

Electrochemical Acylation of Some Activated Olefins

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A number of types of unsaturated compounds have been reductively acylated by electrochemical reduction in polar, aprotic medium in the presence of acetic anhydride. The method is an attractive way of producing the equivalent of an acyl anion, and the synthetic possibilities seem promising.

Electrochemical reductive acylation of aromatic hydrocarbons,¹ activated olefins,^{2,3} activated halides⁴ and ketones⁵ offers a promising method for the preparation of a number of carbonyl compounds. Below is reported the product distribution from the acylation of different types of unsaturated compounds.

In the investigation are included 2-styrylpyridine (1), 4-styrylpyridine (2), ethyl 3-acetoxycinnamate (3), methyl 3-phenylpropynoate (4), methyl 5-phenylpenta-2,4-dienoate (5), and stilbene (6).

RESULTS

Cyclic voltammetry. The cyclic voltammetry of compounds 2⁶ and 6⁷ has been described; for compounds 1 to 6 the first wave is a reversible one-electron wave. In Table 1 are given the peak potentials for the compounds 1 to 6.

In the presence of acetic anhydride (7) the peak height of the substrates 1 to 6 increases, but never more than to approximately twice the original one, and the wave becomes irreversible.

Preparative results. 2-Styrylpyridine (1) yields on electrochemical reductive acetylation 3-phenyl-4-(2-pyridyl)-2-butanone (8) as main product; besides that are isolated minor amounts of the saturated compound 1-phenyl-2-(2-pyridyl)ethane (9), and the *erythro* and

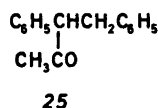
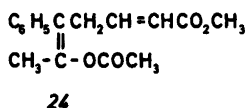
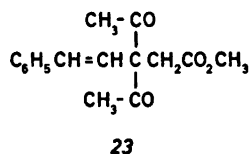
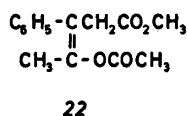
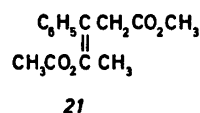
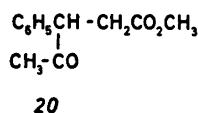
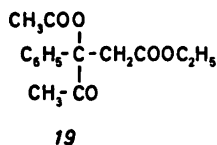
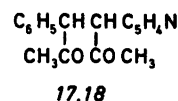
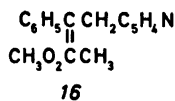
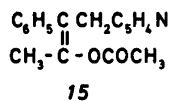
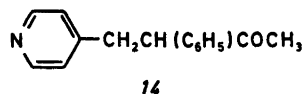
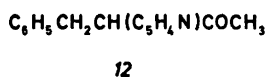
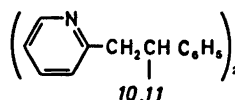
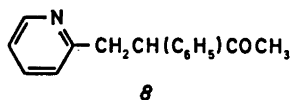
Table 1. Peak potentials (V vs. SCE) of compounds 1 to 7 in dimethylformamide containing 0.2 M tetrabutylammonium iodide.

	1	2	3	4	5	6	7
$-E_p(\text{I})/\text{V}$	1.94	1.81	1.66	1.80	1.54	2.11	2.65 ^a
$-E_p(\text{II})/\text{V}^a$	2.36	2.32	2.20	2.37	2.05	2.54	

^a Irreversible.

threo hydrodimers, 2,3-diphenyl-1,4-di(2-pyridyl)butane (10, 11), but no 4-phenyl-3-(2-pyridyl)-2-butanone (12). The choice between 8 and 12 as the structure for the main product was made from the ¹³C NMR spectrum with selective decoupling of the phenyl protons^{8,9} and observing the 3-bond coupling from the C-2 to the benzylic proton. It may be mentioned that reductive carboxylation of 1 in DMF in the presence of some water similarly yields 2-phenyl-3-(2-pyridyl)propionic acid¹⁰ rather than the isomer analogous to 12.

