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Full Paper

Decarboxylative C–N Bond Formation

One-Pot Transformation of Aliphatic Carboxylic Acids into *N*-Alkylsuccinimides with NIS and NCS/NaI

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Abstract: Primary aliphatic carboxylic acids were treated with *N*-iodosuccinimide (NIS) in 1,2-dichloroethane to form the corresponding alkyl iodides under warming conditions. Based on these results, those aliphatic carboxylic acids were treated with NIS, followed by the reaction with K_2CO_3 to give the corresponding *N*-alkylsuccinimides in good yields in one pot. Moreover, those aliphatic carboxylic acids were treated with *N*-chlorosuccinimide (NCS) and NaI, followed by the reaction with K_2CO_3 to provide the corresponding *N*-alkylsuccinimides in good to moderate yields in one pot. By using the present method, successive treatment of primary aliphatic carboxylic acids (10 mmol) with NIS, K_2CO_3, and then hydrazine provided the corresponding decarboxylated primary amines in good yield.

Introduction

The oxidative functionalization of carboxylic acids is an attractive reaction, because various carboxylic acids, such as fatty acids, are easily available. The decarboxylative halogenation of carboxylic acids, in particular, is useful for organic synthesis. Useful and well-known reactions include the Hunsdiecker–Borodin reaction with RCO_2Ag and bromine, or the modified reaction with carboxylic acids, HgO, and bromine,[1] and the decarboxylative iodination of carboxylic acids with $Pb(OAc)_4$ and iodine.[2] As transition-metal-free methods, the decarboxylative iodination of *N*-acyloxy-2-thiopyridone, prepared from aliphatic carboxylic acids and *N*-hydroxy-2-thiopyridone, with CHI_3 in benzene under refluxing conditions or by tungsten-lamp irradiation was reported.[3] Moreover, the decarboxylative iodination of aliphatic carboxylic acids with (diacetoxyiodo)benzene and iodine in carbon tetrachloride under refluxing and tungsten-lamp irradiation conditions was also reported.[4] Both reactions are useful for the preparation of alkyl iodides. However, some disadvantages remain: the former reaction requires the preparation of moisture- and light-sensitive *N*-acyloxy-2-thiopyridone with 2-pyridyl diiodomethyl sulfide being formed as the co-product, and the latter reaction generates iodobenzene as the co-product. Recently, the effective conversion of aliphatic carboxylic acids into alkyl iodides with 1,3-diiodo-5,5-dimethylhydantoin (DIH) in 1,2-dichloroethane under refluxing conditions was reported.[5] *N*-Iodosuccinimide (NIS) was also studied, but it was found that DIH was much more effective than NIS. Here, as part of our synthetic study of iodine,[6] we would like to report a one-pot conversion of primary aliphatic carboxylic acids into *N*-alkylsuccinimides via alkyl iodides, as *N*-alkylsuccinimides can be smoothly converted into the corresponding primary amines by treatment with hydrazine or aq. KOH solution.

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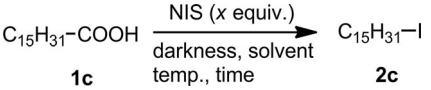
Results and Discussion

Initially, the best conditions for the conversion of palmitic acid into 1-iodopentadecane with NIS (1.2 equiv., 2.0 equiv. 3.0 equiv.) in 1,2-dichloroethane (DCE), carbon tetrachloride, toluene, 1,4-dioxane, acetonitrile, and propionitrile at 80 °C or 100 °C in a 20 mL screw-capped flask were studied, as shown in Table 1, and it was found that the treatment of palmitic acid with NIS (3.0 equiv.) in the presence of iodine (1.0 equiv.) in DCE at 100 °C for 12 h gave 1-iodopentadecane in 96 % yield

Table 1. Optimization for transformation of palmitic acid into 1-iodopentadecane with NIS.



