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# ELECTROREDUCTIVE ACYLATION OF BENZYL CHLORIDE AND RELATED COMPOUNDS WITH ACID CHLORIDES1)

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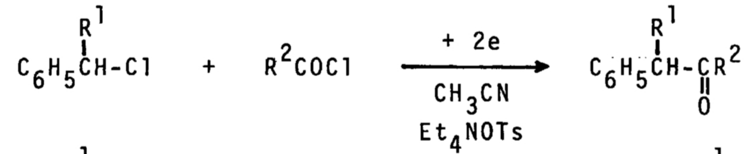
The electroreduction of benzyl chloride and related compounds in the presence of acid chlorides gave alkyl benzyl ketones in moderate yields. The controlled potential electrolysis suggests that the electron transfer from the cathode to benzyl chloride yielding an anionic species is the initiation step of this reductive acylation.

The reductive acylation of electrochemically generated heteroatom anions with acid anhydrides has received much interest in recent years.2-6) The electroreduction of polyene carbonyl compounds,2) 1,3-diketones,3) nitroso and nitro compounds,4) or disulfides5) in the presence of acetic anhydride led to the exclusive acylation of the heteroatom, while the acylation at carbon atom was observed only in the reduction of benzophenone.6) In the present communication, we wish to report the electroreductive acylation of benzyl chloride and related compounds with acid chlorides, which is the first electrochemical C - acylation being useful from the synthetic point of view.



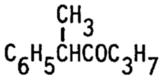
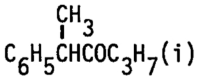
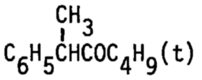
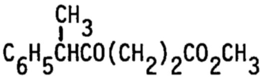
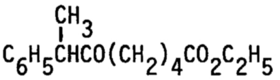
$$C_6H_5\overset{R^1}{\overset{|}{C}}H\text{-}Cl \;+\; R^2COCl \xrightarrow[CH_3CN,\ Et_4NOTs]{+\,2e} C_6H_5\overset{R^1}{\overset{|}{C}}H\text{-}\underset{\underset{O}{\|}}{C}R^2$$

**1**: $R^1 = H$ **3**a - g **4**a - g: $R^1 = H$
**2**: $R^1 = CH_3$ **5**a - g: $R^1 = CH_3$

$R^2 = CH_3$, $C_2H_5$, $C_3H_7$, i-$C_3H_7$, t-$C_4H_9$, $(CH_2)_2CO_2CH_3$, $(CH_2)_4CO_2C_2H_5$

In a typical procedure, the electrolyte, that is, a solution of 20g (0.067 mole) of tetraethylammonium p-toluenesulfonate in 80 ml of anhydrous acetonitrile, was placed in the cathodic (64 ml) and anodic (16 ml) chambers of the electrolysis cell equipped with carbon rod electrodes, a reference electrode, and a ceramic diaphragm. To the catholyte was added 2.53g (0.02 mole) of benzyl chloride and 5.55g (0.06 mole) of propionyl chloride. Stirred with a magnetic bar and cooled with a water bath, the solution was electrochemically reduced at the cathode potential of -2.1 V to -2.4 V vs. SCE until 4 F/mole of electricity was passed (10.7 hr). The usual work-up and distillation afforded benzyl ethyl ketone (**4**b) in 57% yield (1.69g) based on **1**7,8); bp 80°/3mm (lit.9) bp 78°/3mm). In a similar manner, alkyl benzyl ketones **4**a-g or alkyl α-methylbenzyl ketones **5** c-g were obtained in moderate yields as shown in Table I.[10,11)]

Table I. Electroreductive Acylation of the Chloride **1** or **2** with Acid Chlorides **3**[a]

