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Synthesis of 4-(alkoxyamino)chroman-2-ones *via* 6-*exo-trig* cyclization of carbon-centered radicals into oxime ethers

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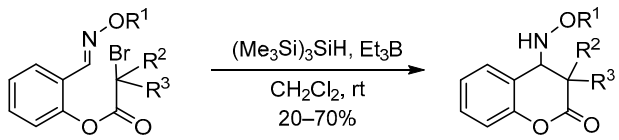


R^1 = CH_2Ph, Me; R^2 = H, Me; R^3 = Me, Et

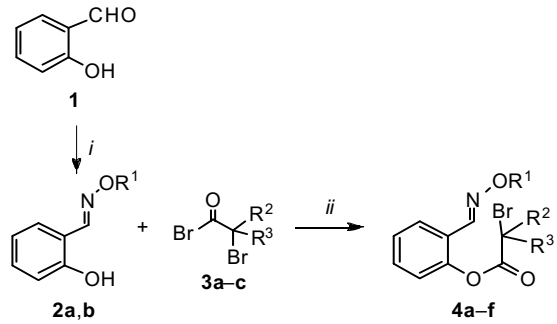
4-(Alkoxyamino)chroman-2-ones were synthesized *via* a 6-*exo-trig* cyclization of alkyl radicals obtained from α-bromoesters containing an oxime ether group. In the case of secondary bromides, the best results were achieved using tris(trimethylsilyl)silane as the chain transfer agent and Et_3B as the initiator in dichloromethane at room temperature; the corresponding chromanones were produced in 58–70% yield. Low yields of the cyclized compounds were obtained in the case of tertiary alkyl bromides (20–25%). Products of premature reduction of carbon-centered radicals and addition of ethyl radicals to C=N bond were also observed.

Keywords: 4-(alkoxyamino)chroman-2-ones, oxime ethers, 6-*exo-trig* radical cyclizations.

Oxime ethers are useful and versatile compounds in organic synthesis. They are easily prepared and relatively stable to moisture, so that they can be stored during long periods in air.[1] Reductive addition of alkyl radicals to oxime ethers is by far the most exploited application of this class of compounds in radical chemistry. Since the first pinacol-type radical cyclization into an oxime ether was reported in 1983,[2] many interesting methodologies that involve inter- and intramolecular versions of this transformation have been published.[3,4] For instance, Naito and coworkers reported the synthesis of 4-(benzyloxyamino)furan-2-ones and 4-(benzyloxyamino)pyran-2-ones from oxime ethers connected with acryloyl and methacryloyl moieties. The synthesis was carried out *via* tandem intermolecular addition of secondary alkyl radicals to the C=C bond of a carbonyl α,β-unsaturated system, followed by intramolecular addition of the stabilized α-ester radical to the C=N bond, using Et_3B and alkyl iodides in a variety of solvents including water.[4c]

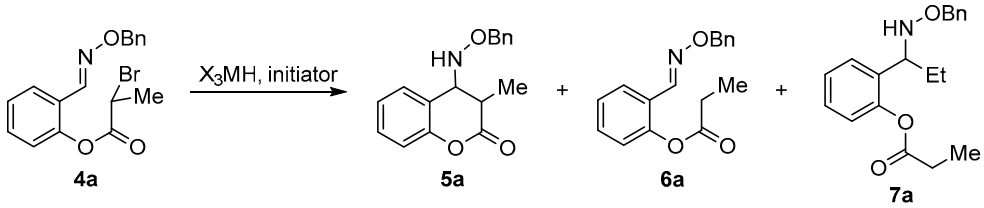
4-(Alkoxyamino)chroman-2-ones are known as important building blocks of biologically active compounds and are considered privileged molecular moieties present in a variety of natural products.[5] With the aim of extending the application of reductive addition of alkyl radicals to oximes, we explored in this work the synthesis of 4-(alkoxyamino)chroman-2-ones from salicylaldehyde oxime ethers connected to α-bromoesters *via* 6-*exo-trig* radical cyclization of secondary and tertiary alkyl radicals at the electrophilic carbon atom of C=N–OR group. In order to evaluate the feasibility of this approach, the requisite oxime ethers were obtained in two steps starting from the reaction of salicylaldehyde (**1**) with *O*-benzyl- or *O*-methylhydroxylamine hydrochloride to obtain compounds **2a**,**b** which were reacted with 2-bromoacylbromides **3a**–**c** to provide the oxime ethers **4a**–**f** in yields up to 69% in two steps (Scheme 1).

Scheme 1



i: $H_2NOR^1 \cdot HCl$, Na_2SO_4, Py, MeOH, rt;
ii: Et_3N, CH_2Cl_2, 0°C, 2–3 h
2a, **4a**,**c**,**e** R^1 = Bn; **2b**, **4b**,**d**,**f** R^1 = Me
3a, **4a**,**b** R^2 = H, R^3 = Me;
3b, **4c**,**d** R^2 = H, R^3 = Et; **3c**, **4e**,**f** R^2 = R^3 = Me

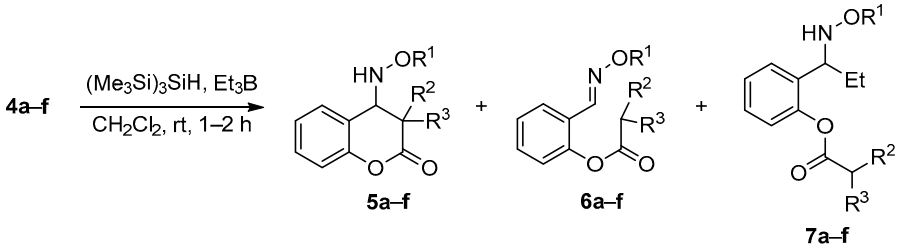
Table 1. Conditions and product ratios for radical cyclization of oxime **4a**



Entry	X_3MH	Initiator	Solvent	Temperature	Reaction time, h	Ratio **5a** : **6a** : **7a***
1	Bu_3SnH	AIBN	PhMe	Reflux	14	9:91:0
2	$(Me_3Si)_3SiH$	AIBN	C_6H_{12}	Reflux	12	17:83:0
3	$(Me_3Si)_3SiH$	Et_3B	CH_2Cl_2	rt	1	58:37:5

* Product ratios established by GC-MS and ^{1}H NMR spectroscopy.

