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REMOTE OXIDATION OF CARBONYL COMPOUNDS IN $Na_2S_2O_8$-NaCN: ESSENTIALLY SIMPLE APPROACH TO γ- AND δ-CYANODERIVATIVES

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Summary. Ketones and aldehydes are converted into γ- and δ-cyanoketones or cyanoacids in one-pot reaction of the remote oxidative cyanation with $Na_2S_2O_8$-NaCN.

In context of our previous investigations of one-step remote oxidative functionalization of compounds of various classes [1-3], we have found recently, that one-electron oxidation of ketones by $Na_2S_2O_8$-$FeSO_4$ leads to γ- and δ-diketones [2].

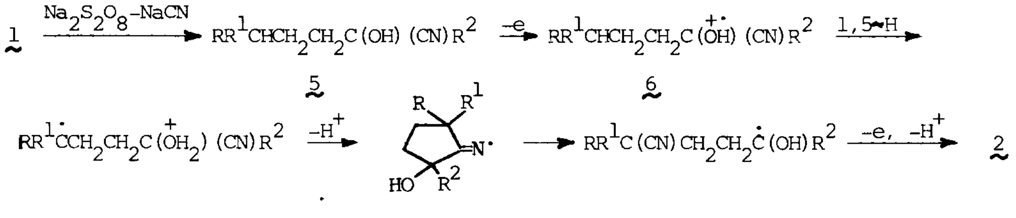
In present work we have found that ketones 1 by treatment with $Na_2S_2O_8$-NaCN (molar ratio 1:$Na_2S_2O_8$:NaCN=1:2:1) undergo an efficient cyanation to γ-cyanoketones 2 (Table). This system was used for oxidative cyanation of amines previously [4].

$$\underset{\textbf{1a-e}}{RR^1CHCH_2CH_2COR^2} \xrightarrow{Na_2S_2O_8\text{-}NaCN} \underset{\textbf{2a-e}}{RR^1C(CN)CH_2CH_2COR^2}$$

a $R=R^2=Me$, $R^1=H$; b $R=Et$, $R^1=H$, $R^2=Me$; c $R=R^1=R^2=Me$; d $R+R^2=(CH_2)_2$, $R^1=H$; e $R+R^2=(CH_2)_3$, $R^1=H$. In oxidation of 1b along with 2b isomeric 6-cyanoheptan-2-one 3 is formed in the ratio 2b:3=1:1,5. In oxidation of 1c besides 2c 13% of 2,5,5-trimethyl-2-cyanotetrahydrofurane 4 was obtained. In all experiments substantial amounts of tar have been also obtained.

Ketone	Conversion, %	Cyanoderivative [5]	Yields(%) based on 1 converted
1a	98	2a	35
1b	74	2b+3	30
1c	88	2c	70
1d	98	2d	30
1e	86	2e	35

We consider the reaction studied to proceed through two competitive routes. The first one includes the formation in situ of cyanohydrins 5 with following oxidative rearrangement [6] through O-centred cation-radicals 6 leading to cyanoketones 2 (scheme [7])

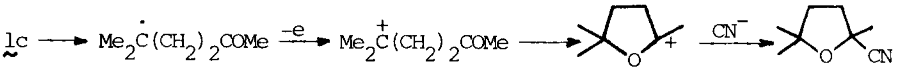


3 is formed as a result of isomerisation of 6b with 1,6-H shift.

The second route involves generation of cation radicals 7 from 1, 1,5-H shift to 8 and subsequent oxidative or homolytic CN-transfer with formation of 2. Exclusively by this route 4-cyanocyclohexanone 2d is formed as it can't be obtained by oxidative rearrangement of 5d

$$\underset{}{1} \xrightarrow{-e} \underset{7}{RR^1CHCH_2CH_2C(R^2)=\overset{+\cdot}{O}} \xrightarrow{1,5-H} \underset{8}{RR^1\dot{C}CH_2CH_2C(R^2)=\overset{+}{O}H} \xrightarrow{-e,\ CN^-} 2$$

Cyanotetrahydrofurane 4 is formed by direct oxidation of 1c, probably according to the scheme:



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A control experiment showed 5c not to be converted into 4 with $Na_2S_2O_8$-NaCN.

Oxidative cyanation of alkanals 9a,b affords γ- and δ-cyanoacids 10a,b and 11b (compare [7]). Yields of 10a and the mixture of 10b and 11b are 60% and 55% respectively, ratio 10b:11b=1:2

$$\underset{9a,b}{R^3(CH_2)_4CHO} \xrightarrow{Na_2S_2O_8\text{-}NaCN} \underset{10a,b}{R^3CH_2CH(CN)(CH_2)_2COOH} + \underset{11b}{R^3CH(CN)(CH_2)_3COOH}$$

R^3=H(a), Me(b)

Typical procedure. A solution of $NaHSO_4$ (4.80 g, 0.04 mole) in 40 ml of water was added to a stirred mixture of 1c (4.56 g, 0.04 mole) and NaCN (1.96 g, 0.04 mole) in 30 ml of water at 20°C. After 20 min the mixture was heated to 80°C and a solution of $Na_2S_2O_8$ (19.04g, 0.08 mole) in 100 ml of water was added dropwise. The mixture was kept at the same temperature for 4.5 h, cooled to 20° and extracted with ether (3x100 ml), extracts were dried (Na_2SO_4). The conversion of 1c (88%) as well as yields of 2c (62%) and 4 (13%) were estimated by g.l.c. analysis of the residue after solvent removal. Distillation of the residue afforded 0.45 g 4 (yield 9%), $C_8H_{13}NO$, b.p. 40-41°C(37 torr), and 2.8 g 2c (yield 51%),b.p.117-118°C(20 torr).

The simplicity of experimental procedure enables us to consider this reaction as an essentially simple route to γ- and δ-cyanosubstituted ketones and acids. The scope and limitations of this method will be discussed in the full paper.

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