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THE ABSOLUTE CONFIGURATIONS OF (α-KETO- AND α-KETO-β-PHENYL-TETRAMETHYLENE)-CYCLOPENTADIENYLMANGANESE TRICARBONYL

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METALLOCENE derivatives with at least two different substituents in one ring are chiral and thus can be resolved into optical antipodes. This has been demonstrated with many ferrocenes (1-3) and also with benzene-chromium-and cyclopentadienylmanganese tricarbonyl derivatives (4,5).

Having so far determined the absolute configurations of several (α-ketotetramethylene)-ferrocenes (6,7), to which the configurations of some other derivatives could be correlated (3), we have now succeeded in establishing the absolute configurations of 1,2-(α-ketotetramethylene)-cyclopentadienylmanganese tricarbonyl (II) and its phenyl derivative, VII.

The racemic ketone II (m.p.74-75°) was prepared by cyclization of the butyric acid I (m.p.78-80°) with polyphosphoric acid (cf.8). Resolution of II could be achieved via its menthydrazone (cf.1,3) (m.p.197-181°) which, after eight recrystallizations from ethanol, furnished the dextrorotatory diastereomer ($[\alpha]_D$ +645°)*. The latter, by hydrolysis in methanolic phosphoric acid in the presence of formaldehyde (3) gave a dextrorotatory ketone ($[\alpha]_D$ +454°; m.p.68-70°).This ketone,

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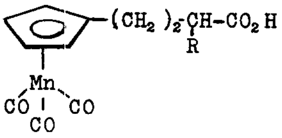
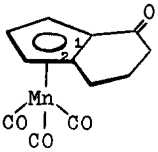
* All rotations in benzene, c = 1.0 - 1.5, t = 18-22°C.

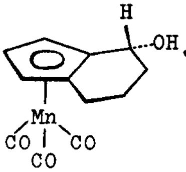
on reduction with $NaBH_4$ afforded a uniform carbinol (thinlayer chromatography (T.L.C.)). The <u>endo</u>-configuration (III) was attributed to this carbinol, taking into consideration a stereoselective reduction (hydride ion attack from the "outside") and on basis of its I.R.spectrum (OH-bands at 3485, 3605 and 3640cm^{-1}, cf.7). Moreover, on $LiAlH_4$-reduction, the <u>exo</u>-carbinol was also formed in small amounts, which, in turn, dehydrated very easily with acid alumina to give the vinyl compound IV. (The <u>endo</u>-carbinol could not be dehydrated under these mild conditions). When, however, (+)-III ($[\alpha]_D$ +22°) was dehydrated by distillation over $KHSO_4$ (0.001mm and 90-100°), a highly laevorotatory vinyl derivative, IV ($[\alpha]_D$ -2040°), was obtained. This result was completely analogous to the result obtained in the ferrocene series, where the ketone, V ($[\alpha]_D$ = +580°), in a similar transformation gave the corresponding vinyl compounds VI ($[\alpha]_D$ -2090°) (3).



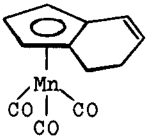
I, R = H
Ia, R = C_6H_5



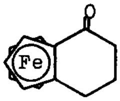
(+)-II



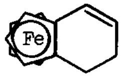
(+)-III



(-)-IV



(+)-V



(-)-VI

In (+)-III, the absolute configuration of the chiral center (the carbinol-C) was elucidated employing Horeau's method of kinetic resolution of racemic phenylbutyric anhydride (9,10).

Since reaction of (+)-III with the anhydride in pyridine furnished a dextrorotatory phenylbutyric acid, the configuration of the carbinol-C was found to be (R). (From 0.85mmoles of III 47% of the ester was obtained; the α_D of the acid was +1.6° (in 2ml of benzene, 1dm-tube) and therefore the optical yield was 51%). Hence, the absolute configuration of the ketone, (+)-II, is as represented in the formula*.

These results are in agreement with those obtained previously for corresponding ferrocene ketones, where the dextrorotatory enantiomers have the 1-(S)-configurations (6,7)*. In addition, both ketones of the same absolute configuration, (+)-II and (+)-V, exhibit a positive circular dichroism in the region of 330 - 350mμ : $\Delta\varepsilon$ +6.9 and +3.9 resp. (7).

Another approach to the problem of correlating the absolute configurations of ketones of the structural type II with the configuration of a chiral center (tetragonal carbon) was accomplished in the following manner.

