A New Synthetic Method to 2-Pyridones

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Abstract: We report here a simple procedure for the preparation of 4,6-disubstituted- and 3,4,6-trisubstituted-2-pyridones and 3-substituted-isoquinol-1-ones, in good yields, from lithium dienediolates and nitriles.

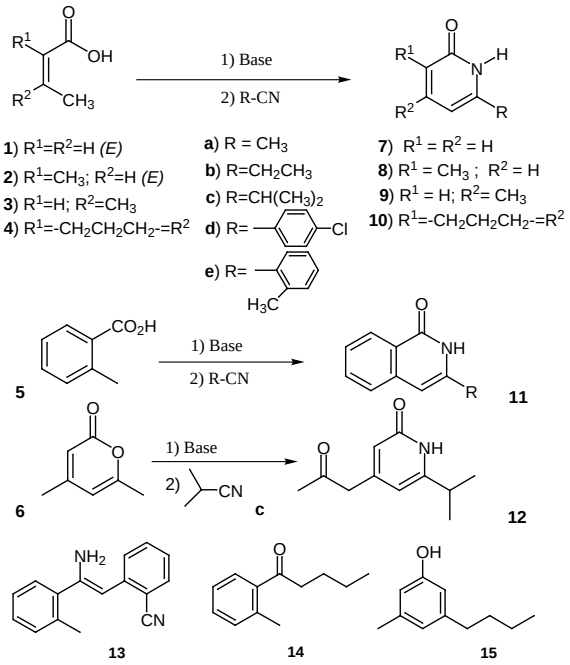
Keywords: pyridones, isoquinolones, nitriles, lithium dienediolates, carboxylic acids

The synthesis of a substituted 2-pyridone ring is a topical area of continuing interest due to the number of biologically active molecules containing this moiety. Over the last decade, natural compounds with this structure have emerged as potent antitumor,[1,2] antiviral[3] and psychotherapeutic[4] agents along with a new antibiotic.[5] Besides, pyridones are key intermediates in the synthesis of the corresponding pyridines.[6] Thus, despite the large number of methods known for their synthesis,[7] new procedures are continuously being developed.[8]

Our studies on the reactivity of dienediolates of unsaturated carboxylic acids has led us to a new convenient synthesis of 4,6-disubstituted- and 3,4,6,-trisubstituted-2-pyridones from lithium dienediolates and nitriles. Synthesis of 1-isoquinolones from nitriles was previously reported[2] by addition of anions derived from *o*-toluamides. The direct use of unsaturated carboxylic acids, however, had remained unexplored until our preliminary communication[9] and we wish to report here a more complete study on the scope of the method.

It is well known that unsaturated carboxylic acids are synthetically useful building blocks. Double deprotonation by lithium amides generate their lithium dienediolates that behave as ambident nucleophiles, through their α or γ carbon atoms, leading to single or clearly predominant compounds when allowed to react with electrophiles under adequate conditions.[10] Thus, α attack predominates for irreversible reactions,[11,12] whereas, highly stereoselective γ-adducts are obtained when reversible additions to carbonyl compounds are carried out under equilibrium conditions.[13,14] Therefore, it seemed reasonable, that γ-adducts resulting from the nucleophilic attack of these dienediolates to nitriles would afford pyridone rings after intramolecular cyclization (Scheme 1).

The results obtained for this tandem reaction show the wide applicability of the method. Several α,β-unsaturated carboxylic acids (**1**−**5**), and both alkyl (**a**-**c**) or aryl (**d**, **e**) nitriles have been used to obtain substituted 2-pyridones (**7**−**10**) and isoquinol-1-ones (**11**), easily isolated in most cases as pure compounds by crystallization from the crude reaction mixture. As a special case, double deprotonation of the 2-pyrone (**6**) leads, under similar reaction conditions, to the 2-pyridone **12** (Scheme 1).



Scheme 1

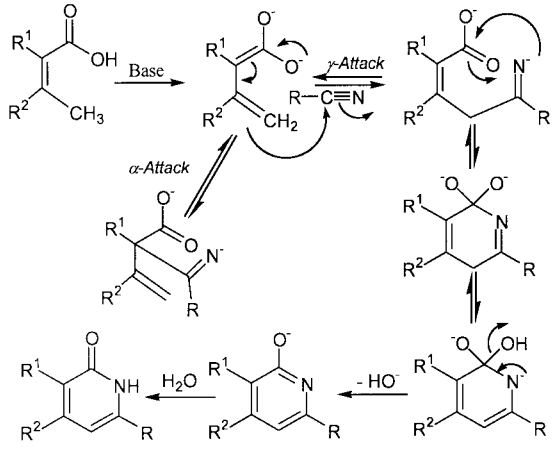
The best results obtained are summarized in Table 1. Although reaction conditions are not critical in order to obtain the corresponding pyridones, for each acid and nitrile, an optimization of time, temperature, proportions of reagents and nature of the base, was performed in order to attain a better yield. Room temperature (25°C) is always the best choice. Lower temperatures led to higher amounts of unreacted material, while higher temperatures promoted the formation of byproducts. At this temperature, a 24-hour reaction time is needed in most cases and a longer reaction time did not improve the yield. Usually, a 1:1 ratio of nitrile and acid were used, as an increase in the amount of nitrile did not improve the results.

Both the amine and its amount are expected to control the aggregation states of dienediolates and were therefore optimized. Use of lithium diisopropylamide (LDA) instead of lithium diethylamide (LDE) as a base led to lower yields in other additions[15] but, in this case, it does not make a great difference and can even be an advantage for the ionization of *o*-toluic acid (Table 1, entries 13 and 15).

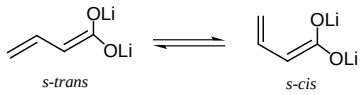
In most cases dienediolates can be generated, without Barbier's reduction or Michael adduct formation, by deprotonation of the corresponding acids with butyllitium and a catalytic amount of an amine.[16] In this case, a smaller amount of amine usually led to pyridones in better yields, but it cannot be considered as a general rule.

Lower yields were obtained for nitriles with acidic protons at primary carbon atoms due to the formation of self-condensation products. Thus, when acetonitrile (**a**) was used, a polymeric material becomes the main product in most cases, whereas use of *o*-tolunitrile (**e**) led to byproduct **13**.

According to our experience on additions of these dienediolates to carbonyl compounds,[14,15] a mechanistic picture of the pyridone forming process can be outlined (Scheme 2). Probably, small amounts of α- and γ-adducts are in equilibrium with starting material and only *cis* γ-adducts can evolve to a stable product that pushes forward the equilibrium. The γ-attack of electrophiles to the dienediolates of unsaturated acids is highly stereoselective leading almost always to a single *cis*- or *trans*-γ-adduct according to the substituents at C-3. Thus, butenoic acids **1** and **2**, which bear no further alkyl substituent at C-3 afford *trans*-γ-adducts, whereas acids **3** to **5**, which bear a methyl group at C-3 lead mainly to *cis*-γ-adducts. Although it may be expected that *s-cis* and *s-trans* conformations of these dianions (Scheme 3) equilibrate in solution,[17] the highly stereoselective *trans*-γ-addition for crotonic acid (**1**) and, especially, tiglic acid (**2**) prevent further intramolecular cyclization. Accordingly, no pyrone **8** could be detected (entries 3 and 4). We tried to force an *s-cis* conformation for these diendiolates by adding coordinative species such as $Fe(CO)_5$, ferrocene or CoI_2 but only starting material was recovered.