Table 2. Structures and yields for products of radical cyclization of oximes **4a**–**f**



Entry	Products **5**–**7**	R^1	R^2	R^3	Product yield, %		
					5 (ratio *trans* : *cis*)	**6**	**7**
1	**a**	Bn	H	Me	58 (8 : 1)	37	5
2	**b**	Me	H	Me	67 (7 : 1)	26	7
3	**c**	Bn	H	Et	63 (4.6 : 1)	31	6
4	**d**	Me	H	Et	70 (6.6 : 1)	25	5
5	**e**	Bn	Me	Me	25	69	6
6	**f**	Me	Me	Me	20	74	6

In order to establish the most favorable reaction conditions for the 6-*exo*-*trig* cyclization to generate 4-(alkoxyamino)chroman-2-ones, we carried out preliminary experiments with compound **4a** (Table 1). The reaction with tri(*n*-butyl)tin hydride (TBTH) and azobisisobutyronitrile (AIBN) in toluene proceeded through the direct reduction of C–Br bond giving rise to compound **6a** (91%) as the main product (entry 1).

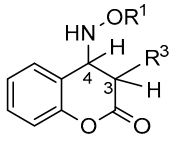
Due to this unfavorable result, we decided to replace TBTH by a weaker hydrogen donor tris(trimethylsilyl)-silane (TTMSS), retaining AIBN as the initiator (entry 2). In this case, the yield of cyclized product **5a** increased, however, the main product as before was the undesired open-chain compound **6a** (83%).

In an attempt to improve the yield of compound **5a** we carried out a third experiment (entry 3) using Et_3B as the initiator, trying to take advantage of its well-known weak Lewis acid character along with the simplification of the experimental procedure, since no heating and deoxygenating processes are needed. The ^{1}H NMR spectrum of the crude mixture after aqueous work-up showed that under these conditions, the desired heterocyclic compound **5a** was generated as the main product (yield 58%), in addition to reduction product **6a** (37%) and a small amount of open-chain product **7a** (5%), likely produced by intermolecular addition of ethyl radicals (donated by Et_3B) to the C=N bond of the oxime function.

Guided by the results of the preliminary experiments, we synthesized a series of 4-(alkoxyamino)chroman-2-ones **5b**–**f** using TTMSS and Et_3B, since these conditions gave rise to a good product ratio **5a** : **6a** (Table 1, entry 3) and required the simplest experimental procedure.

As shown in Table 2, the cyclization of oximes **4a**–**d** took place with diastereoselectivity favoring the *trans*-isomer due to the steric repulsion between the alkyl group tethered to the carbon-centered radical and the oxime ether group NOR[1]. The assignment of *cis/trans* configuration to the cyclized products **5a**–**d** was made by NOESY experiments and examining the $^3J_{HH}$ coupling constants in the ^{1}H NMR spectra (Table 3). The magnitude of coupling

Table 3. ^3J coupling constant values between protons of 3-CH and 4-CH groups in the ^{1}H NMR spectra of compounds **5a**–**d**



Compound	^3J, Hz *trans*	*cis*
5a	2.9	5.1
5b	2.8	5.3
5c	2.1	4.8
5d	2.1	5.0

constants in *trans*-isomer showed protons 3-CH and 4-CH in pseudo-equatorial positions.

In the case of oximes **4e**,**f**, the steric hindrance of the tertiary radical precluded the cyclization to proceed in an efficient way, leading to the formation of chromanones **5e**,**f** in only 20–25% yield, and reduced open-chain compounds **6e**,**f** as the major products.

In conclusion, the synthesis of 4-(alkoxyamino)chroman-2-ones *via* radical cyclization was achieved with reasonably good yields and diastereoselectivity in the case of precursors containing a secondary alkyl bromide and low yields in the case of those containing tertiary alkyl bromides. The experimental protocol to carry out the radical reactions is simple, as is the synthesis of the starting materials.

Experimental

^{1}H and ^{13}C NMR spectra were acquired on a Bruker Avance spectrometer (300 and 75 MHz, respectively) in $CDCl_3$. All chemical shifts are quoted in respect to residual proton signals of $CDCl_3$ (7.28 ppm for ^{1}H nuclei and 77.0 ppm for ^{13}C nuclei). Chemical shifts were assigned with the help of HSQC-edit, HMBC, and COSY experiments. The assignment of *cis/trans* configuration was made by NOESY experiments (mixing time 300 ms) and examining the $^3J_{HH}$ coupling constants in the ^{1}H NMR spectra.

High-resolution mass spectra were recorded on an Agilent 6520 q-TOF-MS instrument with orthogonal ESI. GC-MS analyses were performed on an Agilent 6850 series II gas chromatograph coupled to an Agilent 5975B VL mass spectrometer (electron ionization, 70 eV) equipped with split/splitless inlet (split relation 15:1, 260°C), Agilent 6850 series automatic injector, and Agilent HP-5MS column (30 m × 0.25 mm × 0.25 μm); initial oven temperature 80°C for 1 min, then a temperature ramp of 10°C/min to 320°C (hold 3 min); total run time 28 min. Melting points were determined on a Thermo Fisher Scientific IA 9100 apparatus.

2-[(Benzyloxyimino)methyl]phenol (2a) and 2-[(methoxyimino)methyl]phenol (2b) were synthesized according to previously reported procedures.[4g,6] Oxime **2a** was obtained as a white solid, mp 62–63°C (MeOH) (mp 62.5–63.0°C (AcOEt–hexane)[4g]), and oxime **2b** was obtained as a colorless solid, mp 30–32°C (MeOH) (mp ≤ 30°C (cyclohexane–EtOAc)[6]). The ^{1}H NMR spectra of both compounds were consistent with those reported in literature.

Coupling of oxime ethers with α-bromoesters (General method). A solution of oxime **2a** (0.227 g, 1.0 mmol) or **2b** (0.151 g, 1.0 mmol), an appropriate α-bromoacyl bromide **3a**–**c** (1.5 mmol), and triethylamine (0.28 ml, 2 mmol) in dichloromethane (3.3 ml) was stirred at 0°C for 2–3 h. The reaction mixture was treated with distilled water and extracted with dichloromethane. The organic phase was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude mixtures were purified by column chromatography (silica gel, hexane–CH_2Cl_2, 4:1) to provide products **4a**–**f**.

