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Synthesis of α-Amidoketones from Vinyl Esters via a Catalytic/Thermal Cascade Reaction

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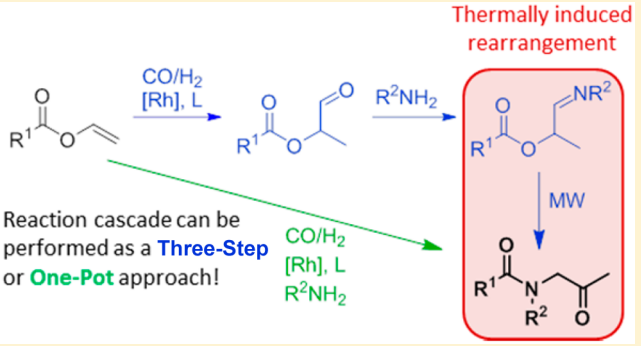
Supporting Information

ABSTRACT: A straightforward, modular, and atom-efficient method is reported for the synthesis of α-amidoketones from vinyl esters via a cascade reaction including hydroformylation, condensation with a primary amine, and a rearrangement step giving water as the only byproduct. The reaction sequence can be performed in one pot or as a three-step procedure. The synthetic applicability is demonstrated by the preparation of different α-amidoketones in moderate to good yields.



The α-amidoketone structural motif can often be found in biologically active compounds such as enzyme inhibitors,[1] herbicides,[2] or fungicides.[3] Several approaches for their synthesis have been reported in recent years. For instance, α-amidoketones are accessible via a palladium-catalyzed oxidation of allylic amides.[4] In 2003 Bunce et al. described a multistep synthesis starting from either nitrophenol or fluorinated nitrobenzene.[2] Cantet et al. reported the synthesis of α-amidoketones from alkynylated amides obtained by direct alkylation using NaH.[5] Cyclic α-amidoketones can be generated by DPU-promoted cyclization of alkynyl-substituted benzamides.[6] Recently, Yamamoto and co-workers described the synthesis of α-amidoketones starting from methyleneaziridines. The palladium catalyzed ring-opening reaction of a methyleneaziridine with a carboxylic acid gives a N,O-acetal which then rearranges to an α-amidoketone.[1] Here, the starting material was prepared by a base-induced 1,2-dehydro-bromination of 2-(bromomethyl)aziridines synthesized from the corresponding aldehydes.[8] Lantos and Zhang described the formation of α-amidoketones via a multihetero Cope rearrangement in 1994.[7] An organocatalytic approach for the synthesis of α-amidoketones via intermolecular aldehyde-imine cross-couplings was reported by Murry et al. in 2001.[9] In 2005 Miller and co-workers introduced an asymmetric version of this cross-coupling reaction.[10] Moreover, α-amidoketones can be synthesized from amino acids through the Dakin−West reaction.[11,12]

During our investigations on the hydroaminomethylation[13] of vinyl esters with primary amines, we found that the reaction did not lead to the expected hydroaminomethylation products but instead the formation of α-amidoketones was observed. Herein we report the synthetic scope of this new atom-efficient method for the preparation of α-amidoketones starting from a primary amine and propanal-2-yl esters, which are obtained from the hydroformylation of easily accessible or even commercially available vinyl esters.

In a preliminary experiment, when vinyl benzoate **1a** was reacted in the presence of a rhodium catalyst with syngas (20 bar) and isopropylamine at 120 °C, substantial amounts of the α-amidoketone *N*-iso-propyl-*N*-(2-oxopropyl)benzamide **4a** were observed in the reaction mixture (Scheme 1).

Thus, the hydrogenation of the imine intermediate **3a** is much slower in comparison to the observed rearrangement leading to the formation of the α-amidoketone **4a**. To verify whether the rearrangement step is Rh-catalyzed, the reaction of the preformed aldehyde **2a** with isopropylamine was investigated separately. Thus, the aldehyde **2a** and isopropylamine were dissolved in ethanol and heated at 120 °C in a sealed vial in a microwave (300 W) for 2 h (Scheme 2). The ^{1}H NMR spectrum of the crude reaction mixture showed nearly full conversion toward the rearranged product **4a** confirming that the rearrangement is just thermally induced.[14]

To study the scope of this approach, different branched aldehydes were prepared by Rh-catalyzed hydroformylation of vinyl esters using vinyl acetate **1b**, vinyl pivalate **1c**, vinyl benzoate **1a**, vinyl butyrate **1g**, vinyl laurate **1h**, vinyl 4-methoxybenzoate **1d**, vinyl 4-fluorobenzoate **1e**, and vinyl 2-naphthoate **1f** as starting materials.[15] The latter three compounds were prepared by Pd-catalyzed esterification of the corresponding acids with vinyl acetate, which served both as reactant and as solvent (Scheme 3).[16]

Various commercially available monodentate and bidentate phosphorus ligands were screened in the Rh-catalyzed hydroformylation using **1a** as the model substrate (see

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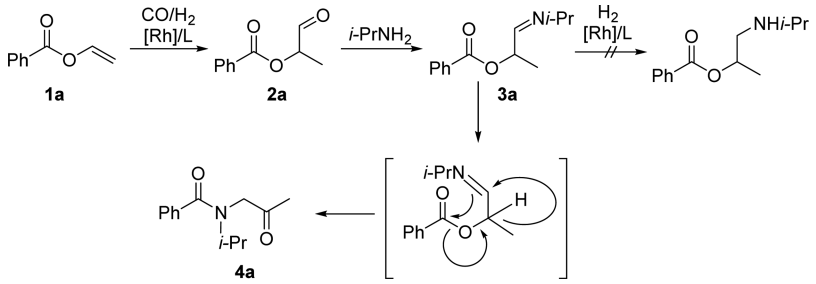
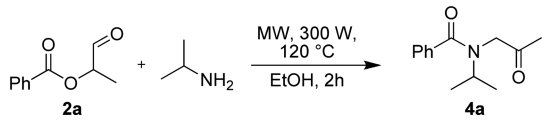
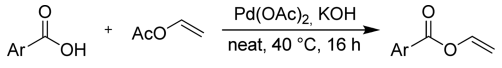
Scheme 1. Cascade Reaction Leading to the Formation of the α-Amidoketone 4a



Scheme 2. Microwave-Promoted Rearrangement Reaction



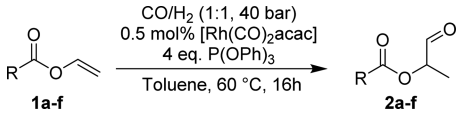
Scheme 3. Synthesis of Noncommercially Available Vinyl Esters by Esterification



d: Ar = 4-Ph-OMe
e: Ar = 4-Ph-F
f: Ar = 2-Nph

Supporting Information for details). Here, the Rh/triphenylphosphite catalyst system led to the best results in terms of activity and regioselectivity at a preparative scale of 5.0 mmol and was therefore used in the hydroformylation of the vinyl esters **1a–h**. The results are summarized in Table 1. Full conversion was achieved for all substrates with regioselectivities of 88–97% toward the branched aldehydes.