Scheme 2



Scheme 3

In order to determine if protonation to the final pyridone was produced in the reaction mixture or in the work-up (Scheme 2), iodomethane was added to the reaction mixture. Methylation of the intermediate was expected, but since no 2-methoxypyridine could be observed, we were led to think that pyridone was already formed before the workup.

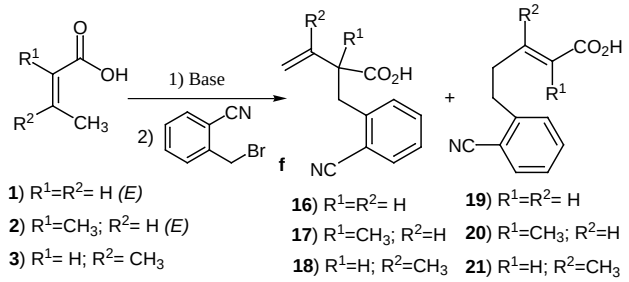
On the other hand, we expected the addition of dienediolates to nitriles to be a slow process as cyano-hydroxy-acids can be prepared, in good yield, by addition of these

Table 1 Nucleophilic Addition of Dienediolates to Nitriles

Entry	Acid	Nitrile	Base BuLi (2 equiv) + Et_2NH (n equiv)	Time (h)	Yield (%) Recovered acid	Pyridone	Other Products
1	**1**	**c**	(2)	24	75	13 (**7c**)	–
2	**1**	**d**	(2)	2	37		
3	**2**	**c**	(2)	5	80		
4	**2**	**d**		3	56		
5	**3**	**a**	(2)	24		38 (**9a**)	Polym.
6	**3**	**b**	(0.4)	24		65 (**9b**)	
7	**3**	**c**	(0)	24		78 (**9c**)	
8	**3**	**d**	(0.4)	24		85 (**9d**)	
9	**3**	**e**	(2)	7		33 (**9e**)	47 (**13**)
10	**4**	**b**	(0.4)	24		60 (**10b**)	
11	**4**	**c**	(0.4)	24		72 (**10c**)	
12	**4**	**d**	(0.4)	24		82 (**10d**)	
13	**5**	**b**	(0.4)[a]	24		40 (**11b**)	3 (**14**)
14	**5**	**c**	(2)	21		84 (**11c**)	
15	**5**	**d**	(0.4)[a]	24		62 (**11d**)	3 (**14**)
16	**6**	**c**	(0.4)	24	40	–	27 (**15**)
17	**6**	**c**	(1)	24	33	11 (**12**)	5 (**15**)
18	**6**	**c**	(2)			32 (**12**)	

[a] $(i\text{-Pr})_2NH$

dienediolates to cyanoaldehydes.[14] However, additions to cyano and aldehyde groups are reversible processes and the preferred attack could be due to thermodynamic control. We expected to establish the rate-determining step in the pyridone forming process, by means of a competition reaction (Scheme 4) with 2-cyanobenzyl bromide (Table 2). Only 2-cyanoalkylation products (**16**−**21**) were obtained, indicating that the irreversible alkylation is much faster than addition to the nitrile.[11] Otherwise, at least traces of the corresponding isoindole was expected. As no isoindole could be detected we deduced that addition of the dienediolate to nitriles should be the rate determining reversible step. On the other hand, the α:γ regioselectivity ratio found was in the normal trend for these kinds of substrates.[12]



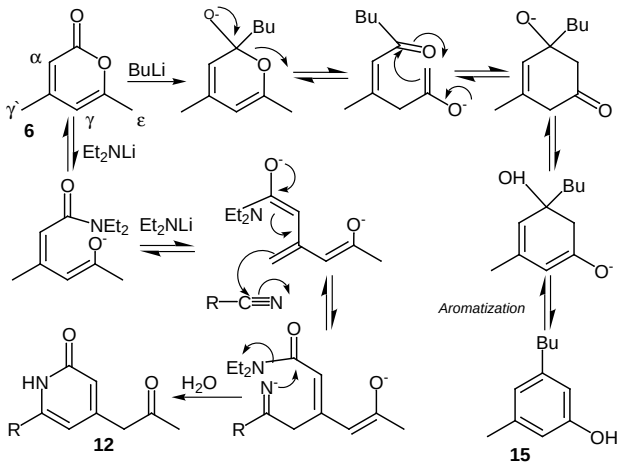
Scheme 4

The conversion of pyrone (**6**) to pyridone (**12**) deserves a special comment. Following the mechanism outlined in Scheme 2, a 5-acyl-6-isopropyl-4-methyl-2-pyridone was expected from γ-attack of the nitrile to the trienolate, generated from pyrone **6** and one equivalent of base. However, this product was not observed in any case and phenol **15** and pyridone **12** were obtained instead (Table 1, entry 17). Lower amounts of amine led mainly to **15**, whereas use of two equivalents of base and amine led to **12** as the main product for this reaction. These results can be explained (Scheme 5) by considering an addition of the base to the pyrone carboxyl instead of deprotonation. When butyllithium is present in the reaction mixture, this is an irreversible process that leads to the phenol **15**. With lithium amides this addition leads to an intermediate which, on γ′ deprotonation and addition to the nitrile, as proposed by Kelly,[2] leads mainly to pyridone **12** which can be isolated as a yellow oil in moderate yield (Table 1, entry 18).

In conclusion, we have found a simple procedure for the preparation of 4,6-disubstituted and 3,4,6-trisubstituted-

Table 2 Competition Reaction: Addition to Nitrile vs Alkylation

Entry	Acid	Yield (%)	Rate (α:γ)
1	**1**	70	**16**:**19** (67:33)
2	**2**	68	**17**:**20** (56:44)
3	**3**	85	**18**:**21** (74:26)



Scheme 5

2-pyridones from the addition of lithium dienediolates, derived from α,β-unsaturated carboxylic acids, to nitriles, which are either commercially available or conveniently prepared by conventional or well stabilised procedures. Besides, the method can be extended to 2-alkylbenzoic acids leading to the 1-isoquinolone moiety. In addition, most 2-pyridones and isoquinol-1-ones are easily isolated from the reaction mixture, as they precipitate on workup with water and can be easily purified by a simple crystallisation.

Mps were determined with a Reichert apparatus and are uncorrected. IR spectral data were obtained for liquid film or KBr discs, with a Perkin−Elmer 281 spectrophotometer. NMR spectra were recorded for $CDCl_3$ solutions, with a Varian Unity 300 or Unity 400 spectrometers. Elemental analyses were determined by "Servicio de Semimicroanálisis del Centro de Investigación y Desarrollo (CSIC) de Barcelona". High resolution mass spectra were determined with a UG Autoespec spectrometer. Silica gel Merck 60 (230−400 mesh) was used for flash column chromatography, with hexane/Et_2O/MeOH mixtures for elution.