2-{[(Benzyloxy)imino]methyl}phenyl 2-bromopropanoate (4a). Yield 0.286 g (79%). Pale-yellow liquid with a pleasant odor. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.95 (3H, d, *J* = 6.9, CH_3); 4.59 (1H, q, *J* = 6.9, CHBr); 5.26 (2H, s, OCH_2Ph); 7.17 (1H, dd, *J* = 8.1, *J* = 1.3, H-6 Ar); 7.24–7.38 (1H, m, H-5 Ar); 7.33–7.51 (6H, m, H-4 Ar, H Ph); 7.85 (1H, dd, *J* = 7.8, *J* = 1.7, H-3 Ar); 8.33 (1H, s, HC=N). ^{13}C NMR spectrum, δ, ppm: 21.4 (CH_3); 39.3 (CHBr); 76.6 (OCH_2Ph); 122.4 (C-6 Ar); 124.7 (C-1 Ar); 126.6 (C-5 Ar); 127.9 (C-3 Ar); 128.1 (C-2,6 Ph); 128.3 (C-4 Ph); 128.5 (C-3,5 Ph); 130.8 (C-4 Ar); 137.4 (C-1 Ph); 144.1 (C=N); 148.3 (C-2 Ar); 168.4 (C=O). Found, *m*/*z*: 362.0398 [M(^{79}Br)+H]$^+$. $C_{17}H_{17}BrNO_3$. Calculated, *m*/*z*: 362.0387.

2-{[(Methoxy)imino]methyl}phenyl 2-bromopropanoate (4b). Yield 0.255 g (89%). Light-yellow liquid. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.97 (3H, d, *J* = 6.9, CH_3); 3.99 (3H, s, OCH_3); 4.65 (1H, q, *J* = 6.9, CHBr); 7.14 (1H, d, *J* = 8.1, H-6 Ar); 7.29 (1H, t, *J* = 7.6, H-5 Ar); 7.42 (1H, t, *J* = 7.7, H-4 Ar); 7.83 (1H, d, *J* = 7.8, H-3 Ar); 8.23 (1H, s, HC=N). ^{13}C NMR spectrum, δ, ppm: 21.4 (CH_3); 39.4 (CHBr); 62.2 (OCH_3); 122.4 (C-6 Ar); 124.7 (C-1 Ar); 126.7 (C-5 Ar); 127.7 (C-3 Ar); 130.7 (C-4 Ar); 143.6 (C=N); 148.2 (C-2 Ar); 168.4 (C=O). Mass spectrum, *m*/*z* (I_{rel}, %): 285 [M(^{79}Br)]$^+$ (5), 152 (9), 151 (100), 120 (23), 119 (41), 107 (17), 91 (37). Found, *m*/*z*: 286.0073 [M(^{79}Br)+H]$^+$. $C_{11}H_{13}BrNO_3$. Calculated, *m*/*z*: 286.0074.

2-{[(Benzyloxy)imino]methyl}phenyl 2-bromobutanoate (4c). Yield 0.301 g (80%). Pale-yellow liquid with a pleasant odor. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.16 (3H, t, *J* = 7.3, $CH_2C\underline{H}_3$); 2.07–2.34 (2H, m, $C\underline{H}_2CH_3$); 4.41 (1H, dd, *J* = 7.9, *J* = 6.5, CHBr); 5.26 (2H, s, OCH_2Ph); 7.13–7.18 (1H, m, H-6 Ar); 7.26–7.47 (7H, m, H-4,5, H Ph); 7.88 (1H, dd, *J* = 7.8, *J* = 1.5, H-3 Ar); 8.34 (1H, s, HC=N). ^{13}C NMR spectrum, δ, ppm: 11.9 ($CH_2\underline{C}H_3$); 28.1 ($\underline{C}H_2CH_3$); 47.1 (CHBr); 76.6 (OCH_2Ph); 122.3 (C-6 Ar); 124.7 (C-1 Ar); 126.6 (C-5 Ar); 127.6 (C-3 Ar); 128.0 (C-4 Ph); 128.3 (C-3,5 Ph); 128.5 (C-2,6 Ph); 130.7 (C-4 Ar); 137.4 (C-1 Ph); 143.9 (C=N); 148.3 (C-2 Ar); 167.9 (C=O). Found, *m*/*z*: 376.0561 [M(^{79}Br)+H]$^+$. $C_{18}H_{19}BrNO_3$. Calculated, *m*/*z*: 376.0543.

2-{[(Methoxy)imino]methyl}phenyl 2-bromobutanoate (4d). Yield 0.267 g (89%). Light-yellow liquid. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.16 (3H, t, *J* = 7.3, $CH_2C\underline{H}_3$); 2.08–2.37 (2H, m, $C\underline{H}_2CH_3$); 4.00 (3H, s, OCH_3); 4.44 (1H, dd, *J* = 8.0, *J* = 6,6, CHBr); 7.14 (1H, dd, *J* = 8.1, *J* =1.3, H-6 Ar); 7.26–7.33 (1H, m, H-5 Ar); 7.39–7.46 (1H, m, H-4 Ar); 7.86 (1H, dd, *J* = 7.8, *J* = 1.8, H-3 Ar); 8.24 (1H, s, HC=N). ^{13}C NMR spectrum, δ, ppm: 12.0 ($CH_2\underline{C}H_3$); 28.1 ($\underline{C}H_2CH_3$); 47.0 (CHBr); 62.2 (OCH_3); 122.4 (C-6 Ar); 124.7 (C-1 Ar); 126.7 (C-5 Ar); 127.5 (C-3 Ar); 130.7 (C-4 Ar); 143.4 (C=N); 148.2 (C-2 Ar); 167.9 (C=O). Mass spectrum, *m*/*z* (I_{rel}, %): 299 [M(^{79}Br)]$^+$ (4), 152 (9), 151 (100), 120 (19), 119 (35), 91 (24). Found, *m*/*z*: 300.0235 [M(^{79}Br)+H]$^+$. $C_{12}H_{15}BrNO_3$. Calculated, *m*/*z*: 300.0230.

2-{[(Benzyloxy)imino]methyl}phenyl 2-bromo-2-methylpropanoate (4e). Yield 0.275 g (73%). Clear yellow liquid. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.14 (6H, s, $CBr(CH_3)_2$); 5.31 (2H, s, OCH_2Ph); 7.20 (1H, d, *J* = 8.1, H-6 Ar); 7.33 (1H, t, *J* = 7.6, H-5 Ar); 7.39–7.52 (6H, m, H-4 Ar, H Ph); 7.95 (1H, d, *J* = 7.8, H-3 Ar); 8.42 (1H, s,

HC=N). ^{13}C NMR spectrum, δ, ppm: 30.6 (C($\underline{C}H_3)_2$); 55.2 ($\underline{C}(CH_3)_2$); 76.6 (OCH_2Ph); 122.3 (C-6 Ar); 124.9 (C-1 Ar); 126.6 (C-5 Ar); 127.5 (C-3 Ar); 128.1 (C-4 Ph); 128.4 (C-3,5 Ph); 128.5 (2C, C-2,6 Ph); 130.8 (C-4 Ar); 137.5 (C-1 Ph); 143.9 (C=N); 148.7 (C-2 Ar); 169.8 (C=O). Found, *m*/*z*: 376.0559 [M(^{79}Br)+H]$^+$. $C_{18}H_{19}BrNO_3$. Calculated, *m*/*z*: 376.0543.

