Organic & Biomolecular Chemistry

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View Article Online
DOI: 10.1039/C9OB01005J

ARTICLE

Tandem double acylation/[3,3]-rearrangement of aliphatic nitro compounds: route to α-oxygenated oxime derivatives

Received 00th January 20xx,
Accepted 00th January 20xx

DOI: 10.1039/x0xx00000x

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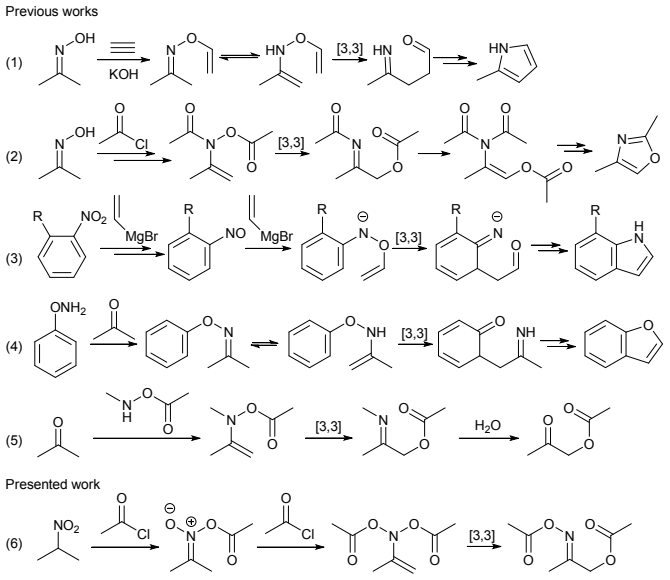
A new tandem double acylation/rearrangement reaction of nitro compounds is described. It has broad substrate scope allowing the mild and efficient synthesis of α-acyloxy oxime esters in high yields and regioselectivity. According to the obtained data, the mechanism for the transformation was proposed. Utility of the obtained α-hydroxy oxime esters was demonstrated.

Introduction

Rearrangement reactions constitute an important class of organic transformations,[1] being particularly attractive the cases assisted by the cleavage of weak N–O bond.[2] Its average bond energy of 240 kJ/mol compared to the energies of other common C–X bonds (290-380 kJ/mol for X=C,N,O) allows the formation of carbon-carbon or carbon-heteroatom bond in a thermodynamically predictable fashion. Representative examples include Beckmann[3] and Neber[4] rearrangements as well as multiple variants of hetero-Claisen rearrangements.[5] In a tandem process, rearrangement reactions are considered as invaluable tools for the quick modification of organic molecules. Some noticeable cases that involve the N–O bond cleavage are Trofimov pyrrole synthesis (tandem oxime vinylation, [3,3]-rearrangement, ring closure) (Scheme 1, eq. 1),[6] exhaustive acylation of oximes (eq. 2),[7] Bartoli indole synthesis (tandem vinylation, [3,3]-rearrangement, ring closure)[8] (eq. 3), Fischer-like benzofuran synthesis (tandem oxime formation, [3,3]-rearrangement, ring closure)[9] (eq. 4) and α-oxygenation of ketone (tandem enamine formation, [3,3]-rearrangement) developed by Tomkinson *et al*. (eq. 5).[10] The majority of the mentioned reactions rely on such starting materials as hydroxylamines or oximes, i.e. compounds that already possess single N–O bond. However, nitro compounds could be useful precursors for the synthesis of compounds possessing N–O-bond, including those with a reactive C=C–N–O-moiety.[11] Thus, the possibility to combine the generation of C=C–N–O-group with N–O-cleavage assisted rearrangement looks very promising. This would allow the functionalization of a carbon backbone of the parent nitro compound and the synthesis of polyfunctional products.[12] Herein we report tandem double acylation/rearrangement of nitro compounds leading to acylated α-hydroxyoxime derivatives (Scheme 1, eq. 6).



Scheme 1 Use of N–O cleavage-assisted rearrangements in tandem reactions.

Results and discussion

For the optimization studies, nitro compound **1a** and pivaloyl chloride were used (Table 1). Among the used solvents (Entries 1-4) the highest yield and regioselectivity was achieved in MeCN. Pyridine and DIPEA resulted in strong deceleration of reaction (Entries 6-9). With NEt_3 reaction was complete in 2 days, while use of DMAP as an additive allowed to shorten the

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Electronic Supplementary Information (ESI) available: [Experimental data, remarks on configuration determination, full optimization table, copies of NMR spectra and HPLC data]. See DOI: 10.1039/x0xx00000x

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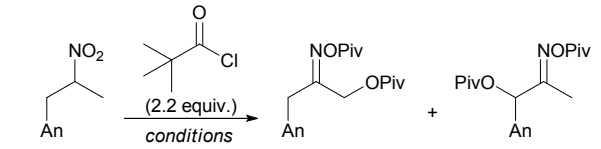
DOI: 10.1039/C9OB01005J

reaction time to 1 day (*cf*. Entries 4 and 10). Decreasing the reaction temperature somewhat increased the regioselectivity, while significantly decreased the reaction rate (Entries 5, 11). Overall an optimal combination of yield/reaction rate/selectivity was achieved using NEt_3 as a base with catalytic amounts of DMAP in MeCN at 0°C (Entry 10).

Table 1 Optimization of the reaction conditions (See ESI for full details).



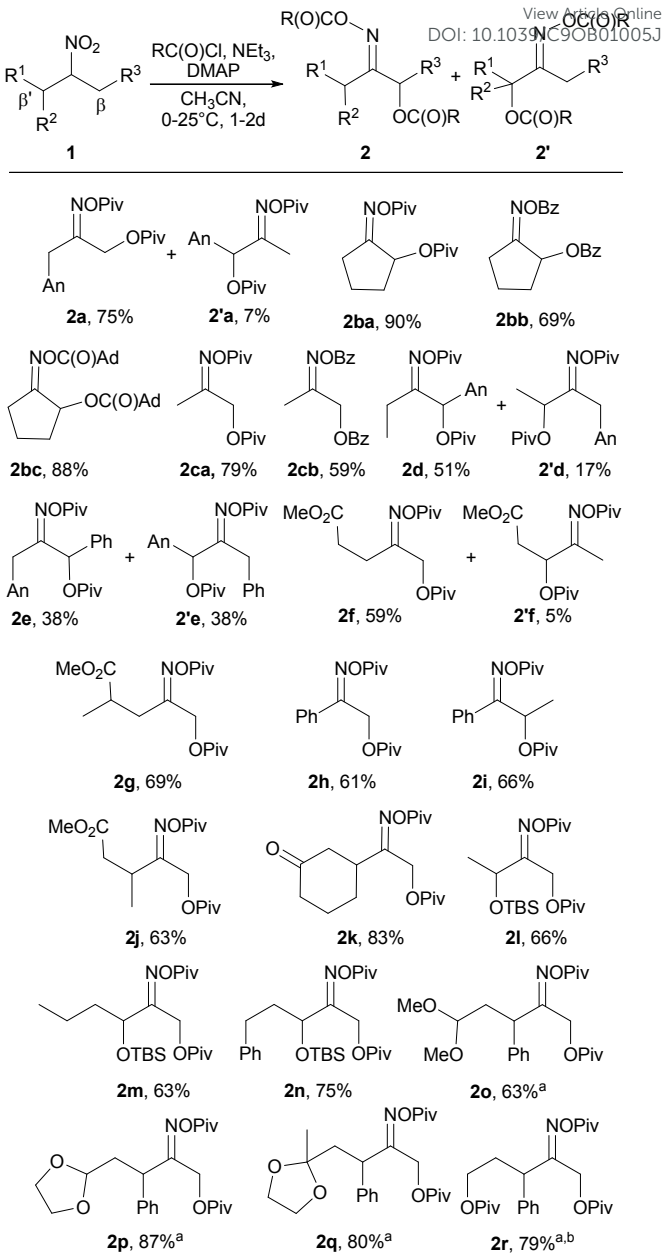
1a **2a** **2'a**

An = 4-$MeOC_6H_4$-

№	Base (equiv.)	Solv.	T, °C	time, h	Recovery **1a**, %[a]	Total yield **2a**+**2'a**, %, (ratio **2a**:**2'a**) [a]
1	NEt_3 (2.5)	CH_2Cl_2	0	24	38	46 (4:1)
2	NEt_3 (2.5)	THF	0	24	87	0
3	NEt_3 (2.5)	DMF	0	48	29	27 (4:1)
4	NEt_3 (2.5)	MeCN	0	48	0	91 (15:1)
5	NEt_3 (2.5)	MeCN	-20	72	25	57 (only **2a**)
6	DIPEA (2.5)	MeCN	0	48	87	2
7	DIPEA (2.5)	MeCN	25	96	73	23 (1:2)
8	NEt_3 (1) + DIPEA (1.5)	MeCN	0	24	40	50 (10:1)
9	Py (2.5)	MeCN	0	24	100	0
10	**NEt_3 (2.5) + DMAP (0.1)**	MeCN	**0**	**24**	**0**	**93 (10:1)**
11	NEt_3 (2.5) + DMAP (0.1)	MeCN	-20	96	20	65 (20:1)

[a] Determined by ^{1}H NMR with an internal standard (1,4-dinitrobenzene).