All reactions were carried out under Ar atm, using standard conditions for exclusion of moisture, in oven dried glassware, in THF freshly distilled from blue benzophenone ketyl and with diethylamine and diisopropylamine distilled from CaH_2. The reaction temperature (-78 °C) was achieved by cooling with a CO_2/acetone bath. Organic extracts were dried over anhyd $MgSO_4$, and solutions were evaporated under reduced pressure with a rotary evaporator and a bath at 40 °C.

2-Methylcyclopent-1-ene carboxylic acid **4** was prepared by the method described by Harding and Clement.[18] The mp and spectroscopic data were in agreement with those already described. Other starting compounds were purchased and used without purification.

2-Pyridones; General Procedure

Carboxylic acid (2.25 mmol) in THF (2 mL) was slowly added to stirred LDE (between 0.2−4.8 mmol, see Table 1) in THF (2 mL) at -78 ºC, according to the method already described.[16] The solution was stirred for 30 min at 0 ºC for unsaturated acids **1**−4 and for 4,6-dimethyl-2H-pyran-2-one (**6**), and 1 h at r.t. for *o*-toluic acid **5**, and

then cooled again to -78 ºC. Nitrile (2.25 mmol) in THF (2 mL) was added dropwise, and the solution stirred at r.t. for the time stated in each case (Table 1). H_2O (20 mL) was added and the product isolated by crystallization from crude in most cases, leading to pure products. In other cases, H_2O was added, extracted with CH_2Cl_2 (3 x 15mL) and the combined organic layers were washed with brine to neutral pH, and dried. Evaporation of the solvent gave crude reaction mixture.

6-Isopropylpyridin-2(1*H*)-one (7c)
From *trans*-but-2-enoic acid (**1**) (194 mg, 2.25 mmol) and isobutyronitrile **c** (0.2 mL, 2.25 mmol), the reaction mixture was stirred at r.t. for 24 h. Yield: 40 mg (13%), yellow waxy material.

IR (film): ν_{max} = 3200, 2964, 2933, 1651, 1618, 1552, 1461, 1157, 998, 932, 804, 736, 558 cm^{-1}.

^1H NMR ($CDCl_3$, 400 MHz): δ = 1.28 [d, 6H, *J* = 6.9 Hz, $(CH_3)_2CH$], 2.88 [m, 1H, $CH(CH_3)_2$], 6.06 (d, 1H, *J* = 7.0 Hz, CH-C-NH), 6.40 (d, 1H, *J* = 9.0 Hz. CH-CO), 7.38 (dd, 1H, *J* = 9.0, 7.0 Hz, CHCHCHN).

^{13}C NMR ($CDCl_3$, 400 MHz): δ = 19.5 (2 CH_3), 29.7 [$CH(CH_3)_2$], 102.3 (CH-C-N), 117.0 (CH-CO), 141.8 (CHCHCHN), 155.5 [C-$CH(CH_3)_2$], 165.5 (CO).

EIMS: *m/z* (%) = 137 (M^+, 60), 122 (M^+-CH_3, 100), 109 (M^+−CO, 13), 104 (29), 94 [$M^+-CH(CH_3)_2$, 22].

HRMS: *m/z* calc for $C_8H_{11}NO$ (M^+) 137.084064. Found: 137.083931.

4,6-Dimethylpyridin-2(1*H*)-one (9a)
From 3-methylbut-2-enoic acid (**3**) (225 mg, 2.25 mmol) and acetonitrile **a** (0.12 mL, 2.25 mmol), the mixture was stirred at r.t. for 24 h. Yield: 105 mg (38%), yellow solid; mp 166−167 °C.

IR (KBr): ν_{max} = 3487, 3265, 3060, 1221, 1560, 1498, 1437, 1369, 928, 834, 765, 739, 726, 591 cm^{-1}.

^1H NMR ($CDCl_3$, 400 MHz): δ = 2.16 (s, 3H, CH_3), 2.29 (s, 3H, CH_3CHN), 5.90 (s, 1H, CH-C-NH), 6.19 (s, 1H, CH-CO).

^{13}C NMR ($CDCl_3$, 400 MHz): δ = 18.8 (CH_3), 21.5 (CH_3CHN), 108.6 (CH-C-N), 115.0 (CH-CO), 149.2 ($NCCH_3$), 153.7 (C-CH_3), 165.9 (CO).

EIMS: *m/z* (%) = 123 (M^+, 85), 108 (M−CH_3, 2), 95 (M−CO, 34), 94 (M−1−CO, 100), 80 (M−CH_3−CO, 22).

HRMS: *m/z* calc for C_7H_9NO (M^+) 123.068414. Found: 123.068038.

6-Ethyl-4-methylpyridin-2(1*H*)-one (9b)
From 3-methylbut-2-enoic acid (**3**) (225 mg, 2.25 mmol) and propionitrile **b** (0.16 mL, 2.25 mmol), the mixture was stirred at r.t. for 24 h. Yield: 200 mg (65%), white solid; mp 147−148 °C (EtOAc).

IR (KBr): ν_{max} = 3291, 3126, 3054, 2968, 2935, 1647, 1545, 1467, 1435, 1216, 989, 946, 868, 808, 610 cm^{-1}.

^1H NMR ($CDCl_3$, 400 MHz): δ = 1.26 (t, 3H, *J* = 7.5 Hz, CH_3-CH_2), 2.17 (s, 3H, CH_3), 2.60 (q, 2H, *J* = 7.6 Hz, CH_2CH_3), 5.90 (s, 1H, CH-C-NH), 6.21 (s, 1H, CH-CO).

^{13}C NMR ($CDCl_3$, 400 MHz): δ = 12.7 (CH_3CH_2), 21.7 (CH_3C), 26.1 (CH_2CH_3), 106.6 (CH-C-N), 115.5 (CH-CO), 150.0 (C-CH_2CH_3), 153.6 (C-CH_3), 165.8 (CO).

EIMS: *m/z* (%) = 137 (M^+, 99), 136 (M−1, 100), 118 (10), 109 (M−CO, 22), 94 (M−CO−CH_3, 43).

HRMS: *m/z* calc for $C_8H_{11}NO$ (M^+) 137.084064. Found: 137.083742.

Anal: $C_8H_{11}NO$ (137.2): calc C, 70.04; H, 8.08; N, 10.21. Found C, 69.93; H, 8.13; N, 10.23.

6-Isopropyl-4-methylpyridin-2(1*H*)-one (9c)
From 3-methylbut-2-enoic acid (**3**) (225 mg, 2.25 mmol) and isobutyronitrile **c** (0.2 mL, 2.25 mmol), the mixture was stirred at r.t. for 24 h. Yield: 263 mg (78%), white solid; mp 145−146 °C (acetone).

IR (KBr): ν_{max} = 3280, 2961, 2900, 1650, 1623, 1548, 1472, 1366, 1317, 1219, 1102, 984, 945, 851, 815, 741, 620 cm^{-1}.

