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STEREOCHEMISTRY OF METALLOCENES

20 YEARS OF PROGRESS AND RECENT ADVANCES

KARL SCHLÖGL
Institut für Organische Chemie der Universität Wien, A-1090 Wien (Austria)

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Introduction and Scope

Metallocenes – highly aromatic transition metal complexes (such as ferrocene, ruthenocene, cymantrene or benchrotrene) have, since the discovery of the first and still the most important representative, bis(cyclopentadienyl)iron (ferrocene), in 1951 [1], inspired many fields of chemistry and initiated a renaissance of organometallic chemistry. In addition to general and important features such as aromaticity and consequently high reactivity towards electrophilic substitution, as well as several theoretical implications and both synthetic and practical applications, their unique molecular ("sandwich") geometry makes them extremely interesting models for stereochemical research. As a consequence of this structure, in addition to classical positional and geometrical isomerism, there is a novel type of enantiomerism; for instance, unsymmetrically 1,2- or 1,3-homoannularly disubstituted ferrocenes have C_1 symmetry and are therefore chiral. Soon after the first separation of a racemic ferrocene into its enantiomers [2] and the beginning of a continuous study of these phenomena in our laboratory, this "molecular asymmetry" was designated as metallocene (asymmetry) chirality. Thus this term (chirality), introduced into chemistry in 1964 [3], was soon afterwards (1965) applied to the metallocene field [4].

The term metallocene chirality avoids the ambiguity which arises from attempts to specify this new molecular chirality. Although in close cooperation with Prof. Prelog and the late Dr. Cahn we agreed to specify metallocene enantiomers according to the rules for centrochiral compounds [5,6], planarchirality seems to be more appropriate, as shown in the example depicted in Fig. 1. Consequently, several authors still prefer to classify these structures as planarchiral [7].

Nevertheless, and apart from this pure formalism, some hundreds of chiral metallocenes of various types have been prepared and separated into their enantiomers in our laboratory since 1963. Moreover, their enantiomeric purities as well as their relative and absolute configurations and conformations have been established and their chiroptical properties determined. Almost 20 years of research have passed, however, since the first review of this topic (1966) [5,8] and it seems

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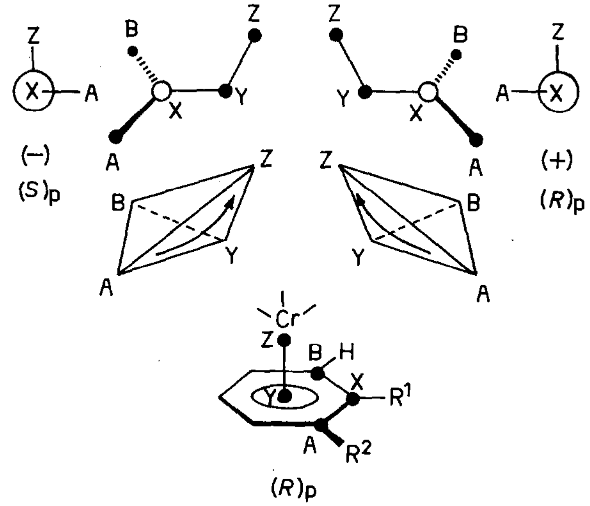


Fig. 1. Planar chirality in metallocenes (Ref. 7).

appropriate to present a more recent, although rather limited and very selective, survey. In the first part of this somewhat personal account some highlights, mainly from our own research, will be presented, and in the second part a more recent topic, the stereochemistry of arenetricarbonylchromium complexes ("benchrotrenes"), will be discussed in more detail. As will be shown, these complexes offer some promising approaches to stereoselective synthesis and novel chiral arenes.

1. Highlights of research on the stereochemistry of metallocenes

In accord with the usual approach in stereochemical research, the following subtopics will be briefly treated:

1.1. Synthesis of chiral metallocenes, especially of novel structures
1.2. Separation of enantiomers, especially by new techniques. Asymmetric synthesis and kinetic resolution
1.3. Enantiomeric purity
1.4. Chiroptical properties - configurational correlation based on Circular Dichroism (CD)
1.5. Relative and absolute configurations and conformations

1.1. Syntheses

Syntheses of unsymmetrically di- or polysubstituted and hence chiral metallocenes – especially in the ferrocene series – require the whole methodology of metallocene chemistry (particularly with regard to synthetic, separation, and analytical aspects, see e.g. refs. 9–11 for ferrocene chemistry). Since unlimited substitutions may give rise to an increasing number of chiral and achiral isomers (see Table 1), selective methods (especially for homoannular substitution) have to be applied: The more important are: Ring closures of suitable starting materials (such as metallocenebutyric acids for metallocene cyclohexenones, cf. **1**) or selective lithiation under the directive influence of suitable hetero atoms (especially of nitrogen in a

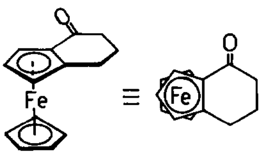
β-position with respect to the ring). These lithiations are also very useful for enantioselective reactions (see section 1.2). Since the range of synthetic procedures is very large, detailed aspects cannot be discussed in this review.

No such problems (such as e.g., directed syntheses of isomers or separation of mixtures) are encountered with arenetricarbonylchromium complexes (benchrotrenes), since these metallocenes are readily accessible from appropriately substituted benzenes and, e.g., hexacarbonylchromium (see also chapter 2).

In addition to these intensively investigated "inherently chiral" metallocenes (cf. **1** for a classical representative), metallocenes may also be part of a more elaborate structure (such as in the allene **4**), or may, by their bulk, impose a stable chiral conformation on an otherwise achiral structure (as e.g. in the tetraferrocenyl ethane **10**).

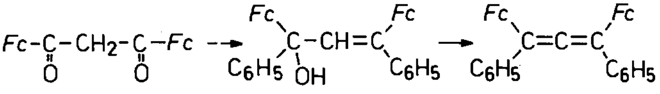
The 1,2-diferrocenyl-1,2-diphenyl allene (**4**) was available by thermal dehydration of **3**, which in turn could be prepared from 1,3-diferrocenyl propanedione-1,3 (**2**) in two steps [12]. Compound **4** could be separated into enantiomers by chromatography on triacetyl cellulose (TAC, see section 1.2).

Titanium-induced reductive coupling of hydroxymethyl arenes is a very versatile method of preparing 1,2-diaryl ethanes [13]. It gives good to excellent yields even with sterically hindered carbinols, such as ferrocenyl t-butyl-, ferrocenyl phenyl- or diferrocenyl-carbinol (**5**, **6**, **7**), furnishing the 1,2-diferrocenyl ethanes **8** and **9**, and the tetraferrocenyl ethane (**10**) in yields of 65, 82 and 82%, respectively. Compound **9** was separated into diastereomers (mesoform and racemate); all the structures were established by X-ray crystallography and ^1H NMR spectroscopy [14]. Compound **10** is of particular interest, since X-ray crystallography revealed a chiral C_2 structure, a conformation resembling a four-bladed propeller (see Fig. 2).

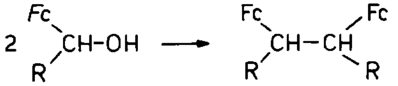


Fc = Ferrocenyl ($C_{10}H_9Fe$)

(+)(1S)-**1**



2 **3** **4**



	R	
5	*t-Bu*	**8**
6	C_6H_5	**9**
7	*Fc*	**10**

For a comprehensive review of the application of arene organo-iron complexes in synthesis (with several stereochemical implications) see Ref. 15.