2-{[(Methoxy)imino]methyl}phenyl 2-bromo-2-methylpropanoate (4f). Yield 0.276 g (92%). Light-yellow liquid. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.11 (6H, s, $CBr(CH_3)_2$); 4.00 (3H, s, OCH_3); 7.14 (1H, dd, *J* = 8.1, *J* = 1.4, H-6 Ar); 7.29 (1H, t, *J* = 7.6, H-5 Ar); 7.43 (1H, t, *J* = 7.7, H-4 Ar); 7.87 (1H, d, *J* = 7.8, H-3 Ar); 8.26 (1H, s, OCH_3). ^{13}C NMR spectrum, δ, ppm: 30.6 (2C, C($\underline{C}H_3)_2$); 55.1 ($\underline{C}(CH_3)_2$); 62.2 (OCH_3); 122.3 (C-6 Ar); 124.8 (C-1 Ar); 126.6 (C-5 Ar); 127.4 (C-3 Ar); 130.7 (C-4 Ar); 143.4 (C=N); 148.5 (C-2 Ar); 169.8 (C=O). Mass spectrum, *m*/*z* (I_{rel}, %): 299 [M(^{79}Br)]$^+$ (12), 151 (60), 123 (80), 121 (86), 120 (44), 119 (100), 91 (55). Found, *m*/*z*: 300.0236 [M(^{79}Br)+H]$^+$. $C_{12}H_{15}BrNO_3$. Calculated, *m*/*z*: 300.0230.

Radical cyclization of compounds 4a–f (General method). A. Experiments using AIBN: a solution of oxime ether **4a** (0.181 g, 0.5 mmol), TTMS or TBTH (0.5 mmol), AIBN (0.025 g, 0.15 mmol) in cyclohexane or toluene (20 ml) was deoxygenated for 1 h by bubbling dry argon and stirred at reflux temperature for 6–8 h. The reactions were monitored by TLC and GC-MS until consumption of starting material. After cooling to room temperature, the solution was concentrated under low pressure. In the case of reaction carried out with TBTH, the crude mixture was dissolved in ethyl acetate (5 ml) and treated with a 20% aqueous solution of KF (5 ml) to eliminate brominated organotin by-products. The crude mixtures were analyzed by ^{1}H NMR spectroscopy and GC-MS.

B. Experiments using Et_3B: a solution of oxime ether **4a–f** (0.5 mmol), TTMS (0.159 ml, 0.5 mmol), and Et_3B (1 M in hexane, 0.75 ml, 0.75 mmol) in dichloromethane (20 ml) was stirred at room temperature under air atmosphere for 1–2 h. The reaction mixture was treated with 10% aqueous $NaHCO_3$ solution and extracted with dichloromethane. The organic phase was dried over Na_2SO_4, filtered, and concentrated. The products were preliminarily identified by GC-MS and ^{1}H NMR spectroscopy. Purification by flash column chromatography using silica gel (hexane–AcOEt, 4:1) afforded compounds **5a–f** which were characterized by HR-MS and ^{1}H and ^{13}C NMR spectroscopy, except compounds **5c**-*cis* and **5d**-*cis*, which were detected and quantified from the crude mixtures. Compounds **6a–f**, **7a**,**b**,**d** were likewise isolated by chromatography and characterized.

***trans*-4-[(Benzyloxy)amino]-3-methylchroman-2-one (*trans*-5a)**. Yield 0.074 g (52%). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.22 (3H, d, *J* = 7.4, 3-CH_3); 3.36 (1H, qd, *J* = 7.4, *J* = 2.9, 3-CH); 4.01 (1H, d, *J* = 2.9, 4-CH); 4.61 (1H, d, *J* = 11.5, OCH_2Ph); 4.70 (1H, d, *J* = 11.5, OCH_2Ph); 7.10 (1H, dd, *J* = 8.1, *J* =1.1, H-8); 7.17 (1H, td, *J* = 7.5, *J* = 1.1, H-6); 7.27–7.41 (7H, m, H-5,7, H Ph). ^{13}C NMR spectrum, δ, ppm: 14.0 (3-CH_3); 38.3 (C-3); 62.6 (C-4); 77.6 ($\underline{C}H_2Ph$); 116.9 (C-8); 119.4 (C-4a); 124.6 (C-7); 128.1 (C-4 Ph); 128.6 (C-3,5 Ph); 128.7 (C-2,6 Ph); 129.6 (C-5); 130.2 (C-6); 137.0 (C-1 Ph); 151.8 (C-8a); 170.7 (C=O). Found, *m*/*z*: 284.1293 [M+H]$^+$. $C_{17}H_{18}NO_3$. Calculated, *m*/*z*: 284.1281.

***cis*-4-[(Benzyloxy)amino]-3-methylchroman-2-one (*cis*-5a)**. Yield 0.008 g (6%). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.50 (3H, d, *J* = 7.0, 3-CH_3); 2.99 (1H, qd, *J* = 7.0, *J* = 5.1, 3-CH); 4.05 (1H, d, *J* = 5.1, 4-CH); 4.38 (1H, d, *J* = 11.7) and 4.45 (1H, d, *J* = 11.6, OCH_2Ph); 7.08–7.13 (1H, m, H-8); 7.16–7.21 (1H, m, H-6); 7.30–7.43 (7H, m, H-5,7, H Ph). ^{13}C NMR spectrum, δ, ppm: 11.5 (3-CH_3); 37.3 (C-3); 60.6 (C-4); 76.9 ($O\underline{C}H_2Ph$); 116.8 (C-8); 122.7 (C-4a); 124.2 (C-6); 127.9 (C-4 Ph); 128.3 (C-2,6 Ph); 128.9 (C-3,5 Ph); 129.5 (C-5); 129.9 (C-7); 136.6 (C-1 Ph); 152.1 (C-8a); 170.4 (C=O). Found, *m*/*z*: 284.1293 [M+H]$^+$. $C_{17}H_{18}NO_3$. Calculated, *m*/*z*: 284.1281.

