

ELECTROREDUCTION OF 3-PHENACYLIDENEINDOLE

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Fundamental polarographic investigation of the $-\text{CO}-\overset{|}{\text{C}}-\text{CO}-$ grouping of the 3-phenacylideneoxindole molecule in aqueous-ethanolic solutions was carried out. Polarographic measurements and preparative electroreductions on a large-area mercury cathode indicated that in acid media a process of a two-electron reduction of the $\text{C}=\text{C}$ double bond takes place in the first cathodic wave, under formation of 3-phenacyloxindole which was isolated and identified polarographically and by means of infrared and $^1\text{H-NMR}$ spectroscopy.

In this paper the electrochemical behaviour of the $-\text{CO}-\overset{|}{\text{C}}-\text{CO}-$ grouping in the molecule of 3-phenacylideneoxindole in aqueous-ethanolic solutions was investigated in comparison with the electroreduction of chalcones¹⁻⁸ or indanediones⁹⁻¹¹ which have an analogous structure, but different polarographic behaviour.

EXPERIMENTAL

3-Phenacylideneoxindole (m.p. 193–194°C) was prepared according to ref.¹² from 3-hydroxy-3-phenacyloxindole (m.p. 169–171°C) by dehydration in acid medium. 3-Hydroxy-3-phenacyloxindole was obtained as a condensation product of dioxindole with acetophenone. On mild reduction of this compound with $\text{Na}_2\text{S}_2\text{O}_4$ 3-phenacylideneoxindole (m.p. 177–178°C) was prepared. The other chemicals used were of analytical grade (Lachema, Brno).

Polarographic measurements were carried out on a polarograph LP 7 (Laboratorní přístroje, Prague) in a thermostated Kalousek vessel. The dropping mercury electrode (70 cm column height) in 1M-KCl and at 0.0 V had a flow rate of 2.7 mg s^{-1} and a drop time 2.3 s. The reference electrode was a saturated calomel electrode (s.c.e.). During our polarographic measurements we used solutions of H_2SO_4 , HCl, NaOH, or solutions of Britton-Robinson buffers. The concentration of the depolarizer used was $2.5 \cdot 10^{-4} \text{ M}$. Total content of ethanol was 40 vol.%. The ionic strength was adjusted to 0.2 by addition of KCl.

The measurement of pH of the solutions was carried out using a pH-meter PHM-26 (Radiometer, Copenhagen) with two electrodes G 202 B and K 401. Solutions of potassium hydrogen phthalate were used as standards.

Preparative electroreduction was carried out with 500 ml aliquots in 0.05N- H_2SO_4 solutions where the concentration of the reduced compound was $2.5 \cdot 10^{-4}$ – $5 \cdot 10^{-4} \text{ M}$, and using 30%

vol. % of acetone. The conductivity of the solutions and other conditions were adjusted as in the case of polarographic measurements. The electroreduction was carried out in a small vessel under nitrogen. The mercury cathode was a 2 cm layer of mercury with approximately 120 cm² surface area. The mercury was stirred with a rotating stirrer LH-10 (Dresden). A saturated calomel electrode served as a reference electrode and it reached with its J-shaped narrowed tip closely above the mercury level. A thin platinum sheet served as the anode, the surface area of which was 10 cm². It was separated from the rest by a salt bridge and fritted glass S4. A stabilized current source (Direct Current Distributor, Tesla) with a 0–500 V range at 0–250 mA served as a source of voltage. For the measurement of the potential differences between the large-area cathode and the calomel electrode a technical compensator QTK (Metra, Blansko) was used. The preparative electroreduction took place within 40–60 minutes at a voltage chosen from the range at the beginning of the limiting current of the first cathodic wave. The cathode potential was maintained manually with a ± 20 mV accuracy. The polarographic control of the reduced solution was carried out at ten minute's intervals. After the end of the electroreduction the solution was neutralized and acetone was evaporated from it under reduced pressure. The pH was adjusted to 4 and the reaction product was extracted with ether in an approximately 85% yield. The product obtained was a white crystalline compound of m. p. 166 to 167°C which was crystallized from a chloroform–tetrachloromethane (1 : 3) mixture. For identification the following measurements were used: polarographic record in comparison with other model compounds, melting point, infrared spectrum, differential infrared spectrum, R_F values in TLC, NMR spectra in comparison with models, *etc.* The chromatographic separation was carried out on Silufol UV 254 sheets (Kavalier, Votice) with dioxan as developing solvent. For detection *p*-nitrophenylhydrazine was used.