TABLE 1

ISOMERIC METALLOCENES [5]

Substitution		No. of possible isomers. Total (chiral, achiral)		
Ring 1	Ring 2 [a]	Bis(CP)metallocenes	Cymantrene	Benchrotrene
R,R		3 (0,3)	2 (0,2)	3 (0,3)
R,R^1		3 (2,1)	2 (2,0)	3 (2,1)
R,R,R,		4 (0,4)	4 (0,2)	3 (1,2)
R,R,R,^{1}		8 (3,5)	4 (2,2)	6 (4,2)
R,R^1,R^2		13 (13,0)	6 (6,0)	10 (10,0)
R,R^1	R,R^1	6 (4,2)	–	–
R,R^1,R^2	R,R^1,R^2	13 (8,5)		

[a] Only for bis(cyclopentadienyl)metallocenes (ferrocene, ruthenocene, osmocene).

1.2. Separation of enantiomers

The first resolution of a chiral metallocene, viz. the ferrocene ketone **1**, was achieved in 1959 by crystallisation of the diastereomeric menthydrazones [2]. Subsequently, many other metallocenes were resolved by classical procedures (see also refs. 5,8,10), e.g. 2-methylferrocenecarboxylic acid and related metallocene carboxylic acids via their α-phenethylamine salts. Soon we turned our attention to more recent techniques for separating enantiomers, such as countercurrent distribution (in

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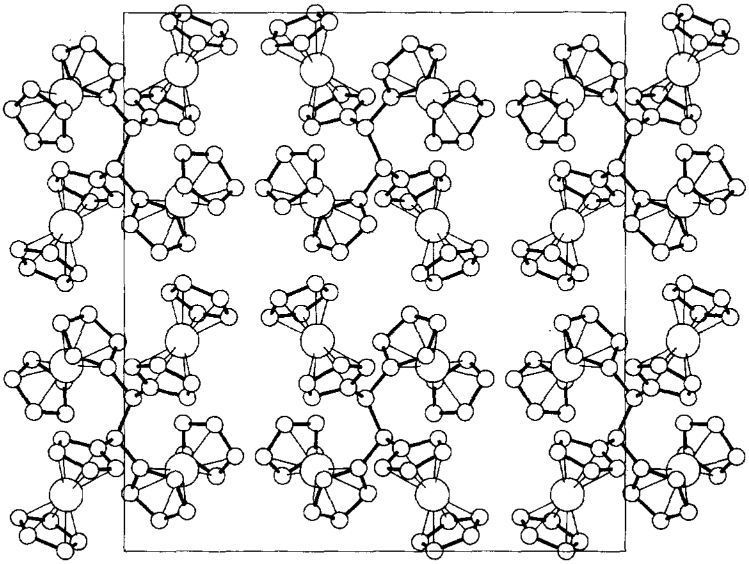
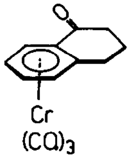
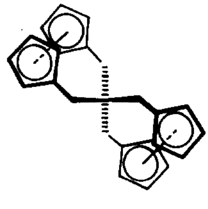


Fig. 2. X-ray crystal structure of tetraferrocenylethane (**10**) [14].

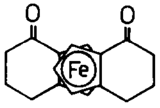
cyclohexane/diethyl tartrate) [16] or chromatography on partially (2.5) acetylated cellulose in benzene. In all these cases (e.g. the ketone **1** and the analogous benchrotrene derivative **11** [17], 2-acetylmethylferrocene [18] or spiro[3]ferrocenophanedione **12** [19], only very unsatisfactory enantiomeric purities (max. 10% e.e.) were obtained.



(+)-**11**



(−)-**12**



(+)-**13**

A breakthrough was achieved by using medium pressure chromatography on microcrystalline triacetylcellulose (TAC) in ethanol at ambient temperatures [20], especially by extending this method into a recycling mode [21]. By this method many axial and planarchiral arenes including ferrocene and especially benzene(tricarbonylchromium) complexes were quantitatively separated into enantiomers. (The latter will be discussed in more detail in chapter 2). Whereas e.g. bis(α-ketotetramethylene)ferrocene (**13**) required 16 cycles [21], the above mentioned diferrocenyl diphenylallene (**4**) was completely resolved in one run (Fig. 3) [20]. The procedure not only gives both enantiomers in semi-preparative amounts, sufficient for the determination of chiroptical properties (see section 1.4) and further transformations (e.g. for configurational correlations), but also enantiomeric purities can be readily established (see 1.3). Since this chromatographic separation may be employed under rather mild condition (e.g. at lower temperatures) it is particularly suitable for (labile) tricarbonylchromium complexes (see chapter 2).

Kinetic resolutions (although rather inefficient with regard to the preparation of pure enantiomers) proved to be a rather versatile method for deducing the absolute chiralities of 2-substituted metallocenecarboxylic acids (see chapter 1.5). Thus if the

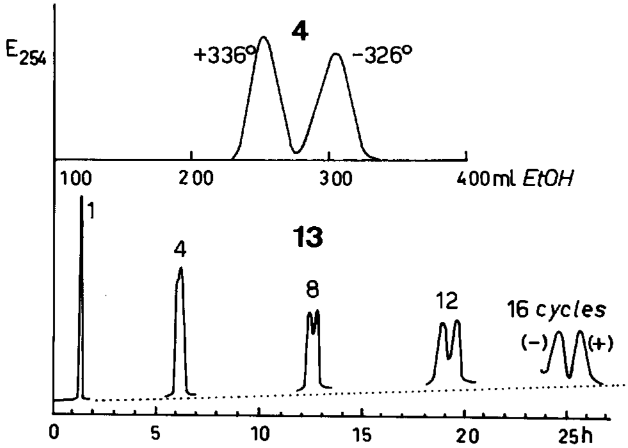


Fig. 3. Separation of chiral ferrocene derivatives **4** and **13** into enantiomers on triacetylcellulose (Refs. 20, 21).

anhydrides of these carboxylic acids are treated with (−)-phenethylamine, an excess of optically active acid is formed (with an e.e. of 3–13%) [8]. In all cases these acids have the same metallocene chirality (1*S*) (cf. refs. 5,6 for its definition; see also 1.5). By analogy, this method was extended to topologically related structures, such as e.g. [2.2]paracyclophane-4-carboxylic acid, where it led to the first assignment of absolute configuration to a cyclophane – i.e. a planarchiral compound [7].

Horeau's method (kinetic resolution of α-phenylbutyric anhydride with an optically active carbinol, or vice versa) was not only very important for the first assignment of absolute chirality to a metallocene derivative (viz. **1**) but also successfully employed for the resolution of the above-mentioned spirobi[3]ferrocenophanedione (**12**) via its diol (with an e.e. of 33% [19]).

The regio and stereospecific lithiation of suitable ferrocenes (as already mentioned in section 1.1) may be applied to the asymmetric syntheses of ferrocenes. Thus whereas asymmetric lithiation of isopropylferrocene with a n-butyl-Li-sparteine complex gave only rather low enantiomeric purities (e.e. ca. 3%) of 1′,3-disubstituted isopropylferrocenes, (*S*)-(+)-(*N*-α-pipecolylmethyl)ferrocene could (after *ortho*-lithiation) be transformed into various optically active 1,2-disubstituted ferrocenes with up to 94% e.e. [23].