^1H NMR ($CDCl_3$, 400 MHz): δ = 1.27 [d, 6H, *J* = 6.9 Hz, $(CH_3)_2CH$], 2.17 (s, 3H, CH_3), 2.84 [m, 1H, $CH(CH_3)_2$], 5.89 (s, 1H, CH-C-NH), 6.21 (s, 1H, CH-CO).

^{13}C NMR ($CDCl_3$, 400 MHz): δ = 21.6 (3 CH_3), 31.8 [$CH(CH_3)_2$], 104.6 (CH-C-N), 115.5 (CH-CO), 153.4 [C-$CH(CH_3)_2$], 154.7 (C-CH_3), 165.9 (CO).

EIMS: *m/z* (%) = 151 (M^+, 52), 136 (M−CH_3, 100), 123 (M−CO, 11), 108 [M−$CH(CH_3)_2$, 17], 91(9), 53 (16).

HRMS: *m/z* calc for $C_9H_{13}NO$ (M^+) 151.099714. Found: 151.099545.

Anal: $C_9H_{13}NO$ (151.1): calc C, 71.49; H, 8.67; N, 9.26. Found C, 71.38; H, 8.74; N, 9.26.

6-(*p*-Chlorophenyl)-4-methylpyridin-2(1*H*)-one (9d)
From 3-methylbut-2-enoic acid (**3**) (225 mg, 2.25 mmol) and *p*-chlorobenzonitrile **d** (309.5 mg, 2.25 mmol), the mixture was stirred at r.t. for 24 h. Yield: 420 mg (85%), white solid; mp 234−235 °C (EtOAc/hexane).

IR (KBr): ν_{max} = 3260, 3070, 2900, 1645, 1615, 1384, 1094, 846, 818 712 cm^{-1}.

^1H NMR ($CDCl_3$, 400 MHz): δ = 2.25 (s, 3H, CH_3), 6.30 (s, 1H, CH-C-NH), 6.35 (s, 1H, CH-CO), 7.45 (d, 2H, *J* = 8.4 Hz, 2 $CH_{arom.}$), 7.65 (d, 2H, *J* = 8.4 Hz, 2 $CH_{arom.}$).

^{13}C NMR ($CDCl_3$, 400 MHz): δ = 21.7 (CH_3), 107.6 (CH-C-N), 117.6 (CH-CO), 128.0, 129.3, 132.0, 136.0 (6 $C_{arom.}$), 144.7 (C-$C_{arom.}$), 152.7 (C-CH_3), 165.2 (CO).

EIMS: *m/z* (%) = 222 (^{37}ClM+1, 6), 221 ($^{37}ClM^+$, 48), 220 (^{35}ClM+1, 17), 219 ($^{35}ClM^+$, 100), 191 (M−CO, 52), 190 (51).

HRMS: *m/z* calc for $C_{12}H_{11}{}^{37}ClNO$ (M^+) 222.049967. Found: 222.049277. *m/z* calc for $C_{12}H_{11}{}^{35}ClNO$ (M^+) 220.052917. Found: 220.053013.

Anal: $C_{12}H_{10}ClNO$ (219.7):Calc C, 65.61; H, 4.59; N, 6.38. Found C, 65.61; H, 4.57; N, 6.30.

4-Methyl-6-(*o*-methylphenyl)pyridin-2(1*H*)-one (9e)
From 3-methylbut-2-enoic acid (**3**) (225 mg, 2.25 mmol) and *o*-methylbenzonitrile **e** (263 mg, 2.25 mmol), the mixture was stirred at r.t. for 7 h. Yield: 148 mg (33%), white solid; mp 204−5 °C (purified by column chromatography).

IR (KBr): ν_{max} = 3260, 3070, 2912, 1637, 1549, 1490, 1460, 1439 1258, 1165, 1028, 948, 937, 831, 756, 721 cm^{-1}.

^1H NMR ($CDCl_3$, 400 MHz): δ = 2.21 (s, 3H, CH_3), 2.34 (s, 3H, CH_3-$C_{arom.}$), 6.00 (s, 1H, CH-C-NH), 6.25 (s, 1H, CH-CO), 7.25−7.34 (m, 4H, 4 $CH_{arom.}$).

^{13}C NMR ($CDCl_3$, 400 MHz) δ = 19.9 (CH_3-$C_{arom.}$), 21.6 (CH_3), 109.5 (CH-C-N), 117.0 (CH-CO), 126.1, 129.1, 129.5, 130.9, 134.1, 135.9 (6 $C_{arom.}$), 146.0 (C-$C_{arom.}$), 152.8 (C-CH_3), 164.6 (CO).

EIMS: *m/z* (%) = 199 (M^+, 91), 198 (M−1, 100), 184 (M−CH_3, 31), 156 (M−CH_3−CO, 10).

HRMS: *m/z* calc for $C_{13}H_{13}NO$ (M^+) 199.099714. Found: 199.099108.

3-Ethyl-2,5,6,7-tetrahydro-1*H*-cyclopenta[*c*]pyridin-1-one (10b)

From 2-methylcyclopent-1-ene carboxylic acid **4** (284 mg, 2.25 mmol) and propionitrile **b** (0.16 mL, 2.25 mmol), the mixture was stirred at r.t. for 24 h. Yield: 220 mg (60%), white prisms; mp 179−80 °C (acetone).

IR (KBr): ν_{max} = 3280, 2937, 2876, 1636, 1562, 1462, 951, 822, 629 599 cm^{-1}.

^1H NMR ($CDCl_3$, 400 MHz): δ = 1.25 (t, 3H, *J* = 7.4 Hz, CH_3-CH_2), 2.05 [m, 2H, $CH_2(CH_2)_2$], 2.60 (q, 2H, *J* = 7.6 Hz, CH_2CH_3), 2.80 (t, 4H, *J* = 7.6 Hz, 2 CH_2C=), 6.02 (s, 1H, CH-C-NH).

^{13}C NMR ($CDCl_3$, 300 MHz): δ = 12.7 (CH_3CH_2), 23.5 [$CH_2(CH_2)_2$], 26.2 (CH_2CH_3), 29.3 (CH_2CCO), 34.3 (CH_2C=CCO), 102.2 (CH-C-N), 128.7 (=C-CO), 148.9 (C=C-CO), 157.5 (C-CH_2CH_3), 162.9 (CO).

EIMS: *m/z* (%) = 163 (M^+, 68), 162 (M-1, 100), 148 (M-CH_3, 7), 134 (M-1-CH_3, 12).

HRMS: *m/z* calc for $C_{10}H_{13}NO$ (M^+) 163.099714. Found: 163.099106.

Anal: $C_{10}H_{13}NO$ (163.1): CalcC, 73.59; H, 8.03; N, 8.58. Found C, 73.42; H, 8.17; N, 8.60.

3-Isopropyl-2,5,6,7-tetrahydro-1*H*-cyclopenta[*c*]pyridin-1-one (10c)

From 2-methylcyclopent-1-ene carboxylic acid **4** (284 mg, 2.25 mmol) and isobutyronitrile **c** (0.20 mL, 2.25 mmol); the mixture was stirred at r.t. for 24 h. Yield: 287 mg (72%), white prisms; mp 184−5 °C.

