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OXIDATIVE COUPLING REACTIONS UNDER PTC CONDITIONS[1]

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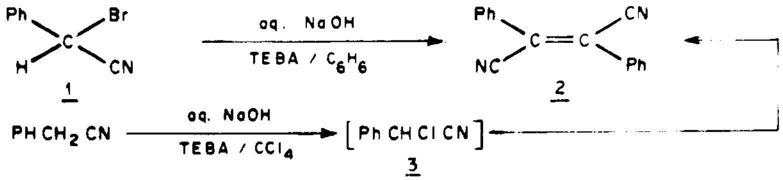
Summary : Succinic acid derivatives have been prepared from cyanohalides under PTC conditions in good yields.

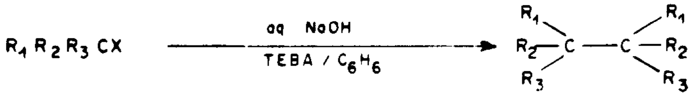
Substitution of primary halides by CN^- under PTC conditions has been one of the most thoroughly studied reactions[2]. However, there is little information available in the literature regarding the substitution of secondary and tertiary halides by CN^-. We happened to try out the substitution of some secondary and tertiary halides by CN^- under PTC conditions wherein we came across new oxidative coupling reactions, which are described in present communication. In the course of further work, it was later found that these reactions can even be carried out in the absence of CN^-.

α-Bromobenzylcyanide[3] 1, failed to react with NaCN in benzene, in presence of TEBA. However, when this reaction was carried out by using 50% aq. NaOH solution (ion pair extraction technique)[4] using TEBA, trans 1,2-dicyano-1,2-diphenylethylene 2 was obtained in good yield. This result offered an independent proof to Makosza's postulation regarding the intermediary of analogous α-chlorobenzyl cyanide 3 in the reaction of benzyl cyanide with CCl_4 in presence of aqueous NaOH and TEBA[5]. Though Makosza has trapped this intermediate[6], this is the first time that the intermediary of 3 has been independently demonstrated.

In the light of this result, it was interesting to find out the fate of α-alkyl-α-halobenzylcyanide under the similar reaction conditions.

Thus α-bromo-α-ethylbenzylcyanide 4[7] and α-bromo-α-n-butylbenzyl cyanide 5 under identical conditions afforded threo-3,4-diphenyl-3,4-dicyanohexane 9 and threo-5,6 diphenyl 5,6-dicyanodecane 10 respectively. The most probable mechanism, that can be suggested for these oxidative coupling reactions, is shown in the chart. Here the anionic species 'A' arising by the abstraction of bromonium cation reacts with the parent compound resulting in the observed succinonitrile derivatives. This formation of anionic species 'A' is parallel to the extraction of chloronium ion





X = Halogen

<u>4</u> $R_1 = Ph$, $R_2 = Et$, $R_3 = CN$

<u>5</u> $R_1 = Ph$, $R_2 = nBu$, $R_3 = CN$

<u>6</u> $R_1 = Ph$, $R_2 = Et$, $R_3 = CO_2Et$

<u>7</u> $R_1 = H$, $R_2 = H$, $R_3 = CO_2Et$

<u>8</u> $R_1 = H$, $R_2 = Me$, $R_3 = CO_2Et$

<u>9</u>, $R_1 = Ph$, $R_2 = Et$, $R_3 = CN$

<u>10</u> $R_1 = Ph$, $R_2 = Et$, $R_3 = CN$

<u>11 A</u> $R_1 = Ph$, $R_2 = Et$, $R_3 = COOH$

<u>11 B</u> $R_1 = Ph$, $R_2 = Et$, $R_3 = CO_2Me$

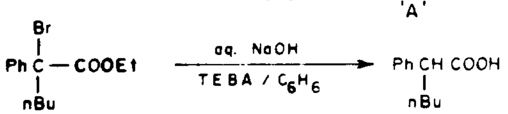
<u>12 A</u> $R_1 = R_2 = H$, $R_3 = CO_2H$