Table 1. Hydroformylation of the Vinyl Ester 1a–h[a]

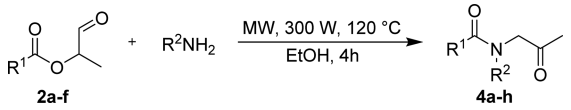


entry	product	R	conv[b] [%]	branched:linear[b]
1	**2b**	Me	>99	92:8
2	**2c**	*t*Bu	>99	88:12
3	**2a**	Ph	>99	97:3
4	**2d**	(4)-MeO-Ph	>99	90:10
5	**2e**	(4)-F-Ph	>99	92:8
6	**2f**	(2)-Nph	>99	92:8
7	**2g**	*n*-C_3H_7	>99	89:11
8	**2h**	*n*-$C_{11}H_{23}$	>99	88:12

[a]Vinyl ester (5.0 mmol), [$Rh(CO)_2acac$] (10 μmol), triphenylphosphite (40 μmol), toluene (0.5 mL), CO/H_2 (1:1, 40 bar), 16 h, 60 °C. [b]Determined by ^1H NMR.

Next, the reaction sequence imine formation/rearrangement was investigated. Control experiments showed that the purification of the aldehydes by column chromatography is not necessary, as identical results were obtained using the crude aldehydes from the hydroformylation reaction as starting material. Consequently, the crude reaction mixtures were directly transferred into the microwave vials and diluted with ethanol. The primary amines were added, and the vials were placed in the microwave. The reactions were performed at 120 °C for 4 h (300 W). The results are summarized in Table 2.

Table 2. Synthesis of α-Amidoketones from Aldehydes and Amines under Microwave Conditions[a]



entry	product	R^1	R^2	yield[b] [%]
1	**4b**	Me	Ph	56
2	**4c**	*t*Bu	Ph	10
3	**4g**	*n*-C_3H_7	Ph	33
4	**4h**	*n*-$C_{11}H_{23}$	Ph	20
5	**4a**	Ph	*i*Pr	34
6	**4i**	Ph	Bn	43
7	**4j**	Ph	Ph	51
8	**4k**	Ph	4-MeO-Ph	38
9	**4l**	Ph	4-F-Ph	52
10	**4m**	Ph	4-CF_3-Ph	46
11	**4d**	(4)-MeO-Ph	Ph	50
12	**4e**	(4)-F-Ph	Ph	21
13	**4f**	(2)-Nph	Ph	52

[a]Vinyl ester (5.0 mmol), amine (5.1 mmol), ethanol (6 mL), 120 °C, 300 W, 4 h. [b]Isolated yield after purification via column chromatography (basic alumina, pentane/ethyl acetate = 2:1–3:1).

Several α-amidoketones with different acyl groups and bearing different substituents at the nitrogen were synthesized and isolated with an ~50% yield in most cases. While a 56% yield was obtained from the acetate derivative **2b** and using aniline as the amine, a lower yield of 10% was obtained starting from propanal-2-yl pivalate **2c**, probably because of the steric bulkiness of the *tert*-butyl group (Table 2, entries 1 and 2). When longer alkyl chains were applied in the R^1 position, the isolated yield decreased with increasing chain length. When the reaction was performed starting from the 1-oxopropan-2-yl butyrate **2g** the corresponding α-amidoketone was isolated in 33% yield (Table 2, entry 3). The α-amidoketone derived from 1-oxopropan-2-yl dodecanoate **2h** was obtained in just 20% yield (Table 2, entry 4). The influence of different amines was investigated using propanal-2-yl benzoate **2a** as the aldehyde component. The highest yield of this series was obtained with 4-fluoroaniline (52%, Table 2, entry 9). It appears that the reaction sequence works best with less basic amines as significantly lower isolated yields were obtained when isopropylamine or benzylamine was used (Table 2, entries 5 and 6). Similar results compared to the benzoate derivative **2a** were achieved using both 2-naphthoate **2f** and the electron-rich

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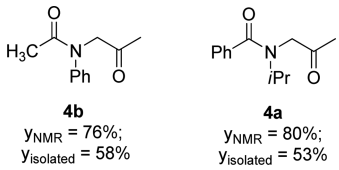
4-OMe-substituted benzoate **2d**. In contrast, a low yield was obtained with the electron-poor 4-fluorobenzoate derivative **2e** (Table 2, entries 11−13).

As mentioned above describing the original experiment leading to the serendipitous discovery of this reaction sequence, it is also possible to perform the complete reaction cascade in a more "user-friendly" one-pot procedure. The reaction control, however, is more challenging as the presence of the amine can hamper the hydroformylation step or side reactions may occur, e.g. the hydrogenation of the aldehyde intermediate.

The ligand set already applied for the hydroformylation (see Supporting Information, Table S1) was tested for the combined hydroformylation/rearrangement reaction using vinyl benzoate **1a** and isopropylamine as starting materials (see Supporting Information, Table S2). When monodentate ligands were used, unreacted starting material was recovered indicating that the presence of the amine completely inhibited the hydroformylation step. In contrast, bidentate phosphine ligands showed good activity in the reaction of vinyl benzoate under "hydroaminomethylation" conditions. Among dppf, dppb, and dppe, the best results were obtained with the latter diphosphine ligand resulting in 53% and 58% yield, respectively (Figure 1).



4b y_{NMR} = 76%; $y_{isolated}$ = 58%

4a y_{NMR} = 80%; $y_{isolated}$ = 53%

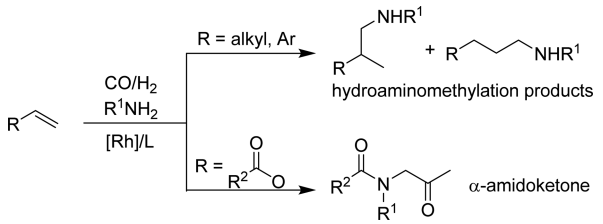
Figure 1. Combined hydroformylation/rearrangement reaction in a one-pot procedure. See Experimental Section for detailed conditions.

It is important to note that a certain level of dilution is necessary to ensure full conversion. Thus, the reactions were performed in 75 mL stainless steel autoclaves at a 3.0 mmol scale using toluene (7.5 mL) as solvent and 1 mol % of rhodium. After 16 h at 120 °C and 40 bar CO/H_2, the reaction of vinyl benzoate with isopropylamine and syngas afforded **4a** in a good yield of 80% (determined by NMR spectroscopy of the crude mixture). The remaining 20% was the imine intermediate **3a**. After purification via column chromatography, **4a** was obtained in 53% isolated yield. A similar trend was observed for the reaction of vinyl acetate and aniline resulting in 76% **4b** and 24% **3b** at full conversion of the starting material. The desired α-amidoketone **4b** was isolated in 58% yield after column chromatography. Thus, for both transformations slightly higher yields were obtained using the one-pot approach when compared to the three-step procedure.

