Short communication

Scandium(III) Triflate Catalyzed 1,4-Addition of Cyano Group to Enones Using Tetraethylammonium Cyanide as the Cyanide Source

Samikannu Ramesh and Appaswami Lalitha*

Department of Chemistry, Periyar University, Periyar Palkalai Nagar, Salem – 636 011, Tamil Nadu, India

** Corresponding author: E-mail: lalitha2531@yahoo.co.in*
Telephone +91-427-2345271, Fax +91-427-2345124

Received: 14-08-2012

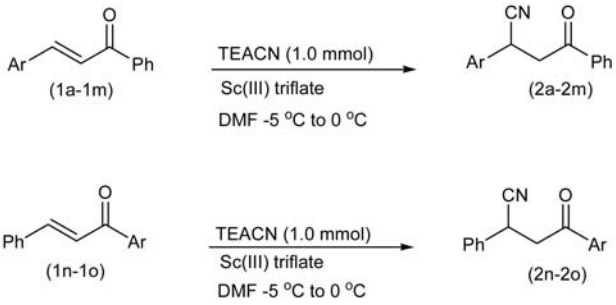
Abstract

A novel and practical method has been developed for the synthesis of β-cyanoketones using tetraethylammonium cyanide (Et_4NCN, TEACN) / Sc(III) triflate and chalcones without the liberation of toxic HCN gas. Availability, safety, easy handling of the reagents, mild conditions of the reaction and high yields, make this method an attractive protocol for the direct synthesis of cyano substituted 1,4-adducts from enones.

Keywords: Scandium(III) triflate; tetraethylammonium cyanide; 1,4-addition; β-cyanoketone; chalcones

1. Introduction

The cyano group serves as a stable and useful key functional group for the synthesis of biologically important compounds. Hydrogen cyanide (HCN) was the most commonly used industrial reagent for the introduction of cyano group.[1–7] However, due to its toxicity and the necessity to follow abundant precautions in handling HCN, newer methods have been developed to substitute it with other potentially less harmful and easily manageable reagents. Cyanide sources, like trimethylsilyl cyanide (Me_3SiCl, TMSCN), tetraethylammonium cyanide (Et_4NCN**,** TEACN), tetrabutylammonium cyanide, etc. along with or without catalysts have been reported for the introduction of cyano group.[8] Depending on the reaction conditions, the hydrocyanation of unsaturated carbonyl compounds leads to β-cyanoketones, β-cyano-cyanohydrins, or vinyl cyanohydrins as a result of 1,2- or 1,4-additions.[9–15] The conjugate addition of α,β-unsaturated carbonyl compounds is one of the most important carbon-carbon bond formation reactions because, the resulting β-cyano adducts can be converted into biologically important γ-aminobutyric acids under reducing conditions (GABA analogues).[16] The conjugate hydrocyanation reaction of enones was recently employed for the total synthesis of natural products like terpenes, alkaloids, steroids etc.[17–21] The reactions of enones with TMSCN in the presence of base catalysts provided selectively the 1,2-adducts; additionally this method also served as a way of protection of the carbonyl groups.[22,23] In contrast, employing Lewis acid catalysts such as Et_2AlCN,[24] Et_3Al,[25] $AlCl_3$, $SnCl_2$,[26] $Pd(OAc)_2$,[27] ionic liquids,[28] and microwave irradiation,[29] resulted in the selective 1,4-additions. Recently, Shibasaki and co-workers employed Ni(0) and $Gd(OTf)_3$ as the co-catalysts in the 1,4-addition of cyanide using TMSCN, and the catalytic enantioselective conjugate addition of cyanide to enones was also disclosed.[30–33] Asymmetric catalytic hydrocyanation of α,β-unsaturated ketones by using TMSCN and [Ru(phgly)$_2$(binap)]/Li salt has been reported very recently.[34] Yanagisawa and co-workers described that unactivated arylalkenes could be effectively converted to benzylic nitriles in the presence of triflic acid and TMSCN.[35] Very recently Fu-Xue Chen and co-workers reported the 1,4-addition of TMSCN to enones in presence of Cs_2CO_3 and CsF catalysts.[36–38] Despite these achievements, practical regioselective 1,4-hydrocyanation of enones using newer cyanide sources is still a demanding task. Scandium(III) triflate has been extensively used as an efficient Lewis acid catalyst for various organic reactions.[39–44] However, its potential application as a catalyst for the hydrocyanation of chalcones has not been explored yet. Herein we report a novel and simple method for the efficient 1,4-addition of cyano group to chalcones, using scandium(III) triflate as the Lewis acid catalyst and TEACN as cyanide source.



