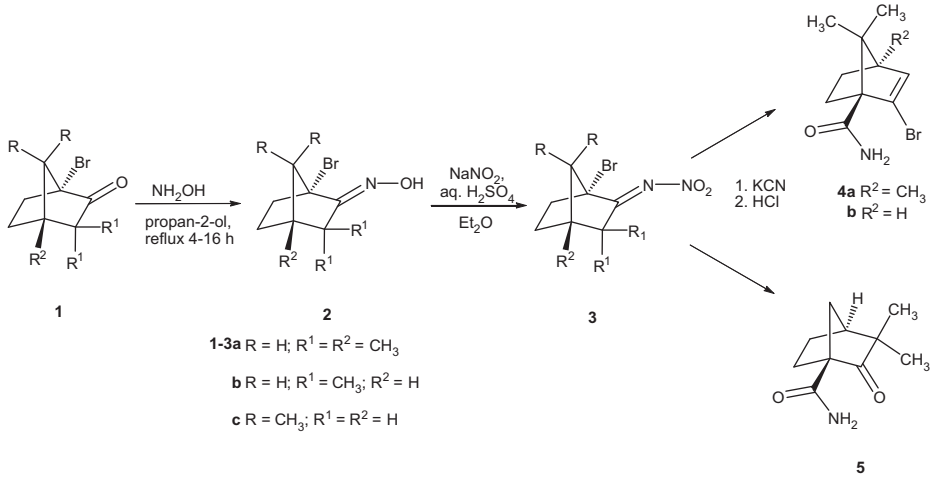
Nitroimines are often used in the synthesis of azomethines ($R^1R^2C{=}NR^3$), hydrazones ($R^1R^2C{=}NNR^3R^4$), and thiocarbonyls ($R^1R^2C{=}S$) *via* substitution of the =N-$NO_2$ moiety by reaction with a primary amine, hydrazine, or hydrogen sulfide, which takes place under much milder conditions compared to reactions involving the carbonyl analogues as starting compounds. The synthesis of conformationally restricted ligands for catalytic asymmetric addition to aldehydes was recently achieved using this synthetic pathway starting from naturally occurring chiral compounds with a norbornyl skeleton.[6] The use of this synthetic methodology enabled the synthesis of enantiopure imidazoline carbene ligands,[7] enantiomerically enriched *vic*-amino alcohols,[8] bornane-derived push-pull butadienes,[9] and the first ever synthesis of stable enantiopure chiral N-H oxaziridines.[10] The syntheses of compounds with antiarrhythmic, local anesthetic, and hypotensive activities[11,12] were recently reported by starting from norbornane nitroimine-derivatives using this approach. High yields and excellent selectivities are common for most of the reactions mentioned above because water and nitrous oxide are the only significant by-products. Sometimes, the loss of the $N_2O$ moiety leads to formation of the carbocationic intermediates, which could react further depending on their structure.[13]

## 2. Results and discussion

Herein we have selected three chiral norbornanones: (1*R*,4*R*)-1-bromo-3,3,4-trimethylbicyclo[2.2.1]heptan-2-one **1a**;[14a,14b] (1*R*,4*R*)-1-bromo-3,3-dimethylbicyclo[2.2.1]heptan-2-one **1b**;[15] and (1*R*,4*S*)-1-bromo-7,7-dimethylbicyclo[2.2.1]heptan-2-one **1c**[16] (Scheme 1), with an α-bromine atom in a bridgehead position which could be easily prepared in both enantiomeric forms starting from a readily accessible naturally occurring material, camphor.

* Corresponding authors. Tel.: +6433642442; fax: +44 1223336033.
*E-mail addresses:* fenchone@gmail.com (O.V. Grytsai), gorichko@chem.univ.kiev.ua (M.V. Gorichko), vladimir.golovko@canterbury.ac.nz (V.B. Golovko).

0957-4166/$ - see front matter © 2013 Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.tetasy.2013.06.001




**Scheme 1.** Synthesis of bromonitroimines 3a-c and rearrangements of the corresponding α-cyanonitroamine salts under acidic conditions.