A novel protocol for the synthesis of α-amidoketones from primary amines and propanal-2-yl esters obtained by regioselective hydroformylation of readily available vinyl esters has been developed. The imine key intermediate, which is formed by condensation of the primary amine with the branched aldehyde, undergoes a thermally induced rearrangement to finally give the desired α-amidoketone. The reaction is highly atom-efficient as the only formed byproduct is water. To demonstrate the synthetic applicability of this method, several α-amidoketones were synthesized in moderate to good yields under microwave conditions by simply mixing a primary amine and a propanal-2-yl ester formed via regioselective Rh-catalyzed hydroformylation of the corresponding vinyl ester.

These individual steps can also be combined, and the whole reaction cascade can be carried out in one pot using a bidentate diphosphine/Rh catalyst for the hydroformylation step. Thus, whereas hydroaminomethylation products are obtained when aryl or alkyl substituted olefins are used as substrates (Scheme 4, upper reaction), vinyl esters afford α-amidoketones (Scheme 4, bottom reaction) under similar conditions in decent yields.

Scheme 4. Hydroaminomethylation (R = Alkyl, Ar) vs α-Amidoketone Formation (R = Acyl)



EXPERIMENTAL SECTION

General Considerations. All reactions and manipulations were performed using standard Schlenk techniques or in a glovebox under an argon atmosphere. Microwave experiments were performed in a CEM Discover/Explorer12 Hybrid microwave equipped with an external infrared sensor for temperature measurement. Chemical shifts were referenced to residual solvent peaks (^{1}H NMR, ^{13}C NMR). For NMR peak assignments ^{1}H,^{13}C-HSQC and ^{1}H,^{13}C-HMBC measurements were used. HRMS analyses were performed with high-pressure-liquid chromatography (HPLC), equipped with a mass spectrometer (MS/MS). Samples were ionized with electrospray ionization (ESI) and quantified with high resolution Orbitrap XL. Dichloromethane and toluene were dried over alumina and molecular sieves with a solvent purification system. Vinyl esters were degassed through freeze−pump−thaw cycles. Vinyl 4-methoxybenzoate **1d**, vinyl 4-fluorobenzoate **1e**, and vinyl 2-naphthoate **1f** were synthesized according to literature procedures.[16]

General Experimental Methods. *GP-1: General Procedure for the Synthesis of Vinyl Esters.* The synthesis of the vinyl esters proceeded in accordance to literature.[16] A Schlenk flask was charged with potassium hydroxide (280.6 mg, 5.0 mmol, 1.25 equiv), palladium(II) acetate (898.0 mg, 4.0 mmol), and carboxylic acid (10.0 mmol, 2.5 equiv). The solids were dissolved in vinyl acetate (100 mL), and the resulting reaction mixture was stirred overnight at 40 °C. The reaction mixture was cooled to room temperature, filtered over a Celite pad, and eluted with DCM. The solvents were removed using the rotary evaporator. The crude product was purified by column chromatography (Silica, pentane/ethyl acetate = 4:1).

GP-2: General Procedure for the Catalytic Hydroformylation. Triphenyl phosphite (12.4 mg, 40.0 μmol, 4.0 equiv) was weighed into a Schlenk tube under air. The Schlenk tube was evacuated and refilled with argon three times. A solution of $[Rh(CO)_2acac]$ in toluene (20.0 mM, 0.5 mL, 10.0 μmol) was added, and the mixture was stirred for 10 min at room temperature. The respective substrate (5.0 mmol, 500 equiv) was added, and the reaction mixture was transferred to a 10 mL stainless steel autoclave equipped with a glass inlet and a stirring bar. The autoclave was pressurized with syngas (40 bar) and stirred for 16 h in a heating cone at 60 °C. After carefully releasing the pressure, the reaction mixture was analyzed by NMR and GC.

GP-3: General Procedure for the Microwave-Assisted Rearrangement Reaction. After the hydroformylation reaction the crude reaction mixture was transferred into a microwave vial and diluted with EtOH (6 mL). The respective amine (5.1 mmol, 1.02 equiv) was added dropwise at 0 °C. The microwave vial was placed into the microwave, and the reaction was performed over 4 h at 120 °C with 300 W. The reaction mixture was transferred into a round-bottom flask, and the solvents were removed using first the rotary evaporator

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and then the high vacuum pump. The crude product was purified by column chromatography (basic Al_2O_3, pentane/ethyl acetate = 2:1−3:1).

GP-4: General Procedure for the Catalytic Hydroformylation and Subsequent Rearrangement Reaction. 1,2-Bis(diphenylphosphino)-ethane (35.9 mg, 90.0 μmol, 3.0 equiv) was weighed into a Schlenk tube under air. The Schlenk tube was evacuated and refilled with argon three times. The ligand was dissolved in DCM (0.5 mL). A solution of $[Rh(CO)_2acac]$ (7.7 mg, 30.0 μmol) in toluene (7.5 mL) was added, and the mixture was stirred for 10 min at room temperature. The respective substrate (3.0 mmol, 100.0 equiv) and amine (3.3 mmol, 110.0 equiv) were added, and the reaction mixture was transferred to a 75 mL stainless steel autoclave equipped with a glass inlet and a stirring bar. The autoclave was pressurized with CO (10 bar) first and afterward with hydrogen (50 bar) to obtain a final pressure of 60 bar. The reaction mixture was stirred in a heating cone for 16 h at 90 °C and then for 24 h at 120 °C. After the pressure was carefully released, the reaction mixture was analyzed by NMR. The solvents were removed using first the rotary evaporator and then the high vacuum pump. The crude product was purified by column chromatography (basic Al_2O_3, pentane/ethyl acetate = 3:1).

Vinyl 4-Methoxybenzoate ***1d.*** The compound was synthesized following the general procedure for the synthesis of vinyl esters GP-1 starting from 4-methoxybenzoic acid. The product was obtained as a colorless solid after column chromatography (Silica, pentane/ethyl acetate = 4:1, R_f = 0.64). The obtained chemical shifts fit the reported ones.[16] Yield: m = 1.39 g (7.8 mmol, 78%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.88 (s, 3H, OCH_3), 4.67 (dd, $^2J_{H,H}$ = 1.5 Hz, $^3J_{H,H}$ = 6.3 Hz, 1H, CH_2), 5.03 (dd, $^2J_{H,H}$ = 1.5 Hz, $^3J_{H,H}$ = 14.0 Hz, 1H, CH_2), 6.94 (m, 2H, Ar−CH), 7.50 (dd, $^3J_{H,H}$ = 6.3 Hz, $^3J_{H,H}$ = 14.0 Hz, 1H, CH), 8.06 (m, 2H, Ar−CH) ppm. $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$): δ = 55.5 (CH_3), 97.7 (CH_2), 113.9 (2× CH, Ar), 121.3 (C_q, Ar), 132.3 (2× CH, Ar), 141.6 (CH), 163.7 (C_q, Ar), 164.4 (C_q, CO) ppm.