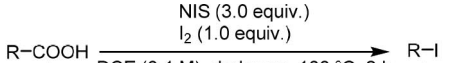
Entry	*x*	Solvent	*T* [°C]	*t* [h]	Yield [%]
1	1.2	DCE (0.5 M)	80	2	19 (78)[a]
2[b]	1.2	DCE (0.5 M)	80	2	11 (84)[a]
3[c]	1.2	DCE (0.5 M)	80	2	n.r.
4[d]	2.0	DCE (0.1 M)	100	12	82 (11)[a]
5	3.0	DCE (0.5 M)	100	4	51 (43)[a]
6	3.0	DCE (0.1 M)	100	6	89 (9)[a]
7	3.0	DCE (0.1 M)	100	12	92
8[d]	3.0	DCE (0.1 M)	100	12	96
9	3.0	CCl_4 (0.1 M)	80	12	76 (18)[a]
10	3.0	toluene (0.1 M)	100	12	89 (5)[a]
11	3.0	1,4-dioxane (0.1 M)	100	12	24 (64)[a]
12	3.0	MeCN (0.1 M)	100	24	46 (48)[a]
13	3.0	EtCN (0.1 M)	110	24	44 (46)[a]

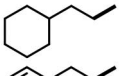
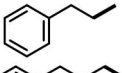
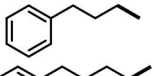
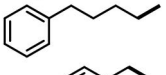
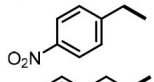
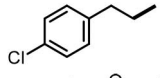
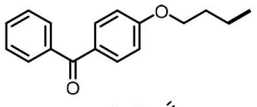
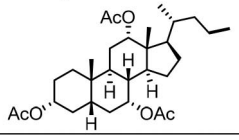
[a] Values in parentheses: recovery of starting carboxylic acid; n.r.: no reaction. [b] K_2CO_3 (10 mol-%) was added. [c] $TsOH{\cdot}H_2O$ (10 mol-%) was added. [d] I_2 (1.0 equiv.) was added.

(Entry 8). Here, iodine works as an effective carbon radical scavenger to form alkyl iodide smoothly.

Based on those results, various primary aliphatic carboxylic acids, such as nonanoic acid, decanoic acid, stearic acid, monomethyl suberate, monomethyl sebacate, 3-cyclohexylpropanoic acid, 3-phenylpropanoic acid, 4-phenylbutanoic acid, 5-phenylpentanoic acid, 2-(*p*-nitrophenyl)ethanoic acid, 3-(*p*-chlorophenyl)propanoic acid, and 4-(4′-benzoylphenoxy)butanoic acid, were treated with NIS (3.0 equiv.) in DCE in a 20 mL screw-capped flask at 100 °C to provide the corresponding alkyl iodides in good yields, as shown in Table 2 (Entries 1, 2, 4–13). Tri-*O*-acetylcholic acid was also converted into the corresponding iodide in good yield under the same reaction conditions (Entry 14). Then, a one-pot transformation of carboxylic acids into *N*-alkylsuccinimides was carried out (Table 3). Treatment of palmitic acid with NIS (3.0 equiv.) in DCE at 100 °C, followed by the reaction with K_2CO_3 in the presence of tetrabutylammonium bromide (TBAB) at 100 °C in a 20 mL screw-capped flask gave the corresponding *N*-pentadecylsuccinimide. However, the yield was dependent on the solvent. Thus, after the first reaction with NIS in DCE, the solvent was removed by evaporation, and acetonitrile, acetone, or 1,4-dioxane was added to the residue, together with K_2CO_3 and TBAB, and the mixture was warmed in the same 20 mL screw-capped flask to give *N*-pentadecylsuccinimide in good yields, as shown in Table 3 (Entries 2, 5, 6). Based on the optimum reaction conditions, various primary aliphatic carboxylic acids, such as nonanoic acid, decanoic acid, stearic acid, monomethyl suberate, monomethyl sebacate, 3-cyclohexylpropanoic acid, 3-phen-

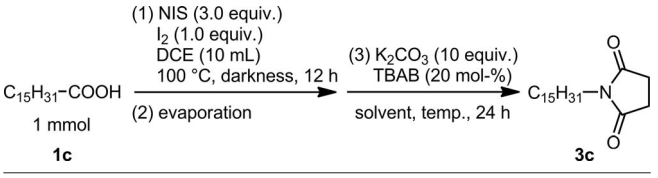
Table 2. Transformation of carboxylic acids into alkyl iodides with NIS.



Entry	R		Yield [%]
1	C_8H_{17}–	**2a**	93
2	C_9H_{19}–	**2b**	90
3[a]	$C_{15}H_{31}$–	**2c**	96
4[a]	$C_{17}H_{35}$–	**2d**	83
5	CH_3O_2C–$(CH_2)_6$–	**2e**	84
6	CH_3O_2C–$(CH_2)_8$–	**2f**	82
7		**2g**	94
8		**2h**	86
9		**2i**	92
10		**2j**	85
11[b]		**2k**	87
12		**2l**	80
13		**2m**	84
14		**2n**	75

[a] Reaction time was 12 h. [b] Reaction time was 4 h.

