[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF PITTSBURGH]

THE CYANOETHYLATION OF CERTAIN KETONES, β-DIKETONES, AND β-KETO ESTERS[1]

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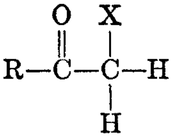
Bruson and Riener (1, 2, 3, 4) have recently reported the cyanoethylation of ketones, cyanoesters, nitroparaffins, aldehydes, and two β-keto esters with acrylonitrile in the presence of the basic condensing agents, potassium hydroxide, sodium methoxide, and benzyltrimethylammonium hydroxide (Triton B).

In the present investigation the cyanoethylation of a number of β-keto esters, β-diketones, and methyl ketones has been studied in the presence of Triton B and benzyltrimethylammonium butoxide (BTAB) as the condensing agents.

The general structure of the active hydrogen compounds studied may be represented by the following formula:



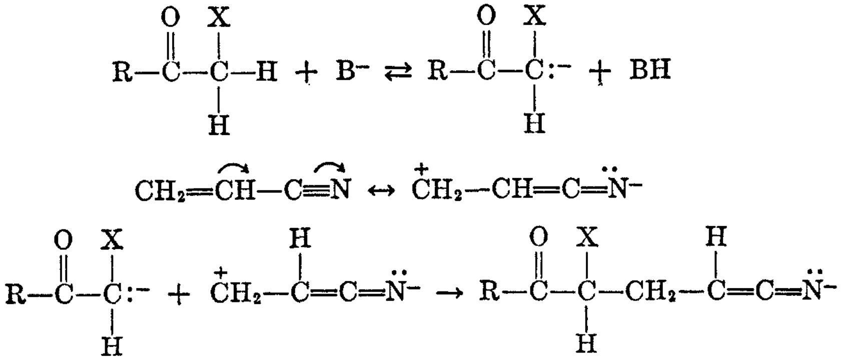
$$R-\overset{O}{\overset{\|}{C}}-\underset{\underset{H}{|}}{\overset{\overset{X}{|}}{C}}-H$$

If X = $\overset{O}{\overset{\|}{C}}$—R, the compound is a β-diketone.

If X = $\overset{O}{\overset{\|}{C}}$—$OC_2H_5$, the compound is a β-keto ester.

If X = H, the compound is a methyl ketone.

The mechanism for the cyanoethylation probably involves the following steps, where B = OH^- or $OC_4H_9\text{-}n^-$



$$\text{(I)}\quad R-\overset{O}{\overset{\|}{C}}-\underset{\underset{H}{|}}{\overset{\overset{X}{|}}{C}}-H + B^- \rightleftarrows R-\overset{O}{\overset{\|}{C}}-\underset{\underset{H}{|}}{\overset{\overset{X}{|}}{C}}:^- + BH$$

$$\text{(II)}\quad CH_2=\overset{\frown}{C}H-C\overset{\frown}{\equiv}N \leftrightarrow \overset{+}{C}H_2-CH=C=\ddot{N}^-$$

$$\text{(III)}\quad R-\overset{O}{\overset{\|}{C}}-\underset{\underset{H}{|}}{\overset{\overset{X}{|}}{C}}:^- + \overset{+}{C}H_2-\overset{\overset{H}{|}}{C}=C=\ddot{N}^- \rightarrow R-\overset{O}{\overset{\|}{C}}-\underset{\underset{H}{|}}{\overset{\overset{X}{|}}{C}}-CH_2-\overset{\overset{H}{|}}{C}=C=\ddot{N}^-$$

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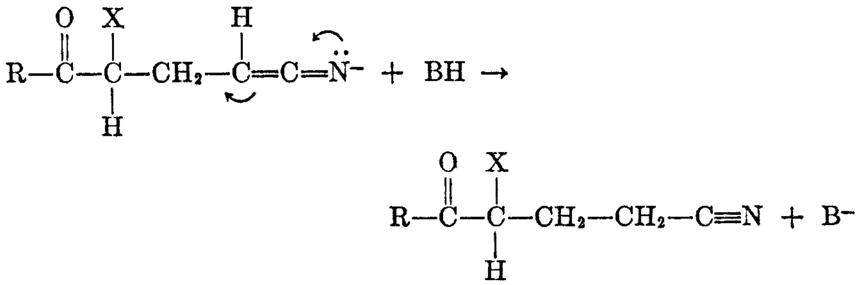
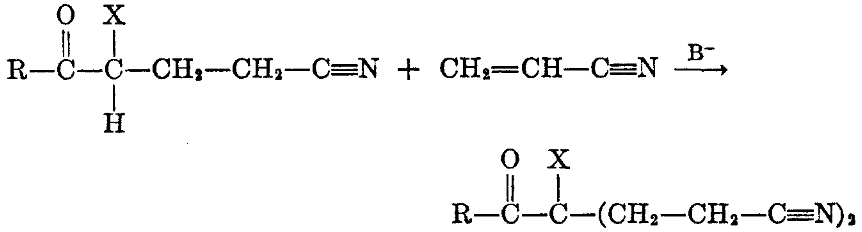
[1] This work is based on a thesis submitted by Glenn R. Zellars in partial fulfillment of the requirements for the degree of Master of Science at the University of Pittsburgh.