***trans*-4-(Methoxyamino)-3-methylchroman-2-one (*trans*-5b)**. Yield 0.061 g (59%). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.22 (3H, d, *J* = 7.4, 3-CH_3); 3.29 (1H, qd, *J* = 7.4, *J* =2.8, 3-CH); 3.50 (3H, s, OCH_3); 3.96 (1H, d, *J* = 2.8, 4-CH); 7.06–7.12 (1H, m, H-8); 7.18 (1H, td, *J* = 7.4, *J* = 1.1, H-6); 7.32 (1H, dd, *J* = 7.4, *J* = 1.5, H-5); 7.38 (1H, td, *J* = 7.9, *J* = 1.7, H-7). ^{13}C NMR spectrum, δ, ppm: 14.1 (3-CH_3), 38.3 (C-3); 62.6 (C-4); 63.3 (OCH_3); 116.8 (C-8); 119.5 (C-4a); 124.6 (C-6); 129.4 (C-5); 130.2 (C-7); 151.7 (C-8a); 170.7 (C=O). Found, *m*/*z*: 208.0966 [M+H]$^+$. $C_{11}H_{14}NO_3$. Calculated, *m*/*z*: 208.0968.

***cis*-4-(Methoxyamino)-3-methylchroman-2-one (*cis*-5b)**. Yield 0.008 g (8%). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.50 (3H, d, *J* = 6.9, 3-CH_3); 2.93–3.01 (1H, m, 3-CH); 3.30 (3H, s, OCH_3); 4.01 (1H, d, *J* = 5.3, 4-CH); 7.09 (1H, d, *J* = 8.2, H-8); 7.17 (1H, t, *J* = 7.5, H-6); 7.30–7.38 (2H, m, H-5,7). ^{13}C NMR spectrum, δ, ppm: 11.5 (3-CH_3); 37.3 (C-3); 60.8 (C-4); 62.6 (OCH_3); 116.8 (C-8); 124.2 (C-6); 128.6 (C-5); 129.9 (C-7); 143.4 (C-4a); 152.3 (C-8a); 170.8 (C=O). Found, *m*/*z*: 208.1001 [M+H]$^+$. $C_{11}H_{14}NO_3$. Calculated, *m*/*z*: 208.0968.

***trans*-4-[(Benzyloxy)amino]-3-ethylchroman-2-one (*trans*-5c)**. Yield 0.077 g (52%). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.05 (3H, t, *J* = 7.5, 3-$CH_2C\underline{H}_3$); 1.47–1.58 (2H, m, 3-$C\underline{H}_2CH_3$); 3.15 (1H, td, *J* = 7.8, *J* = 2.1, 3-CH); 4.10 (1H, d, *J* = 2.1, 4-CH); 4.59 (1H, d, *J* = 11.5, OCH_2Ph); 4.69 (1H, d, *J* = 11.5, OCH_2Ph); 7.08 (1H, dd, *J* = 8.1, *J* =1.1, H-8); 7.15 (1H, td, *J* = 7.5, *J* = 1.1, H-6); 7.24–7.40 (7H, m, H-5,7, H Ph). ^{13}C NMR spectrum, δ, ppm: 11.8 (3-$CH_2\underline{C}H_3$); 22.1 (3-$\underline{C}H_2CH_3$); 45.7 (C-3); 61.2 (C-4); 77.7 ($O\underline{C}H_2Ph$); 116.8 (C-8); 119.4 (C-4a); 124.5 (C-6); 128.0 (C-4 Ph); 128.4 (C-3,5 Ph); 128.7 (C-2,6 Ph); 129.6 (C-5); 130.3 (C-7); 137.0 (C-1 Ph); 151.9 (C-8a); 169.7 (C=O). Found, *m*/*z*: 298.1444 [M+H]$^+$. $C_{18}H_{20}NO_3$. Calculated, *m*/*z*: 298.1438.

***cis*-4-[(Benzyloxy)amino]-3-ethylchroman-2-one (*cis*-5c)**. Yield 0.016 g (11%). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.12 (3H, t, *J* = 7.5, 3-$CH_2C\underline{H}_3$); 1.76–1.88 (2H, m, 3-$C\underline{H}_2CH_3$); 2.65–2.72 (2H, m, 3-CH); 4.18 (1H, d, *J* = 4.8, 4-CH); 4.45 (1H, d, *J* = 11.7) and 4.48 (1H, d, *J* = 11.7, OCH_2Ph); 7.06–7.21 (2H, m, H-6,8); 7.30–7.43 (7H, m, H-5,7, H Ph). Mass spectrum, *m*/*z* (I_{rel}, %): 297 [M]$^+$ (3), 265 (6), 175 (30), 119 (20), 91 (100).

***trans*-3-Ethyl-4-(methoxyamino)chroman-2-one (*trans*-5d)**. Yield 0.067 g (61%). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.01 (3H, t, *J* = 7.4, 3-$CH_2C\underline{H}_3$); 1.43–1.56 (2H, m, 3-$C\underline{H}_2CH_3$); 3.05 (1H, td, *J* = 7.8, *J* = 2.1, 3-CH); 3.45 (3H, s, OCH_3); 4.03 (1H, d, *J* = 2.1, 4-CH); 7.04 (1H, dd, *J* = 8.1, *J* = 1.2, H-8); 7.13 (1H, td, *J* = 7.5, *J* = 1.2, H-6); 7.27 (1H, dd, *J* = 7.5, *J* = 1.7, H-5); 7.34 (1H, td, *J* = 7.8, *J* = 1.7, H-7). ^{13}C NMR spectrum, δ, ppm: 11.7 (3-$CH_2\underline{C}H_3$); 22.1 (3-$\underline{C}H_2CH_3$); 45.6 (C-3); 61.2 (C-4); 63.3 (OCH_3); 116.7 (C-8); 119.6 (C-4a); 124.5 (C-7); 129.5 (C-5); 130.2 (C-6); 151.9 (C-8a); 169.6 (C=O). Found, *m*/*z*: 222.1125 $[M+H]^+$. $C_{12}H_{16}NO_3$. Calculated, *m*/*z*: 222.1125.

***cis*-3-Ethyl-4-(methoxyamino)chroman-2-one (*cis*-5d)**. Yield 0.010 g (9%). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.05 (3H, t, *J* = 7.5, 3-$CH_2C\underline{H}_3$); 1.47–1.57 (2H, m, 3-$C\underline{H}_2CH_3$); 3.09 (1H, td, *J* = 7.7, *J* = 2.1, 3-CH); 3.49 (3H, s, OCH_3); 4.06 (1H, d, *J* = 2.1, 4-CH); 7.08 (1H, dd, *J* = 8.2, *J* =1.1, H-8); 7.16 (1H, td, *J* = 7.4, *J* = 1.2, H-6); 7.30–7.41 (2H, m, H-5,7). Mass spectrum, *m*/*z* (I_{rel}, %): 221 $[M]^+$ (2), 176 (12), 175 (100), 147 (21), 133 (27), 119 (20), 91 (53).