The product mixture from 4-styrylpyridine (2) is more complex. Besides the saturated compound 1-phenyl-2-(4-pyridyl)ethane (13) and 3-phenyl-4-(4-pyridyl)-2-butanone (14), the *E* (15) and *Z* (16) forms of 2-acetoxy-3-phenyl-4-(4-pyridyl)-2-butene and the *erythro* (17) and *threo* (18) forms of 3-phenyl-4-(4-pyridyl)-hexa-2,5-dione were isolated. The choice between the *E* and *Z* structures of 15 and 16 was made on the basis of the chemical shifts of the methyl signals in the ¹H NMR spectrum, as a number of other methods did not give decisive results. The argument for the tentative assignment is that the signal from a methyl group at the



double bond would be expected at a lower field when *cis* to the phenyl ring than when *trans*. For 15 $\text{CH}_3-\text{C}=\text{C}$ is at δ 2.10, whereas for 16 it is at 1.88, for 15 CH_3CO is at δ 1.86, whereas for 16 it is at 2.18. Similar arguments are used for the assignment of *Z/E* to 21 and 22, so if the tentative assignment of one pair later should be proved wrong, the other pair would probably also have to be reversed.

The tentative *erythro/threo* assignment to 17 and 18 rests on considerations of the more probable conformations and their influence on the ^1H NMR spectrum. In the *erythro* isomer the conformer with all groups *anti* is the favoured one, which brings the methyl groups out of the plane of the aromatic rings and their ^1H NMR signals at higher field compared to the *threo* form. The assignment of 17 as the *erythro* is also consistent with the relatively low

mobility during chromatography compared to 18; the *threo* has the acetyl groups close to each other, and they are thus less prone to interact with the silica.

Ethyl 3-acetoxycinnamate (3), the enol acetate of ethyl benzoylacetate, behaves analogously to ethyl cinnamate; the main product is ethyl 3-acetoxy-3-phenyl-4-oxo-pentanoate (19).

4 behaves also analogously to ethyl cinnamate; the main product is methyl 3-phenyl-4-oxo-pentanoate (20); the *Z* (21) and *E* (22) isomers of the enolacetate of 20 are found as minor products.

Methyl styrylacrylate (5) yields, as the only substrate, a main product, *trans* methyl 3,3-diacetyl-5-phenyl-pent-4-enoate (23), with two acetyl groups at the same carbon atom. The structure is based on the ^1H NMR spectrum (see Experimental). Besides the 1,4-addition

product (23), minor amounts of a 1,6-addition product, methyl 5-phenyl-6-oxo-hept-2-enoate enol acetate (24), were isolated.

Stilbene (6) is reduced in the presence of 7 to 3,4-diphenylbutanone-2 (25); bibenzyl was also isolated, but no diacetylated compounds.

DISCUSSION

The half-wave potentials of the olefins are less negative than that of acetic anhydride (Table 1), and in all cases the electroactive species is the olefin. The anion radical of the olefin formed on reduction may dimerize, accept a proton, disproportionate, exchange an electron, initiate polymerization or react with acetic anhydride. The relative rates of these reactions determine the product distribution.

The results from cyclic voltammetry suggest that the mechanism of the electrochemical acetylation and carboxylation reaction is similar; no catalytic current is observed in CV with the substrates 1 to 6. The coupling is thus probably a nucleophilic attack of the radical anion of the substrate on 7 (which could just as well be called an electrophilic attack of 7 on the anion radical); it seems less likely that a major reaction path goes through the dianion (formed by disproportionation) or the anion of the dihydro compound.

Several products are formed in the reaction and their relative importance varies. These variations may be explained if it is assumed that the anion radical may be acylated at the heteroatom in the activating group (if present) or at the carbon atom, where it is found in the product. If the stereochemistry permits, the heteroacylated group may react in an intramolecular acylation of the carbon atom. The reactions are shown with 1 as an example in Scheme 1.

In esters the carbonyl oxygen would play a similar role as the nitrogen in 1 and 2, and a cyclic intermediate, such as 26, could thus be formed from unsaturated esters and explain the rather low yield of diacetylated compounds from cinnamic and similar esters; it could also explain the difference between 1 and 2 with respect to products if it is assumed that the intramolecular acylation of the anion (formation of analogs to 26) is faster than the bimolecular acylation of substrate anion radical

by 7, and that protonation competes better with the bimolecular reaction than with the intramolecular acylation.