With the optimized conditions in hand, we proceeded to apply them on differently substituted nitro compounds **1** to test the substrate scope (Scheme 2). As can be seen a rather high variety of α-acyloxyoxime derivatives **2** was obtained in high yields. Among tested acyl chlorides pivaloyl chloride, benzoyl chloride and 1-adamantanecarbonyl chloride gave target products **2b,c** smoothly. Acyl chlorides possessing α-protons (acetyl chloride, isobutyryl chloride) failed to give target products presumably to the ease of ketene formation. Use of more electrophilic reagent, *e.g. p*-nitrobenzoyl chloride, gave intractable product mixtures. This can be attributed to the instability of intermediate acyl nitronates **3** and their rearrangement into nitroso compounds (see proposed mechanism, Scheme 3), that is in accordance with previous results on the acylation of silyl nitronates.[5a]



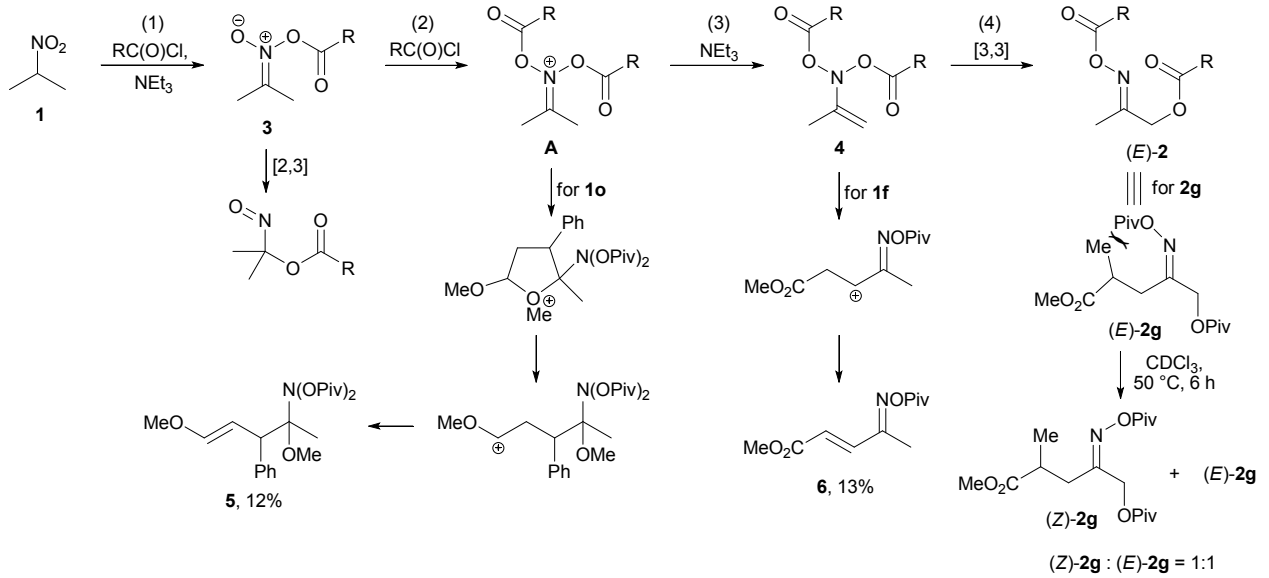
Scheme 2 Synthesis of oxime esters **2** *via* tandem double acylation-rearrangement of nitro compounds **1**. Reagent ratio: RC(O)Cl (2.2 equiv.), NEt_3 (2.5 equiv.), DMAP (0.1 equiv.). MeCN: 0.5 mL / 1 mmol of **1**. Scale: 0.4-5 mmol of starting nitro compound **1**. An = 4-methoxyphenyl; Ad = 1-adamantyl. [a] Average yield for two diastereomers of starting compound **1** (see Experimental/ESI). [b] Starting compound **1r** with unprotected OH-group, 3.4 equiv. of PivCl, 3.8 equiv. of NEt_3 were used.

Reactivity of nitro compounds **1** showed strong dependence on their substitution pattern. Moderately sterically encumbered nitro compounds **1** possessing CH_3 and CH_2-groups at the β-position usually showed a full conversion of starting materials after 1 day at 0 °C. Bulkier substrates, *e.g.* those possessing a tertiary β-carbon, reacted slower thus requiring higher temperatures (25 °C) and prolonged reaction times (2 d). The regiochemistry of the process for non-symmetric nitro compounds depended on the relative bulkiness of β- and β'-positions of the substrate **1**. Thus, products **2a** and **2f** were obtained with moderate

View Article Online DOI: 10.1039/C9OB00051

regiochemistry in favor of CH_3-functionalization (**2a,f**) *vs*. CH_2-functionalization (**2'a,2'f**), while oxime **2g** was obtained as a sole product. Expectedly, low regioselectivity was observed for secondary β- and β'-carbons (**2d**:**2'd** = 3:1, **2e**:**2'e** = 1:1). The competition between primary and tertiary β-positions resulted in the complete selectivity toward CH_3-group (products **2j-2r**). The described tandem acylation/rearrangement process tolerated functional groups such as ester (products **2f,g,j**), acetal (**2o,p**), and ether including silyl ones (**2l,m,n**). The free hydroxyl group was converted into pivalate ester (**2r**) but did not interfere with the desired tandem process. The carbonyl moiety was tolerated for cyclic product **2k**, while for open-chain cases (**2o,p,q**) the protection was needed.[13]

The structures of obtained products were supported by ^{1}H and ^{13}C NMR spectra (including 2D) as well as by HRMS data. For the oxime ester **2q** single crystal X-ray analysis was also performed (Figure 1).[14]



Scheme 3 The proposed mechanism and side-products of the reaction. Substituents R^1-R^3 at major reaction pathway are omitted for clarity.

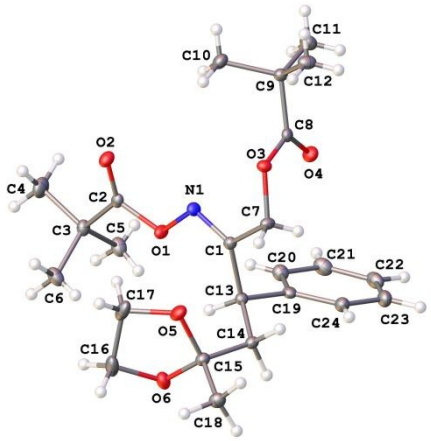
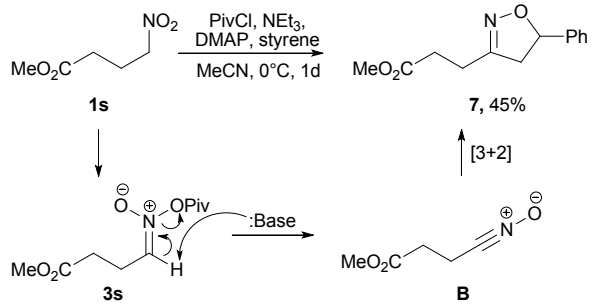


Figure 1 General view of the compound **2q** in representation of atoms *via* thermal ellipsoids at 50% probability level.[14]