IR (KBr): ν_{max} = 3271, 3132, 2960, 2920, 2874, 1645, 1628, 1570, 1456, 1391, 1121, 1058, 946, 818 cm^{-1}.

^1H NMR ($CDCl_3$, 300 MHz): δ = 1.25 (d, 6H, *J* = 6.6 Hz, 2 CH_3-CH), 2.05 [m, 2H, $CH_2(CH_2)_2$], 2.80 [m, 5H, 2 CH_2C= and $CH(CH_3)_2$], 6.02 (s, 1H, CH-C-NH).

^{13}C NMR ($CDCl_3$, 300 MHz): δ = 21.8 (2 CH_3), 23.5 [$CH_2(CH_2)_2$], 29.2 (CH_2CCO), 31.8 [$CH(CH_3)_2$], 34.3 (CH_2C=CCO), 100.4 (CH-C-N), 128.6 (=C-CO), 153.8 (C=C-CO), 157.4 [C-$CH(CH_3)_2$], 162.9 (CO).

EIMS: *m/z* (%) = 177 (M^+, 86), 162 (M−CH_3, 100), 149 (M−CO, 15), 134 (M−CH_3−CO, 13).

HRMS: *m/z* calc for $C_{11}H_{15}NO$ (M^+) 177.115364. Found: 177.115068.

Anal: $C_{11}H_{15}NO$ (177.1): Calc C, 74.54; H, 8.53; N, 7.90. Found C, 74.32; H, 8.47; N, 7.94.

3-(*p*-Chlorophenyl)-2,5,6,7-tetrahydro-1*H*-cyclopenta[c]pyridin-1-one (10d)

From 2-methylcyclopent-1-ene carboxylic acid **4** (284 mg, 2.25 mmol) and *p*-chlorobenzonitrile **d** (309.5 mg, 2.25 mmol), the mixture was stirred at r.t. for 24 h. Yield: 452 mg (82%), white solid; mp dec. (aq EtOH).

IR (KBr): ν_{max} = 3127, 3072, 2959, 2917, 1633, 1608, 1495, 1464, 1092, 1012, 817, 818 578 cm^{-1}.

^1H NMR ($CDCl_3$, 300 MHz): δ = 2.11 [m, 2H, $CH_2(CH_2)_2$], 2.88 (t, 4H, *J* = 8.7 Hz, 2 CH_2C =), 6.44 (s, 1H, CH-C-NH), 7.44 (d, 2H, *J* = 8.7 Hz, 2 $CH_{arom.}$), 7.58 (d, 2H, *J* = 8.7 Hz, 2 $CH_{arom.}$).

^{13}C NMR ($CDCl_3$, 300M Hz): δ = 23.4 [$CH_2(CH_2)_2$], 29.5 (CH_2CCO), 34.4 (CH_2C = CCO), 103.1 (CH-C-N), 122.1 (= C-CO), 127.4, 129.4 (4 $CH_{arom.}$), 132.5, 135.8 (2 $C_{arom.}$), 143.4 (C-$C_{arom.}$), 157.0 (C = C-CO), 162.1 (CO).

(EIMS: *m/z* (%) = 247 ($^{37}ClM^+$, 37), 245 ($^{35}ClM^+$, 100), 230 (M−CH_3), 218 (48), 173 (6), 137 (10).

HRMS: *m/z* calcd for $C_{14}H_{12}{}^{37}ClNO$ (M^+) 247.057792. Found: 247.055699. *m/z* calcd for $C_{14}H_{12}{}^{35}ClNO$ (M^+) 245.060742. Found: 245.059894.

Anal: $C_{14}H_{12}ClNO$ (245.7): Calc C, 68.44; H, 4.92; N, 5.70. Found C, 68.43; H, 4.97; N, 5.75.

3-Ethyl-1,2-dihydroisoquinolin-1(2*H*)-one (11b)

From *o*-toluic acid **5** (306 mg, 2.25 mmol) and propionitrile **b** (0.16 mL, 2.25 mmol), the mixture was stirred at r.t. for 24 h. Yield: 156 mg (40%), white prisms; mp 139−140 °C (acetone).

IR (KBr): ν_{max} = 3293, 3163, 2976, 1657, 1605, 1554, 1475, 1376, 1347, 1257, 1130, 952, 903, 826, 747, 580 cm^{-1}.

^1H NMR ($CDCl_3$, 400 MHz): δ = 1.35 (t, 3H, *J* = 7.5 Hz, CH_3-CH_2), 2.85 (q, 2H, *J* = 7.5 Hz, CH_2CH_3), 6.31 (s, 1H, CH-C-NH), 7.42 (dd, 1H, *J* = 7.5, 7.4 Hz, $CH_{arom.}$), 7.48 (d, 1H, *J* = 7.8 Hz, $CH_{arom.}$), 7.62 (dd, 1H, *J* = 8.0, 7.4 Hz, $CH_{arom.}$), 8.39 (d, 1H, *J* = 8.1 Hz, $CH_{arom.}$).

^{13}C NMR ($CDCl_3$, 400 MHz): δ = 12.4 (CH_3CH_2), 26.4 (CH_2CH_3), 102.9 (CH-C-N), 124.4 (= C-CO), 125.7 (2 $CH_{arom.}$), 127.2, 132.5 (2 $CH_{arom.}$), 138.7 (C=C-CO), 143.3 (C-CH_2CH_3), 164.6 (CO).

EIMS: *m/z* (%) = 173 (M^+, 68), 172 (M−1, 72), 158 (M−CH_3, 49), 145 (M−CO, 14), 131 (16).

HRMS: *m/z* calcd for $C_{11}H_{11}NO$ (M^+) 173.084064. Found: 173.084484.

Anal: $C_{11}H_{11}NO$ (173.2): Calc. C, 76.28; H, 6.40; N, 8.09. Found C, 76.40; H, 6.43; N, 8.15.

3-Isopropyl-1,2-dihydroisoquinolin-1(2*H*)-one (11c)

From *o*-toluic acid **5** (306 mg, 2.25 mmol) and isobutyronitrile **c** (0.20 mL, 2.25 mmol), the mixture was stirred at r.t. for 21 h. Yield: 353 mg (84%), white solid; mp 192−193 °C.

IR (KBr): ν_{max} = 3162, 3008, 2967, 2871, 1661, 1637, 1607, 1554, 1477, 1349, 1256, 1170, 983, 906, 821, 754 637 cm^{-1}.

^1H NMR ($CDCl_3$, 400 MHz): δ = 1.35 (d, 6H, *J* = 6.8 Hz, 2 CH_3-CH), 2.85 [m, 1H, $CH(CH_3)_2$], 6.31 (s, 1H, CH-C-NH), 7.42 (ddd, 1H, *J* = 8.0, 6.8, 1.2 Hz, $CH_{arom.}$), 7.49 (d, 1H, *J* = 8.0 Hz, $CH_{arom.}$), 7.62 (ddd, 1H, *J* = 7.6, 6.4, 1.2 Hz, $CH_{arom.}$), 8.37 (dd, 1H, *J* = 7.6, 1.2 Hz, $CH_{arom.}$).