Optically active *N*,*N*-dimethyl-1-ferrocenylethylamine when *o*-lithiated also gives rise to high asymmetric induction, furnishing one of the two possible diastereomers in 96% excess. Since both Li and the dimethylamino group (via quaternary salts) can be easily substituted, a wide variety of optically active ferrocenes (with known chirality, see section 1.5.) is accessible [24]. Thus in these procedures the stereoselective influence of a chiral centre is used to create (planar) metallocene chirality.

Optically active 2-ferrocenylamines (with a chiral center) were also employed as chiral templates in an asymmetric peptide synthesis (which proceeds via the co-called 4-component condensation of isonitriles) with very high stereoselectivity [25].

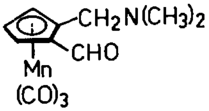
Several functionalized chiral ferrocenylphosphines accessible by the asymmetric lithiation mentioned above, are excellent ligands for rhodium-catalyzed asymmetric hydrogenation with e.e. up to 95% [26].

Like asymmetric lithiation, asymmetric (*ortho*)palladation is also possible, and may lead to optically active transformation products. Thus on the one hand optically active *N*,*N*-dimethyl-1-ferrocenyl ethylamine (vide supra) can be *ortho*-palladated and then transformed into a variety of homoannularly disubstituted derivatives with moderate enantiomeric excess [27], on the other hand, achiral *N*,*N*′-dimethylaminomethyl ferrocene can be cyclopalladated in the presence of *N*-acetyl-valine, with an e.e. of 79%, and the intermediate again transformed into several ferrocenes [28]. This approach was also applied to dimethylamino[3]ferrocenophane; thus with Na_2PdCl_4 in the presence of *N*-acetyl-L-leucine an e.e. of 84% was achieved [29]).

Asymmetrically induced, *ortho*-directed metallation of ferrocenyl alkyl-ethers, however, proceeds only with low regiospecifity. Thus, lithiation followed by reaction with benzophenone of (+)-1-ferrocenyl-1-methoxy-ethane gives a mixture of all three possible isomers (1-, 3- and 1′-) [30].

The diastereoselectivity of reactions of 2- or 3-methyl acyl cymantrenes (as chiral substrates) with either borohydride or Grignard reagents depends, as might be expected, not only on the position of the methyl group (*o*- or *m*- to acyl) but also on the alkyl group R in acyl and/or in the Grignard reagent, and the diastereomeric excess ranges from 10 to 100% [31].

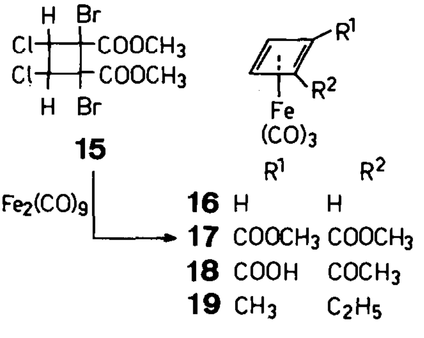
1-(N,N-dimethylaminomethyl)-2-formylcymantrene (**14**) has been resolved into enantiomers through an intermediate formation of diastereomeric complexes with dipeptides (Ala-Ala, Ala-Gly and Gly-Ala) [32].



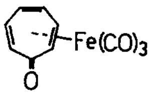
(+)-**14**

Cyclobutadiene can be stabilized as its tricarbonyliron complex (**16**), thereby opening the way to a variety of compounds and interesting reactions [33]. This simple "metallocene" becomes chiral (C_1) upon unsymmetrical disubstitution. The racemic 2-acetyl-1-carboxylic acid (**18**) is accessible by complexation of dibromo-dichloro-cyclobutane-biscarboxylicacid dimethylester (**15**) with $Fe_2(CO)_9$ and transformation of the resulting bis-ester complex **17** by a series of reactions. **18** was resolved via its quinine salts, giving (−)-**18** ($[\alpha]_D - 102°$ in ethanol); its enantiomeric purity was established by using a chiral shift reagent. Subsequent reduction of (−)-**18** furnished the optically active ethylmethyl derivative **19** ($[\alpha]_D - 20°$ in chloroform), which can be decomplexed with Ce^{IV} sals to give optically active cyclobutenes [35].

The tropone tricarbonyliron complex **20** is chiral because of the puckered ring. It was resolved by HPLC on a chiralpack column, and its racemization barrier found to be 108 kJ mol^{-1} [36].



	R^1	R^2
16	H	H
17	$COOCH_3$	$COOCH_3$
18	COOH	$COCH_3$
19	CH_3	C_2H_5



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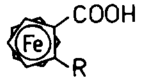
1.3. *Enantiomeric purities*

The enantiomeric purity (e.e.) of 2-methyl ferrocenecarboxylic acid (**21**) was established as early as 1968 by two independent methods, namely isotope dilution employing the $^2H_1$-methyl derivative and an NMR method (based on the relative intensities of the diastereomeric protons in the α-phenethylamides of **21** [37]). The two methods gave consistent results, thus confirming the maximum rotation of **21** as $[\alpha]_D$ 54 ± 2° (in ethanol). Since this key substance (**21**) has been directly or indirectly correlated to more than 150 optically active ferrocenes, the e.e. of all these compounds had been established.

A further approach to the e.e. of chiral carboxylic acids, including the above-mentioned **21** and 2-phenyl ferrocenecarboxylic acid (**22**), is based on HPLC of their diastereomeric α-naphthylethylamides [38]. Furthermore, the previously mentioned



(+)-**21** CH_3
(−)-**22** C_6H_5

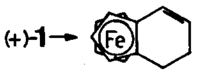
stereorelating metallation (cf. 1.2) of α-dimethylamino alkylferrocenes is also an excellent tool for establishing enantiomeric purities, since the e.e of the starting amine(s) is known [39].

Undoubtedly, however, chromatographic separation of enantiomers on TAC (see section 1.2. and chapter 2) offers the simplest and most reliable method for determing e.e. provided complete separation of the enantiomers is accomplished [20,21].

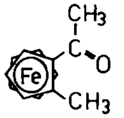
1.4. Chiroptical properties

The chiroptical properties of (optically active) metallocenes, especially their CD spectra, have been extensively studied, mainly with regard to configurational and conformational correlations. The long-wavelength metallocene transition (presumably involving more or less pure *d–d* transitions at the metal [40]) at 440, 350, 330 and 390 nm for ferrocene, ruthenocene, cymantrene and benchrotrene (with bathochromic shifts, if appropriate substituents are present [8]) exhibit corresponding Cotton effects in the ORD and CD spectra, when these inherently achiral chromophores are chirally disturbed [41]. From the relation between rotational and dipole strength of the "ferrocene band" it was concluded that this transition (around 440 nm) is both electrically and magnetically forbidden. On the basis of these assumptions, empirically relations between optically rotations and configurations (based on the known absolute chirality of the ketone **1**) were established and conclusions drawn about the origin of the optical activity of several ferrocenes [42].

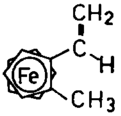
Chiroptical properties and their temperature dependence are powerful tools for establishing the absolute chiralities as well as the preferred conformations of acyl and vinylmetallocenes (such as **23–25**).



(−)-**23**



(−)-**24**

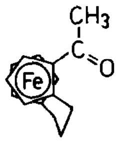


(+)-**25**

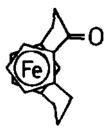
All metalloceno cyclohexenones having the absolute configuration (1*S*), as in (+)-**1** (see section 1.5. for the determination of this configuration), exhibit positive Cotton effects in the region of the metallocene chromophore and have positive rotations at 589 nm. Opposite signs are observed for the corresponding bridged vinyl derivatives, such as **23**.

