

Es hat sich also gezeigt, dass die Tumorbildung des Bastards offensichtlich nichts anderes darstellt als eine übersteigerte Kallusbildung. Histologische und cytologische Untersuchungen haben dies bestätigt. Auch die spontane Tumorbildung kann als übersteigerte Kallusbildung interpretiert werden, denn sie beginnt offenbar stets an endogenen Wundmeristemem, die vermutlich durch Gewebespannungen und -zerreissungen induziert werden¹². Da *N. langsdorffii* nur eine sehr schwache, *N. glauca* hingegen eine sehr starke Potenz zur Kallusbildung zeigt, beruht die Fähigkeit zur Tumorbildung wahrscheinlich vorwiegend auf Erbanlagen des letzteren. Weitere Versuche, die a. a. O. ausführlich erörtert werden, weisen darauf hin, dass das Kalluswachstum von *N. glauca* durch polygene Regulationsfaktoren begrenzt wird. Diese werden durch die Bastardierung mit *N. langsdorffii* offenbar abgebaut oder wenigstens so gestört, dass sich die starke Potenz zur Kallusbildung von *N. glauca* im Bastard ungezügelt manifestieren kann.

Summary. The occurrence of tumours of the amphidiploid hybrid of *Nicotiana glauca* and *N. langsdorffii* can – as was found in organoculture – be connected with the specific formation of callus of *N. glauca*. Those factors of *N. glauca* which hinder callus growth, are obviously disturbed by the hybridization with *N. langsdorffii*, so that

N. glauca's potency in forming callus can manifest itself uninhibitedly and thus produce tumours.

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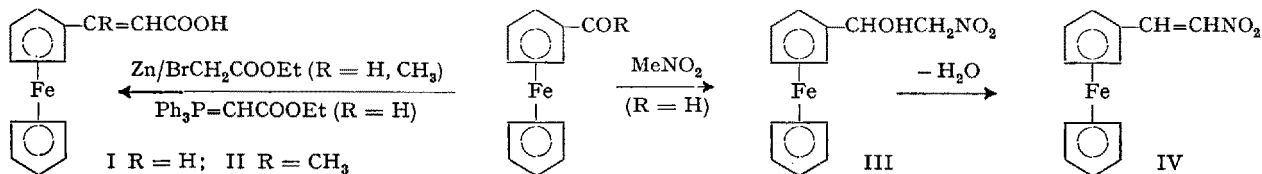
- ¹ Den Herren Prof. Dr. G. DE LATTIN (Zoologisches Institut der Universität des Saarlandes) und Prof. Dr. F. ANDERS (Genetisches Institut der Justus Liebig-Universität, Giessen) bin ich für die Förderung dieser Arbeit zu grösstem Dank verpflichtet.
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Condensation Reactions of Formyl- and Acetyl-Ferrocene

Ferrocene represents a fundamental compound in the recent developments of organometallic chemistry¹; it seems now also to be of interest in the field of practical applications². In this note we wish to report on the preparation of ferrocenylacrylic acids from formyl- and acetylferrocene by means of the Reformatskii and Wittig reactions; as well as on the condensation products of formylferrocene with nitromethane.

β -Ferrocenylacrylic acid (I), which was already obtained by HAUSER and LINDSAY³ on reacting formylferrocene with lithio t-butyl acetate, and by SCHLÖGL⁴ and BROADHEAD et al.⁵ via malonic synthesis, can be also prepared in satisfactory yields from formylferrocene and ethyl bromoacetate under the usual Reformatskii reaction conditions⁶ (1:1 benzene-toluene mixture as solvent; 100% excess of zinc and ethyl bromoacetate). Analogously, acetylferrocene gives the homologous β -ferrocenyl- β -methylacrylic acid (II), not yet described. The intermediate β -hydroxyesters are not isolated, for the reaction mixtures are directly chromatographed on alumina (elution with benzene or respectively 1:2 benzene-petrol ether mixture), where, very probably, dehydration to the corresponding

acrylic esters occurs. Crude acrylic esters (74% yield for ethyl ester of I and 75.5% for ethyl ester of II; the latter a red compound, b.p. 170–175°/1 Torr, m.p. 69–72° (from dil. ethanol); calcd. for $C_{16}H_{18}FeO_2$: C, 64.45; H, 6.08; Fe, 18.73; found: C, 64.31; H, 5.95; Fe, 18.45) are then saponified under alkaline conditions to give the acids I and II, the overall yield being 66% for I and 70% for II (the latter being a red crystalline compound, m.p. 176–177° (dec.) unchanged on sublimation at 140°/0.5 Torr; calcd. for $C_{14}H_{14}FeO_2$: C, 62.25; H, 5.22; Fe, 20.67; found: C, 62.42; H, 5.49; Fe, 20.50).



¹ P. L. PAUSON, in H. ZEISS: *Organometallic Chemistry* Reinhold Publ. Corp., New York 1960, p. 346.