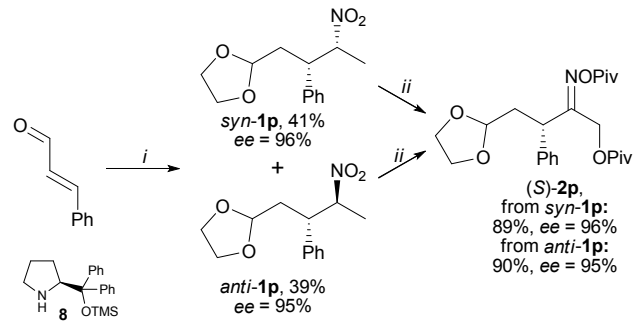
The proposed mechanism for the process is shown in the Scheme 3. At the first step the nitro compound **1** is acylated to give acyl nitronate **3**, thus consuming one equivalent of acyl chloride. At the second step intermediate **3** attacks second equivalent of acyl chloride forming iminium cation **A** (step 2), that is further β-deprotonated[15] by a base giving rise to enamine **4** (step 3). The [3,3]-rearrangement of **4** ultimately gives target oxime ether **2** (step 4). The effect of catalytic amounts of DMAP may be explained by two reasons. Firstly, DMAP is a known Lewis base additive for the acylation reactions *via N*-acyl iminium cations. Secondly, it may accelerate the deprotonation of nitro compound **1** as a less sterically hindered base compared to NEt_3. Next the stability/reactivity of intermediate acyl nitronates **3** should be mentioned. Occasional literature examples describe such compounds as rather unstable even at low temperatures.[16] Thus, they might have been expected to suffer some side reactions like [2,3]-rearrangement or Nef reaction.[17] Nevertheless the high yields of the target oximes **2** suggested the fast step 2, *i.e.* the nitronate **3** is acylated at a much faster rate than other side-processes.[18] The intermediacy of cation **A** is supported by the isolation of nitroso acetal **5** alongside the product **2o**. The formation of **5** should be explained by the electrophilic ring closure and methoxy-group transfer.[19] Side-process associated with the reactivity of enamines **4** results in the formation of enoxime **6**. Here proposed reaction pathway involves the heterolysis of N–O bond and proton abstraction (Scheme 3). Yet rather synchronous nature of the [3,3]-rearrangement is corroborated by the configuration of the formed oxime C=N double bond. The predominant migration of the acyloxy-group *syn*- to the double C=C bond in enamine **4** should be expected. Indeed, usually oximes **2** were isolated as *E*-isomers.[20,21] As exemplified by the product **2g**, the *E*,*Z*-isomerization occurred at elevated temperatures (Scheme 3).

As can be seen from Scheme 2 the tandem acylation/rearrangement smoothly proceeded with secondary nitro compounds **1**. Use of primary nitro compound **1s** did not give any acyloxy-oxime derivatives, that can be ascribed to the decomposition of intermediate nitronate **3s** into nitrile oxide **B**.[22] Performing the reaction in the presence of styrene allowed the isolation of the corresponding [3+2]-cycloaddition product - isoxazoline **7** (Scheme 4).



Scheme 4 Attempted acylation of primary nitro compound **1s**.

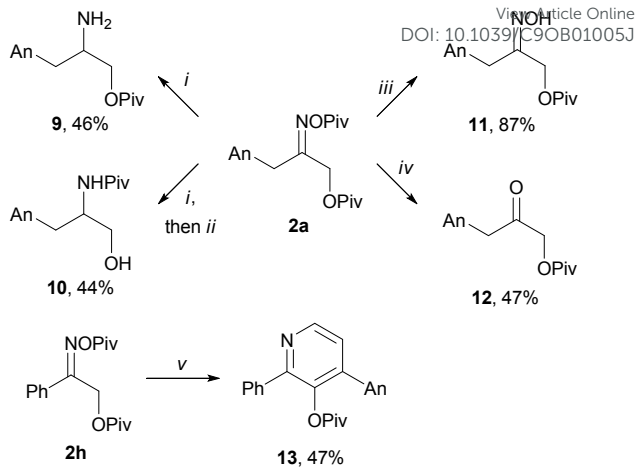
Presented tandem reaction nicely complements asymmetric organocatalysis. The addition of nitroethane to cinnamaldehyde is known to give corresponding γ-nitroaldehydes with high asymmetric induction at CH*–Ph, albeit completely non-diastereoselective.[23] Thus preparation of nitro compound **1p** gave the mixture of *syn*- and *anti*-isomers in nearly equimolar ratio. The tandem acylation/rearrangement sequence removed CH*–NO_2 stereocenter giving rise to one enantiomer of oxime (*S*)-**2p** in perfect yields (Scheme 5).



i: 1. $CH_3CH_2NO_2$, **8** (2 mol%), NEt_3 (10 mol%), AcOH (10 mol%), CH_2Cl_2/MeOH (9/1), r.t., 1d;
2. $HOCH_2CH_2OH$, TsOH (10 mol%), toluene, 80 °C, 1h;
ii: PivCl, NEt_3, DMAP (10 mol%), MeCN, r.t., 2 d

Scheme 5 Asymmetric synthesis and acylation of nitro compounds **1p**.

Acylated oximes are useful intermediates for organic synthesis.[24] Thus, to demonstrate the synthetic utility of obtained products some further transformations were performed (Scheme 6). Hydrogenation was accomplished to give either *O*-protected (**9**) or *N*-protected (**10**) amino alcohol derivatives.[25] Oxime ester was selectively cleaved by the action of methanolic ammonia (product **11**), while the deoximation[26] gave ketone **12**. Finally, tri-substituted pyridine was prepared starting from the oxime ester **2h**.[27]



i: $NaBH_4$, $NiCl_2{\cdot}6H_2O$, EtOH, r.t.,1h ; *ii*: DMAP (10 mol%), toluene, 100°C, 8 h; *iii*: 7M NH_3 in MeOH, r.t., 45 min; *iv*: Fe, TMSCl, AcOH, THF, r.t., 30 min; then H_2O, 15 min; *v*: AnCH=CHCHO, I_2, NEt_3, toluene; 120 °C, 10 h
An = 4-methoxyphenyl

Scheme 6 Synthetic transformations of obtained oxime esters **2**.

Experimental

Determination of configuration of obtained compounds

Determination of *syn*- or *anti*- relative configuration in nitro compounds **1o-r** was made using coupling constants between CH–Ph and CH–NO_2 protons: *J* (anti-isomer) > *J* (*syn*-isomer) (see ESI for more details). Absolute configuration of CH*–Ph stereocenter in *anti*-**1p**, *syn*-**1p** and **2p** was assigned on the basis of the literature data.[23]

General procedure for the synthesis of oxime esters 2 (GP).

The solution of nitro compound **1** in MeCN (2 mL/1 mmol of nitro compound **1**) was cooled to 0 °C in argon atmosphere. NEt_3 (2.5 equiv), DMAP (0.1 equiv), and, after additional 10 min, acyl chloride (2.2 equiv) were consequently added with stirring. The reaction mixture was either left at the same temperature (for **1a-c,f-i**) or warmed to r.t. (for **1d,e,j-r**) and then maintained for 1 d (for **1a-c,f-h,j**) or 2 d (for **1d,e,i,k-r**). After that it was transferred into EtOAc (25 mL)/ H_2O(20 mL). The organic layer was washed with $NaHSO_4$ (0.5 M in H_2O, 20 mL), brine (20 mL), dried (Na_2SO_4) and evaporated. The residue was preadsorbed on Celite and subjected to column chromatography on silica (eluent: PE/EtOAc) to give target oxime esters **2**. *E*,*Z*-configuration of oxime group was determined based on ^{13}C NMR (*anti*-arrangement towards oxime OR-group results in higher chemical shift of α-carbon as compared with *syn*-arrangement).[21] Note: prolonged exposure of oximes **2** at r.t. and higher temperatures (e.g, during evaporation on a rotary evaporator) may result in partial *E*,*Z*-isomerization).

Characterization data for selected products **2** is presented below. For other products **2** see ESI.

3-(4-Methoxyphenyl)-2-(pivaloyloxyimino)propyl pivalate 2a and **1-(4-Methoxyphenyl)-2-(pivaloyloxyimino)propyl pivalate 2'a**

Oxime esters **2a** and **2'a** were obtained from nitro compound **1a** (121 mg, 0.62 mmol) and pivaloyl chloride (0.17 mL, 0.17 g, 1.36 mmol) according to GP (0 °C, 1 d). Column

chromatography (eluent: PE/EtOAc, 10:1) afforded 191 mg (82 %, **2a**:**2'a =** 10:1 (^{1}H NMR)) of target oxime esters as colorless oil, that solidifies in a fridge. R_f = 0.38 (PE/EtOAc, 5:1, anisaldehyde). Pure **2a** was obtained by crystallization from PE/EtOAc, 20:1. mp = 33-35 °C (PE/EtOAc, 20:1). *(E)*-**2a**:*(Z)*-**2a** = 10:1. ^{1}H NMR (300 MHz, $CDCl_3$): *(E)*-**2a**: δ 1.19 (s, 9H, *t*-Bu), 1.28 (s, 9H, *t*-Bu), 3.78 (s, 2H, CH_2Ar), 3.79 (s, 3H, OMe), 4.72 (s, 2H, CH_2–O), 6.85 (d, *J* = 8.6 Hz, 2H, CH_{Ar}), 7.09 (d, *J* = 8.5 Hz, 2H, CH_{Ar}). *(Z)*-**2a** (characteristic signals): δ 3.75 (s, 2H, CH_2Ar), 4.85 (s, 2 H, CH_2–O), 7.20 (d, *J* = 8.6 Hz, 2H, CH_{Ar}). ^{13}C NMR (75 MHz, DEPT, HSQC, HMBC, $CDCl_3$): *(E)*-**2a**: δ 27.1 ($\underline{Me}_3C$), 27.2 ($\underline{Me}_3C$), 32.6 (CH_2Ar), 38.7 ($Me_3\underline{C}$), 38.8 ($Me_3\underline{C}$), 55.3 (OMe), 63.1 (CH_2–O), 114.4 (CH_{Ar}), 125.9 (C_{Ar}), 129.7 (CH_{Ar}), 158.8 ($\underline{C}_{Ar}$–OMe), 163.0 (C=N), 174.7 (C=O), 177.6 (C=O). *(Z)*-**2a** (characteristic signals): δ 36.6 (CH_2Ar), 58.2 (CH_2–O), 129.9 (CH_{Ar}), 164.0 (C=N). **2'a** (characteristic signals): ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.91 (s, 3H, CH_3), 6.41 (s, 1H, CH–O), 7.36 (d, *J* = 8.6, 2H, CH_{Ar}). ^{13}C NMR (75 MHz, DEPT, HSQC, HMBC, $CDCl_3$): δ 11.7 (C(=N)–$\underline{Me}$), 75.2 (CH–O), 127.7 (CH_{Ar}). HRMS (ESI): m/z calcd. for $[C_{20}H_{29}NO_5+Na^+]$: 386.1938, found: 386.1927.