We synthesized stable nitroimine-derivatives **3a-c** of the bromonorbornanones **1a-c** as model starting materials in order to study the acid-induced rearrangement processes of the corresponding α-cyanonitroamines. We recently reported on a detailed study of intramolecular cyclization reactions of 8-bromo substituted camphor nitroimines under similar reaction conditions.[17] However, in the case of our selected compounds, we expected to observe the formation of both products of the rearrangements of carbocationic intermediates as well as products of the intramolecular nucleophilic substitution of a bromine atom.

Despite the significant steric hindrance, the carbonyl groups in compounds **1a-c** could be converted into the corresponding oximes in good yields by heating the starting ketones with hydroxylamine in pyridine. However, in the case of tri-methyl-substituted compound **1a**, this transformation required a longer reaction time (16 hours). Oximes **2a-c** readily yielded the corresponding nitroimine-derivatives **3a-c** upon treatment with nitrous acid generated *in situ* in a mixture of water and ether.

The reaction of unsubstituted camphor-*N*-nitroimine **6** with the cyanide anion resulted in the formation of camphene-1-carboxamide **10** *via* the mechanism illustrated in Scheme 2, according to an earlier report by Kocienski and Kirkup.[13]

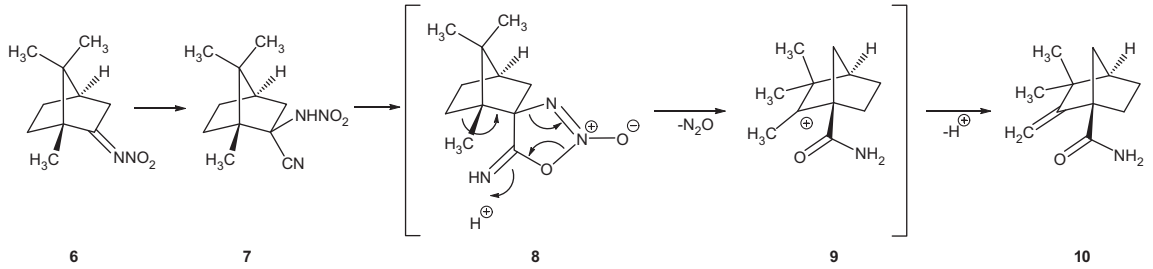
First, the cyanonitramine **7** is generated in virtually quantitative yield *via* the *endo*-addition of the cyanide anion. It is unstable under acidic conditions, and gradually decomposes with the evolution of $N_2O$ from intermediate **8**, which, upon Wagner-Meervein rearrangement, yields a relatively stable tertiary carbocation **9**. Decomposition of the carbocation **9** by the loss of a proton from the nearby methyl group results in formation of the corresponding exocyclic alkene **10**.

The reactivity of brominated derivatives of camphor in this rearrangement could be somewhat different due to the geometric and electronic effects imposed by the bromo-substituents introduced onto the norbornane skeleton, which should affect the stability of the corresponding intermediates. In the case of the nitroimines **3a-c** reported here, the Wagner-Meervein rearrangement yields the formation of the analogous intermediates **12** in which the bromo-substituent is located exactly at the cationic carbon atom (Scheme 3).