Whereas in these bridged derivatives the chromophores are fixed within the total molecular geometry due to the more or less rigid conformation, and consequently the chiroptical properties are temperature independent [8], these properties for the corresponding "open" compounds (such as e.g. 2-methyl acetyl or vinylferrocene, **24**, **25**) are temperature-dependent due to conformational equilibria (with $\Delta G^{\neq}$-values of 2.5–3.4 kJ mol^{-1}). The optical rotations and the Cotton effects have signs opposite to those of the cyclic compounds of the same chirality.

Similar behaviour was observed for chiral ferrocenophanes such as **26** or **27** [43].

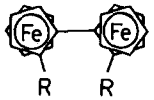


(–)-**26**



(–)-**27**

For 2,2′-disubstituted biferrocenyls, two diastereomers are possible; e.g. of the bis(dimethylaminomethyl)-biferrocenyls one (**28**) was resolvable, and thus was the racemate (the other the mesoform) [44]. In these compounds two elements of chirality are present, since in addition to the metallocene chirality a torsion around the biferrocenyl bond is also possible (representing an element of axial chirality). Whereas the racemate is twisted, with a torsional angle of around 30°, the mesoform is coplanar. Consequently the optically active dimethyl derivative **29** (with a specific rotation of of 1150°) exhibits a temperature-dependent CD spectrum; from this a conformational equilibrium ratio of ca. 85/15 at 20°C was deduced [44].



(+)-**28** $CH_2N(CH_3)_2$
(+)-**29** CH_3

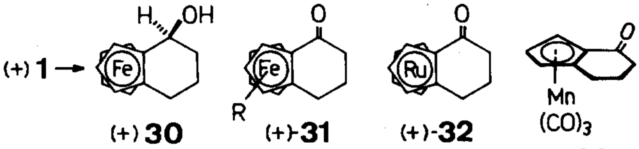
A much more detailed investigation of such phenomena was carried out with biphenyltricarbonylchromium complexes (see chapter 2, especially section 2.3).

1.5. Relative and absolute configuration

The key substance for establishing the absolute configuration of ferrocenes, and hence of other chiral metallocenes, was the cyclic ketone **1**, which was also the first metallocene resolved into enantiomers (cf. section 1.2) [2]. This and related compounds also provided the first examples of application of Horeau's ingenious method outside Professor Horeau's laboratory [45]. This technique, based on the kinetic resolution of racemic α-phenylbutyric anhydride has been described in detail elsewhere [22], along with its application to problems of metallocene chirality. As an illustration, the dextro-rotatory ketone (+)-**1** was unambiguously correlated with the dextro-rotatory *exo*-carbinol **30**, in which the configuration of the chiral center was determined as (*S*) by Horeau's method [45]. This established the absolute chirality of (+)-**1** as shown in the formula [i.e. (1*S*)].

From chiroptical comparison (cf. 1.4) and by application of the classical Freudenberg's "shift-principle" (Verschiebungssatz) the configurations of related metallocenes ketones (**11** and **31–33**) were also deduced [5]. All dextro-rotatory ketones have positive optical rotations (at 589 nm), and after appropriate transformations give rise to highly laevo-rotatory metallocenocyclohexadienes (e.g. **23**). These ketones in turn had been unambiguously correlated to many other optically active metallocenes, particularly in the ferrocene field (where more than 200 derivatives, especially

1,2 and 1,3-disubstituted ferrocenes) had been inter-correlated [5,8,10,11].



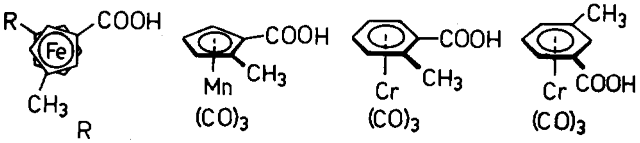
(+)1 → (+)30 (+)-31 (+)-32 (+)-33.

Another useful approach to the determination of the absolute configurations of 2-substituted metallocenecarboxylic acids, the starting materials for many transformations, involves kinetic resolution of the racemic anhydrides with optically active α-phenethylamine [8]. It gave results in agreement with those presented above (see also section 1.2)

More tentative conclusions about the configuration of unsymmetrically disubstituted ferrocenes had been drawn from the results of socalled "stereoregulating syntheses", in which the (known) configuration of a chiral center in a substituent is correlated with the sense of metallocene chirality in the (diastereoselectively) reaction product [39,48].

These early results (the first absolute configuration of a metallocene was known even in 1964) [45] raised the problem of the configurational notation in the metallocene field according to the CIP-system (centro vs. planar chirality). This was briefly mentioned in the introduction of this article and was the main reason why we prefer to use the term "metallocene chirality" [4].

From 1967 onwards all these results on the configuration of optically active metallocenes were unambiguously confirmed by the Bijvoet X-ray technique, which was applied to the optically active methylmetallocenecarboxylic acids **34**–**37** [46].



(+)-34 CH_3 (+)-35 (+)-36 (+)-37
(+)-38 H

The last "missing link" in the chain of configurational correlations was the chemical correlation between (+)-**34** and (+)-**38** performed in 1971 [47] (some doubt having been raised about the applicability of Horeau's method and some of our previous correlations by chiroptical methods [48]). It confirmed all the previous results and conclusions.

These results were and are the basis for all stereochemical research in the metallocene field. They are also of utmost importance for the more recent investigations on tricarbonylchromium complexes (benchrotrenes) discussed in more detail in the next chapter.

2. Stereochemistry of arenetricarbonylchromium and related complexes

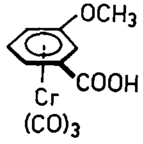
2.1. Introduction and general remarks

Arenetricarbonylchromium complexes (sometimes also referred to as "benchrotrenes") occupy a special position amongst metallocenes (see p. 221) for several important reasons. Thus they are usually rather easily made from corresponding arenes by reaction with hexacarbonylchromium (or triamino-tricarbonylchromium), thus avoiding the problem of formation of isomers (cf. 1.1), and they are coloured, easily to separate and purify (e.g. by chromatography), and are very often nicely crystalline and therefore suitable for X-ray structure analysis. Moreover, and this is of great importance in the use of benchrotrenes, introduction of $Cr(CO)_3$ onto an arene not only changes (sometimes dramatically) the reactivity of the arene moiety (mainly by electron-withdrawal from the σ- and π-framework of the arene) [50], but, which is even important from a stereochemical point of view, also decreases the symmetry, e.g. from C_s to C_1, therefore leading to chiral structures (see e.g. **11** as example). Finally, and equally important, $Cr(CO)_3$ can be removed again under rather mild conditions (e.g. photochemically at low temperatures), thereby restoring an arene which might have been stereoselectively modified at the "benchrotrene" stage. Tricarbonylchromium can thus be regarded and employed as a very efficient and versatile stereoselective protecting group [51].