Scheme 1. Sc(III) OTf-catalyzed 1,4-addition of TEACN with chalcones

In order to determine the most appropriate reaction conditions and to evaluate the efficiency of scandium(III) triflate as the catalyst for the hydrocyanation, synthesis of 4-oxo-2,4-diphenylbutanenitrile was taken as the model reaction (Table 3, entry 8). Among the tested solvents, DMF (Table 1, entry 5) gave the best results for the hydrocyanation of (*E*)-chalcone (1.0 equiv) using TEACN (1.0 equiv) and Sc(III) triflate (30% weight of the employed chalcone). The use of chlorinated solvents, like DCM, 1,2-dichloroethane (EDC), $CHCl_3$, etc. or hydrocarbons as solvents did not provide good yields of the expected product.

Table 1. Effect of solvent in the 1,4-addition of cyano group to enones with TEACN / Sc(III) triflate

Entry[a]	Solvent	Catalyst	Time (h)	Yield (%)
1	CH_3CN	Sc(III)OTf	6	75
2	THF	Sc(III)OTf	12	56
3	EDC	Sc(III)OTf	8	32
4	toluene	Sc(III)OTf	24	–
5	DMF	Sc(III)OTf	2-3	72–92
6	DMSO	Sc(III)OTf	3–6	43
7	dioxane	Sc(III)OTf	12	52
8	DCM	Sc(III)OTf	8	27

[a]All reactions were conducted with 30% of catalyst, 1 mmol of chalcone (benzylideneacetophenone) and 1 mmol of TEACN in 30 vol. of solvent.

This may be attributed to the poor solubility of TEACN in these solvents which give rise to a heterogeneous reaction mixture (TEACN is not freely soluble in non-polar solvents) and may reduce its reactivity. It is noteworthy that the order of addition of reagents was also very important for the success of the reaction. Initially, a mixture of TEACN and chalcones should be prepared in DMF at –5 °C to 0 °C by stirring for 10 min and followed by the addition of scandium(III) triflate. If scandium(III) triflate has been added at the beginning, no reaction was observed. The catalytic activities of various triflates and other catalysts were also investigated using a loading of 30% of the respective catalyst (Table 2) wherein almost all of the catalysts (except scandium(III) triflate) studied were found to be ineffective for the cyano addition to chalcones with TEACN as the cyanide source. Though the TMS(OTf) gave modest yield of the desired product (entry 3), there are difficulties connected with its handling due to its propensity for hydrolysis. $Zn(OTf)_2$ afforded only a trace of the product whereas the other lanthanide triflate, namely, the ytterbium triflate also results in moderate yields leading to the conclusion that Sc(III) triflate is the most promising catalyst for this reaction.

Table 2. Effect of different catalyst in the 1,4-addition of cyano group to enones with TEACN

Entry[a]	Catalyst	Time (h)	Yield (%)
1	Sc(III) OTf	2–3	72–92
2	Yb(III) OTf	2–3	30–40
3	TMS (OTf)	3–6	56–70
4	$Zn(OTf)_2$	12	27
5	Iodine	1	–
6	TFA	1	43
7	HBr	2	37
8	TBABr	12	–
9	TBAF	12	–