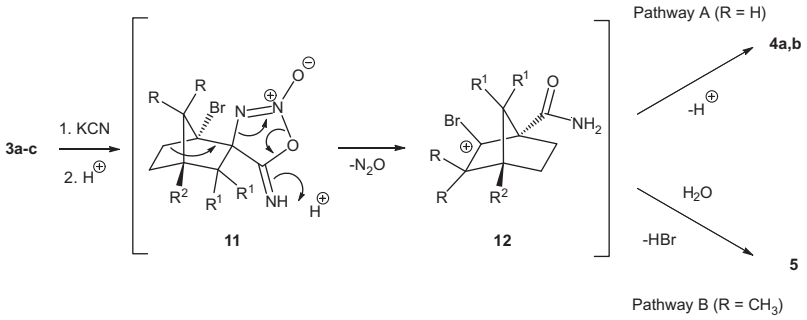
The reactivity of such intermediates appears to be defined by the nature of the other substituents, particularly the R-groups at the nearby *vic*-carbon atom. The presence of a hydrogen at the carbon atom in a vicinal position relative to the carbocation enables its elimination (as a proton) to yield the corresponding bromo-substituted endocyclic alkenes (Scheme 3, Pathway A). Thus, starting from nitroimines **3a** and **3b**, we obtained the corresponding amides (1*R*,4*R*)-2-bromo-4,7,7-trimethylbicyclo-[2.2.1]hept-2-ene-1-carboxamide **4a** and (1*R*,4*R*)-2-bromo-7,7-dimethylbicyclo[2.2.1]hept-2-ene-1-carboxamide **4b** with high yields and selectivity. Only in cases when such elimination is impossible (R = $CH_3$) does the resulting intermediate carbocation react with solvent ($H_2O$) and, after elimination of HBr, form a carbonyl group (Scheme 3, Pathway B). This pathway is illustrated by the reaction of nitroimine **3c**, which under similar conditions, yields (1*S*,4*S*)-3,3-dimethyl-2-oxobicyclo[2.2.1]heptane-1-carboxamide **5**.

The structure of bromo-substituted alkene **4b** was confirmed by using single-crystal X-ray diffraction in order to remove any doubt about potential simultaneous skeletal rearrangements during its formation (Fig. 1).

Compound **5** was prepared independently *via* an alternative pathway starting from the corresponding keto-acid[18] in order to confirm that our assignment of the structure of the rearrangement product of nitroimine **3c** was correct. Compound **5** was prepared by starting from the corresponding keto-acid[18] *via* treatment with thionyl chloride followed by reaction with aqueous ammonia at 0 °C.




**Scheme 2.** Synthesis of camphene-1-carboxamide *via* a Wagner-Meervein rearrangement of cyan nitroamine.




**Scheme 3.** Proposed mechanism of formation of **4a,b** and **5**.

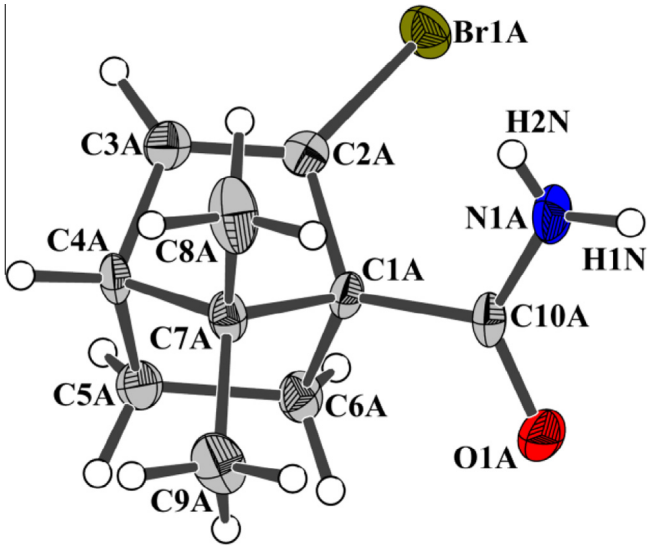



**Fig. 1.** X-Ray crystal structure of (1*R*,4*R*)-2-bromo-7,7-dimethylbicyclo[2.2.1]hept-2-ene-1-carboxamide **4b** showing 50% probability displacement ellipsoids.

The availability of two alternative, highly selective, and high yielding pathways for the rearrangement of intermediate carbocations precisely controlled by the choice of substituents makes the synthetic strategy reported herein particularly attractive for the development of libraries of chiral building blocks for wide ranging applications.

## 3. Conclusion

Precise control over the rearrangement of derivatives of chiral 1-bromo-*N*-nitroiminonorbornanes can be achieved *via* the choice of substituents within a norboranone skeleton. The simplicity of these transformations opens up a novel and straightforward synthetic pathway to enantiopure derivatives of bridgehead norbornane carboxamides in just three steps, starting from 1-bromonorbornanones. The described route constitutes a model procedure for the preparation of a library of norbornane-based functionalized compounds for a wide range of applications.