Stereochemical research in this field has four main aspects:

2.1.1. Study of "simple" metallocene chirality, as outlined and discussed in some detail in chapter 1 (involving, for instance, optical resolution, determination of enantiomeric purities, chiroptical properties, absolute chiralities etc.).

m-Methoxybenchrotrenecarboxylic acid (**39**), the first optically active representative in this series, was obtained in 1963 [49]; the first absolute configuration [of the corresponding methyl derivative (−)-**37**] was established in 1969 [46]; both carboxylic acids had been correlated with many other optically active benchrotrenes [17,52]. The Bijvoet method confirmed our previous conclusions about the absolute chiralities of benchrotrene derivatives (see sub-section 1.5)



(+)-**39**

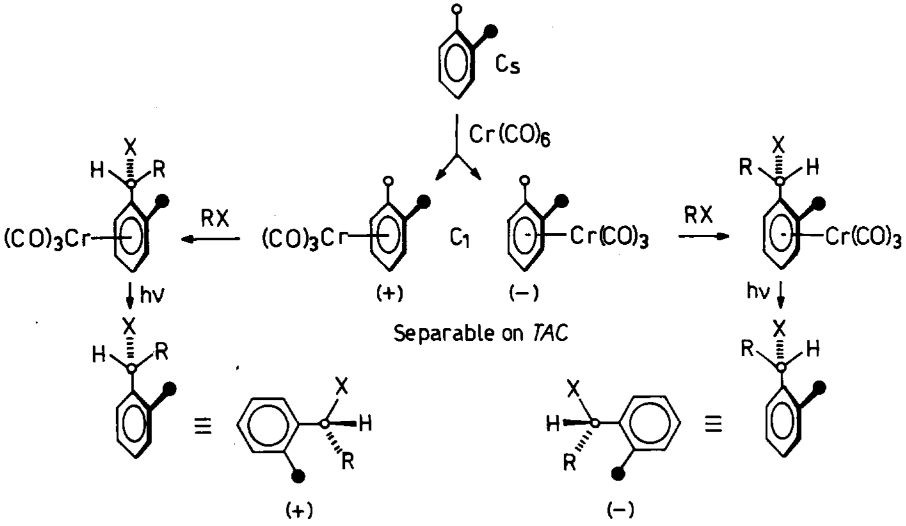
2.1.2. Since the two "faces" of the arene plane are distinguished from each other upon introduction of a $Cr(CO)_3$-unit, the latter can give rise to diastereo- or enantio-selective reactions, as has been demonstrated in several cases (vide infra). Thus, after removal of the $Cr(CO)_3$, stereoisomeric arenes which are otherwise unavailable or only accessibly with difficulty, can be prepared.

2.1.3. The tricarbonylchromium moiety [or appropriately modified ligands, such as $Cr(CO)_2Ph_3$ or $Cr(CO)_2CS$] can influence rotational and inversion barriers, e.g. in biphenyl or diarylmethane derivatives.

2.1.4. In heavily substituted arenes (such as hexaethylbenzene), the rotation of $Cr(CO)_3$ or related ligands itself may be restricted around the Cr–arene bond, and can give rise to what may be called a "chromium carousel".

2.2. Stereoselective syntheses

The directing influence of the tricarbonylchromium moiety in stereoselective syntheses has been utilized for more than a decade. The preferred *exo*-attack (from the "outside") of a nucleophile onto a carbonyl group attached to a benchrotrene



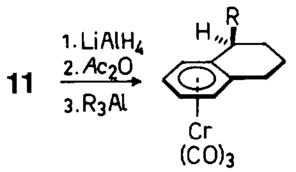
SCHEME 1

unit is the significant feature of these stereoselective reactions in which new chiral centers may be created and thus otherwise unaccessible optically active benzene derivatives may be prepared. This approach is schematically outlined in Scheme 1.

The degree of diastereoselectivity varies, of course, both with the position of the C=O group (either adjacent to a substituent or preferably confined in a ring and consequently almost coplanar) and with the nature of the nucleophile.

Early examples of this technique are reactions of 2- or 3-substituted formylbenchrotrenes with KBH_4 or Grignard reagents [53] and especially the syntheses of optically active 2-substituted indanones, indanols, tetralones and tetralols of known absolute configuration with e.e. up to 95–100% [54]. The intermediate complexes can be used for a stereoselective synthesis of optically active benzobicyclic ring systems with predetermined absolute chiralities [55].

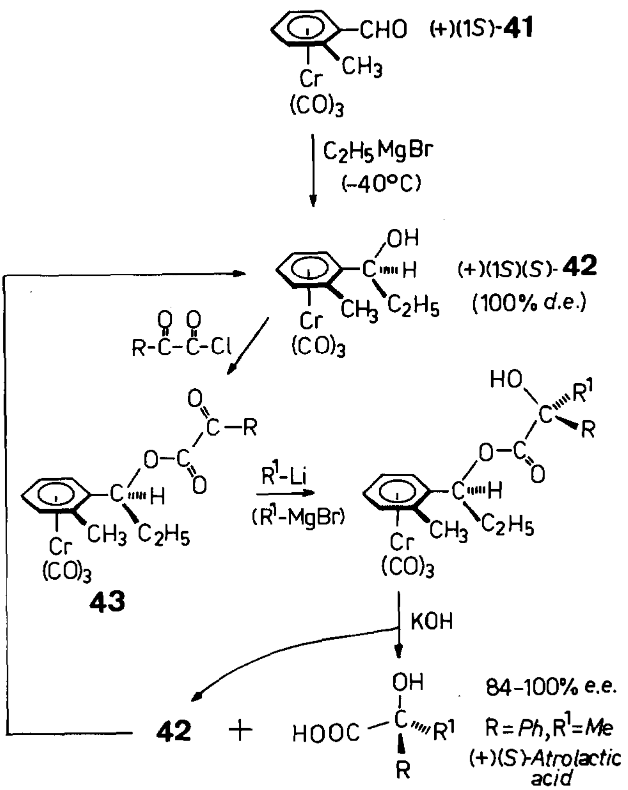
Exo-alkyltricarbonylchromium complexes (e.g. **40**) can be obtained in high yields if benzylic acetates or corresponding hydroxy derivatives of bridged benchrotrenes (such as **11**) are alkylated with trialkyl-Al or diethyl-Zn [56].



40

On the other hand, of course, complexation with $Cr(CO)_6$ can also proceed with a high degree of diastereoselectivity, if appropriate ligands are employed [57].

In 2-methyl formylbenchrotrene [**41**, readily available in both enantiomeric forms via reaction with (S)-(−)-5-(α-phenylethyl)semioxamazide] the asymmetric induction can be increased to 84–100% diastereomeric excess by treatment with perfluoro-



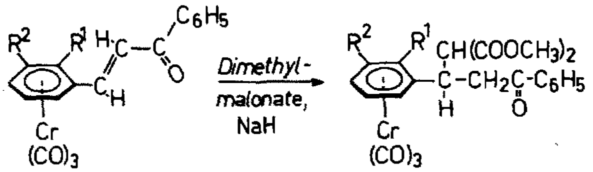
SCHEME 2. Ref. 58.

ethyl-Li or EtMgBr at low temperatures (−40 to −100°C) [58]. Transformation of the optically active carbinols **42** into ketoesters **43** and further reaction with CH_3MgBr followed by hydrolysis yield optically active atrolactic acid with an e.e. of 82%, thus providing a new and advanced version of the well known Prelog-synthesis (cf. Scheme 2).

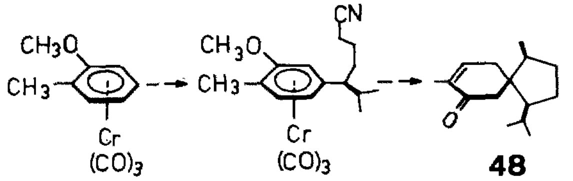
Complexation of benzylic alcohols increases the stability of the corresponding carbenium ions, and allows syntheses of amines or ethers with total stereochemical control, again with exclusive nucleophilic *exo*-attack [59].