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⁵ G. D. BROADHEAD, J. M. OSGERBY, and P. L. PAUSON, J. chem. Soc., Lond. 1958, 650.

⁶ R. L. SHRINER, 'The Reformatskii Reaction' in *Organic Reactions* (John Wiley & Sons Inc., New York 1947), vol. 1, p. 14.

Using the Wittig reaction⁷, after hydrolysis of the intermediate acrylic ester, *acid* I is obtained in 82% yield from formylferrocene and carbethoxymethylenetriphenylphosphorane (in benzene). We have not been able to carry out a similar reaction on acetylferrocene under the various experimental conditions.

Catalytic hydrogenation of I and II on palladinized charcoal in methyl alcohol or acetic ether leads smoothly to the corresponding saturated acids, that is β -ferrocenyl-propionic^{4,8} and β -ferrocenyl- β -methylpropionic acid; the latter not yet described (orange crystals from ligroine, m.p. 95–96°; calcd. for $C_{14}H_{16}FeO_2$: C, 61.79; H, 5.93; found: C, 61.97; H, 5.77) and also characterized as *ethyl ester* (red-orange oil, b.p. 125–130°/0.1 Torr; calcd. for $C_{16}H_{20}FeO_2$: C, 64.01; H, 6.72; Fe, 18.60; found: C, 64.25; H, 6.48; Fe, 18.59) which is obtained on catalytic reduction of the corresponding acrylic ester.

Aldol condensation between formylferrocene and nitromethane, carried out according to the general method of BOILEAU⁹, furnishes in 30% yield a well crystallized product (bronze crystals from ligroine, m.p. 114–115°) to which, on the basis of elemental analysis and IR-spectrum, the structure of 1-ferrocenyl-2-nitroethyl alcohol (III) is just assigned (calcd. for $C_{12}H_{13}FeNO_3$: C, 52.39; H, 4.76; N, 5.09; found: C, 52.48; H, 5.10; N, 5.10. ν_{NO_2} 1550, ν_{OH} (broad) 3400–3500 cm^{-1} , in Nujol). Moreover, by passing a benzene solution of III through alumina or by warming III in acetic acid, its dehydration product, the

ferrocenyl-2-nitroethylene (IV), is obtained in 32–37% yield (brown needles from *n*-hexane, m.p. 139–140°); structure of the latter being also proved by elemental analysis and IR-spectrum (calcd. for $C_{12}H_{11}FeNO_2$: C, 56.06; H, 4.31; N, 5.45; found: C, 56.36; H, 4.04; N, 5.29. $\nu_{C=C}$ 1625, ν_{NO_2} 1500 cm^{-1} , in Nujol).

Riassunto. Si riferisce sulla applicazione delle reazioni di Reformatskii e di Wittig al formil- e all'acetil-ferrocene per preparare i corrispondenti acidi ferrocenilacrilici. Viene anche descritta la condensazione del formilferrocene col nitrometano.

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Physiological Cell Permeability and Pharmacological Action of DMSO

Among the hypotheses that have been put forward to explain the cell membrane permeability, are some which relate it to its lipids and the corresponding peroxide derivatives.

USSING¹ explains the facts observed by considering that the cell membrane is a *lipoid pore-membrane*, provided with specialized 'carriers' for certain substances.

ALLISON² said: 'We suppose that the hyperoxia increases the permeability of lipoprotein membrane of cells and cell organelles, probably as a consequence of lipid peroxidation'. TAPPEL et al.^{3,4} have already demonstrated release of lysosomal enzymes from rabbit liver homogenates by lipid peroxidation damage. But no explanation was given for the stereochemical aspects of the formation of pores. Years ago, one of us (P.P.M.) proposed a hypothetical geometric mechanism of the micropore formation⁵.

This concept of the mechanism of peroxide permeability is as follows: When an unsaturated fatty acid is autoxidated or peroxidated, a shift of double bonds takes place, together with a modification of the geometrical isomerism. In linoleic acid, for instance, the *cis-cis* structure of the hydrocarbon chain is changed by peroxidation to the *cis-trans* form. This stereoisomeric change produces a specific alteration of the IR-spectra. Some published papers deal with this modification and with its application for the study of lipid peroxide formation^{6–8}.

Such a stearic change may be important, especially in the case where a lipidic layer contains saturated fatty acid together with a variety of the non-saturated type. For

instance, in the simpler case of the copresence of stearic and linoleic acids, peroxidation induces structural change in the linoleic acid, whilst stearic acid remains unaffected. This is shown in Figure 1.

When we studied the pharmacological actions of dimethyl sulphoxide (DMSO) on tissues and upon the increasing cellular permeability, we confirmed for the first time some of the surprising experimental results previously published by JACOB et al.⁹ and STOUGHTON and FRISCH¹⁰.

With regard to the stereometric structure of DMSO, and for the known special bond between S and O in the sulphoxides, we studied the possibility that DMSO might produce some change of the isomeric conformation of linoleic acid and oleic acids.

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