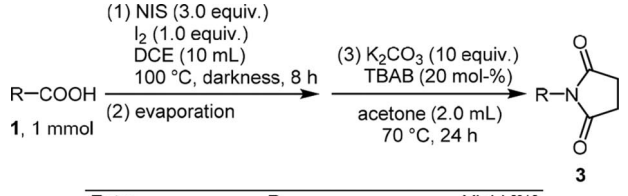
Table 3. Optimization for the transformation of palmitic acid into *N*-pentadecylsuccinimide with NIS.

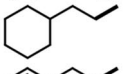
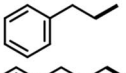
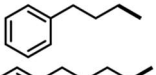
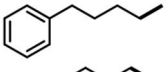
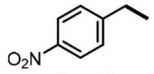
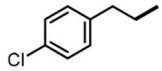
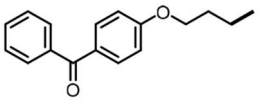
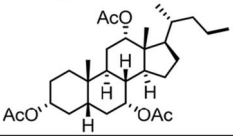


Entry	Solvent	*T* [°C]	Yield [%]
1[b]	DCE	100	13
2	MeCN (2 mL)	80	70
3	MeCN (2 mL)	40	0 (80)[a]
4[b]	MeCN (2 mL)	80	17 (40)[a]
5	acetone (2 mL)	70	71
6	1,4-dioxane (2 mL)	100	70

[a] Values in parentheses: yield of alkyl iodide. [b] Without evaporation after the 1st step.

Table 4. Transformation of carboxylic acids into *N*-alkylsuccinimides with NIS.



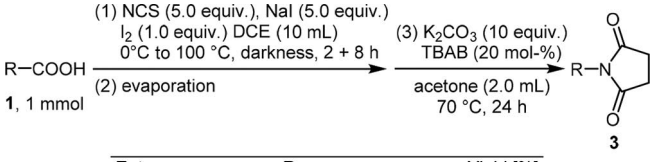
Entry	R		Yield [%]
1	C_8H_{17}–	**3a**	71
2	C_9H_{19}–	**3b**	68
3[a]	$C_{15}H_{31}$–	**3c**	71
4[a]	$C_{17}H_{35}$–	**3d**	70
5	CH_3O_2C–$(CH_2)_6$–	**3e**	80
6	CH_3O_2C–$(CH_2)_8$–	**3f**	75
7		**3g**	84
8		**3h**	64
9		**3i**	81
10		**3j**	60
11[b]		**3k**	59
12		**3l**	55
13		**3m**	65
14[b]		**3n**	54

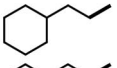
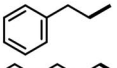
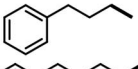
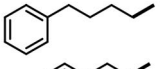
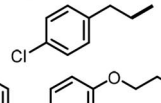
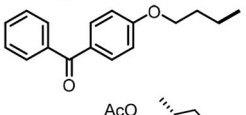
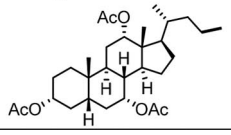
[a] Reaction time for 1st step was 12 h. [b] Reaction time for 1st step was 4 h.

ylpropanoic acid, 4-phenylbutanoic acid, 5-phenylpentanoic acid, 2-(*p*-nitrophenyl)ethanoic acid, 3-(*p*-chlorophenyl)propanoic acid, and 4-(4′-benzoylphenoxy)butanoic acid, were treated with NIS (3.0 equiv.) in DCE at 100 °C in a 20 mL screw-capped flask, followed by the reaction with K_2CO_3 in the presence of TBAB in acetone at 70 °C to provide the corresponding *N*-alkylsuccinimides in good to moderate yields, as shown in Table 4 (Entries 1, 2, 4–13). The same treatment with tri-*O*-acetylcholic acid gave also the corresponding *N*-alkylsuccinimide in moderate yield (Entry 14).

NIS is expensive, whereas *N*-chlorosuccinimide (NCS) is cheap. Therefore, the use of NCS instead of NIS was studied. Treatment of aliphatic carboxylic acids, such as nonanoic acid, decanoic acid, palmitic acid, stearic acid, monomethyl suberate, monomethyl sebacate, 3-cyclohexylpropanoic acid, 3-phenylpropanoic acid, acid, 4-phenylbutanoic acid, 5-phenylpentanoic acid, 3-(*p*-chlorophenyl)propanoic acid, 4-(4′-benzoylphenoxy)butanoic, and tri-*O*-acetyl cholic acid with NCS (5.0 equiv.) and NaI (5.0 equiv.) in DCE in a 20 mL screw-capped flask at 100 °C, followed by the reaction with K_2CO_3 in the presence of TBAB at 70 °C in acetone gave the corresponding *N*-alkylsuccinimides in good to moderate yields, as shown in Table 5 (Entries 1–13).