<u>12 B</u> $R_1 = R_2 = H$, $R_3 = CO_2Me$

<u>13 A</u> $R_1 = H$, $R_2 = Me$, $R_3 = COOH$

<u>13 B</u> $R_1 = H$, $R_2 = Me$ $R_3 = COOMe$

$$R_1R_2R_3CX \xrightarrow[\text{TEBA / } C_6H_6]{\text{aq. NaOH}} \underset{\text{'A'}}{\left[R_1R_2R_3C\right]^{\ominus}} \xrightarrow[-X^{\ominus}]{R_1R_2R_3CX} \text{Succinic acid derivatives}$$



<u>14</u> <u>15</u>

TABLE

NO	REACTANT		PRODUCT	YIELD %	M.P. / B.P	REFERENCES
1	PhCHBrCN	<u>1</u>	<u>2</u>	70	159°C	3
2	PhCEtBrCN	<u>4</u>	<u>9</u>	83	115°C	12
3	PhCnBuBrCN	<u>5</u>	<u>10</u>	66	180-185°C/1mm	12
4	PhCEtBrCO_2Et	<u>6</u>	<u>11 B</u>	62	140-150°C/1mm	–
5	PhCnBuBrCO_2Et	<u>14</u>	<u>15</u>	52	140-150°C/1mm	13
6	$ClCH_2CO_2Et$	<u>7</u>	<u>12 B</u>	59	70-80°C/11mm	3
7	$CH_3CHBrCO_2Et$	<u>8</u>	<u>13 B</u>	50	90°C/8mm	3

I.R., N.M.R., spectral data and elemental analysis were in accordance with the assigned structures.

from CCl_4 under PTC conditions suggested by Makosza[5]. Similar bromonium cation abstraction has been demonstrated by Landini _et al_[8].

Thus this reaction offers a simple route for obtaining succinic acid derivatives and appears to be easier than the existing methods in the literature[9,10].

In an obvious extension of this work ethyl α-bromo- α-phenylbutyrate[11] _6_ was treated with 50% aq. NaOH and TEBA in benzene. The dimerisation did occur along with concomitant hydrolysis resulting in 3,4-diphenylhexane-3,4-dicarboxylic acid _11A_. However, a different result was obtained when ethyl α-bromo- αphenylhexanoate _14_, was subjected to the same reaction conditions. In this case no dimerisation could be observed. Instead only α-phenylhexanoic acid _15_ was obtained. This observation led us to believe that, although the carbanion 'A' is formed by abstraction of bromonium ion, this does not always attack the parent molecule to yield dimerised product. This may be due to steric reasons associated with such an attack. The resultant carbanion 'A' in this case simply picks up a proton from the aq. phase to give _15_.

Closer examination of Makosza's mechanism prompted us to test the ease of abstraction of a halonium ion vis-a-vis a proton. To this goal, it was interesting to study this reaction with esters of α-haloaliphatic acids. Thus in ethyl monochloroacetate _7_, the product expected was either succinic acid derivative if chloronium ion was accessible and fumaric/maleic acid derivative if proton was more easily accessible for abstraction.

In the reactions of ethyl chloroacetate _7_ and α-bromopropionate _8_ with TEBA and aq. NaOH, in benzene, the product isolated were succinic acids _12A_ and _13A_ and no trace of maleic or fumaric acids could be detected. In the latter case an isomeric mixture of _threo_ and _erythro_ dimethyl succinic acid was isolated. This mixture passing over silica gel column yielded _threo_ isomer only.

Having established this dimerisation reaction, its further scope and limitations are under investigation.

EXPERIMENTAL

General procedure for the reaction of bromoalkyl/aryl cyanides _1_, _4_, _5_ and esters _6_, _7_, _8_, _14_ under PTC conditions.

To a stirred mixture of 50% NaOH (0.04 mole) TEBA (0.0004 mole) and benzene (10 ml) the bromo compound (_1_, _4_, _5_, _6_, _7_, _8_, _14_ - 0.01 mole) in benzene (10 ml) was added dropwise..

For compounds 1, 4, 5. The reaction mixture was refluxed for 3 hours. Organic layer was separated, washed with water dried and concentrated in vacuo. Product (2,9,10) were purified by crystallisation/distillation.

For compounds 6, 7, 8, 14. The reaction mixture was stirred at room temperature for one hour. The aqueous layer was washed with benzene, acidified with dilute HCl and then extracted with chloroform. Usual work up of chloroform extract furnished 11A, 12A, 13A and 15 respectively, which were converted to methyl esters and purified by distillation.

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