(IV)


$$\mathrm{R{-}\overset{\overset{O}{\|}}{C}{-}\underset{\underset{H}{|}}{\overset{\overset{X}{|}}{C}}{-}CH_2{-}\overset{\overset{H}{|}}{C}{=}C{=}\ddot{N}^- + BH \rightarrow R{-}\overset{\overset{O}{\|}}{C}{-}\underset{\underset{H}{|}}{\overset{\overset{X}{|}}{C}}{-}CH_2{-}CH_2{-}C{\equiv}N + B^-}$$

(V)


$$\mathrm{R{-}\overset{\overset{O}{\|}}{C}{-}\underset{\underset{H}{|}}{\overset{\overset{X}{|}}{C}}{-}CH_2{-}CH_2{-}C{\equiv}N + CH_2{=}CH{-}C{\equiv}N \xrightarrow{B^-} R{-}\overset{\overset{O}{\|}}{C}{-}\overset{\overset{X}{|}}{C}{-}(CH_2{-}CH_2{-}C{\equiv}N)_3}$$

TABLE I

Cyanoethylation Products of Certain Methyl Ketones

KETONE	PRODUCT	M.P. °C.	YIELD, %	
			BTAB	Triton B
2-Acetylthiophene	1,1,1-tri-(2-cyanoethyl)methyl 2-thienyl ketone	145–146	89	87.7 (4)
2-Acetylfuran	1,1,1-tri-(2-cyanoethyl)methyl 2-furyl ketone	120–121	90	89.2 (4)
Acetophenone	1,1,1-tri-(2-cyanoethyl)acetophenone	127–128	64	57 (1)

In equation (I) the base reacts with the active hydrogen compound and converts it partially to its anion. Equation (II) shows two of the resonance forms of acrylonitrile. The anion of the active hydrogen compound then condenses with the active form of acrylonitrile (equation III) to produce the anion of the condensation product, which then (equation IV) picks up a proton from BH (equation I) to produce the monocyanoethylated product and regenerate the base. If the active hydrogen compound is a β-diketone or a β-keto ester containing two hydrogen atoms on a methylene carbon atom, the series of reactions is repeated to produce the dicyanoethylated product. In the case of the methyl ketones studied (*e.g.*, 2-acetylthiophene) all three of the active hydrogen atoms are replaced by cyanoethyl groups.

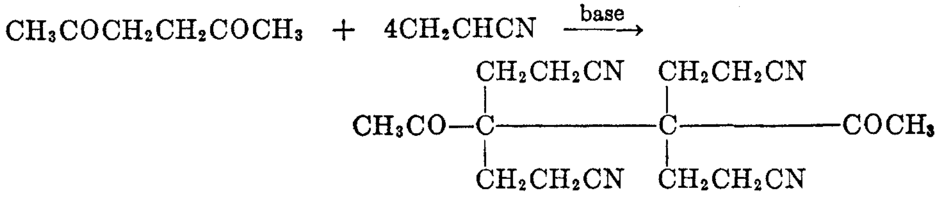
In Table I are found the yields of the tricyanoethylated products of 2-acetylthiophene, 2-acetylfuran, and acetophenone prepared in this investigation using BTAB as the condensing agent. It can be seen that the yields compare favorably with those obtained by Bruson and Riener (1, 4). In Table II are found the yields of the cyanoethylated derivatives of a number of β-keto esters and β-diketones. It will be observed that the yields of the products are fair to good in all cases. In those cases where both Triton B and BTAB were used as the condensing agents, the yields of the cyanoethylation products are about the same, within experimental error.

One 1,4-diketone (acetonylacetone) was also cyanoethylated. Although the structure of the compound has not yet been definitely proven, its analysis indicates the presence of four cyanoethyl groups. It is probably 3,3,4,4-tetra-(2-cyanoethyl)-2,5-hexanedione produced according to the following equation.