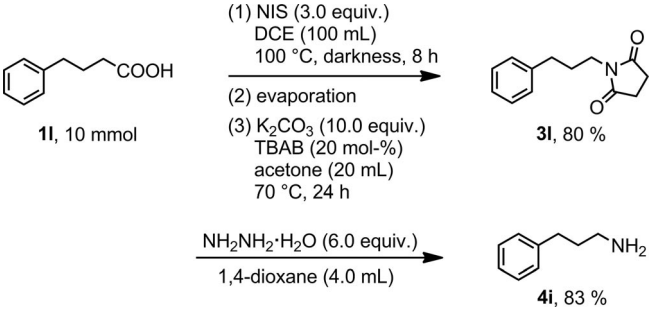
Table 5. Transformation of carboxylic acids into *N*-alkylsuccinimides with NCS and NaI.



Entry	R		Yield [%]
1	C_8H_{17}–	**3a**	51
2	C_9H_{19}–	**3b**	58
3[a]	$C_{15}H_{31}$–	**3c**	74
4[a]	$C_{17}H_{35}$–	**3d**	73
5	$CH_3O_2C–(CH_2)_6$–	**3e**	57
6	$CH_3O_2C–(CH_2)_8$–	**3f**	58
7[b]		**3g**	63
8[b]		**3h**	51
9		**3i**	80
10[b]		**3j**	58
11		**3l**	51
12[b]		**3m**	65
13[b,c]		**3n**	50

[a] Reaction time for 1st step was 12 h. [b] 3rd step conditions: Cs_2CO_3 (5.0 equiv.), acetone (2.0 mL), 70 °C, 24 h. [c] Reaction time for 1st step was 4 h.

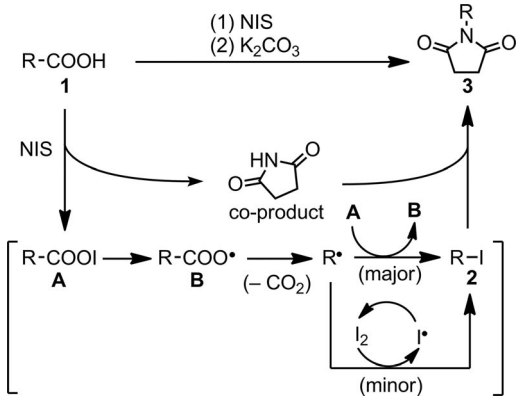
Finally, using the present method, 4-phenylbutanoic acid was converted into 3-phenylpropan-1-amine through the formation of *N*-(3-phenylpropyl)succinimide by treatment with hydrazine hydrate, as shown in Scheme 1. A semi-large-scale conversion of 4-phenylbutanoic acid (10 mmol) into *N*-(3-phenylpropyl)succinimide and *N*-(3-phenylpropyl)succinimide into 3-phenylpropan-1-amine was carried out in 80 % and 83 % yields, respectively. Thus, the present method can be used for the semi-large-scale preparation of primary amines from aliphatic carboxylic acids. This is similar to the Curtius reaction that uses carboxylic acid chlorides and sodium azide to decarboxylatively form primary amines. The important difference is that the present method does not require toxic sodium azide.



Scheme 1. Preparation of primary amine from 4-phenylbutanoic acid.

The same treatment of aromatic carboxylic acids, such as *p*-toluic acid and *p*-chlorobenzoic acid, with NIS under the same conditions gave *p*-iodotoluene and *p*-chloroiodobenzene in 13 % and 10 % yields, respectively, together with much recovered starting aromatic carboxylic acids. Thus, the present method cannot be used for aromatic carboxylic acids.