## 4. Experimental

### 4.1. General

All experiments, unless otherwise stated, were carried under an argon atmosphere. The $^{1}$H and $^{13}$C NMR spectra were recorded on 'Mercury 400' Varian and Bruker AM 400 (400 MHz) spectrometers. Tetramethylsilane was used as the internal standard. IR spectra were obtained on a Perkin Elmer BX II spectrometer. λ max ($cm^{-1}$) values in IR spectra are given for the main absorption bands. Mass spectra were recorded on an R 10-10 C Nermag (70 eV) quadrupolar spectrometer using desorption chemical ionization (DCI), electrospray (ES), or fast atomic bombardment (FAB) techniques. Optical rotations were measured using a sodium D line on P-2000 series Jasco, PTC-262 polarimeter. Melting points are uncorrected. All crystallographic measurements were performed at room temperature on a Bruker Smart Apex II diffractometer operating in the ω and φ scans mode. The structure was solved by direct methods and refined by the full-matrix least-squares technique in the anisotropic approximation for non-hydrogen atoms using the Bruker SHELXTL program package.[19] Full crystallographic data for the structure of **4b** have been deposited with the Cambridge Crystallographic Data Centre under registration number 927999. Copy of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44 1223336033 or e-mail: deposit@ccdc.cam.ac.uk).

#### 4.1.1. Materials

All starting materials were purchased from Acros, Merck, Aldrich and Fluka chemicals. All solvents were distilled before use.[20] Ketones **1a-c** were synthesized by starting from camphor following literature procedures and completely characterized using $^{1}$H and $^{13}$C NMR, MS, and C,H,N analysis *etc.* with all obtained results fitting previously reported literature data (details are not reported here).[14–16]

### 4.2. Synthesis of 1-bromo-bicyclo[2.2.1]heptan-2-one oximes (general procedure)

A single-necked, round-bottomed flask equipped with a magnetic stirring bar was charged with 1 mmol of ketone **1a-c**, 2 mmol (0.139 g) of pyridine and 1.5 mmol (0.119 g) of hydroxylamine hydrochloride in 50 mL of dry isopropanol. The mixture was stirred for 4 hours at reflux (in the case of **1a**, 16 hours), and the solvent was removed under reduced pressure at 40 °C. Dichloromethane (100 mL) and 0.1M hydrochloric acid (50 mL) were added to the resulting solid and the organic phase was separated and washed with 3 × 50 mL of distilled water. The organic phase was dried over magnesium sulfate, filtered, and concentrated by rotary evaporation. The product can be used in the next step without additional purification. An analytical sample can be prepared by recrystallization from isopropanol.

#### 4.2.1. (1*R*,4*R*)-1-Bromo-3,3,4-trimethylbicyclo[2.2.1]heptan-2-one oxime 2a

This compound was obtained from (1*R*,4*R*)-1-bromo-3,3,4-trimethylbicyclo[2.2.1]heptan-2-one **1a** in 86% yield. Mp: 201−203 °C. $[\alpha]_D^{20} = -38.0$ (*c* 0.88, $CHCl_3$). $^{1}$H NMR (400.45 MHz, [$D_6$]DMSO): δ = 1.01 (s, 3H); 1.20 (s, 3H); 1.22 (s, 3H); 1.53 (td, *J* = 12.6, 5.2 Hz, 1H);

1.79–1.97 (m, 3H); 2.09 (d, $J$ = 9.9 Hz, 1H); 2.19 (td, $J$ = 12.6, 3.2 Hz, 1H); 10.37 (s, 1H). $^{13}$C {$^{1}$H} NMR (75 MHz, $CDCl_3$): $\delta$ = 15.12, 19.30, 19.65, 33.87, 39.69, 45.85, 48.08, 51.27, 60.80, 167.17. IR (KBr, $cm^{-1}$): 3272, 3154, 2872, 2929, 2949, 2974, 1549. HRMS (CI, $CH_4$): calculated: 246.0494; found: 246.0505