2-(Pivaloyloxyimino)cyclopentyl pivalate 2ba

Oxime ester **2ba** was obtained from nitro compound **1b** (188 mg, 1.63 mmol) and pivaloyl chloride (0.45 mL, 0.43 g, 3.6 mmol) according to GP (0 °C, 1 d). Column chromatography (eluent: PE/EtOAc, 10:1) afforded 414 mg (90 %) of target oxime ester **2ba** as white solid. R_f = 0.38 (PE/EtOAc, 5:1, anisaldehyde). mp = 56-58 °C (PE). ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.21 (s, 9H, *t*-Bu), 1.28 (s, 9H, *t*-Bu), 1.77-2.01 (m, 3H) and 2.03-2.13 (m, 1H) (2 × CH_2), 2.52-2.77 (m, 2H, CH_2), 5.59 (t, *J* = 5.4 Hz, 1H, CH–O). ^{13}C NMR (75 MHz, DEPT, HSQC, $CDCl_3$): δ 20.6 (CH_2), 27.1 ($\underline{Me}_3C$), 27.3 ($\underline{Me}_3C$), 27.5 (CH_2), 32.0 (CH_2), 38.7 ($Me_3\underline{C}$), 38.8 ($Me_3\underline{C}$), 73.5 (CH–O), 171.1 (C=N), 174.8 (C=O), 177.3 (C=O). HRMS (ESI): m/z calcd. for $[C_{15}H_{25}NO_4+Na^+]$: 306.1671, found: 306.1676.

2-(Pivaloyloxyimino)propyl pivalate 2ca

Oxime ester **2ca** was obtained from nitro compound **1c** (0.45 mL, 0.45 g, 5 mmol) and pivaloyl chloride (1.37 mL, 1.33 g, 11 mmol) according to GP (0 °C, 1 d). Column chromatography (eluent: PE/EtOAc, 7:1) afforded 1.02 g (79 %) of target oxime ester **2ca** as slightly yellow oil. R_f = 0.33 (PE/EtOAc, 5:1, anisaldehyde). NMR matches previously reported data.[5a]

1-(4-Methoxyphenyl)-2-(pivaloyloxyimino)butyl pivalate 2d and **4-(4-Methoxyphenyl)-3-(pivaloyloxyimino)butan-2-yl pivalate 2'd**

Oxime esters **2d** and **2'd** were obtained from nitro compound **1d** (139 mg, 0.67 mmol) and pivaloyl chloride (0.19 mL, 0.18 g, 1.5 mmol) according to GP (r.t., 2 d). Column chromatography (eluent: PE/EtOAc, 15:1, then 10:1) afforded 172 mg (68 %, **2d**:**2'd =** 3:1 (^{1}H NMR)) of target oxime esters as colorless oil, that solidifies upon storage. R_f = 0.19 (PE/EtOAc, 9:1, UV, anisaldehyde). mp (**2d**+**2'd**) = 120-122 °C (PE/EtOAc, 10:1). ^{1}H NMR (300 MHz, COSY, $CDCl_3$): **2d**: δ 0.98 (t, *J* = 7.6 Hz, 3H, $CH_2\underline{Me}$), 1.27 (s, 18H, 2 × *t*-Bu), 2.22-2.38 (m, 2H, $\underline{CH}_2Me$), 3.78 (s, 3H, OMe), 6.39 (s, 1H, CH–O), 6.89 (d, *J* = 8.7 Hz, 2H, CH_{Ar}), 7.34 (d, *J* = 8.7 Hz, 2H, CH_{Ar}). **2'd**: δ 1.12 (s, 9H, *t*-Bu), 1.18 (s, 9H, *t*-Bu), 1.38 (d, *J* = 6.6 Hz, CH$\underline{Me}$), 3.69 (d, *J* = 14.5 Hz, 1H, $CH_{2a}Ar$), 3.76 (s, 2H, CH_2Ar), 3.83 (d, *J* = 14.5 Hz, 1H, $CH_{2b}Ar$), 5.58 (q, *J* = 6.6 Hz, 1 H, CH–O), 6.82 (d, *J* = 8.5 Hz, 2H, CH_{Ar}), 7.06 (d, *J* = 8.5 Hz, 2H, CH_{Ar}). ^{13}C NMR (75 MHz, DEPT, HSQC, HMBC, $CDCl_3$): **2d**: δ 10.9 ($CH_2\underline{Me}$), 20.6 ($\underline{C}H_2Me$), 27.16 ($\underline{Me}_3C$), 27.20 ($\underline{Me}_3C$), 38.7 ($Me_3\underline{C}$), 38.9 ($Me_3\underline{C}$), 55.2 (OMe), 75.0 (CH–O), 114.4 (CH_{Ar}), 127.7 (C_{Ar}), 127.9 (CH_{Ar}), 159.8 ($\underline{C}_{Ar}$–OMe), 167.7 (C=N), 174.6 (C=O), 176.6 (C=O). **2'd**: δ 18.0 (CH$\underline{Me}$), 27.0 ($\underline{Me}_3C$), 27.1 ($\underline{Me}_3C$), 32.0 ($\underline{C}H_2Ar$), 38.6 ($Me_3\underline{C}$), 38.7 ($Me_3\underline{C}$), 55.2 (OMe), 70.2 (CH–O), 114.4 (CH_{Ar}), 126.5 (C_{Ar}), 129.3 (CH_{Ar}), 158.5 ($\underline{C}_{Ar}$–OMe), 165.9 (C=N), 174.6 (C=O), 177.1 (C=O). HRMS (ESI): m/z calcd. for $[C_{21}H_{31}NO_5+Na^+]$: 400.2094, found: 400.2096.

Methyl 2-methyl-5-(pivaloyloxy)-4-(pivaloyloxyimino)pentanoate 2g

Oxime ester **2g** was obtained from nitro compound **1g** (302 mg, 1.7 mmol) and pivaloyl chloride (0.47 mL, 0.46 g, 3.8 mmol) according to GP (0 °C, 1 d). Column chromatography (eluent: PE/EtOAc, 7:1) afforded 409 mg (69 %) of target oxime ester **2g** as colorless oil. R_f = 0.36 (PE/EtOAc, 5:1, anisaldehyde). Maintaining NMR sample of pure *(E)*-**2g** in $CDCl_3$ at 50 °C (oil bath) for 7 h resulted in ratio *(E)*-**2g**:*(Z)*-**2g** = 1:1. ^{1}H NMR (300 MHz, $CDCl_3$): *(E)*-**2g**: δ 1.24 (s, 9H, *t*-Bu), 1.25 (d, overlapped, 3H, CH–$\underline{Me}$), 1.30 (s, 9H, *t*-Bu), 2.60 (dd, *J* = 13.3, 7.9 Hz, 1H, CH_{2a}), 2.76 (dd, *J* = 13.3, 7.3 Hz, 1H, CH_{2b}), 2.89 (app sex, *J* = 7.1 Hz, 1H, CH), 3.69 (s, 3H, CO_2Me), 4.74-4.84 (m, 2H, CH_2–O). *(Z)*-**2g** (characteristic signals): δ 1.25 (s, 9H, *t*-Bu), 1.27 (s, 9H, *t*-Bu), 2.46 (dd, *J* = 15.4, 6.6 Hz, 1H, CH_{2a}), 2.80-2.98 (m, 2H, CH and CH_{2b}), 3.70 (s, 3H, CO_2Me), 4.88-5.04 (m, 2H, CH_2–O). ^{13}C NMR (75 MHz, DEPT, $CDCl_3$):*(E)*-**2g**: δ 17.2 (CH_3), 27.1 ($\underline{Me}_3C$), 27.2 ($\underline{Me}_3C$), 30.8 (CH_2), 36.4 (CH), 38.6 ($Me_3\underline{C}$), 38.8 ($Me_3\underline{C}$), 52.0 ($CO_2\underline{Me}$), 63.5 (CH_2–O), 162.6 (C=N), 174.4 (C=O), 174.9 (C=O), 177.5 (C=O). *(Z)*-**2g** (characteristic signals): δ 17.0 (CH_3), 27.1 ($\underline{Me}_3C$), 27.2 ($\underline{Me}_3C$), 34.4 (CH_2), 36.2 (CH), 38.7 ($Me_3\underline{C}$), 38.8 ($Me_3\underline{C}$), 51.9 ($CO_2\underline{Me}$), 59.4 (CH_2–O), 163.6 (C=N), 174.1 (C=O), 175.6 (C=O), 177.6 (C=O). HRMS (ESI): m/z calcd. for $[C_{17}H_{29}NO_6+Na^+]$: 366.1887, found: 366.1883.