26 would not be a stable species and it has not been possible to detect its presence; if formed, it could react to 27 or be protonated during work-up. 27, which may be produced by the normal bimolecular acylation or through 26, may be protonated or may react with 7 to a diacetylated product. The protonation may also be intramolecular, as the methin proton neighbour to the carbonyl group is a relatively strong acid. The resulting enolate anion may be acylated to the enol acetate or it may be C-acylated to a gem-diacetyl compound.

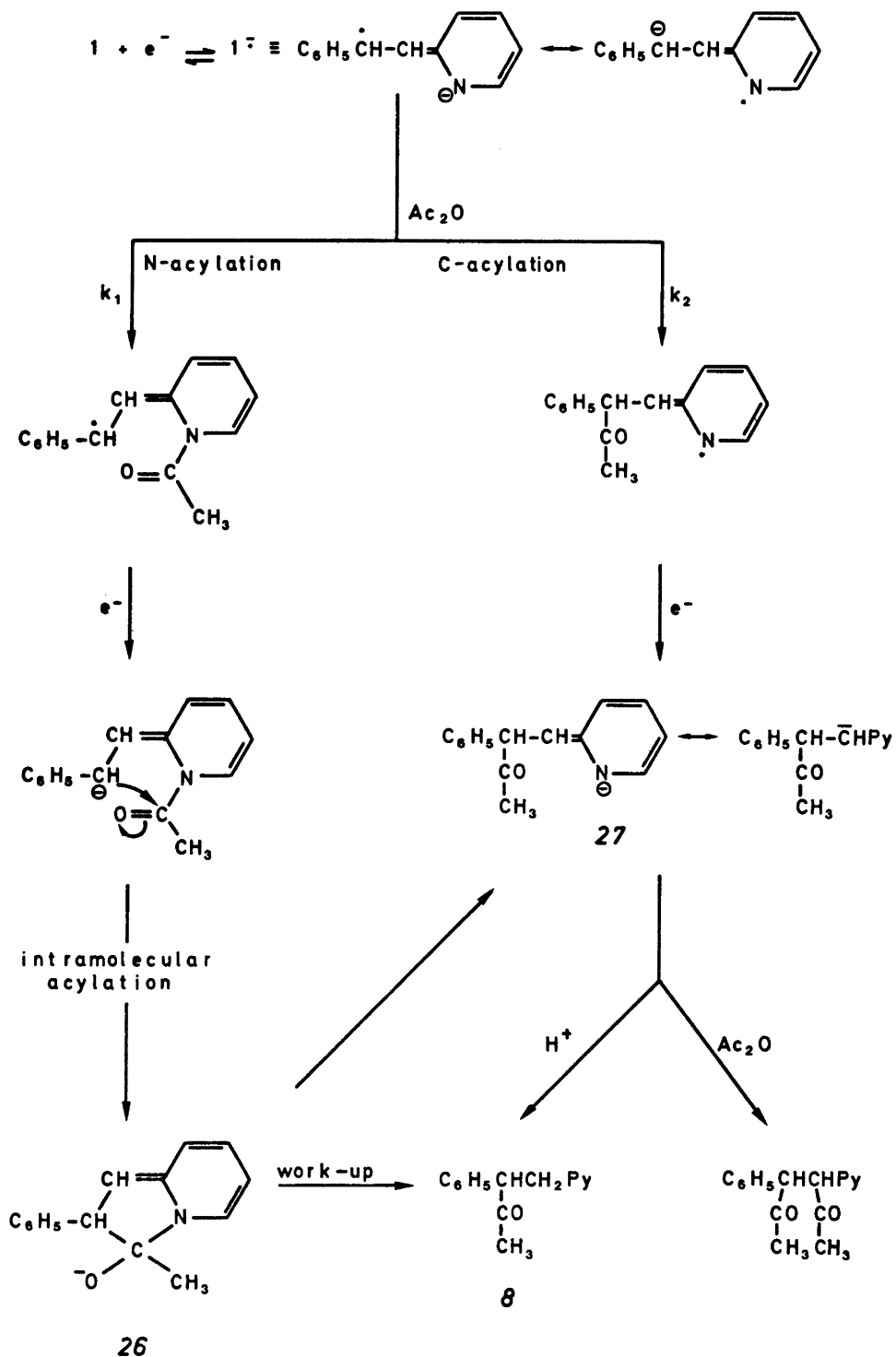
The formation during the reductive acylation of 5 of the 1,4-addition product 23 rather than the 1,6-product is consistent with an intramolecular acylation; the carbanion produced at C-2, possibly after ring-opening of the analog to 26, must then, as described above, be protonated by internal protonation by the stronger acid at C-3 with formation of a C-3 carbanion. The proton at C-3 in the monoacylated product from 5 is activated both by the acetyl and the styryl groups.