| Chloride: $R^1$ | Acid Chloride: $R^2$ | Product | Yield (%)[b] | Bp (°C/mmHg) |
|---|---|---|---|---|
| **1**: H | **3**a: $CH_3$ | $C_6H_5CH_2COCH_3$ (**4**a) | 32 | 81/17 |
| **1**: H | **3**b: $C_2H_5$ | $C_6H_5CH_2COC_2H_5$ (**4**b) | 57 | 80/3 |
| **1**: H | **3**c: $C_3H_7$ | $C_6H_5CH_2COC_3H_7$ (**4**c) | 69 | 95/3 |
| **1**: H | **3**d: $i\text{-}C_3H_7$ | $C_6H_5CH_2COC_3H_7(i)$ (**4**d) | 47 | 83/2 |
| **1**: H | **3**e: $t\text{-}C_4H_9$ | $C_6H_5CH_2COC_4H_9(t)$ (**4**e) | 34 | 89/2 |
| **1**: H | **3**f: $(CH_2)_2CO_2CH_3$ | $C_6H_5CH_2CO(CH_2)_2CO_2CH_3$ (**4**f) | 36 | 102/3 |
| **1**: H | **3**g: $(CH_2)_4CO_2C_2H_5$ | $C_6H_5CH_2CO(CH_2)_4CO_2C_2H_5$ (**4**g) | 37 | 125/3 |
| **2**: $CH_3$ | **3**c: $C_3H_7$ |  $C_6H_5\overset{CH_3}{\overset{\vert}{C}}HCOC_3H_7$ (**5**c) | 71 | 84/2 |
| **2**: $CH_3$ | **3**d: $i\text{-}C_3H_7$ |  $C_6H_5\overset{CH_3}{\overset{\vert}{C}}HCOC_3H_7(i)$ (**5**d) | 47 | 76/2 |
| **2**: $CH_3$ | **3**e: $t\text{-}C_4H_9$ |  $C_6H_5\overset{CH_3}{\overset{\vert}{C}}HCOC_4H_9(t)$ (**5**e) | 27 | 90/2 |
| **2**: $CH_3$ | **3**f: $(CH_2)_2CO_2CH_3$ |  $C_6H_5\overset{CH_3}{\overset{\vert}{C}}HCO(CH_2)_2CO_2CH_3$ (**5**f) | 44 | 110/3 |
| **2**: $CH_3$ | **3**g: $(CH_2)_4CO_2C_2H_5$ |  $C_6H_5\overset{CH_3}{\overset{\vert}{C}}HCO(CH_2)_4CO_2C_2H_5$ (**5**g) | 50 | 132/3 |

[a] The molar ratio of **3** to **2** or **1** is 3:1.
[b] The isolated yield.

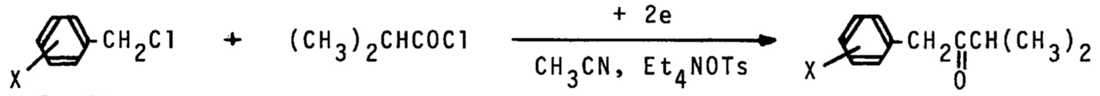
The mixtures of alkyl cinnamyl ketones **7**b-d, β-benzyl vinyl ketones **8**b-d and alkyl γ-phenylpropyl ketones **9**b-d were also obtained from the electroreduction of cinnamyl chloride (**6**) in the presence of acid chlorides **3**b-d under similar conditions.[11)] The products **8**b-d and **9**b-d may be yielded by the rearrangement and the reduction of the first products **7**b-d under the reaction conditions, respectively.

$$\underset{\mathbf{6}}{C_6H_5CH{=}CHCH_2Cl} \quad + \quad \underset{\mathbf{3}\text{b - d}}{RCOCl} \quad \xrightarrow[CH_3CN,\ Et_4NOTs]{+\ 2e}$$

$$\underset{\mathbf{7}\text{b - d}}{C_6H_5CH{=}CHCH_2COR} \quad + \quad \underset{\mathbf{8}\text{b - d}}{C_6H_5CH_2CH{=}CHCOR} \quad + \quad \underset{\mathbf{9}\text{b - d}}{C_6H_5CH_2CH_2CH_2COR}$$

| | R in RCOCl | Total Yield (%) | Product Yield (%) | | |
|---|---|---|---|---|---|
| | | | **7** | **8** | **9** |
| **3**b | $C_2H_5$ | 65 | 33 | 17 | 15 |
| **3**c | $C_3H_7$ | 50 | 19 | 18 | 13 |
| **3**d | i-$C_3H_7$ | 49 | 13 | 20 | 16 |

The introduction of an electron-withdrawing substituent on the phenyl ring of benzyl chloride brought about a considerable increase in the yield of the acylated product (Table II).[11)]



**1**, **10**a - c                **4**d, **11**a - c

Table II.

| Substituent X | Ep (V vs. SCE)[a] | Yield (%) | Bp (°C/mmHg) |
|---|---|---|---|
| p-$CH_3$ | -2.06 (**10**a) | 29 | 121/15 (**11**a) |
| H | -1.97 (**1**)[b] | 47 | 83/2 (**4**d) |
| p-Cl | -1.89 (**10**b) | 63 | 105/5 (**11**b) |
| m-Cl | -1.81 (**10**c) | 73 | 89/2 (**11**c) |

a: The voltammetric peak potential in 0.50 M $Et_4NOTs$-acetonitrile, the sweep rate being 10 mV/sec.

b: The polarographic half-wave potential ($E_{1/2}$) was reported to be -1.94 V vs. SCE in 0.05 M $Et_4NBr$-75% Dioxane.[12)]

Furthermore, the controlled potential electrolysis of **1** in the presence of **3**c at -1.50 V vs. SCE, at which **3**c may be reducible,[13,14)] resulted in almost complete recovery (96%) of **1**, while that at -2.30 V vs. SCE gave the acylated product **4**c in 31% yield together with some recovery (55%) of **1** (Table III).