4-[(Benzyloxy)amino]-3,3-dimethylchroman-2-one (5e). Yield 0.037 g (25%). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.22 (3H, s, 3-CH_3); 1.52 (3H, s, 3-CH_3); 3.69 (1H, s, 4-CH); 4.29 (1H, d, *J* = 11.7) and 4.39 (1H, d, *J* = 11.7, OCH_2Ph); 7.06–7.10 (1H, m, H-8); 7.14–7.20 (3H, m, H-6, H Ph); 7.33–7.41 (5H, m, H-5,7, H Ph). ^{13}C NMR spectrum, δ, ppm: 20.8 (3-CH_3); 24.8 (3-CH_3); 40.4 (C-3); 66.7 (C-4); 76.8 (OCH_2Ph); 116.2 (C-8); 122.1 (C-4a); 124.3 (C-6); 127.8 (C-4 Ph); 128.3 (C-3,5 Ph); 128.4 (C-2,6 Ph); 129.7 (C-5); 129.8 (C-7); 136.8 (C-1 Ph); 151.8 (C-8a); 173.1 (C=O). Found, *m*/*z*: 298.1447 $[M+H]^+$. $C_{18}H_{20}NO_3$. Calculated, *m*/*z*: 298.1438.

4-(Methoxyamino)-3,3-dimethylchroman-2-one (5f). Yield 0.022 g (20%). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.22 (3H, s, 3-CH_3); 1.52 (3H, s, 3-CH_3); 3.24 (3H, s, OCH_3); 3.65 (1H, s, 4-CH); 7.05–7.09 (1H, m, H-8); 7.18 (1H, td, *J* = 7.4, *J* =1.2, H-6); 7.32–7.37 (2H, m, H-5,7). ^{13}C NMR spectrum, δ, ppm: 20.8 (3-CH_3); 24.7 (3-CH_3); 40.2 (C-3); 62.6 (C-4); 66.8 (OCH_3); 116.2 (C-8); 122.1 (C-4a); 124.4 (C-6); 129.5 (C-5); 129.7 (C-7); 151.8 (C-8a); 173.1 (C=O). Found, *m*/*z*: 222.1150 $[M+H]^+$. $C_{12}H_{16}NO_3$. Calculated, *m*/*z*: 222.1125.

2-{[(Benzyloxy)imino]methyl}phenyl propionate (6a). Yield 0.052 g (37%). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.26 (3H, t, *J* = 7.5, $CH_2C\underline{H}_3$); 2.60 (2H, q, *J* = 7.4, $C\underline{H}_2CH_3$); 5.23 (2H, s, OCH_2Ph); 7.11 (1H, d, *J* = 8.1, H-6 Ar); 7.23 – 7.29 (1H, m, H-5 Ar); 7.35 – 7.45 (6H, m, H-4 Ar, H Ph); 7.81 (1H, d, *J* = 7.8, H-3 Ar); 8.22 (1H, s, HC=N). ^{13}C NMR spectrum, δ, ppm: 9.0 ($CH_2\underline{C}H_3$); 27.6 ($\underline{C}H_2CH_3$); 76.6 (OCH_2Ph); 123.0 (C-6 Ar); 124.6 (C-1 Ar); 126.1 (C-5 Ar); 127.8 (C-3 Ar); 128.1 (C-4 Ph); 128.4 (C-2,6); 128.5 (C-3,5); 130.7 (C-4); 137.2 (C-1 Ph); 144.5 (C=N); 148.8 (C-2 Ar); 172.7 (C=O). Mass spectrum, *m*/*z* (I_{rel}, %): 283 $[M]^+$ (1), 210 (10), 91 (100).

2-{[(Methoxy)imino]methyl}phenyl propionate (6b). Yield 0.027 g (26%). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.29 (3H, t, *J* = 7.5, $CH_2C\underline{H}_3$); 2.65 (2H, q, *J* = 7.5, $C\underline{H}_2CH_3$); 3.98 (3H, s, OCH_3); 7.11 (1H, dd, *J* = 8.1, *J* = 1.2, H-6 Ar); 7.25 (1H, td, *J* = 7.5, *J* = 1.2, H-5 Ar); 7.40 (1H, td, *J* = 7.8, *J* = 1.7, H-4 Ar); 7.79 (1H, dd, *J* = 7.8, *J* = 1.7, H-3 Ar); 8.12 (1H, s, HC=N). ^{13}C NMR spectrum, δ, ppm: 9.0 ($CH_2\underline{C}H_3$); 27.6 ($\underline{C}H_2CH_3$); 62.1 (OCH_3); 123.0 (C-6 Ar); 124.5 (C-1 Ar); 126.1 (C-5 Ar); 127.7 (C-3 Ar); 130.6 (C-4 Ar); 144.04 (C=N); 148.7 (C-2 Ar); 172.7 (C=O). Found, *m*/*z*: 230.0798 $[M+Na]^+$. $C_{11}H_{13}NO_3Na$. Calculated, *m*/*z*: 230.0788.

2-{[(Benzyloxy)imino]methyl}phenyl butyrate (6c). Yield 0.046 g (31%). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.06 (3H, t, *J* = 7.4, $(CH_2)_2C\underline{H}_3$); 1.76–1.85 (2H, m, $CH_2C\underline{H}_2CH_3$); 2.56 (2H, t, *J* = 7.4, $C\underline{H}_2CH_2CH_3$); 5.25 (2H, s, OCH_2Ph), 7.12 (1H, d, *J* = 8.1, H-6 Ar); 7.26 (2H, t, *J* = 7.5, H-5 Ar); 7.36–7.45 (6H, m, H-4 Ar, H Ph); 7.83 (1H, d, *J* = 7.8, H-3 Ar); 8.24 (1H, s, HC=N). ^{13}C NMR spectrum, δ, ppm: 13.7 $(CH_2)_2\underline{C}H_3$); 18.3 ($CH_2\underline{C}H_2CH_3$); 36.0 ($\underline{C}H_2CH_2CH_3$); 76.5 (OCH_2Ph); 123.0 (C-6 Ar); 124.6 (C-1 Ar); 126.1 (C-5 Ar); 127.6 (C-3 Ar); 128.0 (C-4 Ph); 128.4 (C-2,6 Ph); 128.5 (C-3,5 Ph); 130.6 (C-4 Ar); 137.3 (C-1 Ph); 144.4 (C=N); 148.8 (C-2 Ar); 171.8 (C=O). Found, *m*/*z*: 298.1453 $[M+H]^+$. $C_{18}H_{20}NO_3$. Calculated, *m*/*z*: 298.1438.