The similarities between the electrochemical carboxylation and acylation reaction suggest that analogous mechanisms are operating and that the acylation reaction will have a synthetic scope comparable to the carboxylation reaction.

EXPERIMENTAL

Materials. 2- and 4-styrylpyridine were prepared according to Refs. 11, 12 and styrylacrylic acid according to Ref. 13. Ethyl 3-acetoxycinnamate was prepared by acylation of the Cu-salt of the enol of ethyl benzoylacetate.¹⁴ Phenylpropionic acid was obtained from Ega-Chemie, BRD.

General procedure. DMF (200 ml) containing 0.1 M tetrabutylammonium iodide (TBAI) and 10 ml acetic anhydride was stirred with active alumina for 2 h; the alumina was allowed to settle and the supernatant introduced into the cathode chamber of the cell. The substrate was added, oxygen removed by a stream of nitrogen, and the substrate reduced at a suitable cathode potential. After completion of the reduction, water was added, the products extracted with ethyl ether which after washing with water (3 times) and drying, was evaporated. The residue was separated on a column of silica.



Scheme 1.

Reduction of 1. 2.0 g of 1 and 10 ml of 7 were reduced at -1.85 V (SCE), $n=2.65$ F mol⁻¹; obtained were 2.3 g of crude product which were purified on silica with a 3:7 mixture of acetone and light petroleum as eluent. Isolated were (in order of elution) 9 (1-phenyl-2-(3-pyridyl)-ethane),¹⁵ 2.5 % yield; 8 (3-phenyl-4-(2-pyridyl)-2-butanone), 1130 mg, 45 %. ¹H NMR (CDCl₃): δ 2.05 (3 H, s), 3.04 (1 H, dd, J_{AB} 14.2 Hz, J_{AM} 6.5 Hz), 3.65 (1 H, dd, J_{AB} 14.2 Hz, J_{BM} 8.0 Hz), 4.47 (1 H, dd, J 6.5, 8.0 Hz), 6.85–7.6 (7 H, m), 8.35–8.55 (1 H, m). IR spectrum, film, cm⁻¹ (intensity): 3050 (w), 1710 (s), 1595 (m), 1490 (w), 1470 (w), 1430 (m), 1345 (m), 1150 (m), 990 (w), 785 (w), 748 (m), 700 (s). 10 (hydrodimer of 1, D,L or meso), yield 3 %, ¹H NMR (CDCl₃): δ 2.8–3.7 (6 H, m), 6.5–7.4 (16 H, m), 8.3–8.5 (2 H, m). *m/e* 364. 11 (hydrodimer of 1, meso or D,L), yield 5 %. ¹H NMR (CDCl₃): δ 2.85–3.8 (6 H, m), 6.65–7.5 (16 H, m), 8.3–8.5 (2 H, m). *m/e* 364.