Another type of high and remarkable diastereoselectivity was observed in the Michael addition of dimethyl malonate to chalcones **44** derived from 2- and 3-substituted formylbenchrotrenes (such as **41**). Optical resolution of these C_1 complexes was achieved by chromatography on triacetylcellulose (see sub-section 1.2) and their absolute chiralities deduced from CD-comparison (cf. 1.4). Shift experiments with $Eu(fod)_3$ using the ^1H NMR spectra of the Michael adducts **45** revealed that *ortho*-substitution (either with Me or OMe) leads to 100% diastereoselectivity, whereas substituents in *meta*-position decrease the stereoselectivity to 18 and 14%, respectively. Chromatography of **44** on TAC confirmed these results [60]. Considerations of the geometry of the transition state(s) of the addition permitted a (tentative) assignment of the absolute configuration of the newly created chiral center(s) in **45** [60].

Stereoselective cyclization of benchrotrene derivatives is also a very useful tool for creating spirocyclic ring structures with a high degree of stereoselectivity. Thus, the complex **46** has been used as a starting compound for the synthesis of acorenone (**48**) via the key intermediate **47** [61].



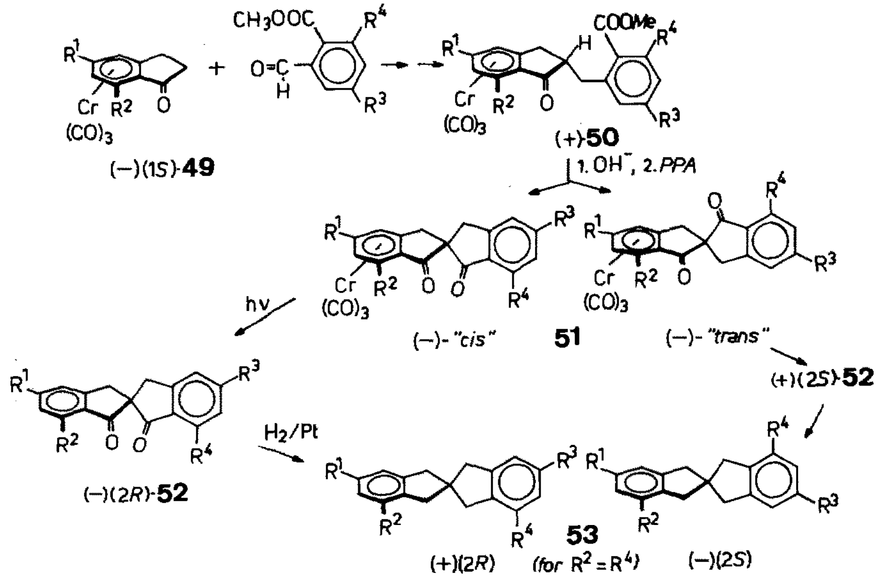
44 (R^1, R^2= H,CH_3,OCH_3,Cl, NMe_2) **45**



46 **47** **48**

The above mentioned optically active indanone-$Cr(CO)_3$ complexes (**49**, of known absolute chirality and enantiomeric purity) were used, in a series of straightforward reactions, to give 2,2′-spirobiindanones (**52**), again of known chirality and e.e. [62]. These can be reduced to chiral 2,2′-spirobiindanes (**53**), which are very useful models for testing the algebraic theory of chirality functions [63]. (It should be noted that attempts to apply this theory to optically active ferrocenes were rather unsuccessful [64]).

The following Scheme 3 outlines the critical steps in and the general strategy for the stereo-controlled synthesis of 2,2′-spirobiindanes.



SCHEME 3. Ref. 62.

TABLE 2

MAXIMUM POSSIBLE NUMBER OF MONO- AND BIS-TRICARBONYLCHROMIUM COMPLEXES, WHICH CAN BE DISTINGUISHED IN A CHIRAL ENVIRONMENT [65]

	Symmetry of ligand						
	C_1				C_2		
	1 [b]	2 [b]			2 [b]		
	Mono	Mono	*trans*-Bis	*cis*-Bis	Mono	*trans*-Bis	*cis*-Bis
Isomers [a]	4	8	4	4	4	4	2
Residual stereoisomers	2	4	2	2	2	2	–

[a] No. of isomers with a rigid skeleton. [b] No. of aryls.

2.3. *Torsional-isomeric tricarbonylchromium complexes*

Complexation of torsional-isomeric arenes with C_1 or C_2 symmetry may result in so called "residual stereoisomers", if (i) the complexation site does not lie within the C_2 axis and (ii) the ligand is converted into its enantiomer by the torsion around the central bond. The number of possible distinguishable isomeric complexes depends on the symmetry of the skeleton, on the number of complexation sites, the number of metal ligands (e.g. $Cr(CO)_3$) and the number of possibilities for isomerizing the skeleton [65]. The maximum numbers of complexes can be calculated; they are summarized in Table 2.

2.3.1. *Biphenyl(tricarbonylchromium) complexes*

Torsional isomerism of biaryls is a classical example of axial chirality (see however Ref. 66 for a discussion on this nomenclature). This type of atropisomerism has been intensively investigated mainly by Mislow and his group [67].

Introduction of one or two tricarbonylchromium moieties into the biphenyl system (by choosing the appropriate stoichiometry in the complexation reaction and/or by chromatographic separation of the complexes) affords complexes with two elements of chirality, namely, the metallocene chirality of the benchrotrene part [the enantiomers being designated as $(R)_m$ and $(S)_m$] and the axial (or biphenyl) chirality of the ligand designated as $(R)_a$ and $(S)_a$ [51,68]. In order to apply a terminology, consistent with the term metallocene chirality (and in accord with Prof. Mislow's recent proposal [66]), we use below the term "biphenyl chirality" and use the symbols $(R)_b$ and $(S)_b$ (whereas in our papers "a" was used for axial chirality) [51,68].

This combination gives rise to four stereoisomers; comprising two diastereomers, each of which is a pair of enantiomers; this situation is depicted schematically in Fig. 4, and summarized as follows:

Mono(tricarbonylchromium)complexes

$(R)_m\text{-}(S)_b \leftrightarrows (R)_m\text{-}(R)_b$

$(S)_m\text{-}(R)_b \leftrightarrows (S)_m\text{-}(S)_b$

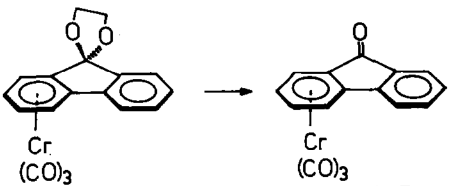
Bis(tricarbonylchromium)complexes

$(R)_m\text{-}(S)_b\text{-}(R)_m \leftrightarrows (R)_m\text{-}(R)_b\text{-}(R)_m$

$(S)_m\text{-}(R)_b\text{-}(S)_m \leftrightarrows (S)_m\text{-}(S)_b\text{-}(S)_m$

Whereas a possible equilibrium (as indicated by the arrows) depends both on the rotational barrier around the biphenyl bond [whereby the biphenyl chirality is reversed, e.g. $(R)_b \rightleftharpoons (S)_b$] and on the energy differences between the diastereomers (especially in the case of the bis-complexes, see Fig. 4 and vide infra), there is no change in the metallocene chirality, i.e. no racemization, at least under the various types of reaction conditions employed: $(R)_m \not\rightleftharpoons (S)_m$. Apart from some decomplexation [69], such racemization of benchrotrenes has never been observed.