^{13}C NMR ($CDCl_3$, 400 MHz): δ = 21.4 (2 CH_3), 32.2 [$CH(CH_3)_2$], 101.4 (CH-C-N), 125.7, 125.9 (2 $CH_{arom.}$), 127.3 (=C-CO), 132.5 (2 $CH_{arom.}$), 138.7 (C=C-CO), 147.3 [C-$CH(CH_3)_2$], 164.5 (CO).

EIMS: *m/z* (%) = 187 (M^+, 89), 186 (M−1, 16), 172 (M−CH_3, 100), 154(18), 145 (5).

HRMS: *m/z* calc for $C_{12}H_{13}NO$ (M^+) 187.099714. Found: 187.099202.

Anal: $C_{12}H_{13}NO$ (187.1): Calc C, 76.98; H, 7.00; N, 7.48. Found C, 76.90; H, 7.03; N, 7.59.

3-(*p*-Chlorophenyl)isoquinolin-1(2*H*)-one (11d)

From *o*-toluic acid **5** (306 mg, 2.25 mmol) and *p*-chlorobenzonitrile **d** (309.5 mg, 2.25 mmol), the mixture was stirred at r.t. for 24 h. Yield: 340 mg (62%), yellow solid (acetone); mp 268−270 °C.

IR (KBr): ν_{max} = 3165, 3038, 1664, 1607, 1487, 1349, 1093, 862, 806 680 cm^{-1}.

^1H NMR (DMSO-d_6, 300 MHz): δ = 6.93 (s, 1H, CH-C-NH), 7.48 (m, 1H, $CH_{arom.}$); 7.54 (d, 2H, *J* = 8.4, 2 $CH_{arom.}$ disubstituted), 7.70 (m, 2H, $CH_{arom.}$); 7.79 ((d, 2H, *J* = 8.4, 2 $CH_{arom.}$ disubstituted), 8.18 (d, 1H, *J* = 7.8 Hz, $CH_{arom.}$-C-CONH).

^{13}C NMR (DMSO-d_6, 300 MHz): δ = 104.3 (CH-C-N), 115.8 ($C_{arom.}$), 125.6 ($C_{arom.}$), 127.3 (2 $CH_{arom.}$), 127.5 (2 $CH_{arom.}$), 129.2 (2

$CH_{arom.}$), 129.4 (2 $CH_{arom.}$), 133.4 ($CH_{arom.}$), 134.6 ($C_{arom.}$), 138.4 ($C_{arom.}$), 139.5 (= C-NH), 163.4 (CO).

EIMS: *m/z* (%) = 258 (^{37}ClM+1, 8), 257 (^{37}ClM$^+$, 8), 256 (^{35}ClM+1, 24), 255 (^{35}ClM$^+$, 15), 239 (^{37}ClM−H_2O, 100).

HRMS: *m/z* calc for $C_{15}H_{10}{}^{35}ClNO$ (M^+) 255.045092. Found: 255.045659.

6-Isopropyl-4-(2-oxopropyl)pyridin-2(1*H*)-one (12)
From 4,6-dimethyl-2H-pyran-2-one (**6**) (279 mg, 2.25 mmol) and isobutyronitrile **c** (0.20 mL, 2.25 mmol), the mixture was stirred at r.t. for 24 h. Yield: 139 mg (32%), yellow oil.

IR (film): ν_{max} = 3123, 2970, 1716, 1651, 1546, 1456, 1360, 1214, 1160, 961, 869 737 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 1.28 (d, 6H, *J* = 6.9 Hz, 2 CH_3-CH), 2.21 (s, 3H, CH_3CO), 2.84 [m, 1H, $CH(CH_3)_2$], 3.53 (s, 2H, CH_2CO), 5.93 (s, 1H, CH-C-NH), 6.27 (s, 1H, CHCO).

^{13}C NMR ($CDCl_3$, 400 MHz): δ = 21.6 (2 CH_3), 29.7 (CH_3CO), 32.2 [$CH(CH_3)_2$], 50.7 (CH_2CO), 104.2 (CH-C-N), 117.1 (=C-CO), 149.2 (C=C-CO), 155.0 [C-$CH(CH_3)_2$], 165.2 (CON), 202.3 (CO ketone).

EIMS: *m/z* (%) = 193 (M^+, 76), 178 (M−CH_3, 46), 165 (M−CO, 7), 151(M−CH_3CCH_3, 100), 136 (20).

HRMS: *m/z* calc for $C_{11}H_{15}NO_2$ (M^+) 193.110279. Found: 193.110328.

2-[2-Amino-2-(2-methylphenyl)-1-ethenyl]benzonitrile (13)
Yield: 123 mg (47%), yellow solid; mp 192−193 °C (by column chromatography).

IR (film): ν_{max} = 3359, 3292, 3005, 2921, 2840, 2219, 1647, 1463, 1223, 987, 965, 935, 817, 615, 564 530 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 2.30 (s, 3H, CH_3-$C_{arom.}$), 5.25 (br s, 2H, NH_2), 6.90 (s, 1H, CH=), 7.05 (m, 3H, $CH_{arom.}$), 7.45 (m, 2H, $CH_{arom.}$), 7.60 (t, 1H, *J* = 6.0 Hz, $CH_{arom.}$), 7.65 (d, 1H, *J* = 6.0 Hz, $CH_{arom.}$), 7.75 (d, 1H, *J* = 6.0 Hz, $CH_{arom.}$).

^{13}C NMR ($CDCl_3$, 400 MHz): δ = 20.8 (CH_3), 112.6 ($C_{arom.}CN$), 116.8 (CN), 123.0, 126.1, 126.3, 127.7, 128.2, 130.0, 130.6, 131.0, 136.4, 138.3, 141.3, 152.4 (11$C_{arom.}$ and CH =), 155.8 (=C-NH_2).

EIMS: *m/z* (%) = 234 (M^+, 56), 233 (M−1, 100), 216 (M−NH_4^+, 17), 90 (M−NH_4^+−CN, 5).

HRMS: *m/z* calc for $C_{16}H_{14}N_2$ (M^+) 234.115699. Found: 234.114879.

1-(2-Methylphenyl)pentan-1-one (14)
Yield: 12 mg (3%), yellow oil (by column chromatography).

IR (film): ν_{max} = 2959, 2929, 2872, 1733, 1688, 1601, 1456, 1286, 1073, 967, 755 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 0.93 (t, 3H, *J* = 7.6 Hz, CH_3-CH_2), 1.38 (m, 2H, $CH_3CH_2CH_2$), 1.66 (m, 2H, $CH_2CH_2CH_2$),. 2.48 (s, 3H, CH_3-$C_{arom.}$), 2.88 (t, 2H, *J* = 7.2 Hz, CH_2CH_2CO), 7.25 (m, 2H, $CH_{arom.}$), 7.35(t, 1H, *J* = 7.2 Hz, $CH_{arom.}$), 7.60 (d, 1H, *J* = 6.4 Hz, $CH_{arom.}$).