2-{[(Methoxy)imino]methyl}phenyl butyrate (6d). Yield 0.028 g (25%). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.07 (3H, t, *J* = 7.4, $(CH_2)_2C\underline{H}_3$); 1.78–1.88 (2H, m, $CH_2C\underline{H}_2CH_3$); 2.61 (2H, t, *J* = 7.4, $C\underline{H}_2CH_2CH_3$); 3.99 (3H, s, OCH_3); 7.09–7.13 (1H, m, H-6 Ar); 7.23–7.29 (1H, m, H-5 Ar); 7.38–7.44 (1H, m, H-4 Ar); 7.81 (1H, dd, *J* = 7.8, *J* = 1.7, H-3 Ar); 8.13 (1H, s, HC=N). ^{13}C NMR spectrum, δ, ppm: 13.7 ($(CH_2)_2\underline{C}H_3$); 18.3 ($CH_2\underline{C}H_2CH_3$); 36.1 ($\underline{C}H_2CH_2CH_3$), 62.2 (OCH_3); 123.0 (C-6 Ar); 124.5 (C-1 Ar); 126.1 (C-5 Ar); 127.5 (C-3 Ar); 130.6 (C-4 Ar), 143.9 (C=N); 148.7 (C-2 Ar); 171.8 (C=O). Found, *m*/*z*: 244.0955 $[M+Na]^+$. $C_{12}H_{15}NNaO_3$. Calculated, *m*/*z*: 244.0944.

2-{[(Benzyloxy)imino]methyl}phenyl isobutyrate (6e). Yield 0.10 g (69%). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.36 (6H, d, *J* = 6.8, $CH(C\underline{H}_3)_2$); 2.85 (1H, hept, *J* = 6.8, $C\underline{H}(CH_3)_2$); 5.25 (2H, s, OCH_2Ph), 7.10 (1H, d, *J* = 8.1, H-6 Ar); 7.26 (1H, t, *J* = 7.5, H-5 Ar); 7.35–7.47 (6H, m, H-4 Ar, H Ph), 7.87 (1H, dd, *J* = 7.8, *J* = 1.7, H-3 Ar); 8.24 (1H, s, HC=N). ^{13}C NMR spectrum, δ, ppm: 18.9 (2C, $CH(\underline{C}H_3)_2$); 34.2 ($\underline{C}H(CH_3)_2$); 76.6 (OCH_2Ph); 122.9 (C-6 Ar); 124.6 (C-1 Ar); 126.1 (C-5 Ar); 127.3 (C-3 Ar); 128.1 (C-4 Ph); 128.4 (C-3,5 Ph); 128.5 (C-2,6 Ph); 130.7 (C-4 Ar); 137.3 (C-1 Ph); 144.1 (C=N); 148.9 (C-2 Ar); 175.2 (C=O). Found, *m*/*z*: 298.1454 $[M+H]^+$. $C_{18}H_{20}NO_3$. Calculated, *m*/*z*: 298.1438.

2-{[(Methoxy)imino]methyl}phenyl isobutyrate (6f). Yield 0.08 g (74%). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.35 (6H, d, *J* = 7.0, $CH(C\underline{H}_3)_2$); 2.86 (1H, hept, *J* = 7.0, $C\underline{H}(CH_3)_2$); 3.97 (3H, s, OCH_3); 7.07 (1H, dd, *J* = 8.1, *J* = 1.2, H-6 Ar); 7.23 (1H, t, *J* = 7.3, H-5 Ar); 7.35–7.41 (1H, m, H-4 Ar); 7.82 (1H, dd, *J* = 7.8, *J* = 1.8, H-3 Ar); 8.12 (1H, s, HC=N). ^{13}C NMR spectrum, δ, ppm: 18.9 (2C, $CH(\underline{C}H_3)_2$); 34.1 ($\underline{C}H(CH_3)_2$); 62.1 (OCH_3); 123.0 (C-6 Ar); 124.8 (C-1 Ar); 126.0 (C-5 Ar); 127.2 (C-3 Ar); 130.6 (C-4 Ar); 143.6 (C=N); 148.5 (C-2 Ar); 169.8 (C=O). Mass spectrum, *m*/*z* (I_{rel}, %): 221 $[M]^+$ (7), 152 (11), 151 (100), 120 (24), 119 (38), 91 (39).

2-{1-[(Benzyloxy)amino]propyl}phenyl propionate (7a). Yield 0.008 g (5%). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.01 (3H, t, *J* = 7.2, $CHCH_2C\underline{H}_3$); 1.15 (3H, t, *J* = 7.5, $COCH_2C\underline{H}_3$); 2.02–2.16 (1H, m, $CHC\underline{H}_2CH_3$); 2.30–2.53 (2H, m, $COC\underline{H}_2CH_3$); 2.56–2.70 (1H, m, $CHC\underline{H}_2CH_3$); 4.60 (1H, d, *J* = 10.2) and 4.65 (1H, d, *J* = 10.3, OCH_2Ph); 5.51 (1H, dd, *J* = 9.7, *J* = 5.4, C<u>H</u>NH); 6.91 (1H, t, *J* = 7.5, H-5 Ar); 7.00 (1H, d, *J* = 8.0, H-6 Ar); 7.21–7.40 (7H, m, H-3,4 Ar, H Ph); 8.86 (1H, s, NH). ^{13}C NMR spectrum, δ, ppm: 8.8 ($COCH_2\underline{C}H_3$); 11.3 ($CHCH_2\underline{C}H_3$); 22.3 ($CH\underline{C}H_2CH_3$); 25.5 ($CO\underline{C}H_2CH_3$); 57.2 (<u>C</u>HNH); 79.1 (OCH_2Ph); 117.7 (C-6 Ar); 119.7 (C-5 Ar); 125.1 (C-1 Ar); 126.9 (C-3 Ar); 128.7 (C-4 Ph); 128.9 (C-2,6 Ph); 129.0 (C-3,5 Ph); 129.8 (C-4 Ar); 134.0 (C-1 Ph); 156.0 (C-2 Ar); 178.1 (C=O). Found, *m*/*z*: 336.1587 $[M+Na]^+$. $C_{19}H_{23}NNaO_3$. Calculated, *m*/*z*: 336.1570.