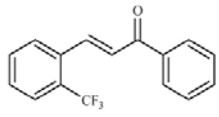
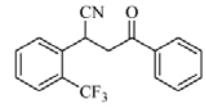
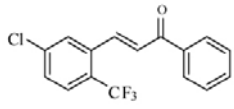
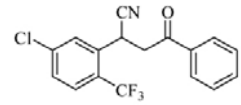
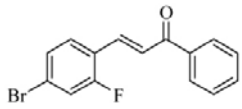
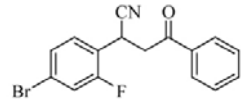
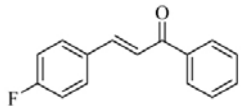
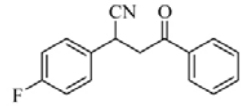
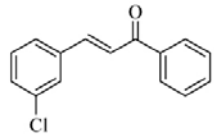
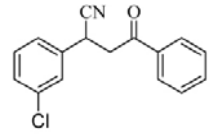
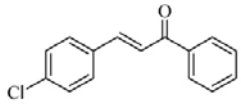
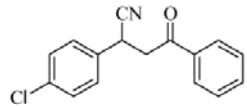
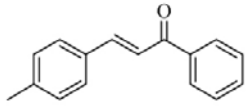
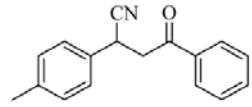
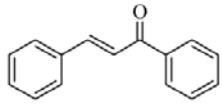
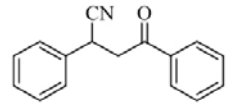
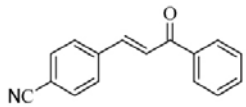
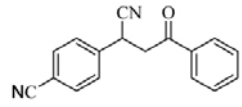
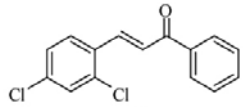
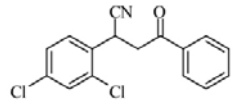
[a]All reactions were conducted with 30% of catalyst, 1 mmol of chalcone (benzylideneacetophenone) and 1 mmol of TEACN in 30 vol. of solvent.

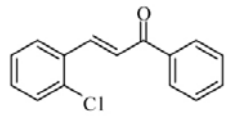
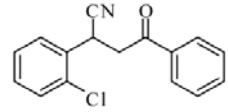
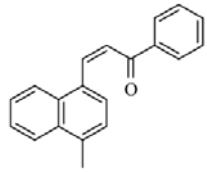
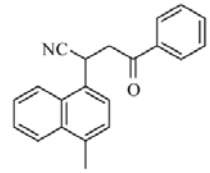
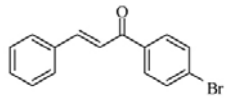
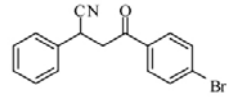
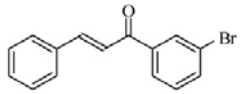
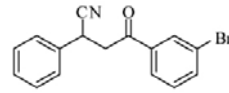
2. Results and Discussion

In order to extend the scope of the scandium(III) triflate catalyzed hydrocyanation reaction, various chalcones were subjected to this transformation (Table 3). Interestingly, no substituent effects on the yields were noted.

Thus, the chalcones with either electron withdrawing or electron donating groups at any positions, gave the 1,4-adducts in good to moderate yields (Table 3, entries 1–14). It was observed that no 1,2-adduct was obtained in any of the reactions. In order to clarify the scope and limitation of the present method, some reactions of the enones other than chalcones were performed under same reaction conditions. Unfortunately, cyclohexenone and α,β-unsaturated esters such as methyl cinnamate did not undergo 1,4-addition at all, and the starting materials were recovered. The mechanism of the reaction is not completely understood at this stage. However, since the order of the addition of reagents is crucial for the success of the reaction, we can give a reasonable explanation as shown in the Scheme 2. It has been observed that if scandium(III) triflate is added at the beginning no reaction takes place. Besides, there should be an induction period of 10 min after the addition of TEACN to chalcones and before the addition of the triflate salt.

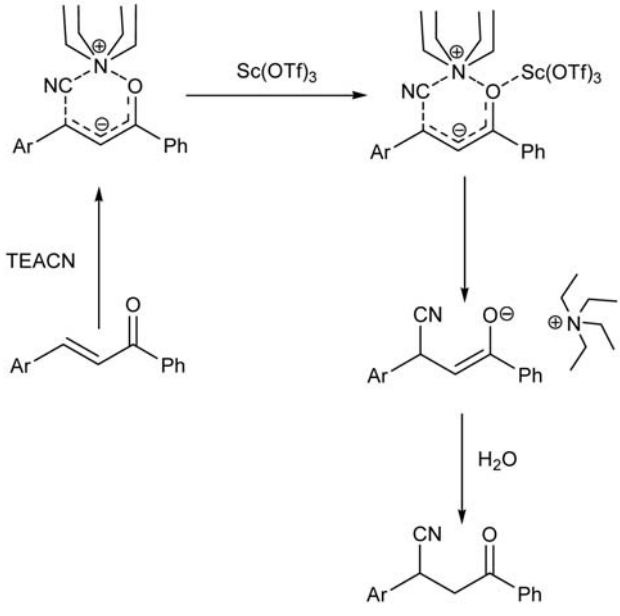
Table 3. Synthesis of 4-oxo-2,4-diphenylbutanenitrile derivatives