2-Phenyl-2-(pivaloyloxyimino)ethyl pivalate 2h

Oxime ester **2h** was obtained from nitro compound **1h** (150 mg, 1.0 mmol) and pivaloyl chloride (0.27 mL, 0.27 g, 2.2 mmol) according to GP (0 °C, 1 d). Column chromatography (eluent: PE/EtOAc, 15:1) afforded 196 mg (61 %) of target oxime ester **2h** as colorless oil, that solidifies in a fridge. R_f = 0.49 (PE/EtOAc, 5:1, anisaldehyde). mp = 85-87 °C (PE). *(E)*-**2h**:*(Z)*-**2h** = 1.7:1. ^{1}H NMR (300 MHz, $CDCl_3$): *(E)*-**2h**: δ 1.01 (s, 9H, *t*-Bu), 1.09 (s, 9H, *t*-Bu), 5.11 (s, 2H, CH_2–O), 7.35-7.44 (m, 5H, CH_{Ph}). *(Z)*-**2h**: δ 1.01 (s, 9H, *t*-Bu), 1.33 (s, 9H, *t*-Bu), 5.29 (m, 2 H, CH_2–O), 7.35-7.44 (m, 3H, CH_{Ph}), 7.61 (d, *J* = 7.8 Hz, 2H, CH_{Ph}). ^{13}C NMR (75 MHz, DEPT, $CDCl_3$): *(E)*-**2h**: δ 26.8 ($\underline{Me}_3C$), 26.9 ($\underline{Me}_3C$), 38.4 ($Me_3\underline{C}$), 38.7 ($Me_3\underline{C}$), 63.5 (CH_2–O), 127.7 (CH_{Ph}), 128.2 (CH_{Ph}), 130.0 (CH_{Ph}), 130.3 (C_{Ph}), 162.5 (C=N), 174.8 (C=O), 177.4 (C=O). *(Z)*-**2h** (characteristic signals): δ 26.8 ($\underline{Me}_3C$), 27.2 ($\underline{Me}_3C$), 38.6 ($Me_3\underline{C}$), 38.8 ($Me_3\underline{C}$), 57.3 (CH_2–O), 128.1 (CH_{Ph}), 128.3 (CH_{Ph}), 130.5 (CH_{Ph}), 131.7 (C_{Ph}), 162.8 (C=N), 174.4 (C=O), 177.5 (C=O). HRMS (ESI): m/z calcd. for $[C_{18}H_{25}NO_4+Na^+]$: 342.1676, found: 342.1674.

1-Phenyl-1-(pivaloyloxyimino)propan-2-yl pivalate 2i

Oxime ester **2i** was obtained from nitro compound **1i** (77 mg, 0.47 mmol) and pivaloyl chloride (0.13 mL, 0.13 g, 1.03 mmol)

according to GP (0 °C, 2 d). Column chromatography (eluent: PE/EtOAc, 30:1, then 15:1) afforded 103 mg (66 %) of target oxime ester **2i** as colorless oil, that solidifies in a fridge. R_f = 0.56 (PE/EtOAc, 9:1, anisaldehyde). mp = 115-118 °C (PE/EtOAc, 10:1). *(E)*-**2i**:*(Z)*-**2i** = 1:1. ^{1}H NMR (300 MHz, COSY, for *(E,Z)*-mixture, $CDCl_3$): δ 0.93 (s, 9H, *t*-Bu), 1.05 (s, 9H, *t*-Bu), 1.08 (s, 9H, *t*-Bu), 1.35 (s, 9H, *t*-Bu), 1.55 (d, *J* = 6.6 Hz, 3H, (*E*)-isomer, Me), 1.73 (d, *J* = 7.0 Hz, 3H, (*Z*)-isomer, Me), 5.83 (q, *J* = 6.6 Hz, 3H, (*E*)-isomer, CH–O), 6.13 (q, *J* = 7.0 Hz, 3H, (*Z*)-isomer, CH–O), 7.28-7.43 (m, 5H ((*E*)-isomer) + 3H ((*Z*)-isomer), CH_{Ph}), 7.59 (d, *J* = 7.9 Hz, 2H, (*Z*)-isomer, CH_{Ph}). ^{13}C NMR (75 MHz, DEPT, HSQC, for *(E,Z)*-mixture, $CDCl_3$): δ 17.8 (Me, (*E*)-isomer), 18.2 (Me, (*Z*)-isomer), 26.7 ($\underline{Me}_3C$), 26.9 (2 × $\underline{Me}_3C$), 27.3 ($\underline{Me}_3C$), 38.4 (2 × $Me_3\underline{C}$), 38.6 ($Me_3\underline{C}$), 38.8 ($Me_3\underline{C}$), 66.3 (CH–O, (*Z*)-isomer), 70.3 (CH–O, (*E*)-isomer), 127.4 (CH_{Ph}), 128.0 (CH_{Ph}),128.1 (CH_{Ph}), 128.6 (CH_{Ph}), 129.4 (CH_{Ph}), 130.1 (CH_{Ph}), 131.1 (C_{Ph}), 131.2 (C_{Ph}), 166.4 (C=N), 167.4 (C=N), 174.3 (C=O), 174.7 (C=O), 177.3 (2 × C=O). HRMS (ESI): m/z calcd. for [$C_{19}H_{27}NO_4$+Na$^+$]: 356.1832, found: 356.1838.

3-(*tert*-Butyldimethylsilyloxy)-2-(pivaloyloxyimino)butyl pivalate 2l

Oxime ester **2l** was obtained from nitro compound **1l** (111 mg, 0.48 mmol) and pivaloyl chloride (0.13 mL, 0.13 g, 1.06 mmol) according to GP (r.t., 2 d). Column chromatography (eluent: PE/EtOAc, 20:1) afforded 127 mg (66 %) of target oxime ester **2l** as colorless oil. R_f = 0.67 (PE/EtOAc, 5:1, anisaldehyde). *(E)*-**2l**:*(Z)*-**2l** = 1:4. ^{1}H NMR (300 MHz, COSY, $CDCl_3$): *(Z)*-**2l**: δ 0.07 (s, 3 H, MeSi), 0.09 (s, 3 H, MeSi), 0.90 (s, 9H, *t*-BuSi), 1.25 (s, 9H, *t*-Bu-C), 1.29 (s, 9H, *t*-Bu-C), 1.43 (d, *J* = 6.5 Hz, 3H, CH_3), 4.67 (d, *J* = 13.7 Hz, 1H, $C\underline{H}_{2a}$–OPiv), 5.12 (d, *J* = 13.7 Hz, 1H, $C\underline{H}_{2b}$–OPiv), 5.12 (q, *J* = 6.5 Hz, 1H, C<u>H</u>–OTBS). *(E)*-**2l** (characteristic signals): δ 4.74 (q, *J* = 6.6 Hz, 1H, C<u>H</u>–OTBS), 4.82-4.92 (m, 2H, $C\underline{H}_2$–OPiv). ^{13}C NMR (75 MHz, DEPT, HSQC, $CDCl_3$): *(Z)*-**2l**: δ -5.3 (MeSi), -4.9 (MeSi), 18.0 (<u>C</u>-Si), 21.6 (CH_3), 25.6 (*t*-BuSi), 27.2 (2 × $Me_3\underline{C}$–C), 38.7 ($Me_3\underline{C}$), 38.8 ($Me_3\underline{C}$), 60.9 (CH_2–O), 64.8 (CH–O), 167.4 (C=N), 174.0 (C=O), 177.6 (C=O). *(E)*-**2l** (characteristic signals): δ 22.0 (CH_3), 54.8 (CH_2–O), 68.8 (CH–O). HRMS (ESI): m/z calcd. for [$C_{20}H_{39}NO_5Si$+Na$^+$]: 424.2490, found: 424.2485.