As an experimental proof, optically active fluorenone tricarbonylchromium (**55**, accessible either by asymmetric reduction of racemic **55** with a chiral $LiAlH_4$-complex with an e.e. of 80% [70] or by chromatography of the corresponding 1,3-dioxolane **54** on triacetylcellulose [20]) was treated under various conditions: It is optically stable in several solvents at elevated temperatures (e.g. isooctane, 3 d at 80°C) [70] and so no intramolecular shift of $Cr(CO)_3$ occurs (see also Ref. 71).



(+)-**54** (+)-**55**

Figure 4 shows that for the bis-complex one of the two diastereomers (the *exo*) should be favoured because of the steric interactions of the large residues R and $Cr(CO)_3$ in the other (the *endo*, shown underneath). From similar considerations, and on the basis of chromatographic and NMR results (including the lanthanide-induced-shift (LIS) technique) a combination involving two unlike (ul) [72] metallocene chiralities [e.g. $(R)_m$-$(S)_b$-$(S)_m$] could be excluded. Subsequent X-ray structure analyses revealed, at least for two key compounds ($R = R' = COOCH_3$ and $R = COOCH_3$, R' = protected CHO) that only one pair of enantiomers is, in fact, present, namely the one with all four groups (e.g. two tricarbonylchromium and two esters) pointing towards four different quadrants in a Newman-projection and with an torsional angle of ca. 100° (see Fig. 5) [73,74].

Many mono- and bis-complexes of diphenic acid derivatives (e.g. of its dimethylester) were prepared and intercorrelated by straightforward reactions [51,68].

At the beginning of this work, optical resolution of these complexes caused some problems, since classical methods (such as crystallization of α-phenethylamine salts) as well as asymmetric syntheses (e.g. reduction of an aldehyde with a chiral $LiAlH_4$ complex [51]) were rather unsatisfactory. Later, chromatography on TAC (especially by the recycling technique, see section 1.2) proved to be the method of choice for the separation of enantiomers of these (sometimes unstable) complexes [20,21,75,76]. (Cf. also the discussion below on complexes of bridged biphenyls; Fig. 6).

The chiroptical properties of most of the optically active complexes were recorded, and some tentative conclusions as to the absolute chiralities drawn on the basis of CD-comparison with "simple" benchrotrenes of known chirality [51] which had been established previously by the Bijvoet-technique (see 1.5). Subsequently, these results were unambiguously confirmed by a combination of methods, as outlined for the $Cr(CO)_3$-complex **57** of 6,6′-dimethyl diphenicacid dimethylester **56** in Scheme 4.

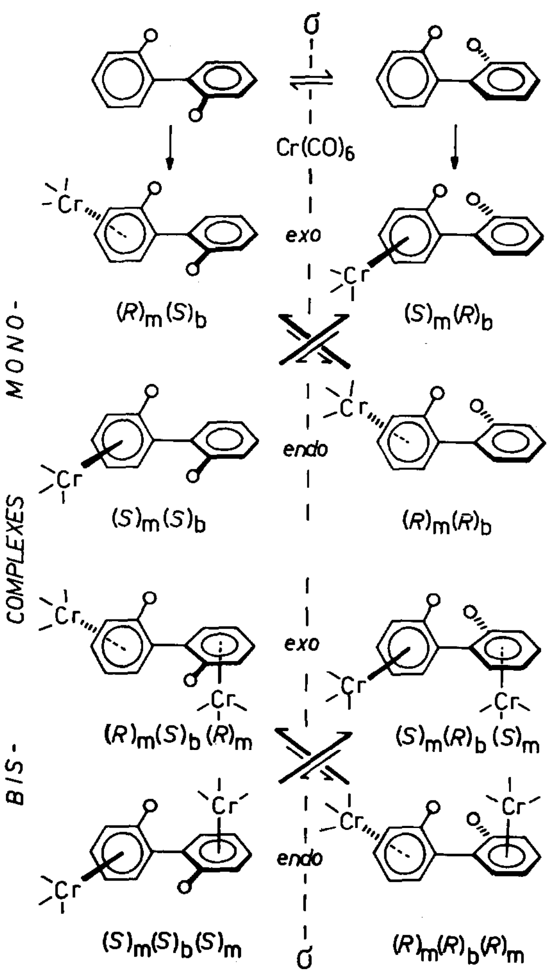


Fig. 4. Stereoisomerism in tricarbonylchromium complexes of *o,o'*-disubstituted biphenyls (Refs. 51, 68),

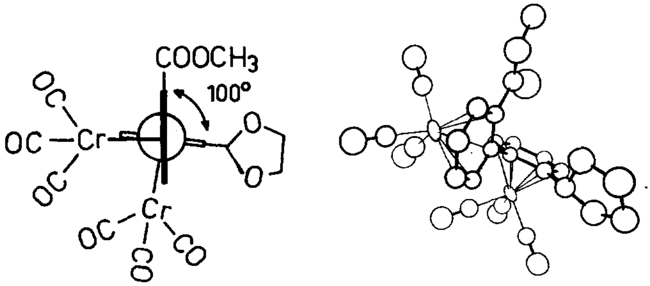
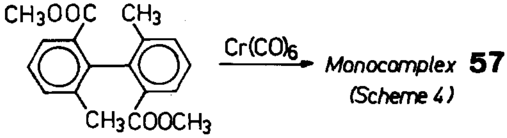
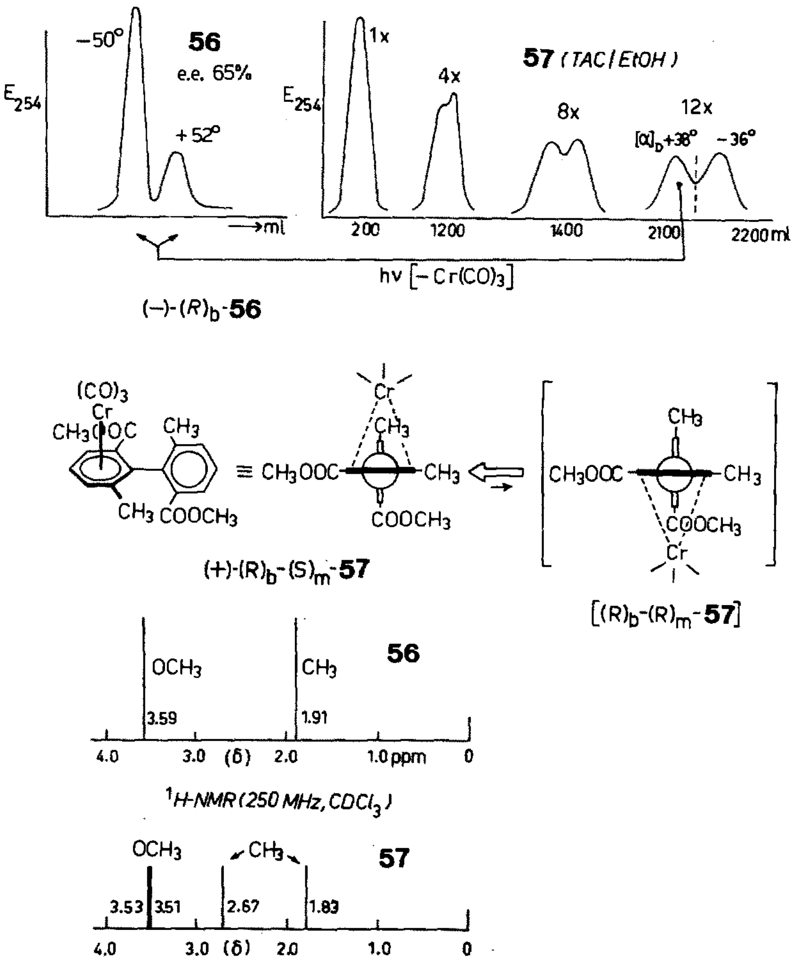


Fig. 5. X-ray crystal structure of a bis(tricarbonylchromium)biphenyl complex (Ref. 73).