Vinyl 4-Fluorobenzoate ***1e.*** The compound was synthesized following the general procedure for the synthesis of vinyl esters GP-1 starting from 4-fluorobenzoic acid. The product was obtained as a colorless solid after column chromatography (Silica, pentane/ethyl acetate = 4:1, R_f = 0.73). The obtained chemical shifts fit the reported ones.[16] Yield: m = 1.08 g (6.5 mmol, 65%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.70 (dd, $^2J_{H,H}$ = 1.7 Hz, $^3J_{H,H}$ = 6.3 Hz, 1H, CH_2), 5.06 (dd, $^2J_{H,H}$ = 1.7 Hz, $^3J_{H,H}$ = 14.0 Hz, 1H, CH_2), 7.13 (m, 2H, Ar−CH), 7.48 (dd, $^3J_{H,H}$ = 6.3 Hz, $^3J_{H,H}$ = 14.0 Hz, 1H, CH), 8.12 (m, 2H, Ar−CH) ppm. $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$): δ = 98.4 (CH_2), 115.8 (d, $^2J_{C,F}$ = 22.1 Hz, 2× CH, Ar), 125.2 (d, $^4J_{C,F}$ = 3.0 Hz, C_q, Ar), 132.6 (d, $^3J_{C,F}$ = 9.5 Hz, 2× CH, Ar), 141.3 (CH), 162.7 (C_q, CO), 166.2 (d, $^1J_{C,F}$ = 255.1 Hz, C_q, Ar) ppm. ^{19}F NMR (282 MHz, $CDCl_3$): δ = −104.4 ppm.

Vinyl 2-Naphthoate ***1f.*** The compound was synthesized following the general procedure for the synthesis of vinyl esters GP-1 starting from 2-naphthoic acid. The product was obtained as a colorless liquid after column chromatography (Silica, pentane/ethyl acetate = 4:1, R_f = 0.87). Analytical data agree with literature.[17] Yield: m = 1.49 g (7.5 mmol, 75%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.63 (dd, $^2J_{H,H}$ = 1.7 Hz, $^3J_{H,H}$ = 6.3 Hz, 1H, CH_2), 5.02 (dd, $^2J_{H,H}$ = 1.7 Hz, $^3J_{H,H}$ = 14.0 Hz, 1H, CH_2), 7.37−7.53 (m, 3H, 2× Ar−CH, CH), 7.74 (m, 2H, Ar−CH), 7.82 (m, 1H, Ar−CH), 7.97 (m, 1H, Ar−CH), 8.54 (s, 1H, Ar−CH) ppm. $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$): δ = 98.3 (CH_2), 125.2 (CH), 126.1 (C_q, Ar), 126.8 (CH, Ar), 127.8 (CH, Ar), 128.4 (CH, Ar), 128.6 (CH, Ar), 129.5 (CH, Ar), 131.8 (CH, Ar), 132.4 (C_q, Ar), 135.8 (C_q, Ar), 141.6 (CH), 163.8 (C_q) ppm. IR (ATR): $\tilde{\nu}$ = 3060, 1724, 1643, 1631, 1598, 1509, 1467, 1389, 1355, 1294, 1277, 1265, 1222, 1190, 1134, 1127, 1081, 946, 911, 864, 823, 773, 759, 696, 634, 597, 585, 528, 516, 471 cm^{-1}. HR-MS (ESI): m/z = 199.0754, calculated for $C_{13}H_{11}O_2^+$ ($M-H^+$): 199.0754.

1-Oxopropan-2-yl Benzoate ***2a.*** Analytical data agree with literature.[17] ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.45 (d, $^3J_{H,H}$ = 7.2 Hz, 3H, CH_3), 5.21 (q, $^3J_{H,H}$ = 7.2 Hz, 1H, CH), 7.40 (m, 2H, Ar−CH), 7.52 (m, 1H, Ar), 8.00 (m, 2H, Ar−CH), 9.50 (s, 1H, CHO) ppm. $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ = 14.4 (CH_3), 75.0 (CH), 128.4 (2× CH, Ar), 129.1 (C_q, Ar), 129.6 (2× CH, Ar), 133.0 (CH, Ar), 166.6 (C_q, CO), 198.7 (CHO).

1-Oxopropan-2-yl Acetate ***2b.*** Analytical data agree with literature.[17] ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.30 (d, $^3J_{H,H}$ = 7.2 Hz, 3H, CH_3), 2.07 (s, 3H, CH_3), 4.97 (q, $^3J_{H,H}$ = 7.2 Hz, 1H, CH), 9.39 (s, 1H, CHO) ppm. $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$): δ = 13.6 (CH_3), 21.1 (CH_3), 74.4 (CH), 170.0 (C_q, CO), 197.9 (CHO) ppm.

1-Oxopropan-2-yl Pivalate ***2c.*** Analytical data agree with literature.[17] ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.18 (s, 9H, $C(CH_3)_3$), 1.33 (d, $^3J_{H,H}$ = 7.2 Hz, 3H, CH_3), 4.96 (q, $^3J_{H,H}$ = 7.2 Hz, 1H, CH), 9.40 (s, 1H, CHO) ppm. $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$): δ = 14.2 (CH_3), 27.2 (3× CH_3), 38.8 (C_q) 74.5 (CH), 178.1 (C_q, CO), 198.6 (CHO) ppm.

1-Oxopropan-2-yl 4-Methoxybenzoate ***2d.*** Analytical data agree with literature.[17] ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.51 (d, $^3J_{H,H}$ = 7.2 Hz, 3H, CH_3), 3.86 (s, 3H, OCH_3), 5.24 (q, $^3J_{H,H}$ = 7.2 Hz, 1H, CH), 7.93 (m, 2H, Ar−CH), 8.04 (m, 2H, Ar−CH), 9.65 (s, 1H, CHO) ppm. $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 14.5 (CH_3), 55.5 (OCH_3), 74.9 (CH), 113.9 (2× CH, Ar), 121.5 (C_q, Ar), 132.0 (2× CH, Ar), 163.9 (C_q, Ar), 165.8 (C_q, CO), 199.1 (CHO) ppm. IR (ATR): $\tilde{\nu}$ = 2938, 2841, 1707, 1646, 1604, 1581, 1511, 1458, 1422, 1316, 1292, 1250, 1167, 1097, 1069, 1025, 911, 846, 822, 785, 768, 732, 696, 636, 610, 512, 414 cm^{-1}. HR-MS (ESI): m/z = 209.0802, calculated for $C_{11}H_{13}O_4^+$ ($M-H^+$): 209.0808.