5,5-Dimethoxy-3-phenyl-2-(pivaloyloxyimino)pentyl pivalate 2o

Oxime ester **2o** was obtained from nitro compound *syn*-**1o** (125 mg, 0.49 mmol) and pivaloyl chloride (0.13 mL, 0.13 g, 1.1 mmol) according to GP (r.t., 2 d). Column chromatography (eluent: PE/EtOAc, 15:1, then 9:1) afforded 15 mg of nitroso acetal **5**, 71 mg of mixture **2o**+**5** (**2o**:**5** = 6:1 (^{1}H NMR)) and 71 mg of oxime ester **2o** as colorless oils. Total yields: **2o**: 64 %, **5**: 12 %. Similar procedure for *anti*-**1o** (177 mg, 0.7 mmol) gave 182 mg (62%) of target oxime ester **2o**. Oxime ester **2o:** R_f = 0.36 (PE/EtOAc, 5:1, anisaldehyde). Only *(E)*-**2o**. ^{1}H NMR (300 MHz, COSY, $CDCl_3$): δ 1.15 (s, 9H, *t*-Bu), 1.28 (s, 9H, *t*-Bu), 2.32 (dd, *J* = 7.9, 5.7 Hz, 1H, CH_2), 3.30 (s, 3H, OMe), 3.31 (s, 3H, OMe), 4.34 (t, *J* = 5.7 Hz, 1H, $C\underline{H}(OMe)_2$), 4.62 (t, *J* = 7.9 Hz, 1H, C<u>H</u>Ph), 4.68 (s, 2 H, CH_2–O), 7.24-7.35 (m, 5H, Ph). ^{13}C NMR (75 MHz, DEPT, HSQC, $CDCl_3$): δ 27.0 ($\underline{Me}_3C$), 27.1 ($\underline{Me}_3C$), 33.9 (CH_2), 38.6 ($Me_3\underline{C}$), 38.7 ($Me_3\underline{C}$), 40.3 (<u>C</u>HPh), 52.4 (OMe), 53.7 (OMe), 62.8 (CH_2–O), 102.3 ($\underline{C}H(OMe)_2$), 127.5 (CH_{Ph}), 127.7 (CH_{Ph}), 128.9 (CH_{Ph}), 137.7 (C_{Ph}), 164.1 (C=N), 174.6 (C=O), 177.5 (C=O). HRMS (ESI): m/z calcd. for [$C_{23}H_{35}NO_6$+Na$^+$]: 444.2357, found: 444.2353.

4-(1,3-Dioxolan-2-yl)-3-phenyl-2-(pivaloyloxyimino)butyl pivalate 2p

Oxime ester **2p** was obtained from nitro compound *anti*-**1p** (86 mg, 0.35 mmol) and pivaloyl chloride (0.10 mL, 0.10 g, 0.84 mmol) according to GP (r.t., 2 d). Column chromatography (eluent: PE/EtOAc, 6:1) afforded 131 mg (89 %) of target oxime ester **2p** as colorless oil. R_f = 0.28 (PE/EtOAc, 5:1, anisaldehyde). Similar procedure for *syn*-**1p** (98 mg, 0.39 mmol) gave 140 mg (86%) of target oxime ester **2p**. Similar procedure for (+)-*anti*-**1p** (97 mg, 0.39 mmol) gave 145 mg (90%, ee = 95%) of target oxime ester (–)-**2p**. Similar procedure for (+)-*syn*-**1p** (90 mg, 0.36 mmol) gave 133 mg (89%, ee = 96%) of target oxime ester (–)-**2p**. (–)-(*S*)-**2p**: $[\alpha]^{24}_D$ = -93.5 (*c* = 1.0, MeOH, 96% ee, *E*-isomer). ^{1}H NMR (300 MHz, COSY, $CDCl_3$): (*E*)-**2p**: δ 1.11 (s, 9H, *t*-Bu), 1.26 (s, 9H, *t*-Bu), 2.26-2.48 (m, 2H, CH_2), 3.77-3.84 and 3.88-3.97 (m, 4H, OCH_2CH_2O), 4.66 (d, *J* = 13.1 Hz, 1H, $C\underline{H}_{2a}$–OPiv), 4.73 (d, *J* = 13.1 Hz, 1H, $C\underline{H}_{2b}$–OPiv), 4.76 (t, *J* = 7.7 Hz, 1H, CHPh), 4.87 (t, *J* = 4.6 Hz, 1H, $C\underline{H}(OCH_2)_2$), 7.18-7.35 (m, 5H, Ph). (*Z*)-**2p**: δ 1.13 (s, 9H, *t*-Bu), 1.28 (s, 9H, *t*-Bu), 2.17 (ddd, *J* = 13.9, 7.6, 4.3 Hz, 1H, CH_{2a}), 2.51 (ddd, *J* = 13.9, 7.6, 5.8 Hz, 1H, CH_{2a}), 3.75-3.85 and 3.87-3.96 (m, 4H, OCH_2CH_2O), 4.13 (t, *J* = 7.6 Hz, 1H, CHPh), 4.52 (d, *J* = 14.7 Hz, 1H, $C\underline{H}_{2a}$–OPiv), 4.84 (dd, *J* = 5.8, 4.3 Hz, 1H, $C\underline{H}(OCH_2)_2$), 4.94 (d, *J* = 14.7 Hz, 1H, $C\underline{H}_{2b}$–OPiv), 7.22-7.34 (m, 5H, Ph). ^{13}C NMR (75 MHz, DEPT, HSQC, $CDCl_3$): (*E*)-**2p**: δ 27.0 ($\underline{Me}_3C$), 27.1 ($\underline{Me}_3C$), 34.9 (CH_2), 38.6 ($Me_3\underline{C}$), 38.7 ($Me_3\underline{C}$), 39.5 (<u>C</u>HPh), 62.8 ($\underline{C}H_2$–OPiv), 64.9 and 65.0 (OCH_2CH_2O), 102.2 ($\underline{C}H(OCH_2)_2$), 127.4 (CH_{Ph}), 127.7 (CH_{Ph}), 128.8 (CH_{Ph}), 137.8 (C_{Ph}), 164.2 (C=N), 174.6 (C=O), 177.5 (C=O). (*Z*)-**2p**: δ 27.0 ($\underline{Me}_3C$), 27.2 ($\underline{Me}_3C$), 37.0 (CH_2), 38.7 ($Me_3\underline{C}$), 38.8 ($Me_3\underline{C}$), 43.6 (<u>C</u>HPh), 58.2 ($\underline{C}H_2$–OPiv), 64.8 (OCH_2CH_2O), 102.4 ($\underline{C}H(OCH_2)_2$), 127.4 (CH_{Ph}), 128.3 (CH_{Ph}), 128.8 (CH_{Ph}), 138.7 (C_{Ph}), 165.4 (C=N), 174.5 (C=O), 177.5 (C=O). HRMS (ESI): m/z calcd. for [$C_{23}H_{33}NO_6$+H$^+$]: 420.2381, found: 420.2374. HPLC separation conditions: column: Chiralpak AD-3, 250 x 4.6 mm, temp. 25 °C, eluent: Hexane-*i*-PrOH, 90:10, 1 mL/min, detection at 207 nm. t_R = 4.9 min (*Z*-isomer, minor), 5.2 min (*Z*-isomer, major), 6.3 min (*E*-isomer, major), 7.1 (*E*-isomer, minor).

3-Phenyl-2-(pivaloyloxyimino)pentane-1,5-diyl bis(2,2-dimethylpropanoate) 2r

Oxime ester **2r** was obtained from nitro compound *syn*-**1r** (86 mg, 0.42 mmol) according to GP (r.t., 2 d) with the change: increasing amounts of pivaloyl chloride (3.4 equiv., 0.18 mL, 0.17 g, 1.4 mmol) and NEt_3 (3.8 equiv., 0.22 mL, 0.16 g, 1.6 mmol) were taken. Column chromatography (eluent: PE/EtOAc, 10:1) afforded 156 mg (82 %) of target oxime ester **2r** as colorless oil, that solidifies in a fridge. R_f = 0.44 (PE/EtOAc, 5:1, anisaldehyde). mp = 73-75 °C (PE/EtOAc, 10:1). Similar procedure for *anti*-**1r** (94 mg, 0.45 mmol) gave 160 mg (77 %) of target oxime ester **2r**. Only *(E)*-**2r**. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.16 (s, 18H, 2 × *t*-Bu), 1.27 (s, 9H, *t*-Bu), 2.37 (app q, *J* = 7.0 Hz, CH_2(4)), 4.00-4.18 (m, 2H, CH_2(5)–OPiv), 4.55 (app t, *J*= 7.8 Hz, CHPh), 4.62-4.72 (m, 2H, CH_2(1)–OPiv), 7.23-7.33 (m, 5H, Ph). ^{13}C NMR (75 MHz, DEPT, HSQC, $CDCl_3$): δ 27.07 ($\underline{Me}_3C$), 27.12 ($\underline{Me}_3C$), 27.18 ($\underline{Me}_3C$), 29.8 (CH_2(4)), 38.63

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DOI: 10.1039/C9OB01005J

(Me_3C), 38.68 (Me_3C), 38.74 (Me_3C), 41.4 (CHPh), 62.2 (CH_2(5)–OPiv), 62.7 (CH_2(1)–OPiv), 127.7 (CH_{Ph}), 127.8 (CH_{Ph}), 129.0 (CH_{Ph}), 137.2 (C_{Ph}), 163.4 (C=N), 174.3 (C=O), 177.4 (C=O), 178.2 (C=O). HRMS (ESI): m/z calcd. for $[C_{26}H_{39}NO_6+Na^+]$: 484.2670, found: 484.2659.