A plausible reaction pathway for the present reaction is shown in Scheme 2. Aliphatic carboxylic acid **1** (RCOOH) reacts with NIS to form acyl hypoiodite **A** (RCOOI) and succinimide. Acyl hypoiodite **A** is reactive under thermal conditions to form carboxyl radical **B** (RCOO•) and an iodine atom. Once carboxyl radical **B** is formed, it rapidly decarboxylates to produce an alkyl radical (R•) and carbon dioxide. The alkyl radical reacts with RCOOI (**A**) (major process) and iodine (minor process) to form alkyl iodide **2**. Treatment of alkyl iodide **2** with K_2CO_3 in the presence of TBAB in acetone induces the *N*-alkylation of succin-



Scheme 2. Plausible reaction mechanism.

imide formed in situ at the second reaction step, generating *N*-alkylsuccinimide **3** by an S_N2 pathway.

Conclusions

Various primary aliphatic carboxylic acids were treated with NIS in 1,2-dichloroethane, followed by the reaction with K_2CO_3 in acetone to give *N*-alkylsuccinimides in one pot. Moreover, those carboxylic acids were also treated with NCS and NaI in 1,2-dichloroethane, followed by the reaction with K_2CO_3 in acetone to provide *N*-alkylsuccinimides. A semi-large-scale transformation of aliphatic carboxylic acid into *N*-alkylsuccinimide and conversion into primary alkylamine were also carried out successfully. We believe the present method should be useful for the transformation of primary aliphatic carboxylic acids into decarboxylated *N*-alkylsuccinimides in one pot.

Experimental Section

General: ^1H and ^{13}C NMR spectra were obtained with JEOL-JNM-ECX400, JEOL-JNM-ECS400, and JEOL-JNM-ECA500 spectrometers. Chemical shifts are expressed in ppm downfield from TMS in δ units. Mass spectra were recorded with a Thermo Fisher Exactive spectrometer. IR spectra were measured with a JASCO FT/IR-4100 spectrometer. Melting points were determined with a Yamato Melting Point Apparatus Model MP-21. Silica gel $60F_{254}$ (Merck) was used for TLC, and Silica gel 60 (Kanto Kagaku Co.) was used for short column chromatography.

General Experimental Procedure with NIS: To a solution of RCOOH (**1**) (1.0 mmol) of 1,2-dichloroethane (DCE) (10 mL) in a 20 mL screw-capped flask were added *N*-iodosuccinimide (3.0 mmol, 675.0 mg) and molecular iodine (1.0 mmol, 253.8 mg). The mixture was stirred at 100 °C for 4–12 h. After cooling to room temperature, the solvent was removed by evaporation, and acetone (2 mL) was added to the residue, together with K_2CO_3 (10 mmol, 1382.0 mg) and TBAB (0.2 mmol, 64.5 mg). Then, the mixture was stirred in the same 20 mL screw-capped flask at 70–100 °C for 4–12 h. After cooling to room temperature, the reaction mixture was filtered, and the vessel was washed with EtOAc (3 × 5 mL). The filtrate obtained was concentrated under reduced pressure, and then the residue was purified by short column chromatography on silica gel (AcOEt/hexane, 1:2) to afford the desired product **3**.

General Experimental Procedure with NCS and NaI: A mixture of *N*-chlorosuccinimide (5.0 mmol, 667.7 mg) and NaI (5.0 mmol, 749.5 mg) in DCE (10 mL) was stirred at 0 °C for 2 h. Then, RCOOH (**1**) (1.0 mmol) and molecular iodine (1.0 mmol, 253.8 mg) were added. The obtained mixture was stirred at 100 °C for 4–12 h. After cooling to room temperature, the solvent was removed by evaporation, and acetone (2 mL) was added to the residue, together with K_2CO_3 (10 mmol, 1382 mg) and TBAB (0.2 mmol, 64.5 mg). Then, the mixture was stirred in the same 20 mL screw-capped flask at 70–100 °C for 4–12 h. After cooling to room temperature, the reaction mixture was filtered, and the vessel was washed with EtOAc (3 × 5 mL). The filtrate obtained was concentrated under reduced pressure, and then the residue was purified by short column chromatography on silica gel (AcOEt/hexane, 1:2) to afford the desired product **3**.

1-Octylpyrrolidine-2,5-dione (3a): Yield: 150.0 mg (71 %); colorless oil. IR (neat): $\tilde{\nu}$ = 1695, 2856, 2926 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 0.87 (t, *J* = 6.9 Hz, 3 H), 1.26–1.29 (m, 10 H), 1.55 (quint, *J* = 7.2 Hz, 2 H), 2.70 (s, 4 H), 3.49 (t, *J* = 7.5 Hz, 2 H) ppm. ^{13}C NMR (125 Hz, $CDCl_3$): δ = 14.03, 22.56, 26.81, 27.66, 28.10, 29.06, 31.69, 38.86, 177.26 ppm. HRMS (APCI): calcd. for $C_{12}H_{22}O_2N$ $[M + H]^+$ 212.1645; found 212.1649.