#### 4.2.2. (1*R*,4*R*)-1-Bromo-3,3-dimethylbicyclo[2.2.1]heptan-2-one oxime 2b

This compound was obtained from (1*R*,4*R*)-1-bromo-3,3-dimethylbicyclo[2.2.1]heptan-2-one **1b** in 94% yield. Mp: 222–223 °C. $[\alpha]_D^{20} = -59.6$ ($c$ 0.87, $CHCl_3$). $^{1}$H NMR (400.45 MHz, [$D_6$]DMSO): $\delta$ = 1.29 (s, 6H), 1.705–1.94 (m, 5H), 2.10 (td, $J$ = 12.1, 3.4 Hz, 1H), 2.19 (d, $J$ = 9.6 Hz, 1H), 10.34 (s, 1H). $^{13}$C {$^{1}$H} NMR (75 MHz, $CDCl_3$): $\delta$ = 22.14, 23.06, 38.10, 26.13, 44.08, 46.23, 47.07, 61.35, 166.30. IR (KBr, $cm^{-1}$): 3275, 3165, 2890, 2949, 2989, 1452. HRMS (CI, $CH_4$): calculated: 232.0337; found: 232.0344.

#### 4.2.3. (1*R*,4*S*)-1-Bromo-7,7-dimethylbicyclo[2.2.1]heptan-2-one oxime 2c

This compound was obtained from (1*R*,4*S*)-1-bromo-7,7-dimethylbicyclo[2.2.1]heptan-2-one **1c** in 91% yield. Mp: 190–191 °C. $[\alpha]_D^{20} = -49.3$ ($c$ 0.85, $CHCl_3$). $^{1}$H NMR (400.45 MHz, [$D_6$]DMSO): $\delta$ = 0.92 (s, 3H); 1.05 (s, 3H); 1.34–1.43 (m, 1H); 1.95–2.07 (m, 3H); 2.18–2.30 (m, 2H); 2.63–2.71 (m, 1H); 9.7 (br s, 1H). $^{13}$C {$^{1}$H} NMR (75 MHz, $CDCl_3$): $\delta$ = 163.52, 70.17, 50.47, 40.44, 36.14, 33.32, 28.44, 19.80, 18.83. IR (KBr, $cm^{-1}$): 3304, 2890, 2935, 2965, 2983,1437. HRMS (CI, $CH_4$): calculated: 232.0337; found: 232.0349.

### 4.3. Synthesis of *N*-nitroimines (general procedure)

To a solution of 1 mmol oxime **2a-c** in dry ether was added a concentrated aqueous solution of 2.4 mmol (0.166 g) of sodium nitrite. Concentrated sulfuric acid (1 mmol, 0.096 g) diluted to a 20% aqueous solution was then added cautiously over 10 min with vigorous swirling. The ether layer turned brown within 10 minutes from the start of the addition of the acid. The ether layer was separated and solvent was removed on a rotary evaporator with the water bath temperature not exceeding 40 °C. Complete removal of the ether coincided with the disappearance of the brown coloration. Next, crude *N*-nitroimine was dissolved in dichloromethane (50 mL) washed with distilled water three times, dried over magnesium sulfate, and filtered. The solvent was removed by rotary evaporation with the water bath temperature not exceeding 40 °C. The compounds obtained can be used in the next step without further purification.