^{13}C NMR ($CDCl_3$, 400 MHz): δ = 13.9 (CH_3-CH_2), 21.1 (CH_3-$C_{arom.}$), 22.4 ($CH_3CH_2CH_2$), 26.5 ($CH_2CH_2CH_2$), 41.4 (CH_2CH_2CO), 125.6, 128.2, 131.0, 131.9 (4 $CH_{arom.}$), 137.8, 138.1 (2 $C_{arom.}$), 205.4 (CO).

EIMS: *m/z* (%) = 177 (M^++1, 16), 176 (M^+, 7), 161 (M−CH_3, 6), 147 (M−CH_2CH_3, 2), 119 (M−butyl, 100).

HRMS: *m/z* calc for $C_{12}H_{16}O$ (M^+) 176.120115. Found: 176.120586.

3-Butyl-5-methylphenol (15)
Yield: 100 mg (27%), yellow oil (by column chromatography).

IR (film): ν_{max} = 3411, 2929, 2859, 1620, 1597, 1457, 1297, 1152, 968, 840 697 cm^{-1}.

^{1}H NMR ($CDCl_3$, 300 MHz): δ = 0.93 (t, 3H, *J* = 6.0 Hz, CH_3-CH_2), 1.34 (m, 2H, $CH_3CH_2CH_2$), 1.56 (m, 2H, $CH_2CH_2CH_2$), 2.28 (s, 3H, CH_3-$C_{arom.}$), 2.52 (t, 2H, *J* = 7.5 Hz, $CH_2CH_2C_{arom.}$), 5.00 (br s, 1H, OH), 6.48 (s, 2H, 2 $CH_{arom.}$), 6.59 (s, 1H, $CH_{arom.}$).

^{13}C NMR ($CDCl_3$, 300 MHz): δ = 13.9 (CH_3-CH_2), 21.3 (CH_3-$C_{arom.}$), 22.4 ($CH_3CH_2CH_2$), 33.5 ($CH_2CH_2CH_2$), 35.5 ($CH_2CH_2C_{arom.}$), 112.4, 113.3, 121.9 (3 $CH_{arom.}$), 139.4, 144.7, 152.4 (3 $C_{arom.}$).

EIMS): *m/z* (%) = 165 (M^++1, 8), 164 (M^+, 52), 149 (M−CH_3, 9), 135 (M−CH_2CH_3, 60), 121(M−$CH_3CH_2CH_2$, 96), 107 (M−$CH_3CH_2CH_2CH_2$, 94), 91 (86), 56 (100).

HRMS: *m/z* calc for $C_{11}H_{16}O$ (M^+) 164.120115. Found: 164.119589.

2-(2-Cyanobenzyl)but-3-enoic Acid (16)
Yield: 212 mg (47%), yellow oil (by column chromatography).

IR (film): ν_{max} = 3070, 2226, 1697, 1485, 1422, 1287, 1213, 929, 763 cm^{-1}.

^{1}H NMR ($CDCl_3$, 300 MHz): δ = 3.08 (dd, 1H, *J* = 13.9, 7.6 Hz, $CH_2C_{arom.}$), 3.29 (dd, 1H, *J* = 13.8, 7.6 Hz, $CH_2C_{arom.}$), 3.42 (m, 1H, $CHCO_2H$) 5.07 (d, 1H, *J* = 17.2 Hz, =CH_2*trans*), 5.14 (d, 1H, *J* = 10.2 Hz, =CH_2*cis*), 5.85 (ddd, 1H, *J* = 17.2, 10.2, 8.5 Hz, CH = CH_2), 7.1−7.5 (m, 4H, 4 $CH_{arom.}$).

^{13}C NMR ($CDCl_3$, 300 MHz): δ = 36.2 (CH_2-$C_{arom.}$), 50.8 ($CHCO_2H$), 112.8 ($C_{arom.}CN$), 117.9 (CN), 119.0 (= CH_2), 128.3, 130.2, 132.8 (4 $C_{arom.}$), 133.7 (CH = CH_2), 142.2 ($C_{arom.}$), 178.0 (CO_2H).

EIMS: *m/z* (%) = 201 (M^+, 7), 183 (M−H_2O, 27), 155 (M−H_2O−CO, 68), 116 (M−$C_4H_5O_2$, 100).

HRMS: *m/z* calc for $C_{12}H_{11}NO_2$ (M^+) 201.078979. Found: 201.078447.

2-(2-Cyanobenzyl)-2-methylbut-3-enoic Acid (17)
Yield: 199 mg (44%), yellow solid (by column chromatography); mp 93−94ºC.

IR (KBr): ν_{max} = 3068, 2983, 2939, 2226, 1707, 1691, 1487, 1289, 1221, 926, 767, 662 cm^{-1}.

^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.32 (s, 3H, CH_3), 3.24 (d, 1H, *J* = 13.4 Hz, $CH_2C_{arom.}$), 3.34 (d, 1H, *J* = 13.4 Hz, $CH_2C_{arom.}$), 5.12 (d, 1H, *J* = 17.4 Hz, = CH_2*trans*), 5.23 (d, 1H, *J* = 10.8 Hz , = CH_2*cis*), 6.13 (dd, 1H, *J* = 17.4, 10.8 Hz, CH =), 7.29 (m, 2H, 2 $CH_{arom.}$), 7.47 (t, 1H, *J* = 6.0 Hz, $CH_{arom.}$), 7.62 (d, 1H, *J* = 6.6 Hz, $CH_{arom.}$).

^{13}C NMR ($CDCl_3$, 300 MHz): δ = 19.4 (CH_3), 42.3 (CH_2-$C_{arom.}$), 50.0 (C-CO), 114.3 ($C_{arom.}CN$), 115.8 (CH_2 =), 118.5 (CN), 127.3, 131.1, 132.3, 132.9, 139.5, 140.8 (5 $C_{arom.}$ and CH = CH_2), 180.3 (CO_2H).

EIMS: *m/z* (%) = 215 (M^+, 1), 197 (M−H_2O, 8), 170 (M−CO_2H, 10), 157 (17), 116 (M−$C_5H_7O_2$, 100).

HRMS: *m/z* calc for $C_{13}H_{13}NO_2$ (M^+) 215.094629. Found: 215.095664.

2-(2-Cyanobenzyl)-3-methylbut-3-enoic Acid (18)
Yield: 320 mg (63%), yellow solid (by column chromatography); mp 92−93ºC.

IR (KBr): ν_{max} = 2969, 2736, 2650, 2223, 1702, 1640, 1441, 1418, 1248, 936, 897, 765, 547 cm^{-1}.

^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.84 (s, 3H, CH_3C=), 3.13 (dd, 1H, *J* = 14.1, 6.9 Hz, $CH_2C_{arom.}$), 3.34 (dd, 1H, *J* = 14.1, 8.4 Hz, $CH_2C_{arom.}$), 3.49 (dd, 1H, *J* = 8.4, 6.9 Hz, =$CCHCH_2$), 4.91 (d, 1H, *J* = 0.6 Hz, =CH_2), 4.95 (d, 1H, *J* = 1.2 Hz, =CH_2), 7.32 (m, 2H, 2

$CH_{arom.}$), 7.47 (dt, 1H, *J* = 7.5, 1.5 Hz, $CH_{arom.}$), 7.63 (dd, 1H, *J* = 7.8, 0.6 Hz, $CH_{arom.}$),

^{13}C NMR ($CDCl_3$, 300 MHz): δ = 19.8 (CH_3), 30.8 (CH_2-$C_{arom.}$), 46.5 (CH-CO), 111.1 ($C_{arom.}CN$), 114.9 (CH_2 =), 117.9 (CN), 126.4, 129.4, 132.0, 132.4, 140.5, 141.3 (5 $C_{arom.}$ and C=CH_2), 178.3 (CO_2H).