1-Nonylpyrrolidine-2,5-dione (3b): Yield: 143.7 mg (68 %); colorless oil. IR (neat): $\tilde{\nu}$ = 1696, 2855, 2925 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 0.88 (t, *J* = 6.9 Hz, 3 H), 1.25–1.29 (m, 12 H), 1.55 (quint, *J* = 7.2 Hz, 2 H), 2.74 (s, 4 H), 3.49 (t, *J* = 7.5 Hz, 2 H) ppm. ^{13}C NMR (125 Hz, $CDCl_3$): δ = 14.08, 22.62, 26.83, 27.69, 28.13, 29.13, 29.18, 29.40, 31.79, 38.89, 177.29 ppm. HRMS (APCI): calcd. for $C_{13}H_{24}O_2N$ $[M + H]^+$ 226.1802; found 226.1806.

1-Pentadecylpyrrolidine-2,5-dione (3c): Yield: 219.7 mg (71 %); white solid; m.p. 61–64 °C. IR (neat): $\tilde{\nu}$ = 1698, 2849, 2916 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 0.88 (t, *J* = 6.9 Hz, 3 H), 1.25–1.32 (m, 24 H), 1.55 (quint, *J* = 7.2 Hz, 2 H), 2.70 (s, 4 H), 3.49 (t, *J* = 7.6 Hz, 2 H) ppm. ^{13}C NMR (125 Hz, $CDCl_3$): δ = 14.11, 22.68, 26.86, 27.71, 28.13, 29.15, 29.34, 29.46, 29.54, 29.64 (3 C), 29.66 (2 C), 31.91, 38.90, 177.28 ppm. HRMS (APCI): calcd. for $C_{19}H_{36}O_2N$ $[M + H]^+$ 310.2741; found 310.2748.

1-Heptadecylpyrrolidine-2,5-dione (3d): Yield: 236.3 mg (70 %); white solid; m.p. 65–68 °C. IR (neat): $\tilde{\nu}$ = 1699, 2849, 2916 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 0.88 (t, *J* = 7.0 Hz, 3 H), 1.25–1.32 (m, 28 H), 1.55 (quint, *J* = 7.2 Hz, 2 H), 2.70 (s, 4 H), 3.49 (t, *J* = 7.7 Hz, 2 H) ppm. ^{13}C NMR (125 Hz, $CDCl_3$): δ = 14.09, 22.66, 26.83, 27.68, 28.11, 29.13, 29.33, 29.45, 29.52, 29.59, 29.63 (2 C), 29.66 (4 C), 31.89, 38.88, 177.28 ppm. HRMS (APCI): calcd. for $C_{21}H_{40}O_2N$ $[M + H]^+$ 338.3054; found 338.3056.

Methyl 7-(2′,5′-Dioxopyrrolidin-1′-yl)heptanoate (3e): Yield: 193.0 mg (80 %); colorless oil. IR (neat): $\tilde{\nu}$ = 1694, 2941 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.28–1.36 (m, 4 H), 1.55–1.63 (m, 4 H), 2.30 (t, *J* = 7.6 Hz, 2 H), 2.71 (s, 4 H), 3.49 (t, *J* = 7.4 Hz, 2 H), 3.66 (s, 3 H) ppm. ^{13}C NMR (125 Hz, $CDCl_3$): δ = 24.63, 26.39, 27.42, 28.06, 28.51, 33.81, 38.62, 51.39, 174.01, 177.21 ppm. HRMS (APPI): calcd. for $C_{12}H_{20}O_4N$ $[M + H]^+$ 242.1387; found 242.1387.

Methyl 9-(2′,5′-Dioxopyrrolidin-1′-yl)nonanoate (3f): Yield: 202.0 mg (75 %); colorless oil. IR (neat): $\tilde{\nu}$ = 1695, 2857, 2932 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.22–1.26 (m, 8 H), 1.53–1.63 (m, 4 H), 2.30 (t, *J* = 7.6 Hz, 2 H), 2.70 (s, 4 H), 3.49 (t, *J* = 7.4 Hz, 2 H), 3.67 (s, 3 H) ppm. ^{13}C NMR (125 Hz, $CDCl_3$): δ = 24.83, 26.72, 27.63, 28.12, 28.88, 28.95, 29.01, 34.01, 38.81, 51.43, 174.26, 177.28 ppm. HRMS (APPI): calcd. for $C_{14}H_{24}O_4N$ $[M + H]^+$ 270.1700; found 270.1695.