#### 4.3.1. (1*R*,4*R*)-1-Bromo-3,3,4-trimethyl-*N*-nitrobicyclo[2.2.1]heptan-2-imine 3a

This compound was obtained as a mixture of *syn*- and *anti*-isomers (1: 1) from (1*R*,4*R*)-1-bromo-3,3,4-trimethylbicyclo[2.2.1]-heptan-2-one oxime **2a** in 90% yield. Mp: 144–146 °C. $[\alpha]_D^{20} = -65.3$ ($c$ 0.86, $CHCl_3$). $^{1}$H NMR (300 MHz, $CDCl_3$): $\delta$ = 1.28 (s, 3H); 1.05 (s, 3H); 1.10 (s, 3H); 1.14 (s, 3H); 1.16 (s, 3H); 1.22 (s, 3H); 1.57–1.70 (m, 2H); 1.82–1.99 (m, 4H); 2.07–2.17 (m, 1H); 2.21– 2.43 (m, 5H). $^{13}$C {$^{1}$H} NMR (75 MHz, $CDCl_3$): $\delta$ = 184.99, 183.36, 59.51, 57.92, 53.44, 50.41, 49.54, 49.25, 49.19, 46.63, 39.16, 38.81, 33.25, 32.94, 24.19, 22.12, 21.41, 19.82, 14.95, 14.87. IR (KBr, $cm^{-1}$): 1307, 1465, 1567, 1648, 2877, 2934, 2975, 3434. MS (CI): $m/z$ 275.1 (M+H).

#### 4.3.2. (1*R*,4*R*)-1-Bromo-3,3-dimethyl-*N*-nitrobicyclo[2.2.1]heptan-2-imine 3b

This compound was obtained from (1*R*,4*R*)-1-bromo-3,3-dimethylbicyclo[2.2.1]heptan-2-one oxime **2b** in 81% yield. Mp: 130–131 °C. $[\alpha]_D^{20} = -73.2$ ($c$ 0.93, $CHCl_3$). $^{1}$H NMR (300 MHz, $CDCl_3$): $\delta$ = 1.24 (s, 3H); 1.36 (s, 3H); 1.81–1.88 (m, 2H); 2.01–2.14 (m, 3H); 2.24–2.34 (m,1H); 2.37–2.42 (m, 1H). $^{13}$C {$^{1}$H} NMR (75 MHz, $CDCl_3$): $\delta$ = 22.69, 25.32, 25.60, 37.67, 45.49, 47.45, 48.42, 60.18, 184.64. IR (KBr, $cm^{-1}$): 1307, 1314, 1560, 1647, 2876, 2936, 2974, 2988. MS (CI): $m/z$ 261.1 (M+H).

#### 4.3.3. (1*R*,4*S*)-1-Bromo-7,7-dimethyl-*N*-nitrobicyclo[2.2.1]heptan-2-imine 3c

This compound was obtained from (1*R*,4*S*)-1-bromo-7,7-dimethylbicyclo[2.2.1]heptan-2-one oxime **2c** in 85% yield. Mp: 42–43 °C. $[\alpha]_D^{20} = -41.25$ ($c$ 0.91, $CHCl_3$). $^{1}$H NMR (300 MHz, $CDCl_3$): $\delta$ = 0.97 (s, 3H); 1.09 (s, 3H); 1.42–1.51 (m, 1H); 2.03–2.19 (m, 3H); 2.27 (d, $J$ = 18.6 Hz, 1H); 2.31–2.42 (m, 1H); 2.77–2.85 (m, 1H). $^{13}$C {$^{1}$H} NMR (75 MHz, $CDCl_3$): $\delta$ = 183.80, 69.12, 51.33, 40.34, 35.18, 34.92, 27.82, 19.62, 18.91. IR (KBr, $cm^{-1}$): 1295, 1313, 1575, 1647, 1654, 2879, 2941, 2972, 3429. HRMS (CI, $CH_4$): calculated: 261.0239; found: 261.0228.

### 4.4. Reaction of *N*-nitroimines 3a-c with a cyanide ion (general procedure)

A solution of nitrimine (1 mmol) in methanol (10 mL) was added to the mixture of acetone cyanohydrin (2 mmol, 0.170 g) and potassium hydroxide (1.5 mmol, b0.084 g) in distilled water (10 mL). The resulting mixture was stirred magnetically and refluxed for 20 min. After cooling in ice, an excess of 3 M aqueous hydrochloric acid was added over 5 min with vigorous stirring. Almost immediate precipitation of carboxamide **4a,b** or **5** was accompanied by gas ($N_2O$) evolution. The amide was filtered off, washed with distilled water (2 × 10 mL), dried in a vacuum desiccator overnight, and recrystallized from absolute 2-propanol.