Entry[a]	Chalcones	Time (h)	Product	Yield[c] (%)
1	 1a	3	 2a	74[b]
2	 1b	3	 2b	72[b]
3	 1c	3	 2c	75[b]
4	 1d	2	 2d	80[29,45]
5	 1e	2	 2e	90[46]
6	 1f	2	 2f	92[29,47]
7	 1g	2	 2g	87[29,38,47]
8	 1h	2	 2h	92[29,47]
9	 1i	3	 2i	73[45]
10	 1j	3	 2j	80[38,48]

Entry[a]	Chalcones	Time (h)	Product	Yield[c] (%)
11	 1k	2	 2k	72[49]
12	 1l	3	 2l	72[b]
13	 1m	2	 2m	92[29]
14	 1n	2	 2n	90[29]

[a]All reactions were conducted with 30% of catalyst, 1 mmol of chalcone and 1 mmol of TEACN in 30 volume of dry DMF, [b]New compounds, [c]Isolated yield.

These two facts indicate that a weak interaction is needed between chalcone and TEACN at the beginning of the reaction to initiate the transfer of the cyano group.



Scheme 2. Plausible mechanism for the Sc(III) OTf-catalyzed 1,4-addition of TEACN with chalcones

Once scandium(III) triflate is added it coordinates with the carbonyl oxygen and helps the delocalization of electron through a six member cyclic transition state (Scheme 2) and in this step the cyanide is added in 1,4-fashion rather than the 1,2-fashion.

Finally, during quenching the neutral product is generated. This model thus takes into account the importance of the order of addition of reagents and selectivity of the reaction. If scandium(III) triflate is added at the beginning it gives rise to a strong interaction with the carbonyl oxygen and does not allow the TEACN salt to interact with the chalcone. Hence no reaction takes place.

3. Conclusions

The present investigation has demonstrated that the use of TEACN/scandium(III) triflate offers a novel, simple, and convenient method for the conversion of wide varieties of chalcones to their corresponding β-cyanoketones, without the liberation of HCN gas. This method shows excellent selectivity giving the 1,4-adduct in good yields. The ready availability of the reagents, easy handling of them, the absence of generation of HCN during the reaction, mild reaction conditions and high yield of the product make this method attractive for direct synthesis of cyano substituted 1,4-adducts from enones.

4. Experimental Section

All the melting points of the products were measured using a Büchi melting point (B-545) apparatus. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker 400 MHz instrument using $CDCl_3$ as the solvent with tetramethylsilane (TMS) as the internal standard. Mass spectra were recorded on an Agilent 6330 ion trap instrument. Elemental analysis for C, H and N were obtained using a Vario-micro-cube CHN-O-Rapid analyzer. TEACN from Alfa Aesar (purity >97%), and scandium(III) triflate from Aldrich (purity >98%) were used as obtained.

4. 1. Material and Methods of Synthesis

The chalcones used in the present study have been prepared as per literature procedures. TEACN (1 mmol) was dissolved in DMF (30 vol) at room temperature, then cooled to –5 °C to 0 °C. To that, chalcone (1 mmol) was added and stirred at –5 °C to 0 °C for 10 min and then, scandium(III) triflate (30% weight of chalcone taken) was added at 0 °C, and the reaction mixture was slowly warmed to 25 °C. It was stirred for appropriate time at 25 °C under N_2 atmosphere. The reaction was monitored by thin layer chromatography. After completion (about 3 h), the reaction mixture was quenched with water (5 mL) and extracted with diethyl ether (3 × 10 mL). The combined organic layer was dried (over anhydrous $MgSO_4$), filtered, concentrated and purified by column chromatography with silica gel (230–400 Mesh) (hexane/ethyl acetate 8:2) to give the desired product. All the products were characterized by ^{1}H and ^{13}C NMR, LCMS, melting point and elemental analysis. The characterization data for those products that are not novel are given in the supporting information.