1-Oxopropan-2-yl 4-Fluorobenzoate ***2e.*** Analytical data agree with literature.[17] ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.54 (d, $^3J_{H,H}$ = 7.2 Hz, 3H, CH_3), 5.28 (q, $^3J_{H,H}$ = 7.2 Hz, 1H, CH), 7.12 (m, 2H, Ar−CH), 8.10 (m, 2H, Ar−CH), 9.64 (s, 1H, CHO) ppm. $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 14.3 (CH_3), 75.2 (CH), 115.7 (d, $^2J_{C,F}$ = 22.1 Hz, 2× CH, Ar), 125.4 (d, $^4J_{C,F}$ = 3.0 Hz, C_q, Ar), 132.5 (d, $^3J_{C,F}$ = 9.5 Hz, 2× CH, Ar), 165.0 (C_q, CO), 166.1 (d, $^1J_{C,F}$ = 254.9 Hz, C_q, Ar), 198.3 (CHO) ppm. ^{19}F NMR (377 MHz, $CDCl_3$): δ = −104.5 ppm. IR (ATR): $\tilde{\nu}$ = 2992, 1716, 1646, 1603, 1507, 1449, 1412, 1325, 1292, 1260, 1237, 1154, 1130, 1105, 1088, 1069, 1014, 948, 852, 824, 800, 764, 687, 624, 607, 503 cm^{-1}. HR-MS (ESI): m/z = 197.0606, calculated for $C_{10}H_{10}O_3F^+$ ($M-H^+$): 197.0608.

1-Oxopropan-2-yl 2-Naphthoate ***2f.*** Analytical data agree with literature.[17] ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.45 (d, $^3J_{H,H}$ = 7.2 Hz, 3H, CH_3), 5.24 (q, $^3J_{H,H}$ = 7.2 Hz, 1H, CH), 7.36−7.48 (m, 2H, Ar−CH), 7.72 (m, 2H, Ar−CH), 7.80 (d, $^3J_{H,H}$ = 8.0 Hz, 1H, Ar−CH), 7.96 (m, 1H, Ar−CH), 8.54 (s, 1H, Ar−CH), 9.59 (s, 1H, CHO) ppm. $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 14.1 (CH_3), 75.0 (CH), 124.9 (CH, Ar), 126.1 (C_q, Ar), 126.6 (CH, Ar), 127.5 (CH, Ar), 128.1 (CH, Ar), 128.3 (CH, Ar), 129.1 (CH, Ar), 131.3 (CH, Ar), 132.2 (C_q, Ar), 135.5 (C_q, Ar), 165.8 (C_q, CO), 198.4 (CHO) ppm. IR (ATR): $\tilde{\nu}$ = 3060, 2988, 2939, 2820, 1710, 1645, 1631, 1599, 1578, 1508, 1466, 1388, 1354, 1325, 1275, 1266, 1224, 1193, 1129, 1088, 1067, 955, 911, 865, 825, 776, 760, 731, 634, 596, 584, 516, 472 cm^{-1}. HR-MS (ESI): m/z = 229.0862, calculated for $C_{14}H_{13}O_3^+$ ($M-H^+$): 229.0859.

1-Oxopropan-2-yl Butyrate ***2g.*** Analytical data agree with literature.[18] ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.97 (t, $^3J_{H,H}$ = 7.4 Hz, 3H, CH_3), 1.38 (d, $^3J_{H,H}$ = 7.2 Hz, 3H, CH_3), 1.69 (m, 2H, CH_2), 2.39 (dt, $^3J_{H,H}$ = 7.5 Hz, $^2J_{H,H}$ = 2.2 Hz, 2H, CH_2), 5.06 (q, $^3J_{H,H}$ = 7.2 Hz, 1H, CH), 9.51 (s, 1H, CHO) ppm. $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 13.6 (CH_3), 14.1 (CH_3), 18.4 (CH_2), 35.8 (CH_2), 74.4 (CH), 173.1 (C_q, CO), 198.6 (CHO) ppm.

1-Oxopropan-2-yl Dodecanoate ***2h.*** Analytical data agree with literature.[18] ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.87 (t, $^3J_{H,H}$ = 6.7 Hz, 3H, CH_3), 1.21−1.34 (m, 16H, 8× CH_2), 1.38 (d, $^3J_{H,H}$ = 7.3 Hz, 3H, CH_3), 1.65 (m, 2H, CH_2), 2.40 (dt, $^3J_{H,H}$ = 7.5 Hz, $^2J_{H,H}$ = 2.0 Hz, 2H, CH_2), 5.06 (q, $^3J_{H,H}$ = 7.2 Hz, 1H, CH), 9.52 (s, 1H, CHO) ppm. $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 14.1 (CH_3), 14.2 (CH_3), 22.7 (CH_2), 24.9 (CH_2), 29.1 (CH_2), 29.2 (CH_2), 29.3 (CH_2), 29.4 (CH_2), 29.6 (2× CH_2), 31.9 (CH_2), 34.0 (CH_2), 74.4 (CH), 173.3 (C_q, CO), 198.6 (CHO) ppm.

N-Isopropyl-N-(2-oxopropyl)benzamide ***4a.*** The compound was obtained as a colorless liquid after column chromatography (basic Al_2O_3, pentane/ethyl acetate = 3:1, R_f = 0.23). Yield: m = 372.8 mg (1.7 mmol, 34%). ^{1}H NMR(400 MHz, $CDCl_3$): δ = 1.00 (d, $^3J_{H,H}$ =

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6.7 Hz, 6H, 2×CH_3), 2.16 (s, 3H, CH_3), 3.95 (sept, $^3J_{H,H}$ = 6.7 Hz, 1H, CH), 4.00 (s, 2H, CH_2), 7.32 (s, 5H, 5× Ar−CH) ppm. $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ [ppm]: 20.8 (2× CH_3), 27.3 (CH_3), 49.9 (CH), 49.9 (CH_2), 126.1 (2× CH, Ar), 128.5 (2× CH, Ar), 129.4 (CH, Ar), 136.3 (C_q, Ar), 171.4 (C_q, NCO), 202.8 (C_q, CO) ppm. IR (ATR): $\tilde{\nu}$ = 2977, 2934, 1730, 1625, 1601, 1578, 1496, 1433, 1400, 1360, 1341, 1223, 1201, 1170, 1127, 1073, 1040, 1026, 986, 919, 882, 851, 783, 736, 700, 657, 630, 617, 609, 570, 544, 496, 479, 409 cm^{-1}. HR-MS (ESI): m/z = 220.1343, calculated for $C_{13}H_{18}NO_2^+$ ($M-H^+$): 220.1332.