#### 4.4.1. (1R,4*R*)-2-Bromo-4,7,7-trimethylbicyclo[2.2.1]hept-2-ene-1-carboxamide 4a

This compound was obtained from (1*R*,4*R*)-1-bromo-3,3,4-dimethyl-*N*-nitrobicyclo[2.2.1]heptan-2-imine **3a** in 88% yield. Mp: 146–148 °C. $[\alpha]_D^{20} = +73.35$ ($c$ 0.85, $CHCl_3$). $^{1}$H NMR (300 MHz, $CDCl_3$): $\delta$ = 0.83 (s, 3H); 0.97 (s, 3H); 1.07 (s, 3H); 1.18–1.37 (m, 2H); 1.73 (ddd, $J$ = 11.7, 8.5, 3.3 Hz, 1H); 2.28 (ddd, $J$ = 11.7, 8.6, 3.0 Hz, 1H); 5.63 (br s, 1H); 5,97 (s, 1H); 6,39 (br s, 1H). $^{13}$C {$^{1}$H} NMR (75 MHz, $CDCl_3$): $\delta$ = 172.16, 141.95, 121.28, 70.21, 60.70, 57.25, 33.18, 27.61, 18.35, 17.77, 13.28. IR (KBr, $cm^{-1}$): 3503, 3371, 3199, 2957, 2929, 1664, 1606, 1439, 1389. HRMS (CI, $CH_4$): calculated: 258.0494; found: 258.0497.

#### 4.4.2. (1*R*,4*R*)-2-Bromo-7,7-dimethylbicyclo[2.2.1]hept-2-ene-1-carboxamide 4b

This compound was obtained from (1*R*,4*R*)-1-bromo-3,3-dimethyl-*N*-nitrobicyclo[2.2.1]heptan-2-imine **3b** in 82% yield. Mp: 163–164 °C. $[\alpha]_D^{20} = +75.65$ ($c$ 0.81, $CHCl_3$). $^{1}$H NMR (300 MHz, $CDCl_3$): $\delta$ = 0.94 (s, 3H); 1.07–1.14 (m, 4H); 1.29 (ddd, $J$ = 12.3, 9.2, 3.6 Hz, 1H); 1.92–2.01 (m, 1H); 2.24–2.32 (m, 1H); 2.46 (t, $J$ = 3.4 Hz, 1H); 5.64 (br s, 1H); 6.20 (d, $J$ = 3.3 Hz, 1H); 6.72 (br s, 1H). $^{13}$C {$^{1}$H} NMR (75 MHz, $CDCl_3$): $\delta$ = 172.21, 138.01, 122.31, 68.55, 59.49, 54.19, 27.08, 25.54, 20.62, 20.51. IR (KBr, $cm^{-1}$): 1385, 1398, 1612, 1679, 2886, 2964, 3151, 3489, 3453, 3151. HRMS (CI, $CH_4$): calculated: 244.0337; found: 244.0341.

#### 4.4.3. (1*S*,4*S*)-3,3-Dimethyl-2-oxobicyclo[2.2.1]heptane-1-carboxamide 5

This compound was obtained from (1*R*,4*S*)-1-bromo-7,7-dimethyl-*N*-nitrobicyclo[2.2.1]heptan-2-imine **3c** in 78% yield. Mp: 158–159 °C. $[\alpha]_D^{20} = -52.5$ ($c$ 1.30, $CHCl_3$). $^{1}$H NMR (500 MHz, $CDCl_3$): $\delta$ = 1.06 (s, 3H); 1.07 (s, 3H); 1.61 (dt, $J$ = 12.9, 6.9 Hz, 1H); 1.82 (m, 2H); 2.05–2.11 (m, 1H); 2.21–2.27 (m, 1H);

6.02 (br s, 1H); 7.55 (br s, 1H). $^{13}C$ {$^{1}H$} NMR (125 MHz, $CDCl_3$): $\delta$ = 220.21, 172.77, 61.04, 49.00, 44.78, 38.67, 31.71, 24.39, 23.20, 21.68. Anal. Calcd: C, 66.27; H, 8.34; N, 7.73; Found: C, 66.24; H, 8.37; N, 7.75.