Spectral measurement. The infrared spectra were measured with a UR-20 (Zeiss, Jena) apparatus, in chloroform solutions of $5 \cdot 10^{-2}$ M concentration and in cells 0.1 mm thick, and in tetrachloromethane solutions of 10^{-4} M concentration and in cells 4 cm thick. The ¹H-NMR spectra were measured on a spectrometer Tesla, Model BS 487, provided with proton stabilization (80 MHz). The measurements were carried out at 0.2 M concentration in deuteriochloroform with hexamethyldisiloxan as internal standard. Solutions of perdeuterated dimethyl sulfoxide and acetone, 1 : 4, with or without addition of heavy water, were also used.

RESULTS AND DISCUSSION

3-Phenacylideneoxindole is reduced in Britton–Robinson's buffers, within their whole pH range, in two, and at pH < 5, in one cathodic wave. The limiting current of the positive cathodic wave is constant within the whole pH range. The half-wave potential of this wave is linearly dependent on pH. In the pH 1–13 range it assumes the values from +20 to –720 mV (s.c.e.) and follows the equation $E_{1/2} = k \cdot \text{pH} + E^0$, where $E^0 = +40$ mV (s.c.e.) is the extrapolated value at pH 0 and the gradient k has the value –60 mV/pH. In the whole pH range the wave is well developed and the effect of acidobasic equilibrium was not observed on it. From the dependence of the limiting current of this wave on temperature, concentration and mercury column height it is evident that the limiting current is a diffusion current. On the basis of the comparison of the limiting current value of this wave with the values of the limiting currents of model compounds dioxindole and 3-oximoxindole, as well as on the basis of the further mentioned results of preparative electroreduction,

this positive cathodic wave corresponds to a two-electron process of electroreduction of the C=C bond. The half wave potential of the more negative cathodic wave assumes the value -1200 to -1400 mV (s.c.e.) in dependence on the concentration of protons in the 5–13 pH range. The limiting current of this wave does not achieve the limiting current value of the first wave. The wave is insufficiently developed and in acid solutions it almost merges with the wave of the basic electrolyte. The half-wave potential of this wave is close to the half wave potential of the cathodic waves of acetophenone and 3-methylbenzoyloxindole, as is evident from Figs 1, 2. The value of the half-wave potential of this wave and especially the limiting current value are affected by the type of the buffer solution used, the concentration of the organic solvent used, the concentration of the depolarizer, as well as the possible insufficient capacity of the buffer. On the basis of the results of the polarographic study of dioxindole and its numerous derivatives¹³, as well as of acetophenone and 3-phenacyloxindole, the negative wave represents the electroreduction of the CO group in the benzoyl substituent.

During preparative electroreduction of 3-phenacylideneoxindole in 0.05N- H_2SO_4 at -200 mV (s.c.e.) polarographic control indicated a continual decrease of the cathode wave under simultaneous decolorization of the yellow solution. In these media the reduction product was not sensitive to air oxidation. After working up a white crystalline substance was isolated of m.p. $166-167^\circ C$. This value alone excluded the possibility of the formation of dimeric products which were proved in the case of chalcones^{2,14}. The different melting points of the reduction product and of the 3-phenacyloxindole prepared according to ¹² may be probably best

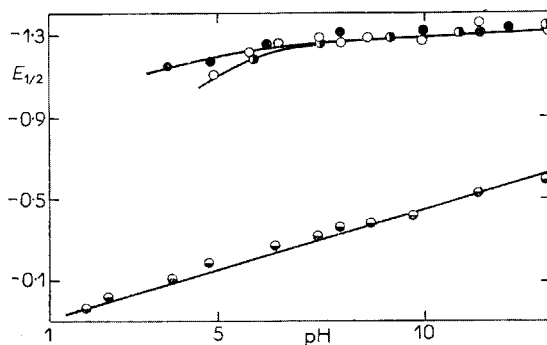


FIG. 1

Dependence of the Half-Wave Potential of Cathodic Waves on pH in Britton–Robinson Buffers (conc. $2.5 \cdot 10^{-4} M$, 40 vol.% of ethanol)

○ 1st wave of 3-phenacylideneoxindole; ○ 2nd wave of 3-phenacylideneoxindole; ● wave of the reduction product; ● wave of acetophenone.

explained on the basis of different crystal modifications of this compound, which was evident during a microscopic observation of the melting point. Polarographic record (Fig. 2) and R_C values in thin-layer chromatography are consistent with the values measured for 3-phenacyloxindol.