Table III. Controlled Potential Electrolysis of **1** in the Presence of **3**c.

| Cathode Potential (V vs. SCE) | F/mole | $C_6H_5CH_2COC_3H_7$ **4**c | $C_6H_5CH_2Cl$ **1** |
|---|---|---|---|
| -1.20 | 1.8 | 0% | 98% |
| -1.50 | 2.0 | 0% | 96% |
| -2.30 | 1.5 | 31% | 55% |

These facts would indicate that the mechanism of the reductive acylation involves the formation of an anionic species by the initial electron transfer from the cathode to benzyl chlorides, and the nucleophilic attack of the active species to acid chlorides. In view of its simplicity and generality, the electroreductive method described herein is to be one of the promising methods of the syntheses of alkyl benzyl ketones.[15)]

## References and NOtes

1) Electroorganic Chemistry XXVIII. Part XXVII: T. Shono, J. Hayashi, H. Omoto, and Y. Matsumura, Tetrahedron Lett., in press.
2) E. A. H. Hall, G. P. Moss, J. H. P. Utley, and B. C. L. Weedon, J. Chem. Soc., Chem. Commun., 1976, 589.
3) T. J. Curphey, C. W. Amelotti, T. P. Layloff, R. L. McCartney, and J. H. Williams, J. Am. Chem. Soc., 91, 2817 (1969); T. J. Curphey and R. L. McCartney, Tetrahedron Lett., 1969, 5295.
4) L. H. KLemm, P. E. Iverson, and H. Lund, Acta Chem. Scand. B, 28(5), 593 (1974).
5) P. E. Iverson and H. Lund, ibid. B, 28(7), 827 (1974).
6) T. J. Curphey, T. D. Trivedi, and T. Layloff, J. Org. Chem., 39, 3831 (1974).
7) The catholyte was poured into 100 ml of saturated aqueous sodium chloride solution and extracted with three 100ml portions of ether. After the ethereal solution was dried and evaporated, the residual oil was distilled to give 3.11 g (0.042 mole) of propionic acid, a small amount of toluene (2-3%), and **4**b. The formation of bibenzyl was negligible.
8) The yield of **4**b was 63% based on the consumed **3**b.
9) E. H. Sund and H. R. Henze, J. Chem. Eng. Data, 15, 200 (1970).
10) The substitution of acetonitrile by N,N-dimethylformamide as the solvent generally brought about a considerable decrease in the acylated products. The yields of ketones **4**a-e under this reaction condition were 13%, **4**a; 40%, **4**b; 12%, **4**c; 19%, **4**d and 27%, **4**e.
11) Satisfactory spectroscopic and elemental analyses were obtained for all products.
12) M. von Stackelberg and W. Stracke, Z. Electrochem., 53, 118 (1949).
13) The half-wave reduction potential ($E_{1/2}$) of n-butyryl chloride (**3**c) in lithium chloride-acetone solution was reported to be -1.24 V vs. the acetone-saturated calomel electrode (or -1.00 V vs. Hg pool).[14] The cyclic voltammetry of **3**c in acetonitrile containing 0.1 M tetraethylammonium p-toluenesulfonate showed a reduction wave at -1.16 V (Ep) vs. SCE, though the active species generated from **3**c at the potential was not necessarily known.
14) P. Arthur and H. Lyons, Anal. Chem., 24, 1422 (1952).
15) Some recent references on the syntheses of alkyl benzyl ketones. a) M. J. Jorgenson, Org. Reactions, 18, 1 (1970); b) ref. 9; c) B. D. Raymonde, D. Patrick, and D. Brigritte, C. R. Acad. Sci. Ser. C, 272, 1664 (1971): Chem. Abstr., 75, 35334n (1971); d) R. A. Rossi and J. F. Bunnett, J. Am. Chem. Soc., 94, 683 (1972); e) A. I. Meyers and E. M. Smith, J. Org. Chem., 37, 4289 (1972); f) A. McKillop, J. D. Hunt, F. Kienzle, E. Bigham, and E. C. Taylor, J. Am. Chem. Soc., 95, 3635 (1973); g) S. L. Hegedus and R. K. Stiverson, ibid., 96, 3250 (1974).

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