The α-phenyl derivative, Ia, of the butyric acid I was prepared by acylation of cyclopentadienylmanganese tricarbonyl with phenylsuccinic anhydride followed by Clemmensen-reduction of the resulting mixture of keto acids and chromatographic separation of their methylesters. Both the α- and β-phenylbutyric acids were obtained pure (m.p. 115-117° and 129-130° resp.) and characterized by their mass spectra. The α-phenyl acid Ia

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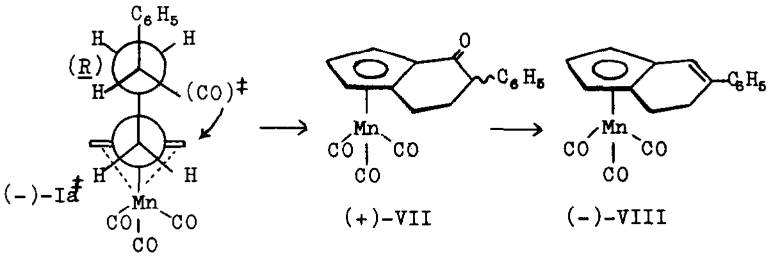
* According to our previous nomenclature suggested for ferrocene-asymmetric compounds and based on the concept of planar chirality of metallocenes (3,6,7), this configuration would be assigned (R). The configuration 1-(S), however, can be assigned, if the recent suggestion is adopted (11), according to which chiral metallocenes may be regarded as compounds having a chiral center (i.e. C_1 in II). (Cf.also 7).

was resolved by recrystallization of its (-)-α-phenylethylamine salt from ethanol (m.p. 144-147°, $[\alpha]_D$ +13.7°, and from the mother liquid: m.p. 144-150°, $[\alpha]_D$ -22°). From these salts the corresponding acids ($[\alpha]_D$ +48° and -41°) were obtained, but apparently not in an optically pure form. They exhibited plain ORD-curves (positive and negative resp.), at least in the region 656 - 486mμ. On the basis of results obtained with an analogous ferrocene derivative (7) and taking into consideration ORD-studies (12), the (S)-configuration could be assigned to the (+)-enantiomer and vice versa.

Cyclization of these acids, Ia, of known configuration, with polyphosphoric acid gave mixtures of the exo- and endo-phenyl ketones, VII, which could be separated by preparative T.L.C. (Attempts to effect cyclization with trifluoroacetic anhydride - T.F.A.A. - failed as in the case of unsubstituted I). The (+)-(S)-acid afforded the laevorotatory ketones ($[\alpha]_D$ -92° and -126°), whereas from the (-)-acid the dextrorotatory compounds ($[\alpha]_D$ +120° and +95°) were obtained. Therefore, the direction of ring closure appears to be governed by the configuration of the chiral center in Ia. For reasons discussed previously for an analogous case in the ferrocene series (7) and based on the preferred conformation of the transition state of the cyclization step ($Ia^{\ddagger}$), the stereoselective ring closure of the (R)-acid, (-)-Ia, would be expected to afford predominantly the 1-(S)-ketone (depicted in the formula VII) and vice versa.

In a fast (and hence largely kinetically controlled) reaction (as with T.F.A.A. in the ferrocene series), the stereo-



selectivity is very high (probably > 95%) (7), whereas in a slow process (treatment with polyphosphoric acid for 20-30 hours at 90°) the enantiomeric ketone also could be formed. Moreover, by the latter reaction, some racemization might also occur at the chiral center. Since the optical purity of the acids, Ia, has not been established so far, nothing can be said concerning the degree of stereoselectivity or the extend of epimerization.

To eliminate the ambiguity with regard to the configuration of the chiral center (Cβ) in VII, the mixtures of (+)-and (-)-ketones were reduced (NaBH$_4$), resp., and the carbinols obtained were dehydrated (KHSO$_4$ in refluxing benzene). Thus, from the mixture of (+)-ketones, a laevorotatory vinyl derivative and from the (-)-ketones a dextrorotatory vinyl derivative was obtained (VIII, $[\alpha]_D$ -81° and +130° resp.). Hence, on account of the stereoselective cyclization mechanism, the chiral center in Ia (of known absolute configuration) has been correlated with the configuration of the optically active metallocenes, VII and VIII. In addition, according to Freudenberg's displacement rule, the remarkable shift of r tation (II → IV, V → VI, VII → VIII; cf.also 7) can b ly regarded as support for the absolute configurat ketones in question (VII). Therefore, here too, as in the ferrocene series, the 1-(*S*)-configurations can be attributed to the dextrorotatory ketones and vice versa.

Acknowledgements

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