4. 2. Spectral Data of Novel Compounds

4-Oxo-4-phenyl-2-(2-(trifluoromethyl)phenyl) butanenitrile (2a): Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.42 (dd, *J* = 3.6, 18.0 Hz, 1H), 3.72 (dd, *J* = 10.4, 18.0 Hz, 1H), 4.89 (dd, *J* = 3.6, 10.4 Hz, 1H), 7.48–7.54 (m, 3H, ArH), 7.62–7.65 (t, *J* = 8.0 Hz, 1H, ArH), 7.67–7.71 (t, *J* = 8.0 Hz, 1H, ArH), 7.74–7.76 (d, *J* = 8.0 Hz, 1H, ArH), 7.84–7.86 (d, *J* = 8.0 Hz, 1H, ArH), 7.95–7.97 (d, *J* = 8.0 Hz, 1H, ArH) ppm.^{13}C NMR (100 MHz, $CDCl_3$) δ = 28.81, 44.70, 120.01, 123.79 (q, *J* = 274.8 Hz, $\underline{C}F_3$), 126.84 (q, *J* = 6.0 Hz, ortho carbon to CF_3), 127.61, 127.92, 128.12, 128.75, 128.87, 129.88, 132.95, 133.96, 135.43, 193.91 ppm. ^{19}F NMR (376 MHz, $CDCl_3$) δ = –59.22 ppm. MS: *m/z* = 303.29 $(M)^+$. Anal. Calcd. for $C_{17}H_{12}F_3NO$: C, 67.33; H, 3.99; N, 4.62%. Found: C, 67.30; H, 3.93, N, 4.64%.

2-(5-Chloro-2-(trifluoromethyl)phenyl)-4-oxo-4-phenylbutanenitrile (2b): Yellow pasty mass. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.43 (dd, *J* = 4.0, 18.0 Hz, 1H), 3.77 (dd, *J* = 10.4, 18.0 Hz, 1H), 4.89 (dd, *J* = 3.6, 10.4 Hz, 1H), 7.49–7.53 (t, *J* = 8.4 Hz, 3H, ArH), 7.61–7.64 (m, 1H, ArH) 7.68–7.70 (d, *J* = 8.4 Hz, 1H, ArH), 7.83 (s, 1H, ArH), 7.95–7.99 (d, *J* = 16.0 Hz, 2H, ArH) ppm. ^{13}C NMR (100.66 MHz, $CDCl_3$) δ = 28.74, 44.41, 119.46, 123.51 (q, *J* = 273.8 Hz, $\underline{C}F_3$), 126.24 (q, *J* = 31.2 Hz, $\underline{C}$–CF_3), 128.28 (q, *J* = 5.0 Hz, ortho carbon to CF_3), 128.62, 128.91, 129.07, 130.18, 134.15, 135.25, 135.90, 136.53, 139.40, 193.50 ppm. MS: *m/z* = 337.04 $(M)^+$. Anal. Calcd. for $C_{17}H_{11}ClF_3NO$: C, 60.46; H, 3.28; N, 4.15% . Found: C, 60.43; H, 3.26, N, 4.18%.

2-(4-Bromo-2-fluorophenyl)-4-oxo-4-phenylbutanenitrile (2c): White solid; mp 118.2–119.7 °C, ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.56 (dd, *J* = 5.7, 18.0 Hz, 1H), 3.72 (dd, *J* = 8.0, 18.0 Hz, 1H), 4.70 (dd, *J* = 5.7, 7.8 Hz, 1H), 7.26–7.34 (m, 2H, ArH), 7.43–7.51 (m, 3H, ArH), 7.59–7.64 (m, 1H, ArH), 7.91–7.94 (d, 2H, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ = 26.35, 42.05, 118.92, 119.59, 119.91, 121.32, 123.04, 128.02, 128.82, 130.73, 134.00, 135.32, 159.64 (broad d, *J* = 251.3 Hz, F attached carbon), 194.07 ppm. ^{19}F NMR (376 MHz, $CDCl_3$) δ = –114.04 ppm. MS: *m/z* = 332.17 $(M)^+$. Anal Calcd. for $C_{16}H_{11}$ BrFNO: C, 57.85; H, 3.34; N, 4.22%. Found: C, 57.82; H, 3.31, N, 4.25%.