***O*-Pivaloyl-*N*-(pivaloyloxy)-*N*-((3*E*)-1,4-dimethoxy-1-methylbut-3-en-1-yl)hydroxylamine 5**

Obtained as a side-product during acylation of *syn*-**1o**. R_f = 0.44 (PE/EtOAc, 5:1, anisaldehyde). Relative configuration of stereocenters was not determined. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.13 (s, 9H, *t*-Bu), 1.25 (s, 9H, *t*-Bu), 1.28 (s, 3H, Me), 3.51 (s, 3H, N–C–OMe), 3.52 (s, 3H, =CHOMe), 3.84 (d, *J* = 9.2 Hz, 1H, CHPh), 5.36 (dd, *J* = 12.7, 9.2 Hz, =CH–CH), 6.21 (d, *J* = 12.7 Hz, 1H, =CH–O), 7.19-7.35 (m, 5H, Ph). ^{13}C NMR (75 MHz, DEPT, HSQC, HMBC, $CDCl_3$): δ 17.9 (Me), 26.8 (Me_3C), 27.0 (Me_3C), 38.4 (Me_3C), 38.5 (Me_3C), 50.6 (CHPh), 52.2 (N–C–OMe), 56.2 (=CHOMe), 98.7 (C–N), 104.1 (=CH–CH), 126.4 (CH_{Ph}), 128.3 (CH_{Ph}), 129.3 (CH_{Ph}), 142.7 (C_{Ph}), 148.1 (=CH–O), 174.2 (C=O), 174.5 (C=O). HRMS (ESI): m/z calcd. for $[C_{23}H_{35}NO_6+Na^+]$: 444.2357, found: 444.2374.

Methyl 3-(5-phenyl-4,5-dihydroisoxazol-3-yl)propanoate 7

The solution of nitro compound **1s** (115 mg, 0.78 mmol) in MeCN (1.55 mL) was cooled to 0 °C in argon atmosphere. Styrene (0.27 mL, 0.24 g, 2.3 mmol), NEt_3 (0.27 mL, 0.19 g, 2.0 mmol), DMAP (9.5 mg, 0.08 mmol), and, after additional 10 min, pivaloyl chloride (0.21 ml, 0.21 g, 1.7 mmol) were consequently added with stirring. The reaction mixture was maintained at the same temperature for 1 d, transferred into EtOAc (50 mL)/ H_2O(40 mL). The organic layer was washed with $NaHSO_4$ (0.5 M in H_2O, 40 mL), brine (40 mL), dried (Na_2SO_4) and evaporated. The residue was subjected to column chromatography (eluent: PE/EtOAc, 6:1, then 3:1) to give 82 mg (45%) of isoxazoline **7** as colorless oil. R_f = 0.42 (PE/EtOAc, 1:1, anisaldehyde). NMR matches previously reported data.[28]

2-Amino-3-(4-methoxyphenyl)propyl pivalate 9

To the solution of oxime ester **2a** (98 mg, 0.27 mmol) and $NiCl_2{\cdot}6H_2O$ (130 mg, 0.55 mmol) in EtOH (2.8 mL) $NaBH_4$ (102 mg, 2.7 mmol) was added portionwise during 30 min at 0 °C. The reaction mixture was stirred at r.t. for 1 h and transferred into EtOAc (100 mL)/ H_2O(75 mL). The water layer was extracted with EtOAc (3 × 20 mL). The combined organic layer was washed with brine (150 mL), dried (Na_2SO_4) and evaporated to give crude amine **9**. Column chromatography (eluent: PE/EtOAc, 1:1, then PE/EtOAc/MeOH, 1:1:0.2) afforded 33 mg (46 %) of target amine **9** as colorless oil. R_f = 0.13 (EtOAc, ninhydrine). ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.25 (s, 9H, *t*-Bu), 1.90 (br s, 2H, NH_2), 2.57 (dd, *J* = 13.6, 8.0 Hz, 1H, CH_{2a}–Ar), 2.78 (dd, *J* = 13.6, 5.5 Hz, 1H, CH_{2b}–Ar), 3.29 (app br quint, *J* = 6.2 Hz, 1H, CH–N), 3.80 (s, 3H, OMe), 3.92 (dd, *J* = 10.9, 6.8 Hz, 1H, CH_{2a}–O), 4.05 (dd, *J* = 10.9, 4.5 Hz, 1H, CH_{2b}–O), 6.86 (d, *J* = 8.5 Hz, 2H, CH_{Ar}), 7.13 (d, *J* = 8.5 Hz, 2H, CH_{Ar}). ^{13}C NMR (75 MHz, DEPT, HMBC, $CDCl_3$): δ 27.3 (Me_3C), 38.9 (Me_3C), 39.5 (CH_2–Ar), 51.7 (CH–N), 55.3 (OMe), 68.4 (CH_2–O), 114.0 (CH_{Ar}), 130.0 (C_{Ar}), 130.2 (CH_{Ar}), 158.3 (C_{Ar}–OMe), 178.3 (C=O). HRMS (ESI): m/z calcd. for $[C_{15}H_{23}NO_3+H^+]$: 266.1751, found: 266.1743.

***N*-(1-Hydroxy-3-(4-methoxyphenyl)propan-2-yl)pivalamide 10**

Oxime ester **2a** (94 mg, 0.26 mmol) was subjected to hydrogenation as described for the synthesis of amine **9**. Then the solution of crude amine **9** and DMAP (3.1 mg, 0.03 mmol) in toluene (0.52 mL) was heated at 100 °C (oil bath) for 8 h. The reaction mixture was evaporated and preadsorbed on Celite®. Column chromatography (eluent: PE/EtOAc, 1:1, then PE/EtOAc/MeOH, 1:1:0.1) afforded 30 mg (44 %) of target amide **10** as colorless oil. R_f = 0.13 (PE/EtOAc, 1:1, Hanessian stain). ^{1}H NMR (300 MHz, COSY, $CDCl_3$): δ 1.13(s, 9H, *t*-Bu), 2.77 (dd, *J* = 13.9, 7.6 Hz, 1H, CH_{2a}–Ar), 2.87 (dd, *J* = 13.9, 6.9 Hz, 1H, CH_{2b}–Ar), 3.44 (br s, 1H, OH), 3.60 (dd, *J* = 11.0, 5.3 Hz, 1H, CH_{2a}–O), 3.68 (dd, *J* = 11.0, 3.6 Hz, 1H, CH_{2b}–O), 3.79 (s, 3H, OMe), 4.03-4.15 (m, 1H, CH–N), 5.89 (br d, *J* = 6.6 Hz, 1H, NH), 6.85 (d, *J* = 8.5 Hz, 2H, CH_{Ar}), 7.14 (d, *J* = 8.5 Hz, 2H, CH_{Ar}). ^{13}C NMR (75 MHz, DEPT, HSQC, HMBC, $CDCl_3$): δ 27.5 (Me_3C), 36.0 (CH_2–Ar), 38.7 (Me_3C), 52.9 (CH–N), 55.3 (OMe), 64.6 (CH_2–O), 114.0 (CH_{Ar}), 129.6 (C_{Ar}), 130.2 (CH_{Ar}), 158.4 (C_{Ar}–OMe), 179.4 (C=O). HRMS (ESI): m/z calcd. for $[C_{15}H_{23}NO_3+H^+]$: 266.1751, found: 266.1748.