In the infrared spectra of the reduction product and of 3-phenacyloxindole a most intensive band at 1735 cm^{-1} in the carbonyl region was also observed, due to the stretching vibration of the CO group in the isatin ring. At 1690 cm^{-1} a shoulder of the stretching band of the 3-phenacyl CO group was observed. The value of this wave-number is increased in comparison with that of 3-phenacylidene derivative, due to the lack of conjugation. 3-Phenacylideneoxindole shows in the $\nu(\text{CO})$ stretching region two separated intensive bands at 1739 and 1677 cm^{-1} which correspond to the $\nu(\text{CO})$ of the carbonyl group in the isatin ring and in the phenacylidene substituent. In this compound a band of a higher activity appears in the $\nu(\text{C}=\text{C})$ region, which corresponds to the ethylene group and the aromatic nuclei. In the $\nu(\text{O}-\text{H})$ region no absorption was observed in the reduction product or in the synthesized¹² 3-phenacyloxindole. The stretching vibrations of the free and the bound NH group appeared in the reduction product and in 3-phenacyl derivative at 3220 and 3450 cm^{-1} , while in 3-phenacylideneoxindole they were at 3240 and 3460 cm^{-1} . In the spectra of 3-phenacyl derivative, as well as in the spectra of the reduction product in CCl_4 solutions of 10^{-4} M concentration two strong bands in the $\nu(\text{NH})$ region appeared at 3300 and 3460 cm^{-1} , due to the vibrations of the bound and the free NH group. As on the basis of Dreiding models the existence of an intramolecular hydrogen bond of the $-\text{NH}\cdots\text{O}=\text{C}-\text{C}_6\text{H}_5$ type may be excluded, this compound

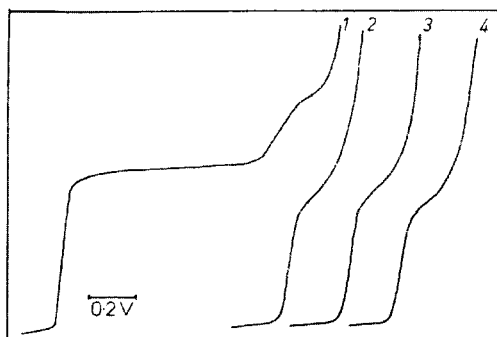


FIG. 2

Polarographic Records in Britton-Robinson's Buffer of pH 9.5 (conc. $2.5 \cdot 10^{-4}\text{ M}$, 40 vol.% of ethanol)

1 3-Phenacylideneoxindole, start -400 mV (s.c.e.), 2 product of electroreduction, start -1200 mV (s.c.e.), 3 3-phenacyloxindole, start -1200 mV (s.c.e.), 4 acetophenone, start -1200 mV (s.c.e).

forms a strong intermolecular hydrogen bond between the NH group and the carbonyl group of the phenacyl substituent. The results of the IR spectrography, the identity of the $^1\text{H-NMR}$ spectra of the reduction product and the synthetically prepared 3-phenacyloxindole, as well as the interpretation of the NMR spectra confirm unambiguously the identity of the reduction product with 3-phenacyloxindole, which shows that in acid media the first cathodic polarographic wave represents a two-electron process of reduction of the $\text{C}=\text{C}$ bond.

In the $^1\text{H-NMR}$ spectrum of 3-phenacylideneoxindole in CHCl_3 strong bands of overlapping multiplets of aromatic protons may be observed at $\delta \approx 6.6-8.0$ p.p.m.. On the basis of the comparison of this spectrum with that of 3-phenacyl derivative, as well as on the basis of the comparison of the areas under single peaks we assign the narrow singlet with the highest amplitude at $\delta \approx 7.7$ p.p.m. to the ethylenic proton $\text{C}=\text{CH}-\text{CO}-$. In the spectrum of the reduction product this singlet is missing. In 3-phenacylidene derivative the NH proton appears at $\delta \approx 10.5$ p.p.m.. The ratio of the areas under the curves of CH, NH and aromatic protons is 1 : 1 : 9. In 3-phenacyloxindole the aromatic nucleus protons appear as strong bands in multiplets at $\delta \approx 6.6-8.0$ p.p.m. and the NH proton as a broader band at 8.8 p.p.m.. In the $\delta \approx 3.2-3.9$ p.p.m. region overlapping bands of doublets corresponding to OH and CH_2 groups protons can be observed. In the interpretation of this part of the spectrum we made use of the analysis of the spectrum of 3-hydroxy-3-phenacyloxindole where the bands at $\delta \approx 3.4-4.2$ p.p.m. were interpreted as bands corresponding to the resonance of non-equivalent CH_2 protons of the AB system. The non-equivalence of the protons may be explained by the formation of an intramolecular hydrogen bond between the CO group of the isatin ring and one hydrogen of the CH_2 group. This system appeared in the spectrum in the form of two doublets, where the distance of the second band of the first doublet from the first band of the second doublet was $\nu_{2,3} = 14$ Hz. The spin-spin coupling constant was $J_{\text{AB}} = 18$ Hz, $\nu_{\text{AB}} = 26.5$ Hz, and the chemical shifts were 3.65 and 3.97 p.p.m.. Between the CH_2 protons and the OH group there was no spin-spin coupling.