Reduction of 2. 2.0 g of 2 and 10 ml of 7 were reduced at -1.80 V (SCE), $n=2.2$ F mol⁻¹. Isolated were 2.46 g crude product, purified on a column of silica with a 3:7 mixture of acetone–light petroleum as eluent. Isolated were, in order of elution: 13 (1-phenyl-2-(4-pyridyl)ethane,¹⁶ 429 mg (21 %). 15 (*E* 2-acetoxy-3-phenyl-4-(4-pyridyl)-butene, 203 mg, 7 %. ¹H NMR (CDCl₃): δ 1.86 (3 H, s, CH₃CO), 2.10 (3 H, s(br.)), CH₃C=C), 3.75 (2 H, s(br.)), 6.9–7.4 (7 H, m), 8.2–8.6 (2 H, m). 16 (*Z* 2-acetoxy-3-phenyl-4-(4-pyridyl)-2-butene) 167 mg, 6 %. ¹H NMR (CDCl₃): δ 1.88 (3 H, s(br.)), CH₃C=C), 2.18 (3 H, s, CH₃CO), 3.65 (2 H, s(br.)), 6.9–7.4 (7 H, m), 8.3–8.6 (2 H, m). 18 (*threo* 3-phenyl-4-(4-pyridyl)-hexa-2,5-dione), 88 mg, 3 %. ¹H NMR (CDCl₃): δ 2.15 (3 H, s), 2.20 (3 H, s), 4.42 (2H, s), 6.8–7.3 (7 H, m), 8.2–8.5 (2 H, m). 14 (3-Phenyl-4-(4-pyridyl)-2-butanone), 323 mg, 13 %. ¹H NMR (CDCl₃): δ 2.90 (1 H, dd, J_{AB} 14 Hz, J_{AC} 8 Hz), 3.40 (1 H, dd, J_{AB} 14 Hz, J_{BC} 7 Hz), 3.90 (1 H, dd, J_{AC} 8 Hz, J_{BC} 7 Hz). IR spectrum (film) cm⁻¹ (intensity): 3000 (m), 1710 (s), 1600 (s), 1490 (w), 1440 (w), 1410 (m), 1350 (m), 1220–1150 (m), 810 (m), 750 (m), 700 (s). 17 (*erythro* isomer of 18), m.p. 215 °C (CH₂Cl₂/hexane), 210 mg, 7 %. ¹H NMR (CDCl₃): δ 1.85 (3 H, s), 1.91 (3 H, s), 4.58 (2 H, s), 7.2–7.5 (7 H, m), 8.5–8.7 (2 H, m).

Reduction of 3. 2.0 g of 3 and 10 ml of 7 were reduced at -1.70 V (SCE), $n=2.2$ F mol⁻¹. Isolated were 1.97 g crude product, GLC showed that 80 % of crude product was 19. It was purified on a column of silica with methylene chloride as eluent. 19 (Ethyl 3-acetoxy-3-phenyl-4-oxopentanoate), 68 %. ¹H NMR (CCl₄): δ 0.92 (3 H, tr, J 7.1 Hz), 1.87 (3 H, s), 2.23 (3 H, s), 3.28 (1 H, d, J 14.5 Hz), 3.43 (1 H, d, J 14.5 Hz), 3.84 (2 H, q, J 7.1 Hz), 7.1–7.5 (5 H, m).

Reduction of 4. 2.0 g of 4 and 10 ml of 7 were reduced at -1.9 V (SCE), $n=4$ F mol⁻¹.

The crude product (1.7 g) was purified on a silica column with a mixture of 3:7 ether–light petroleum. 21 (*Z* enol acetate of 20), 70 mg, 2 %. ¹H NMR (CDCl₃): δ 2.13 (3 H, s, CH₃CO), 2.33 (3 H, s (br.)), CH₃C=C), 3.60 (2 H, s(br.)), 3.65 (3 H, s), 7.20 (5 H, s(br.)). 20 (Methyl 3-phenyl-4-oxopentanoate),¹⁷ 400 mg, 16 %. ¹H NMR (CDCl₃): δ 2.10 (3 H, s), 2.45 (1 H, dd, J 17 Hz, 6 Hz), 3.23 (1 H, dd, J 17 Hz, 9.5 Hz), 3.62 (3 H, s), 4.20 (1 H, dd, J 9.5 Hz, 6 Hz), 7.28 (5 H, s(br.)). 22 (*E* enol acetate of 20) 250 mg, 8 %. ¹H NMR (CDCl₃): δ 1.90 (3 H, s(br.)), CH₃C=C), 2.19 (3 H, s, CH₃CO), 3.30 (2 H, s), 3.60 (3 H, s), 7.28 (5 H, s(br.)).