2-(Hydroxyimino)-3-(4-methoxyphenyl)propyl pivalate 11 and **2-(Hydroxyimino)-1-(4-methoxyphenyl)propyl pivalate 11'**

Mixture of oxime esters **2a+2'a** (121 mg, 0.33 mmol) was dissolved in the solution of NH_3 in MeOH (7M, 1.43 mL). Reaction mixture was stirred for 45 min at r.t., transferred into EtOAc (50 mL) / H_2O(40 mL). The organic layer was washed with $NaHSO_4$ (0.5 M in H_2O, 30 mL), brine (40 mL), dried (Na_2SO_4) and evaporated. Column chromatography (eluent: PE/EtOAc, 6:1) afforded 80 mg (87 %) of target oxime **11+11'** (**11**:**11'** = 12:1 (^{1}H NMR)) as colorless oil, that solidifies in a fridge. R_f = 0.33 (PE/EtOAc, 5:1, UV, anisaldehyde). mp = 58-60 °C (PE/EtOAc, 20:1). *(E)*-**11**:*(Z)*-**11** = 10:1. ^{1}H NMR (300 MHz, $CDCl_3$): *(E)*-**11**: δ 1.21 (s, 9H, *t*-Bu), 3.76 (s, 2H, CH_2Ar), 3.80 (s, 3H, OMe), 4.59 (s, 2H, CH_2–O), 6.85 (d, *J* = 8.6 Hz, 2H, CH_{Ar}), 7.19 (d, *J* = 8.6 Hz, 2H, CH_{Ar}), 9.22 (br s, 1H, NOH). *(Z)*-**11** (characteristic signals): δ 3.59 (s, 2H, CH_2Ar), 4.95 (s, 2 H, CH_2–O). ^{13}C NMR (75 MHz, DEPT, HSQC, HMBC, $CDCl_3$): *(E)*-**11**: δ 27.1 (Me_3C), 30.8 (CH_2Ar), 38.8 (Me_3C), 55.3 (OMe), 63.6 (CH_2–O), 114.1 (CH_{Ar}), 127.5 (C_{Ar}), 130.1 (CH_{Ar}), 155.4 (C=N), 158.4 (C_{Ar}–OMe), 178.0 (C=O). *(Z)*-**11** (characteristic signals): δ 36.3 (CH_2Ar), 58.4 (CH_2–O), 129.8 (CH_{Ar}). **11'** (characteristic signals): ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.86 (s, 3H, CH_3), 6.30 (s, 1H, CH–O), 7.31 (d, *J* = 8.7, 2H, CH_{Ar}). ^{13}C NMR (75 MHz, DEPT, HSQC, HMBC, $CDCl_3$, characteristic signals): δ 10.4 (C(=N)–Me), 75.6 (CH–O), 127.8 (CH_{Ar}). HRMS (ESI): m/z calcd. for $[C_{15}H_{21}NO_4+Na^+]$: 302.1363, found: 302.1362.

3-(4-Methoxyphenyl)-2-oxopropyl pivalate 12 and **3-(4-methoxyphenyl)-2-oxopropyl pivalate 12'**

Ketone **12** was obtained similar to the reported procedure.[26] To the solution of oxime esters **2a+2'a** (145 mg, 0.4 mmol) in THF (4 mL) Fe powder (223 mg, 4 mmol), AcOH (2 drops) and TMSCl (2 drops) were consequently added. The reaction mixture was stirred at r.t. for 0.5 h. Water (4 mL) was added. The mixture was stirred for additional 15 min, transferred into

EtOAc (55 mL)/ H_2O (15 mL). The organic layer was washed with $NaHCO_3$ (sat. aq., 50 mL), brine (50 mL), dried (Na_2SO_4) and evaporated. The residue was preadsorbed on Celite® and subjected to column chromatography (eluent: PE/EtOAc, 10:1) to give 50 mg (47 %) of target ketones **12+12'** (**12**:**12'**=11:1) as colorless oil, that solidifies in a fridge. R_f = 0.47 (PE/EtOAc, 5:1, anisaldehyde). mp = 29-31 °C (PE). **12**: ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.28 (s, 9H, *t*-Bu), 3.68 (s, 2H, CH_2–Ar), 3.81 (s, 3H, OMe), 4.69 (s, 2H, CH_2–O), 6.89 (d, *J* = 8.5 Hz, 2H, CH_{Ar}), 7.15 (d, *J* = 8.8 Hz, 2H, CH_{Ar}). ^{13}C NMR (75 MHz, DEPT, $CDCl_3$): δ 27.2 (Me_3C), 38.7 (Me_3C), 45.4 (CH_2–Ar), 55.3 (OMe), 67.4 (CH_2–O), 114.3 (CH_{Ar}), 124.8 (C_{Ar}), 130.5 (C_{Ar}), 158.9 (C_{Ar}–OMe), 177.8 (COO), 201.7 (C=O). **12'**: ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.30 (s, 9H, *t*-Bu), 2.12 (s, 3H, Me), 3.83 (s, 3H, OMe), 5.89 (s, 1H, CH–O), 6.94 (d, *J* = 8.7 Hz, 2H, CH_{Ar}), 7.35 (d, *J* = 8.7 Hz, 2H, CH_{Ar}). HRMS (ESI): m/z calcd. for [$C_{15}H_{20}O_4$+Na^+]: 287.1254, found: 287.1255.

4-(4-Methoxyphenyl)-2-phenylpyridin-3-yl pivalate 13

Substituted pyridine **13** was obtained similar to the reported procedure.[27] The solution of oxime ester **2h** (82.3 mg, 0.26 mmol), *p*-methoxycinnamaldehyde (63 mg, 0.39 mmol), NEt_3 (18 µL, 13 mg, 0.13 mmol) and I_2 (33 mg, 0.13 mmol) in toluene (1.3 mL) was heated at 120 °C (oil bath) for 9 h. The reaction mixture was transferred into EtOAc (50 mL)/ H_2O (20 mL). The organic layer was washed with brine (30 mL), dried (Na_2SO_4) and evaporated. Column chromatography (eluent: PE/EtOAc, 9:1, then 7:1) afforded 43.7 mg (47 %) of target pyridine **13** as yellow oil. R_f = 0.18 (PE/EtOAc, 5:1, UV). ^{1}H NMR (300 MHz, COSY, $CDCl_3$): δ 0.93 (s, 9H, *t*-Bu), 3.86 (s, 3H, OMe), 6.98 (d, *J* = 8.6 Hz, 2H, CH_{Ar}), 7.30 (d, *J* = 5.0 Hz, 1H, CH(5)), 7.29-7.47 (m, 5H, CH_{Ar} and CH_{Ph}), 7.67 (d, *J* = 8.0 Hz, 2H, CH_{Ph}), 8.60 (d, *J* = 5.0 Hz, 1H, CH(6)). ^{13}C NMR (75 MHz, DEPT, HSQC, HMBC, $CDCl_3$): δ 26.8 (Me_3C), 38.7 (Me_3C), 55.4 (OMe), 113.8 (CH_{Ar}), 124.1 (CH(5)), 127.7 (C_{Ar}), 128.0, 128.5, 129.1 and 130.2 (3×CH_{Ph} and CH_{Ar}), 137.3 (C_{Ph}), 142.7 (C(3)), 144.0 (C(4)), 146.9 (CH(6)), 153.7 (C(2)), 159.9 (C_{Ar}–OMe), 175.6 (C=O). HRMS (ESI): m/z calcd. for [$C_{23}H_{23}O_3$+H^+]: 362.1751, found: 362.1752.

Conclusions

In summary, a new tandem double acylation/rearrangement of nitro compounds was investigated. The overall process represents the C-H functionalization of β-position of starting nitro compound with the concomitant conversion of nitro to oxime moiety. Considering ready availability of starting nitro compounds by simple means (Henry, Michael reactions) this allows a quick increase in molecular complexity in a few steps. The reaction has rather broad substrate scope, proceeds with high regioselectivity and can be used in asymmetric synthesis. Based on the obtained data, the mechanism for the transformation including possible side-reactions was proposed. Synthetic utility of the obtained α-hydroxy oxime esters was demonstrated.

Conflicts of interest

There are no conflicts to declare.

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DOI: 10.1039/C9OB01005J

Acknowledgements

This work was supported by the Russian Science Foundation (grant 17-13-01411). The authors thank Dr. N. G. Kolotyrkina and Dr. A. O. Chizhov (N. D. Zelinsky Institute of Organic Chemistry) for registration of HRMS. X-ray diffraction data were collected with the financial support from Ministry of Science and Higher Education of the Russian Federation using the equipment of the Center for molecular composition studies of INEOS RAS.

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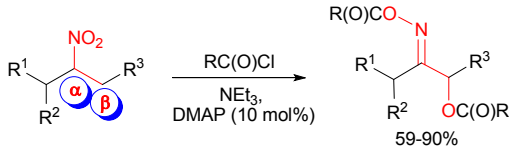

- **one-pot**
- **carbon chain activation**
- **broad substrate scope**
- **high regioselectivity**

Novel efficient regioselective method for the carbon chain activation of aliphatic nitro compounds is described using tandem double acylation/[3,3]-rearrangement sequence.

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DOI: 10.1039/C9OB01005J