EIMS: *m/z* (%) = 215 (M^+, 2), 197 (M−H_2O, 25), 182 (M−H_2O−CH_3, 7), 169 (M−H_2O−CO, 14), 154 (M−H_2O−CO−CH_3, 21), 116 (M−$C_5H_7O_2$, 65), 99 ($C_5H_7O_2$, 100).

HRMS: *m/z* calcd for $C_{13}H_{13}NO_2$ (M^+) 215.094629. Found: 215.094605.

***(E)*-5-(2-Cyanophenyl)pent-2-enoic Acid (19)**
Yield: 105 mg (23%), yellow oil (by column chromatography).

IR (film): ν_{max} = 2930, 2858, 2225, 1695, 1493, 1410, 1320, 1220, 1101, 870, 740 cm^{-1}.

^1H NMR ($CDCl_3$, 300 MHz): δ = 2.60 (m, 2H, CH_2CH =), 2.92 (m, 2H, $C_{arom.}CH_2$), 5.85 (d, 1H, *J* = 17.2 Hz, = CH 6.92 (t, 1H, *J* = 7.5 Hz, CH =), 7.32 (m, 2H,. $CH_{arom.}$), 7.52 (dt, 1H, *J* = 7.8, 1.5 Hz, $CH_{arom.}$), 7.63 (dd, 1H, *J* = 7.5. 1.5 Hz, $CH_{arom.}$).

^{13}C NMR ($CDCl_3$, 300 MHz): δ = 30.5 (CH_2CH =), 33.2 (CH_2-$C_{arom.}$), 112.2 ($C_{arom.}CN$), 117.9 (CN), 126.8, 129.4, 129.8, 132.9, 133.8, 142.9, 143.9 (5 $C_{arom.}$ and CH = CHCO), 171.4 CO_2H).

EIMS: *m/z* (%) = 201 (M^+, 5), 183 (M−H_2O, 78), 155 (M−H_2O−CO, 30), 116 (100).

HRMS: *m/z* calc for $C_{12}H_{11}NO_2$ (M^+) 201.078979. Found: 201.078633.

***(E)*-5-(2-cyanophenyl)-2-methylpent-2-enoic Acid (20)**
Yield: 156 mg (34%), yellow solid (by column chromatography); mp 101−102ºC.

IR (KBr): ν_{max} = 2928, 2867, 2224, 1685, 1637, 1425, 1304, 1270, 1075, 943, 759, 750, 616, 552 cm^{-1}.

^1H NMR ($CDCl_3$, 300 MHz): δ = 1.76 (s, 3H, CH_3), 2.62 (dt, 2H, *J* = 7.8, 7.5 Hz, CH_2CH_2CH =), 3.00 (t, 2H, *J* = 7.8 Hz, $C_{arom.}CH_2CH_2$), 6.92 (t, 1H, *J* = 7.5 Hz, CH =), 7.32 (m, 2H, $CH_{arom.}$), 7.52 (dt, 1H, *J* = 7.8, 1.5 Hz, $CH_{arom.}$), 7.63 (dd, 1H, *J* = 7.5. 1.5 Hz, $CH_{arom.}$).

^{13}C NMR ($CDCl_3$, 300 MHz): δ = 11.9 (CH_3), 29.8 (CH_2CH =), 33.2 (CH_2-$C_{arom.}$), 112.3 ($C_{arom.}CN$), 117.8 (CN), 126.9, 128.6, 129.6, 132.9, 133.0, 142.1, 144.7 (5 $C_{arom.}$ and CH = CCO), 173.2 CO_2H).

EIMS: *m/z* (%) = 215 (M^+, 3), 197 (M−H_2O, 83), 182 (M−H_2O−CH_3, 5), 169 (M−H_2O−CO, 21), 157 (46), 116 (M−$C_5H_7O_2$, 100).

HRMS: *m/z* calc for $C_{13}H_{13}NO_2$ (M^+) 215.094629. Found: 215.093983.

5-(2-Cyanophenyl)-3-methylpent-2-enoic Acid (21)
Yield: 112 mg (22%), waxy material (by column chromatography).

IR (KBr): ν_{max} = 2938, 2225, 1692, 1666, 1637, 1488, 1449, 1434, 1410, 1380, 1246, 1161, 862, 761 cm^{-1}.

^1H NMR ((*Z*)-isomer, $CDCl_3$, 300 MHz): δ = 1.96 (s, 3H, CH_3), 2.20−2.40 (m, 4H, $C_{arom.}CH_2CH_2C$ =), 5.91 (d, 1H, *J* = 1.5 Hz, CH =), 7.27 (m, 2H,. $CH_{arom.}$), 7.51 (m, 1H, $CH_{arom.}$), 7.60 (m, 1H, $CH_{arom.}$).

^1H NMR ((*E*)-isomer, $CDCl_3$, 300 MHz): δ = 2.23 (s, 3H, CH_3), 2.50 (t, 2H, *J* = 7.5 Hz, CH_2CH_2C =), 3.01 (t, 2H, *J* = 7.5 Hz, $C_{arom.}CH_2CH_2$), 5.67 (d, 1H, *J* = 0.9 Hz, CH =), 7.27 (m, 2H,. $CH_{arom.}$), 7.51 (m, 1H, $CH_{arom.}$), 7.60 (m, 1H, $CH_{arom.}$).

^{13}C NMR ((*Z*)-isomer, $CDCl_3$, 300 MHz): δ = 24.6 (CH_3), 43.0 (CH_2-$C_{arom.}$), 49.1 (CH_2CH =), 112.3 ($C_{arom.}CN$), 117.9 (CN), 125.4, 126.8, 129.5, 129.8, 132.9, 133.1, 144.1 (5-$C_{arom.}$ and C = CHCO), 171.6 (CO_2H).

^{13}C NMR ((*E*)-isomer, $CDCl_3$, 300 MHz): δ = 19.0 (CH_3), 32.5 (CH_2-$C_{arom.}$), 41.9 (CH_2CH =), 112.2 ($C_{arom.}CN$), 116.2 (C = CHCO), 117.8 (CN), 125.6, 127.0, 129.4, 132.8, 132.9, 144.6 (5 $C_{arom.}$ and C = CHCO), 171.3 (CO_2H).

EIMS: *m/z* (%) = 215 (M^+, 8), 197 (M−H_2O, 100), 182 (M−H_2O−CH_3, 13), 169 (M−H_2O−CO, 36), 154 (M−H_2O−CO−CH_3, 30), 116 (M−$C_5H_7O_2$, 99).

HRMS: *m/z* calc for $C_{13}H_{13}NO_2$ (M^+) 215.094629. Found: 215.095117.

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