2-[1-(Methoxyamino)propyl]phenyl propionate (7b). Yield 0.008 g (7%). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.99 (3H, t, *J* = 7.2, $CHCH_2C\underline{H}_3$); 1.19 (3H, t, *J* = 7.4, $COCH_2C\underline{H}_3$); 1.96–2.11 (1H, m) and 2.55–2.69 (1H, m, $CHC\underline{H}_2CH_3$); 2.34–2.50 (2H, m, $COC\underline{H}_2CH_3$); 3.57 (3H, s, OCH_3); 5.42 (1H, dd, *J* = 9.7, *J* = 5.6, C<u>H</u>NH); 6.88 (1H, t, *J* = 7.6, H-5 Ar); 6.95 (1H, d, *J* = 8.2, H-6 Ar); 7.22 (1H, t, *J* = 7.6, H-4 Ar); 7.33 (1H, d, *J* = 7.6, H-3 Ar); 8.80 (1H, s, NH). ^{13}C NMR spectrum, δ, ppm: 8.8 ($COCH_2\underline{C}H_3$); 11.3 ($CHCH_2\underline{C}H_3$); 22.1 ($CH\underline{C}H_2CH_3$); 25.3 ($CO\underline{C}H_2CH_3$); 56.6 (<u>C</u>HNH); 65.2 (OCH_3); 117.7 (C-6 Ar); 119.6 (C-5 Ar); 125.2 (C-1 Ar); 126.9 (C-3 Ar); 129.6 (C-4 Ar); 155.7 (C-2 Ar); 177.6 (C=O). Found, *m*/*z*: 260.1272 $[M+Na]^+$. $C_{13}H_{19}NNaO_3$. Calculated, *m*/*z*: 260.1257.

2-[1-(Methoxyamino)propyl]phenyl butyrate (7d). Yield 0.007 g (5.5%). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.98 (3H, t, *J* = 7.4, $CH_2CH_2C\underline{H}_3$); 0.99 (3H, t, *J* = 7.3, $CHCH_2C\underline{H}_3$); 1.72 (2H, hept, *J* = 7.3, $CH_2C\underline{H}_2CH_3$); 1.96–2.11 (1H, m, $CHC\underline{H}_2CH_3$); 2.32–2.46 (2H, m, $C\underline{H}_2CH_2CH_3$); 2.51–2.64 (1H, m, $CHC\underline{H}_2CH_3$); 3.57 (3H, s, OCH_3); 5.44 (1H, dd, *J* = 9.6, *J* = 5.5, C<u>H</u>NH); 6.87 (1H, td, *J* = 7.5, *J* = 1.3, H-5 Ar); 6.95 (1H, dd, *J* = 8.2, *J* = 1.3, H-6 Ar); 7.22 (1H, ddd, *J* = 8.2, *J* = 7.3, *J* = 1.7, H-4 Ar); 7.33 (1H, dd, *J* = 7.3, *J* = 1.7, H-3 Ar); 8.77 (1H, s, NH). ^{13}C NMR spectrum, δ, ppm: 11.2 ($CHCH_2\underline{C}H_3$); 13.8 ($CH_2CH_2\underline{C}H_3$); 18.0 ($CH_2\underline{C}H_2CH_3$); 22.1 ($CH\underline{C}H_2CH_3$); 33.7 ($\underline{C}H_2CH_2CH_3$); 56.5 (<u>C</u>HNH); 65.2 (OCH_3); 117.7 (C-6 Ar); 119.6 (C-5 Ar); 125.2 (C-1 Ar); 126.9 (C-3 Ar); 129.6 (C-4 Ar); 155.7 (C-2 Ar); 176.8 (C=O). Found, *m*/*z*: 274.1424 $[M+Na]^+$. $C_{14}H_{21}NNaO_3$. Calculated, *m*/*z*: 274.1414.

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References

1. Mikhaleva, A. I.; Zaitsev, A. B.; Trofimov, B. A. *Russ. Chem. Rev.* **2006**, 75, 797. [*Usp. Khim.* **2006**, *75*, 884.]
2. Corey, E.; Pyne, S. *Tetrahedron Lett.* **1983**, *24*, 2821.
3. For some reviews of radical addition to oxime ethers, see: (a) Friestad, G. *Tetrahedron* **2001**, *57*, 5461. (b) Subramanian, H.; Landais, Y.; Sibi, M. P. In *Comprehensive Organic Synthesis II*; Molander, G.; Knochel, P., Eds.; Elsevier: Amsterdam, 2014, Vol. 4, p. 699.
4. For some examples of radical addition to oxime ethers, see: (a) Miyata, O.; Takahashi, S. A.; Tamura, U. M.; Naito, T. *Tetrahedron.* **2008**, *64*, 1270. (b) Jaramillo-Gómez, L. M.; Loaiza, A. E.; Martin, J.; Ríos, L. A.; Wang, P. G. *Tetrahedron Lett*. **2006**, *47*, 3909. (c) Miyabe, H.; Ueda, M.; Fujii, K.; Nishimura, A.; Naito, T. *J. Org. Chem.* **2003**, *68*, 5618. (d) Miyabe, H.; Ueda, M.; Yoshioko, N.; Yamakawa, K.; Naito, T. *Tetrahedron* **2000**, *56*, 2413. (e) Miyabe, H.; Ueda, M.; Naito, T. *J. Org. Chem*. **2000**, *65*, 5043. (f) Miyabe, H.; Tanaka, H.; Naito, T. *Tetrahedron Lett*. **1999**, *40*, 8387. (g) Miyabe, H.; Shibata, R.; Sangawa, M.; Ushiro, C.; Naito, T. *Tetrahedron* **1998**, *54*, 11431. (h) Miyabe, H.; Shibata, R.; Ushiro, C.; Naito, T. *Tetrahedron Lett.* **1998**, *39*, 631.
5. (a) Dong, S.; Liu, X.; Zhang, Y.; Lin, L.; Feng, X. *Org. Lett.* **2011**, *13*, 5060. (b) El-Saghier, A. M.; Naili, M. B.; Rammash, B. Kh.; Saleh, N. A.; Kreddan, K. M. *ARKIVOC* **2007**, (xvi), 83. (c) Di Braccio, M.; Grossi, G.; Roma, G.; Marzano, C.; Baccichetti, F.; Simonato, M.; Bordin, F. *Farmaco* **2003**, *58*, 1083. (d) Roma, G.; Di Braccio, M.; Carrieri, A.; Grossi, G.; Leoncini, G.; Signorello, M.; Carotti, A. *Biorg. Med. Chem.* **2003**, *11*, 123.
6. Otto, N.; Opatz, T. *Beilstein J. Org. Chem*. **2012**, *8*, 1105.