Reduction of 5. 2.0 g of 5 and 10 ml of 7 were reduced at -1.80 V (SCE), $n=1.8$ F mol⁻¹. The crude product (2.2 g) was purified on a silica column using a mixture of 1:4 ether/light petroleum as eluent. 24 (enol acetate of *E* methyl 5-phenyl-6-oxohept-2-enoate) 435 mg, 15 %. ¹H NMR (CDCl₃): δ 1.78 (3 H, s(br.)) CH₃C=C), 2.25 (3 H, s, CH₃CO), 3.12 (2 H, d(br.)), J 7.2 Hz), 3.63 (3 H, s), 5.22 (1 H, double tr., J 16 Hz, 7.2 Hz), 6.57 (1 H, d(br.)), J 16 Hz), 7.0–7.5 (5 H, m). UV spectrum (96 % ethanol) λ_{max} 243 nm, ϵ 1.5×10^4 . 23 (*E* methyl 3,3-diacetyl-5-phenylpent-4-enoate), m.p. 62.5–65.5 °C (ether/light petrol) 880 mg 30 %. ¹H NMR (CDCl₃): δ 2.20 (6 H, s), 3.35 (2 H, s), 3.68 (3 H, s), 6.62 (1 H, d, J 16 Hz), 6.97 (1 H, d, J 16 Hz), 7.15–7.50 (5 H, m).

Reduction of stilbene. 2.0 g of stilbene and 10 ml of 7 were reduced at -2.3 V (SCE), $n=2.3$ F mol⁻¹. The residue (2.2 g) was separated on a column of silica using light petroleum as eluent. Besides bibenzyl (20 %) was isolated 25, 3,4-diphenylbutanone-2 (60 %). ¹H NMR (CDCl₃): δ 1.93 (3 H, s), 2.92 (1 H, dd, J 14 Hz, 7.2 Hz), 3.43 (1 H, dd, J 14 Hz, 7.1 Hz), 3.92 (tr, J 7.2 Hz), 7.0–7.3 (5 H, m).

REFERENCES

- Lund, H. *Acta Chem. Scand. B* 31 (1977) 424.
- Lund, H. and Degrand, C. *Tetrahedron Lett.* (1977) 3593.
- Shono, T., Nishiguchi, I. and Ohmizu, H. *J. Am. Chem. Soc.* 99 (1977) 7396.
- Shono, T., Nishiguchi, I. and Ohmizu, H. *Chem. Lett.* (1977) 1021.
- Curphey, T. J., Trivedi, L. D. and Layloff, T. *J. Org. Chem.* 39 (1974) 3831.
- Alwair, K., Archer, J. F. and Grimshaw, J. *J. Chem. Soc. Perkin Trans. 2* (1972) 1663.
- Funt, B. L. and Gray, D. G. *J. Electrochem. Soc.* 117 (1970) 1020.
- Hansen, M. and Jakobsen, H. J. *J. Magn. Reson.* 10 (1973) 74.
- Sørensen, S., Hansen, M. and Jakobsen, H. J. *J. Magn. Reson.* 12 (1973) 340.
- Lund, H. and Nielsen, J. *J. Unpublished observation.*

11. Baurath, H. *Ber. Dtsch. Chem. Ges.* 20 (1187) 2719.
12. Friedländer, C. *Ber. Dtsch. Chem. Ges.* 38 (1905) 159.
13. Doebner, O. *Ber. Dtsch. Chem. Ges.* 35 (1902) 2129.
14. Bernhard, A. *Ann.* 282 (1894) 153.
15. Baurath, H. *Ber. Dtsch. Chem. Ges.* 21 (1888) 818.
16. Friedländer, C. *Ber. Dtsch. Chem. Ges.* 38 (1905) 2837.
17. Corey, E. J. and Hegedus, L. S. *J. Am. Chem. Soc.* 91 (1969) 4926.

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