2-(4-Methylnaphthalen-1-yl)-4-oxo-4-phenylbutanenitrile (2l): Yellow solid; mp 132.4–134.7 °C, ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.71 (s, 3H), 3.56 (dd, *J* = 4.0, 18.0 Hz, 1H), 3.86 (dd, *J* = 9.6, 18.0 Hz ,1H), 5.31 (dd, *J* = 3.8, 10.0 Hz, 1H), 7.35–7.37 (m, 1H, ArH), 7.44–7.46 (m, 2H, ArH), 7.48–7.61 (m, 3H, ArH), 7.67–7.69 (m, 1H ArH), 7.93–7.96 (m, 3H, ArH), 7.97–8.07 (m, 1H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 19.52, 28.97, 43.84, 12.79, 122.51, 125.54, 125.61, 126.13, 126.86, 128.15, 128.83, 129.73, 133.29, 133.90, 135.70, 194.98 ppm. MS: *m/z* = 299.38 $(M)^+$. Anal. Calcd. for $C_{21}H_{17}NO$: C, 84.25; H, 5.72; N, 4.68%. Found: C, 84.28; H, 5.69, N, 4.68%.

5. References

1. A. Lapworth, *J. Chem. Soc. Trans*. **1903**, *83*, 995–1005.
2. P. Kurtz, *Ann. Chem*. **1951**, *572*, 23–82.
3. C. F. H. Allen, H. B. Johnsons, Organic Synthesis, Wiley, New York, **1963**, Collect Vol. IV, pp. 804
4. W. C. Groutas, D. Felker, *Synthesis* **1980**, 861–868.
5. I. N. Nazarov, J. Zavyalov, *Gen. Chem., USSR Engl. Transl*. **1954**, *24*, 475–478.
6. H. O. House, Modern Synthetic Reactions, 2nd ed.; Benjamin, Inc.; New York, **1972**, pp 623– 628.
7. Y. Kawasaki, A. Fujii, Y. Nakano, S. Sakaguchi, Y. Ishii, *J. Org. Chem*. **1999**, *64*, 4214–4216.
8. N. Iranpoor, H. Firouzabadi, B. Akhlaghinia, N. Nowrouzi, *J. Org. Chem*. **2004**, 69, 2562–2564.