N-(2-Oxopropyl)-N-phenylacetamide **4b**. Analytical data agree with literature.[5] The compound was obtained as a dark orange oil after column chromatography (basic Al_2O_3, pentane/ethyl acetate = 3:1, R_f = 0.23). Yield: m = 535.4 mg (2.8 mmol, 56%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.84 (s, 3H, CH_3), 2.08 (s, 3H, CH_3), 4.36 (s, 2H, CH_2), 7.21−7.36 (m, 5H, 5× Ar−CH) ppm. $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 22.1 (CH_3), 27.1 (CH_3), 59.3 (CH_2), 127.9 (2× CH, Ar), 128.1 (CH, Ar), 129.7 (2× CH, Ar), 143.5 (C_q, Ar), 170.7 (C_q, NCO), 202.4 (C_q, CO) ppm. HR-MS (ESI): m/z = 192.1012, calculated for $C_{11}H_{14}NO_2^+$ ($M-H^+$): 192.1019.

N-(2-Oxopropyl)-N-phenylpivalamide **4c**. The compound was obtained as a dark orange oil after column chromatography (basic Al_2O_3, pentane/ethyl acetate = 3:1, R_f = 0.22). Yield: m = 116.7 mg (0.5 mmol, 10%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.04 (s, 9H, $C(CH_3)$), 2.15 (s, 3H, CH_3), 4.27 (s, 2H, CH_2), 7.30−7.42 (m, 5H, 5× Ar−CH) ppm. $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 27.2 (CH_3), 29.4 (3× CH_3), 40.7 (C_q), 62.9 (CH_2), 128.3 (CH, Ar), 129.2 (2× CH, Ar), 129.7 (2× CH, Ar), 144.3 (C_q, Ar), 177.8 (C_q, NCO), 202.7 (C_q, CO) ppm. IR (ATR): $\tilde{\nu}$ = 3353, 2960, 2932, 2873, 1727, 1633, 1594, 1495, 1480, 1452, 1442, 1408, 1396, 1358, 1298, 1228, 1202, 1167, 1061, 1027, 1003, 973, 936, 771, 750, 703, 652, 617, 583, 565, 490, 432 cm^{-1}. HR-MS (ESI): m/z = 234.1487, calculated for $C_{14}H_{20}NO_2^+$ ($M-H^+$): 234.1489.

4-Methoxy-N-(2-oxopropyl)-N-phenylbenzamide **4d**. The compound was obtained as light yellow crystals after column chromatography (basic Al_2O_3, pentane/ethyl acetate = 3:1, R_f = 0.19), mp = 125.0 °C. Yield: m = 708.3 mg (2.5 mmol, 50%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.23 (s, 3H, CH_3), 3.73 (s, 3H, OCH_3), 4.64 (s, 2H, CH_2), 6.66 (m, 2H, 2× Ar−CH), 7.18−7.06 (m, 3H, 3× Ar−CH), 7.32−7.19 (m, 4H, 4× Ar−CH) ppm. $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 27.3 (CH_3), 55.2 (OCH_3), 60.5 (CH_2), 113.0 (2× CH, Ar), 126.7 (CH, Ar), 127.0 (C_q, Ar), 127.3 (2× CH, Ar), 129.2 (2× CH, Ar), 131.1 (2× CH, Ar), 144.4 (C_q, Ar), 160.9 (C_q, Ar), 170.0 (C_q, NCO), 202.7 (C_q, CO) ppm. IR (ATR): $\tilde{\nu}$ = 3073, 3018, 2963, 2934, 2840, 2052, 1979, 1900, 1724, 1632, 1606, 1593, 1578, 1514, 1495, 1462, 1453, 1445, 1410, 1370, 1325, 1310, 1283, 1251, 1228, 1185, 1173, 1155, 1117, 1071, 1039, 1025, 974, 958, 916, 846, 820, 807, 799, 772, 759, 709, 699, 693, 656, 630, 599, 564, 534, 491, 479, 447, 433 cm^{-1}. HR-MS (ESI): m/z = 284.1279, calculated for $C_{17}H_{18}NO_3^+$ ($M-H^+$): 284.1281.

4-Fluoro-N-(2-oxopropyl)-N-phenylbenzamide **4e**. The compound was obtained as a dark yellow oil after column chromatography (basic Al_2O_3, pentane/ethyl acetate = 3:1, R_f = 0.23). Yield: m = 284.9 mg (1.1 mmol, 21%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.09 (s, 3H, CH_3), 4.51 (s, 2 H, CH_2), 6.70 (m, 2H, 2× Ar−CH), 6.94 (m, 2H, 2× Ar−CH), 7.01(m, 1H, Ar−CH), 7.08 (m, 2H, 2× Ar−CH), 7.20 (m, 2H, 2× Ar−CH) ppm. $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 27.3 (CH_3), 60.4 (CH_2), 114.9 (d, $^2J_{C,F}$ = 22 Hz, 2× CH, Ar), 127.0 (CH, Ar), 127.3 (2× CH, Ar), 129.3 (2× CH, Ar), 131.1 (d, $^4J_{C,F}$ = 3.3 Hz, C_q, Ar), 131.2 (d, $^3J_{C,F}$ = 8.7 Hz, 2× CH, Ar), 143.9 (C_q, Ar), 163.4 (d, $^1J_{C,F}$ = 250.3 Hz, C_q, Ar), 169.4 (C_q, NCO), 202.2 (C_q, CO) ppm. ^{19}F NMR (377 MHz, $CDCl_3$): δ = −109.57 ppm. IR (ATR): $\tilde{\nu}$ = 3378, 3055, 2928, 1725, 1636, 1600, 1506, 1493, 1455, 1441, 1411, 1372, 1320, 1307, 1268, 1224, 1178, 1153, 1113, 1100, 1090, 1070, 1035, 1013, 992, 964, 915, 851, 815, 767, 749, 698, 690, 630, 607, 596, 558, 519, 483, 443, 407 cm^{-1}. HR-MS (ESI): m/z = 272.1078, calculated for $C_{16}H_{15}NO_2F^+$ ($M-H^+$): 272.1081.