1-(2′-Cyclohexylethyl)pyrrolidine-2,5-dione (3g): Yield: 175.8 mg (84 %); colorless oil. IR (neat): $\tilde{\nu}$ = 1695, 2851, 2922 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 0.88–0.98 (m, 2 H), 1.08–1.30 (m, 4 H), 1.41–1.47 (m, 2 H), 1.62–1.77 (m, 5 H), 2.69 (s, 4 H), 3.52 (t, *J* = 7.9 Hz, 2 H) ppm. ^{13}C NMR (125 Hz, $CDCl_3$): δ = 26.11, 26.44, 28.16, 32.94, 35.00, 35.48, 36.93, 177.24 ppm. HRMS (APCI): calcd. for $C_{12}H_{20}O_2N$ $[M + H]^+$ 210.1489; found 210.1493.

1-(2′-Phenylethyl)pyrrolidine-2,5-dione (3h): Yield: 130.0 mg (64 %); white solid; m.p. 133–135 °C. IR (neat): $\tilde{\nu}$ = 1693, 2940 cm^{-1}. H NMR (400 MHz, $CDCl_3$): δ = 2.65 (s, 4 H), 2.88 (t, *J* = 7.9 Hz, 2 H), 3.75 (t, *J* = 7.9 Hz, 2 H), 7.21–7.31 (m, 5 H) ppm. ^{13}C NMR (125 Hz, $CDCl_3$): δ = 28.04, 33.50, 39.89, 126.65, 128.49, 128.79, 137.70, 176.96 ppm. HRMS (APCI): calcd. for $C_{12}H_{14}O_2N$ $[M + H]^+$ 204.1019; found 204.1024.

1-(3′-Phenylpropyl)pyrrolidine-2,5-dione (3i): Yield: 176.0 mg (81 %); colorless oil. IR (neat): $\tilde{\nu}$ = 1692, 2940 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.94 (quint, *J* = 7.6 Hz, 2 H), 2.56 (s, 4 H), 2.64 (t, *J* =

7.9 Hz, 2 H), 3.56 (t, *J* = 7.3 Hz, 2 H), 7.15–7.19 (m, 3 H), 7.25–7.29 (m 2 H) ppm. ^{13}C NMR (125 Hz, $CDCl_3$): δ = 27.99, 28.32, 33.08, 38.58, 125.89, 128.11, 128.26, 140.84, 177.19 ppm. HRMS (APCI): calcd. for $C_{13}H_{16}O_2N$ $[M + H]^+$ 218.1176; found 218.1178.

1-(4′-Phenylbutyl)pyrrolidine-2,5-dione (3j): Yield: 138.8 mg (60 %); white solid; m.p. 85–88 °C. IR (neat): $\tilde{\nu}$ = 1687, 2946 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.61 (m, 4 H), 2.63 (t, *J* = 7.1 Hz, 2 H), 2.68 (s, 4 H), 3.53 (t, *J* = 7.1 Hz, 2 H), 7.15–7.19 (m, 3 H), 7.25–7.29 (m 2 H) ppm. ^{13}C NMR (125 Hz, $CDCl_3$): δ = 27.25, 28.11, 28.59, 35.30, 38.58, 125.80, 128.30, 128.38, 141.88, 177.23 ppm. HRMS (APCI): calcd. for $C_{14}H_{18}O_2N$ $[M + H]^+$ 232.1332; found 232.1333.

1-(4′-Nitrobenzyl)pyrrolidine-2,5-dione (3k): Yield: 138.2 mg (59 %); white solid; m.p. 146–147 °C. IR (neat): $\tilde{\nu}$ = 1692, 2952 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.77 (s, 4 H), 4.75 (s, 2 H), 7.56 (d, *J* = 8.8 Hz, 2 H), 8.17 (d, *J* = 9.2 Hz, 2 H) ppm. ^{13}C NMR (125 Hz, $CDCl_3$): δ = 28.19, 41.63, 123.91, 129.76, 142.54, 147.62, 176.59 ppm. HRMS (APCI): calcd. for $C_{11}H_{11}O_4N_2$ $[M + H]^+$ 235.0713; found 235.0716.