The problem of the interpretation of the spectrum of 3-phenacyloxindole is more complex in spite of the fact that $>\text{CH}-\text{CH}_2-$ represents an ABC system. In addition to an AB spin-spin coupling, AC and AB couplings are also involved. In the spectrum of this compound the multiplets of the aromatic protons are overlapped in the $\delta = 6-8$ p.p.m. region. At $\delta \sim 3.2-4.1$ twelve bands appear of the ABC system with spin-spin couplings $J_{\text{AB}} = 18$ Hz, $J_{\text{AC}} = 8$ Hz, and $J_{\text{BC}} = 4$ Hz. The chemical shifts are: 3.4 p.p.m. (A), 3.8 p.p.m. (B), and 4.1 p.p.m. (C). The region of the CH proton resonance (C) is 3.9-4.1 p.p.m. and the region of the CH_2 protons (A, B) is 3.2-3.9 p.p.m.. Proton NH appears as a broader band at $\delta = 8.8$ p.p.m.. The ratio of the peak areas $\text{NH} : \text{CH} : \text{CH}_2 = 1 : 1 : 2$. In the solutions of the compounds studied in deuterated acetone and deuterated dimethyl sulfoxide the bands of NH and OH groups do not appear in consequence of isotopic exchange.

In alkaline solutions the results of preparative electroreduction are not as unambiguous. It is true that on electroreduction 3-phenacyloxindole is probably formed, but this product undergoes a reaction catalysed by the medium, under formation of isatinic acid. The reversibility of the reaction is affected by NaOH concentration. After 40 hours' standing of the reduction product in the original solution oxidation was observed *via* an unidentified intermediate, and a part of 3-phenacylideneoxindole was isolated.

In the electroreduction of 3-phenacylideneoxindole the formation of a one-electron product, or dimeric products formed from it, was not observed. Our results correspond to those from ref.⁴. During the electrochemical study of the —CO—CH=C— —CO— grouping in the 3-phenacylideneoxindole the one-electron product of reduction was not observed, as stated in papers^{1,2,15-17}.

REFERENCES

1. Martinet P., Simonet J.: *Bull. Soc. Chim. Fr.* 1967, 3534.
2. Simonet J., Albisson A.: *Bull. Soc. Chim. Fr.* 1971, 1125.
3. Simonet M.: *Bull. Soc. Chim. Fr.* 1970, 1534.
4. Tiroufflet J., Laviron E., Metzger J., Boichard J.: *This Journal* 25, 3277 (1960).
5. Tiroufflet J., Boichard J.: *C. R. Acad. Sci. (Paris)* 250, 1861 (1960).
6. Holleck L., Marquand D.: *Naturwissenschaften* 49, 468 (1922).
7. Ryvolová-Kejharová A., Zuman P.: *J. Electroanal. Chem. Interfacial Electrochem.* 21, 197 (1969).
8. Zuman P., Michl J.: *Nature* 192, 655 (1961).
9. Zacharová-Kalavská D., Perjéssy A.: *This Journal* 36, 1407 (1971).
10. Zacharová-Kalavská D., Perjéssy A., Hrnčiar P.: *This Journal* 38, 2461 (1973).
11. Zacharová-Kalavská D., Perjéssy A., Vida M.: *This Journal* 38, 892 (1973).
12. Lindwall H. G., MacLennan J. S.: *J. Amer. Chem. Soc.* 54, 4739 (1932).
13. Košturiak A.: *Thesis*. University P. J. Šafárik, Košice 1971.
14. Simonet J.: *C. R. Acad. Sci. (Paris)* 267, 1548 (1968).
15. Pasternak R.: *Helv. Chim. Acta* 31, 753 (1948).
16. Arijan Z. S., Mooney B., Stonehill H. I.: *J. Chem. Soc.* 1962, 2239.
17. Zahradník P., Leška J.: *This Journal* 36, 44 (1971).

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