9. P. Seokan, K. Hae-Jo, *Chem. Commun*. **2010**, *46*, 9197–9199.
10. J. Wang, L. W. Liu, Y. Chu, Y. Lin, L. X. Liu, X. Feng, *Org. Lett*. **2010**, *12*, 1280–1283.
11. C. Mazet, E. N. Jacobsen, *Angew. Chem. Int. Ed*. **2008**, *47*, 1762–1765.
12. N. Madhavan, M. Weck, *Adv. Synth. Catal*. **2008**, *350*, 419–425.
13. I. Fujimori, T. Mita, K. Maki, M. Shiro, A. Sato, S. Furusho, M. Kanai, M. Shibasaki, *Tetrahedron* **2007**, *63*, 5820–5831.
14. D. T. Mowry, *Chem. Rev*. **1948**, *42*, 189–283.
15. W. Nagata, T. Okumura, M. Yoshioka, *J. Chem. Soc*. **1970**, 2347–2355.
16. A. Baeza, C. Nájera, M. de G. Retamosa, J. M. Sansano, *Synthesis* **2005**, 2787–2797.
17. A. Siwicka, D. Cuperly, L. Tedeschi, R. Le Vezouet, A. J. P. White, A. G. M. Barrett, *Tetrahedron* **2007**, *63*, 5903–5917.
18. H. Muratake, M. Natsume, *Tetrahedron* **2006**, *62*, 7071–7092.
19. L. N. Mander, R. J. Thomson, *J. Org. Chem*. **2005**, *70*, 1654–1670.
20. S. M. A. Rahman, H. Ohno, H. Yoshino, N. Satoh, M. T. Sukaguchi, K. Murakami, C. Iwata, N. Maezaki, T. Tanaka, *Tetrahedron* **2001**, *57*, 127–134.
21. S. M. A. Rahman, H. Ohno, N. Maezaki, C. Iwata, T. Tanaka, *Org. Lett*. **2000**, *2*, 2893–2895.
22. B. He, Y. Li, X. Feng, *Synlett* **2004**, 1776–1778.
23. K. Higuchi, M. Onaka, Y. Izumi, *Bull. Chem. Soc. Jpn*. **1993**, *66*, 2016–2032.
24. W. Nagata, M. Yoshioka, *Org. React*. **1977**, *25*, 255–476.
25. K. Utimoto, M. Obayashi, Y. Shishiyama, M. Inoue, H. Nozaki, *Tetrahedron Lett*. **1980**, *21*, 3389–3392.
26. K. Utimoto, Y. Wakabayashi, T. Horiie, M. Inoue, Y. Shishiyama, M. Obayashi, H. Nozaki, *Tetrahedron* **1983**, *39*, 967–973.
27. M. Hayashi, H. Kawabata, S. Shimono, A. Kakehi, *Tetrahedron Lett*. **2000**, *41*, 2591–2594.
28. L. D. S. Yadav, C. Aswathi, A. Rai, *Tetrahedron Lett*. **2008**, *49*, 6360–6363.
29. H. Iida, T. Moromizato, H. Hamana, K. Matsumoto, *Tetrahedron Lett*. **2007**, *48*, 2037–2039.
30. Y. Tanaka, M. Kanai, M. Shibasaki, *J. Am. Chem. Soc*. **2008**, *130*, 6072–6073.
31. K.Yamatsugu, S. Kamijo, Y. Suto, M. Kanai, M. Shibasaki, *Tetrahedron Lett*. **2007**, *48*, 1403–1406.
32. T. Mita, K. Sasaki, M. Kanai, M. Shibasaki, *J. Am. Chem. Soc*. **2005**, *127*, 514–515.
33. Y. Tanaka, M. Kanai, M. Shibasaki, *Synlett* **2008**, 2295–2298.
34. K. Nobuhito, N. Noriyuki, S. Yusuke, U. Masato, O. Takeshi, *Angew. Chem. Int. Ed*. **2011**, *50*, 5541–5544.
35. A. Yanagisawa, T. Nezu, S. Mohri, *Org. Lett*. **2009**, *11*, 5286–5289.
36. J. Yang, Y. Shen, F. X. Chen, *Synthesis* **2010**, 1325–1333.
37. J. Yang, S. Wu, F. X. Chen, *Synlett* **2010**, *18*, 2725–2728.
38.J. Yang, Y. Wang, S. Wu, F. X. Chen, *Synlett* **2009**, *20*, 3365–3367.
39. M. Aki, J. K. Sami, M. P. Ari, *J. Org. Chem*. **2007**, *72*, 5411–5413.
40. K. Surya, A. Richard, *Tetrahedron Lett*. **2005**, *46*, 1811–1813.
41. S. Kobayashi, M. Siguira, H. Kitagawa, W. W. Lam, *Chem. Rev*. **2002**, *102*, 2227–2302.
42. S. Kobayashi, *Eur. J. Org. Chem*. **1999**, 15–27.
43. S. Kobayashi, *Chem. Soc. Rev*. **1999**, *28*, 1–15.
44. J. S. Yadav, B. V. S. Reddy, C. Parisse, P. Carvalho, T. P. Rao, *Tetrahedron Lett*. **2002**, *43*, 2999–3002.
45. J. E. Ellis, M. Davis, P. L. Brower, *Org. Process Res. Dev*. **1997**, *1*, 250–252.
46. L. Sultzbaugh, K. W. Johnson, F. Gacta, Patent, US2007/191365 A1, 2007.
47. J. A. Ciller, C. Seoane, J. L. Soto, *Liebigs Ann. Chem*. **1985**, 51–57.
48. Y. Jingya, C. Fuxue, *Chin. J. Chem*. **2010**, *28*, 981–987.
49. R. Davis, *J. Org. Chem*. **1959**, *24*, 879–880.

Povzetek

Razvili smo novo in praktično metodo za sintezo β-cianoketonov iz halkonov, ki vključuje uporabo tetraetilamonijevega cianida (Et_4NCN, TEACN) in skandijevega(III) triflata. Pomembno je poudariti, da pri tem ne pride do sproščanja strupenega plina HCN. Dostopnost, varnost, enostavnost uporabe reagentov, nežni reakcijski pogoji ter visoki izkoristki so odlike tega protokola, ki iz enonov omogoča neposredno sintezo ciano substituiranih 1,4-aduktov.