N-(2-Oxopropyl)-N-phenyl-2-naphthamide **4f**. The compound was obtained as a yellow oil, which slowly crystallizes after column chromatography (basic Al_2O_3, pentane/ethyl acetate = 3:1, R_f = 0.41), mp = 73.1 °C. Yield: m = 788.7 mg (2.6 mmol, 52%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.27 (s, 3H, CH_3), 4.72 (s, 2 H, CH_2), 7.22−7.06 (m, 5H, 5× Ar−CH), 7.46−7.34 (m, 3H, 3× Ar−CH), 7.59 (m, 1H, Ar−CH), 7.75−7.68 (m, 2H, 2× Ar−CH), 7.94 (m, 1H, Ar−CH) ppm. $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 27.4 (CH_3), 60.5 (CH_2), 125.5 (CH, Ar), 126.4 (CH, Ar), 126.9 (CH, Ar), 127.2 (CH, Ar), 127.3 (CH, Ar), 127.4 (2× CH, Ar), 127.6 (CH, Ar), 128.7 (CH, Ar), 129.2 (2× CH, Ar), 129.7 (CH, Ar), 132.4 (C_q, Ar), 132.5 (C_q, Ar), 133.7 (C_q, Ar), 144.0 (C_q, Ar), 170.4 (C_q, NCO), 202.5 (C_q, CO) ppm. IR (ATR): $\tilde{\nu}$ = 3367, 3053, 2962, 2929, 1962, 1735, 1719, 1635, 1626, 1593, 1574, 1497, 1468, 1458, 1410, 1380, 1351, 1325, 1313, 1285, 1245, 1228, 1196, 1169, 1149, 1124, 1094, 1083, 1067, 1036, 1016, 1002, 987, 971, 965, 957, 917, 902, 864, 823, 774, 761, 729, 699, 662, 640, 623, 585, 551, 515, 476, 440, 433, 412 cm^{-1}. HR-MS (ESI): m/z = 304.1326, calculated for $C_{20}H_{18}NO_2^+$ ($M-H^+$): 304.1332.

N-(2-Oxopropyl)-N-phenylbutyramide **4g**. The compound was obtained as a dark yellow oil after column chromatography (basic Al_2O_3, pentane/ethyl acetate = 2:1, R_f = 0.42). Yield: m = 361.1 mg (1.6 mmol, 33%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.74 (t, $^3J_{H,H}$ = 7.4 Hz, 3H, CH_3), 1.50 (m, 2H, CH_2), 2.02 (t, $^3J_{H,H}$ = 7.4 Hz, 2H, CH_2), 2.07 (s, 3H, CH_3), 4.34 (s, 2 H, CH_2), 7.20−7.27 (m, 3H, 3× Ar−CH), 7.28−7.34 (m, 2H, 2× Ar−CH) ppm. $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 13.7 (CH_3), 18.6 (CH_2), 27.1 (CH_3), 35.5 (CH_2), 59.4 (CH_2), 128.0 (3× Ar−CH), 129.6 (2× Ar−CH), 143.1 (C_q, Ar), 173.1 (C_q, NCO), 202.5 (C_q,CO) ppm. IR (ATR): $\tilde{\nu}$ = 1733, 1652, 1595, 1495, 1411, 1383, 1350, 1293, 1212, 1169, 1067, 700, 552 cm^{-1}. HR-MS (ESI): m/z = 220.1326, calculated for $C_{13}H_{18}NO_2^+$ ($M-H^+$): 220.1332.

N-(2-Oxopropyl)-N-phenyldodecanamide **4h**. The compound was obtained as a dark yellow oil after column chromatography (basic Al_2O_3, pentane/ethyl acetate = 2:1, R_f = 0.45). Yield: m = 351.5 mg (1.0 mmol, 20%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.87 (t, $^3J_{H,H}$ = 6.8 Hz, 3H, CH_3), 1.10−1.33 (m, 16H, 8× CH_2), 1.55 (m, 2H, CH_2), 2.11 (m, 2H, CH_2), 2.16 (s, 3H, CH_3), 4.41 (s, 2H, CH_2), 7.24−7.44 (m, 5H, 5× Ar−CH) ppm. $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 14.1 (CH_3), 22.7 (CH_2), 25.3 (CH_2), 27.2 (CH_3), 29.2 (CH_2), 29.3 (2× CH_2), 29.4 (CH_2), 29.6 (2× CH_2), 31.9 (CH_2), 33.7 (CH_2), 59.4 (CH_2), 128.1 (Ar−CH), 128.1 (2× Ar−CH), 129.7 (2× Ar−CH), 143.2 (C_q, Ar), 173.5 (C_q, NCO), 202.6 (C_q, CO) ppm. IR (ATR): $\tilde{\nu}$ = 2922, 2853, 1735, 1657, 1596, 1495, 1412, 1382, 1357, 1169, 700, 552 cm^{-1}. HR-MS (ESI): m/z = 332.2577, calculated for $C_{21}H_{34}NO_2^+$ ($M-H^+$): 332.2584.

N-Benzyl-N-(2-oxopropyl)benzamide **4i**. Analytical data agree with literature.[1] The compound was obtained as yellow crystals after column chromatography (basic Al_2O_3, pentane/ethyl acetate = 3:1, R_f = 0.41), mp = 77.8 °C. Yield: m = 574.8 mg (2.2 mmol, 43%). **Rotation isomer *major*:** ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.15 (s, 3H, CH_3), 4.19 (s, 2H, CH_2), 4.56 (s, 2H, CH_2), 7.12−7.57 (m, 10H, 10x Ar−CH) ppm. $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 27.5 (CH_3), 53.9 (CH_2), 54.2 (CH_2), 126.9 (2× CH, Ar), 127.0 (2× CH, Ar), 127.9 (CH, Ar), 128.6 (2× CH, Ar), 129.0 (2× CH, Ar), 130.0 (CH, Ar), 135.3 (C_q, Ar), 136.2 (C_q, Ar), 172.5 (C_q, NCO), 202.6 (C_q, CO) ppm. **Rotation isomer *minor*:** ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.88 (s, 3H, CH_3), 3.90 (s, 2H, CH_2), 4.76 (s, 2H, CH_2), 7.12−7.57 (m, 10H, 10x Ar−CH) ppm. $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 27.0 (CH_3), 49.1 (CH_2), 57.6 (CH_2), 126.4 (2× CH, Ar), 127.8 (CH, Ar), 128.5 (2× CH, Ar), 128.6 (2× CH, Ar), 128.8 (2× CH, Ar), 129.9 (CH, Ar), 136.0 (C_q, Ar), 136.5 (C_q, Ar), 172.4 (C_q, Ar), 203.1 (C_q, CO) ppm. HR-MS (ESI): m/z = 268.1347, calculated for $C_{17}H_{18}NO_2^+$ ($M-H^+$): 268.1332.