1-(4′-Chlorophenylethyl)pyrrolidine-2,5-dione (3l): Yield: 130.7 mg (55 %); yellow solid; m.p. 149–151 °C. IR (neat): $\tilde{\nu}$ = 1687, 2934 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.66 (s, 4 H), 2.86 (t, *J* = 7.8 Hz, 2 H), 3.73 (t, *J* = 7.8 Hz, 2 H), 7.15 (d, *J* = 8.5 Hz, 2 H), 7.26 (d, *J* = 8.5 Hz, 2 H) ppm. ^{13}C NMR (125 Hz, $CDCl_3$): δ = 28.05, 32.82, 39.63, 128.67, 130.15, 132.55, 136.13, 176.93 ppm. HRMS (APPI): calcd. for $C_{12}H_{13}O_2NCl$ $[M + H]^+$ 238.0629; found 238.0626.

1-[3′-(4′′-Benzoylphenoxy)propyl]pyrrolidine-2,5-dione (3m): Yield: 219.2 mg (65 %); yellow oil. IR (neat): $\tilde{\nu}$ = 1693, 2942 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.13 (quint, *J* = 6.6 Hz, 2 H), 2.72 (s, 4 H), 3.76 (t, *J* = 7.0 Hz, 2 H), 4.08 (t, *J* = 6.1 Hz, 2 H), 6.93 (d, *J* = 8.8 Hz, 2 H), 7.48 (t, *J* = 7.9 Hz, 2 H), 7.57 (t, *J* = 7.6 Hz, 1 H), 7.75 (d, *J* = 7.3 Hz, 2 H), 7.82 (d, *J* = 8.8 Hz, 2 H) ppm. ^{13}C NMR (125 Hz, $CDCl_3$): δ = 27.36, 28.14, 36.26, 65.96, 113.90, 128.16, 129.70, 130.26, 131.89, 132.56, 138.18, 162.26, 177.18, 195.54 ppm. HRMS (APCI): calcd. for $C_{20}H_{20}O_4N$ $[M + H]^+$ 338.1387; found 338.1393.

3n: Yield: 317.4 mg (54 %); white solid; m.p. 65–68 °C. IR (neat): $\tilde{\nu}$ = 1698, 2968 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.72 (s, 3 H), 0.90–0.92 (m, 6 H), 1.03–2.03 (m, 22 H), 2.05 (s, 3 H), 2.10 (s, 3 H), 2.14 (s, 3 H), 2.70 (s, 4 H), 3.40–3.57 (m, 2 H), 4.57 (m, 1 H), 4.90 (s 1 H), 5.08 (s, 1 H) ppm. ^{13}C NMR (125 Hz, $CDCl_3$): δ = 12.09, 17.74, 21.35, 21.41, 21.59, 22.47, 22.67, 25.46, 26.79, 27.04, 28.08, 28.78, 29.50, 31.13, 33.18, 33.29, 34.23, 34.50, 34.59, 36.27, 37.62, 40.82, 43.23, 44.98, 47.02, 70.58, 73.98, 75.22, 170.33, 170.41, 170.48, 177.14 ppm. HRMS (ESI): calcd. for $C_{33}H_{49}O_8NNa$ $[M + Na]^+$ 610.3350; found 610.3345.

3-Phenylpropan-1-amine (**4i**, commercially available): To a solution of **3i** (1 mmol, 217.3 mg) in dry 1,4-dioxane (4.0 mL) was added $NH_2NH_2{\cdot}H_2O$ (0.5 mL). The mixture was stirred under reflux conditions for 48 h. After cooling to room temperature, the reaction mixture was filtered, and the vessel was washed with $CHCl_3$ (3 × 5 mL). The filtrate obtained was concentrated under reduced pressure, and then the residue was purified by short column chromatography on silica gel (CH_2Cl_2/MeOH/NH_4OH, 80:20:1) to afford the desired product **4i**. Yield: 112.2 mg (83 %); colorless oil. IR (neat): $\tilde{\nu}$ = 3362, 3287 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.77 (quint, *J* = 7.5 Hz, 2 H), 2.65 (t, *J* = 7.9 Hz, 2 H), 2.71 (t, *J* = 7.2 Hz, 2 H), 7.18–7.19 (m, 3 H), 7.26–7.29 (m, 2 H) ppm. ^{13}C NMR (125 Hz, $CDCl_3$): δ = 32.64, 33.16, 35.08, 41.48, 125.70, 128.26, 141.96 ppm.

Supporting Information (see footnote on the first page of this article): Copies of ^{1}H and ^{13}C NMR spectra of all *N*-alkylsuccinimides.

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