TABLE II

CYANOETHYLATION PRODUCTS OF CERTAIN β-KETO ESTERS AND DIKETONES

ACTIVE HYDROGEN COMPOUND	PRODUCT	YIELD, %		M.P. °C.	N ANALYSIS	
		Triton B	BTAB		Calc'd	Found
Ethyl acetoacetate	Ethyl 2,2-di-(2-cyanoethyl)-3-ketobutanoate	79	80	81 - 81.5 (1)		
Ethyl *n*-butyrylacetate	Ethyl 2,2-di-(2-cyanoethyl)-3-ketohexanoate	34	36	40.3- 41.5	10.60	10.87
Ethyl isovalerylacetate	Ethyl 2,2-di-(2-cyanoethyl)-3-keto-5-methylhexanoate	65	68	53.5- 54.4	10.06	10.18
Ethyl benzoylacetate	Ethyl 2,2-di(2-cyanoethyl)-2-benzoylethanoate	53		61.5- 62	9.39	9.19
Ethyl 2-thenoylacetate	Ethyl 2,2-di-(2-cyanoethyl)-2-(2-thenoyl)ethanoate	32		100.5-101	9.21	9.13
Ethyl 2-furoylacetate	Ethyl 2,2-di-(2-cyanoethyl)-2-(2-furoyl)ethanoate	25		91 - 91.5	9.73	10.01
Acetylacetone	3,3-Di-(2-cyanoethyl)-2,4-pentanedione	49	55	180 -180.4	13.58	13.30
Acetylbenzoylmethane	1-Benzoyl-1,1-di-(2-cyanoethyl)propanone	22		107 -107.2	10.44	10.53
Acetyl-2-thenoylmethane	1-(2-Thenoyl)-1,1-di-(2-cyanoethyl)propanone	40		127 -127.5	10.21	10.12
Acetonylacetone	3,3,4,4-Tetra-(2-cyanoethyl)-2,5-hexanedione	46	50	179 -179.5	17.46	17.29



$$\mathrm{CH_3COCH_2CH_2COCH_3} + \mathrm{4CH_2CHCN} \xrightarrow{\text{base}} \mathrm{CH_3CO}-\underset{\mathrm{CH_2CH_2CN}}{\overset{\mathrm{CH_2CH_2CN}}{\mathrm{C}}}-\underset{\mathrm{CH_2CH_2CN}}{\overset{\mathrm{CH_2CH_2CN}}{\mathrm{C}}}-\mathrm{COCH_3}$$

Some support for believing that the cyanoethyl groups were introduced on the methylene carbon atoms may be obtained from the work of Bruson and Riener

(1). They have shown that ketones which have the grouping, —CH_2COCH_3 are primarily cyanoethylated at the methylene carbon atom. This tetra-cyanoethylated derivative of acetonylacetone was prepared earlier by Bruson (9).

EXPERIMENTAL

Starting Materials

Triton B and benzyltrimethylammonium butoxide. These compounds were generously supplied by the Rohm and Haas Company, Philadelphia, Pa.

Acetonylacetone. This diketone supplied by the Carbide and Carbon Corp., Charleston, W. Va.

2-Acetylthiophene. This ketone was purchased from the Socony-Vacuum Oil Co., Paulsboro, N. J.

2-Acetylfuran. This ketone was prepared by the method of Heid and Levine (5).

All the β-keto esters, with the exception of ethyl acetoacetate, which was purchased from the Eastman Kodak Co., and the β-diketones used in this investigation, were prepared by methods already described in the literature (6, 7, 8).

Preparation of cyanoethylated β-keto esters. The apparatus used in these reactions consists of a 500-ml. three-necked round-bottomed flask equipped with ground-glass joints, a mercury-sealed stirrer, a reflux condenser, and an addition funnel. To the rapidly stirred solution of 0.1 mole of the β-keto ester, 0.2 mole of *t*-butyl alcohol and 3 g. of Triton B or 5 g. of BTAB, 0.2 mole of acrylonitrile is added slowly over a period of 20 minutes. The temperature of the reaction mixture is kept near room temperature by occasionally immersing the flask in an ice-water bath. The reaction mixture is stirred for two hours after the addition of the acrylonitrile is complete. The contents of the flask is then poured into ice-water. In those cases where a solid is formed at this point, it is filtered on a Büchner. In those cases where a solid does not form in ice-water, the reaction mixture is extracted with ether. The ethereal solution is dried over Drierite, the ether distilled, and the *t*-butyl alcohol removed in a vacuum. The remaining viscous liquid is dissolved in cold acetone or ethyl alcohol and allowed to crystallize. Usually at this point a tarry mass is obtained. The tar is washed out by adding more acetone or alcohol, leaving behind the cyanoethylated β-keto ester. The crystalline residue is recrystallized from ethyl alcohol. The cyanoethylated β-keto esters prepared are found in Table II.

Preparation of cyanoethylated diketones. The apparatus used is the same as that described above. The proportions of reactants are also the same as described above except in the case of acetonylacetone, in which 0.4 mole of nitrile was used for 0.1 mole of the diketone. The rapidly stirred solution of the diketone, *t*-butyl alcohol, and base is warmed to 40°, and the acrylonitrile added slowly. After the addition of the acrylonitrile is complete, the solution is stirred and refluxed gently for two hours longer. The products are then isolated as described above.

Preparation of cyanoethylated ketones. The procedure used is the same as that described by Bruson and Riener (4) except that BTAB is used as the base instead of Triton B. The compounds prepared are found in Table I.

SUMMARY

A number of β-keto esters, β-diketones, and one γ-diketone have been cyanoethylated in fair to good yields.

Three methyl ketones have been cyanoethylated using BTAB as the condensing agent. The yields of the compounds compare satisfactorily with those obtained earlier in the presence of Triton B.

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