N-(2-Oxopropyl)-N-phenylbenzamide **4j**. The compound was obtained as yellow crystals after column chromatography (basic Al_2O_3, pentane/ethyl acetate = 3:1, R_f = 0.40), mp = 88.1 °C. Yield: m = 645.9 mg (2.6 mmol, 51%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.12 (s, 3H, CH_3), 4.56 (s, 2H, CH_2), 6.99−7.13 (m, 8H, 8× Ar−CH), 7.23−7.25 (m, 2H, 2× Ar−CH) ppm. $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 27.3 (CH_3), 60.3 (CH_2), 126.9 (CH, Ar), 127.4 (2× CH, Ar), 127.7 (2× CH, Ar), 128.8 (2× CH, Ar), 129.2 (2× CH, Ar), 129.9 (CH, Ar), 135.1 (C_q, Ar), 143.9 (C_q, Ar), 170.5 (C_q, NCO), 202.4 (C_q, CO) ppm. IR (ATR): $\tilde{\nu}$ = 3057, 3026, 2969, 2927, 1724,

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1646, 1595, 1493, 1455, 1445, 1410, 1381, 1342, 1322, 1311, 1277, 1223, 1166, 1115, 1068, 1040, 1025, 1002, 977, 914, 785, 770, 727, 715, 694, 662, 628, 563, 521, 452 cm^{-1}. HR-MS (ESI): m/z = 254.1180, calculated for $C_{16}H_{16}NO_2^+$ ($M-H^+$): 254.1176.

N-(4-Methoxyphenyl)-N-(2-oxopropyl)benzamide **4k**. The compound was obtained as a dark yellow oil after column chromatography (basic Al_2O_3, pentane/ethyl acetate = 2:1, R_f = 0.32). Yield: m = 532.3 mg (1.9 mmol, 38%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.21 (s, 3H, CH_3), 3.71 (s, 3H, OCH_3), 4.61 (s, 2H, CH_2), 6.66−6.72 (m, 2H, 2× Ar−CH), 6.99−7.06 (m, 2H, 2× Ar−CH), 7.12−7.19 (m, 2H, 2× Ar−CH), 7.20−7.25 (m, 1H, Ar−CH), 7.29−7.35 (m, 2H, 2× Ar−CH) ppm. $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 27.3 (CH_3), 55.4 (OCH_3), 60.5 (CH_2), 114.3 (2× CH, Ar), 127.7 (2× CH, Ar), 128.7 (2× CH, Ar), 128.8 (2× CH, Ar), 129.7 (CH, Ar), 135.2 (C_q, Ar), 136.8 (C_q, Ar), 158.2 (C_q, Ar), 170.6 (C_q, NCO), 202.5 (C_q, CO) ppm. IR (ATR): $\tilde{\nu}$ = 1730, 1638, 1508, 1446, 1425, 1407, 1374, 1322, 1291, 1246, 1225, 1173, 1026, 838, 721, 701, 611, 565 cm^{-1}. HR-MS (ESI): m/z = 284.1288, calculated for $C_{17}H_{18}NO_3^+$ ($M-H^+$): 284.1281.

N-(4-Fluorophenyl)-N-(2-oxopropyl)benzamide **4l**. The compound was obtained as a dark yellow oil after column chromatography (basic Al_2O_3, pentane/ethyl acetate = 2:1, R_f = 0.37). Yield: m = 701.4 mg (2.6 mmol, 52%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.23 (s, 3H, CH_3), 4.63 (s, 2H, CH_2), 6.85−6.92 (m, 2H, 2× Ar−CH), 7.05−7.13 (m, 2H, 2× Ar−CH), 7.14−7.21 (m, 2H, 2× Ar−CH), 7.25 (m, 1H, Ar−CH), 7.28−7.34 (m, 2H, 2× Ar−CH) ppm. $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 27.3 (CH_3), 60.2 (CH_2), 116.0 (d, $^2J_{CF}$ = 22.4 Hz, 2× Ar−CH), 127.9 (2× Ar−CH), 128.7 (2× Ar−CH), 129.3 (d, $^3J_{CF}$ = 8.8 Hz, 2× Ar−CH), 130.0 (Ar−CH), 134.9 (C_q), 140.0 (d, $^4J_{CF}$ = 3.1 Hz, C_q), 161.0 (d, $^1J_{CF}$ = 247.8 Hz, C_q), 170.6 (C_q, NCO), 202.2 (C_q,CO) ppm. ^{19}F NMR (377 MHz, $CDCl_3$): δ = −114.27 ppm. IR (ATR): $\tilde{\nu}$ = 1729, 1638, 1509, 1446, 1424, 1407, 1373, 1321, 1291, 1246, 1224, 1172, 1162, 1039, 1025, 838, 782, 720, 700, 611, 564 cm^{-1}. HR-MS (ESI): m/z = 272.1080, calculated for $C_{16}H_{15}FNO_2^+$ ($M-H^+$): 272.1081.

N-(2-Oxopropyl)-N-(4-(trifluoromethyl)phenyl)benzamide **4m**. The compound was obtained as a dark yellow oil after column chromatography (basic Al_2O_3, pentane/ethyl acetate = 2:1, R_f = 0.34). Yield: m = 744.1 mg (2.3 mmol, 46%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.25 (s, 3H, CH_3), 4.69 (s, 2 H, CH_2), 7.16−7.23 (m, 4H, 4× Ar−CH), 7.27−7.7.35 (m, 3H, 3× Ar−CH), 7.43−7.49 (m, 2H, 2× Ar−CH) ppm. $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 27.3 (CH_3), 60.0 (CH_2), 121.6 (q, $^1J_{CF}$ = 272.2 Hz, CF_3), 126.3 (q, $^3J_{CF}$ = 3.6 Hz, 2× Ar−CH), 127.4 (2× Ar−CH), 128.1 (2× Ar−CH), 128.2 (q, $^2J_{C,F}$ = 51.5 Hz, C_q, Ar), 128.8 (2× Ar−CH), 130.5 (Ar−CH), 134.4 (C_q, Ar), 147.1 (C_q, Ar), 170.5 (C_q, NCO), 202.0 (C_qCO) ppm. ^{19}F NMR (377 MHz, $CDCl_3$): δ = −62.52 ppm. IR (ATR): $\tilde{\nu}$ = 1652, 1612, 1320, 1161, 1107, 1065, 101, 834, 709 cm^{-1}. HR-MS (ESI): m/z = 322.1058, calculated for $C_{17}H_{15}F_3NO_2^+$ ($M-H^+$): 322.1049.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b02851.

NMR spectra, IR spectra, and additional Tables S1 and S2 (PDF)

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Notes

The authors declare no competing financial interest.

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(14) The imine intermediate **3a** and the product **4a** were obtained in approximately equal amounts at 100 °C, whereas at 140 °C higher amounts of **4a** were formed albeit with several unidentified side products deriving from the degradation of the imine intermediate. The addition of water scavengers (4Å molecular sieve, $MgSO_4$) does not have a significant influence while acidic or basic additives (HBF_4, NEt_3) led to reduced conversion. Consequently, all following experiments were performed at 120 °C and without additives.

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