## References


1. a Shafiullah; Ansari, M. R.; Husain, S. *Bull.Chem. Soc. Japan* **1987**, *60*, 3411–3414; (b) Boswell; George, A. *Chem. Ind.-London* **1965**, *47*, 1929–1930; (c) Brooks, S. G.; Evans, R. M.; Green, G. F. H.; Hunt, J. S.; Long, A. G.; Mooney, B.; Wyman, L. J. *J. Chem. Soc.* **1958**, 4614–4628; (d) Ranise, A.; Bondavalli, F.; Schenone, P.; Mugnoli, A.; Pani, M. J. *Chem. Soc. Perkin Trans.* **1990**, *1*, 3053–3060; (e) Ranise, A. Journal of Chemical Research *Synopses* **1988**, *9*, 282–283.
2. Angeli, A.; Rimini, E. *Berichte* **1895**, *28*, 1077–1078.
3. Freeman, J. P. *J. Org. Chem.* **1961**, *26*, 4190–4193.
4. Li, J. *J. Science of Synthesis* **2004**, *27*, 825–842.
5. (a) Gawinecki, R.; Kolehmainen, E.; Rasala, D.; Suontamo, R. *J. Phys. Org. Chem* **1995**, *8*, 689–695; (b) Sepiol, J.; Tomasik, P. *Acta Chimica Hungarica* **1983**, *113*, 159–164.
6. Parrott, R. W.; Hitchcock, S. R. Tetrahedron *Asymmetry* **2008**, *19*, 19–26.
7. Pelegri, A. S.; Elsegood, M. R. J.; McKee, V.; Weaver, G. W. *Org. Lett.* **2006**, *8*, 3049–3051.
8. Squire, M. D.; Burwell, A.; Ferrence, G. M.; Hitchcock, S. R Tetrahedron *Asymmetry* **2002**, *17*, 1849–1854.
9. Lalk, M.; Peseke, K.; Reinke, H. *Journal fuer Praktische Chemie* **1999**, *341*, 552–556.
10. Bulman Page, P. C.; Murrell, V. L.; Limousin, C.; Laffan, D. D. P.; Bethell, D.; Slawin, A. M. Z.; Smith, T. A. D. *J. Org. Chem.* **2000**, *65*, 4204–4207.
11. Ranise, A.; Bondavalli, F.; Bruno, O.; Schenone, P.; Faillace, G.; Coluccino, A.; Filippelli, W.; Di Sarno, A.; Marmo, E. *Farmaco* **1990**, *45*, 187–202.
12. Bondavalli, F.; Bruno, O.; Ranise, A.; Schenone, P.; Susanna, V.; Lisa, M.; Maione, S.; Marmo, E. *Farmaco* **1987**, *42*, 947–953.
13. Kocienski, P. J.; Kirkup, M. *J. Org. Chem.* **1975**, *40*, 1681–1682.
14. (a) Brown, F. C.; Morris, D. G. J. Chem. Soc *Perkin Trans* **1977**, *2*, 125–127; (b) Nesmeyanov, A. N.; Kritskaya, I. I. *Russ. Chem. Bull.* **1966**, *9*, 1652–1653.
15. Antkowiak, R.; Antkowiak, W. Z. *Pol. J. Chem.* **1994**, *68*, 2297–2308.
16. Fong, W. C.; Thomas, R.; Kirby, V.; Scherer, Jr. *Tetrahedron Lett.* **1971**, *41*, 3789–3790.
17. Gorichko, M. V.; Grygorenko, O. O.; Komarov, I. V. *Tetrahedron Lett.* **2002**, *43*, 9411–9412.
18. Nickon, A.; Nishida, T.; Frank, J.; Muneyuki, R. *J. Org. Chem.* **1971**, *36*, 1075–1078.
19. Sheldrick, G. M. *Acta Cryst. A.* **2008**, *64*, 112–122.
20. Armarego, W. L. F.; Chai, C. *Purification of Laboratory Chemicals*, 5th Edition; Bultesworth-Heinemann: Oxford, 2003.