56



SCHEME 4. Ref. 76.

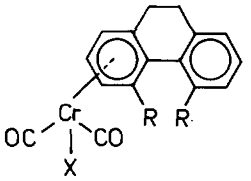
The complex **57** was partially resolved on TAC after 12 cycles. The dextro-rotatory fraction was decomplexed and the (−)-ligand **56** quantitatively separated into enantiomers on TAC, revealing an e.e. of 65%. The configuration of **56** was known to be (−)-$(R)_b$ [67]. The metallocene chirality of **57** was established by ^{1}H NMR spectroscopy both of the ligand and the complex; since in **57** one of the methyl signals is shifted downfield, it seems evident that the complex has a structure with $Cr(CO)_3$ on "the same side" as the methyl, thus acting as an internal shift reagent for the latter. These results confirm the "ul" chirality of **57** as (−)-$(R)_b$-$(S)_m$ (and hence of several bis-complexes which had been chemically correlated with **57** [51]).

Tricarbonylchromium complexes of bridged biphenyls, in addition to the results on "open" biphenyls, show several new and promising aspects e.g. with regard to torsional barriers and to modifications of the complex (vide infra).

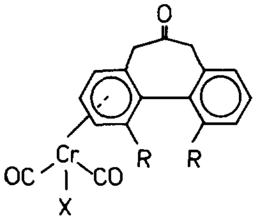
Figure 6 shows the general situation in a schematic representation. Again there are two diastereomers, "*exo*" and "*endo*" with respect to the bridge to $Cr(CO)_3$, which can be interconverted by torsion rotation the central biphenyl bond, changing thereby $(R)_b$ into $(S)_b$ and vice versa [75,77].

This possibility is of course absent, if the bridged ligand is (almost) coplanar, as in fluorene, fluorenone, diphenyl oxide or carbazole. The mono tricarbonylchromium complexes of these ligands were resolved on TAC, and conclusions about their absolute chiralities were drawn from their chiroptical properties [76].

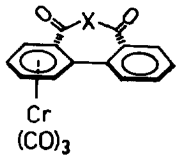
Other bridged biphenyls studied included dihydrophenanthrene, the cyclic ketone (cf. **64** for its complex), their 6,6′-dimethyl derivatives [77] as well as diphenic acid anhydride [78] or imide [76] and the lactone **72** and its bis-complex **73** [68,78].



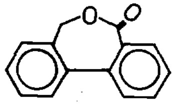
	R	X
58	H	CO
59	CH_3	CO
60	H	CS
61	CH_3	CS
62	H	PPh_3
63	CH_3	PPh_3



	R	X
64	H	CO
65	CH_3	CO
66	H	CS
67	CH_3	CS
68	H	PPh_3
69	CH_3	PPh_3



	X
(+)-**70**	O
(+)-**71**	NH



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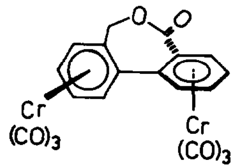


(−)-**73**

Table 3 summarizes the complexation results, the torsional angles and the rotational barriers for both the ligands and the complexes **58**, **59**, **64**, **65**, as well as the absolute chiralities of the latter.

Whereas in the unmethylated biphenyls (**58**, **64**) the *exo*-isomers predominate by more than 90%, the dimethylated ligands yield an almost equal mixture of the *exo*- and *endo*-isomers.

Although it is possible to separate all four possible stereoisomers in one run on TAC (which gives satisfactory results in some cases, cf. Fig. 7 for **65**) [75], it is advisable to perform this separation in two steps, first into the stable "metallocene enantiomers" on TAC (necessarily in the ratio of 1/1), and subsequently into *exo-endo* isomers by medium pressure chromatography (in variable ratios, see Table

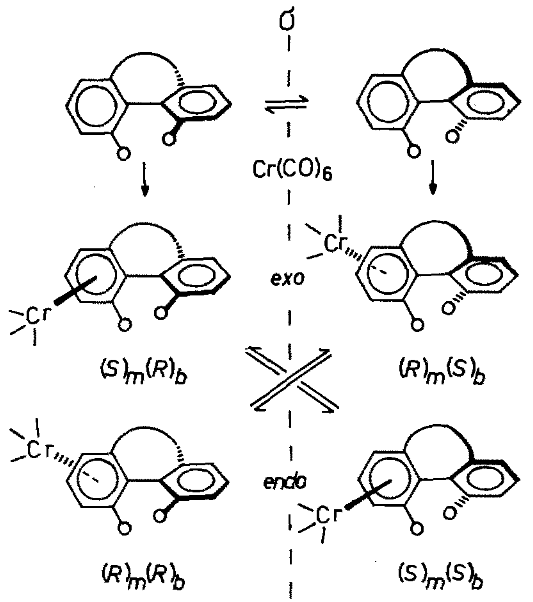


Fig. 6. Stereoisomerism in tricarbonylchromium complexes of bridged biphenyls. *Exo* and *endo* refers to bridge/Cr(CO)$_3$. o = H or CH$_3$. (Refs. 75, 77).

3; at temperatures which depend on the rotational barriers, this separation can be performed down to −20°C).

The configurational assignment (*exo, endo*) as well as the *exo/endo* ratios were based on ^{1}H NMR data (especially for the bridge proton signals [77]). These ratios can easily be explained by steric interactions between methyl- and tricarbonylchromium in the *exo* form of **59** and **65**, which are absent in the unmethylated complexes **58** and **64**, therefore favouring the *exo*-isomers [77].

LIS-NMR-experiments revealed that complexation does not significantly change the torsional angles [77].

The torsional barriers were determined both by temperature dependent ^{1}H NMR spectroscopy and by racemization studies with the optically active complexes, easily accessible by chromatography on TAC in ethanol (vide supra and Fig. 7 for **65**) [75].

CD-kinetics revealed a barrier of $\Delta G^{\neq}$ 90 kJ mol^{-1} for the *exo* $\rightleftharpoons$ *endo* conversion in **59**, compared with that of 97 kJ mol^{-1} for the ligand. In this case at least, complexation decreases the inversion barrier! [75].

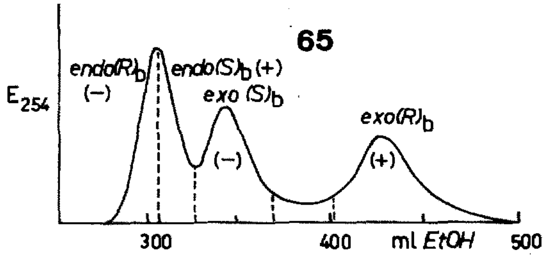


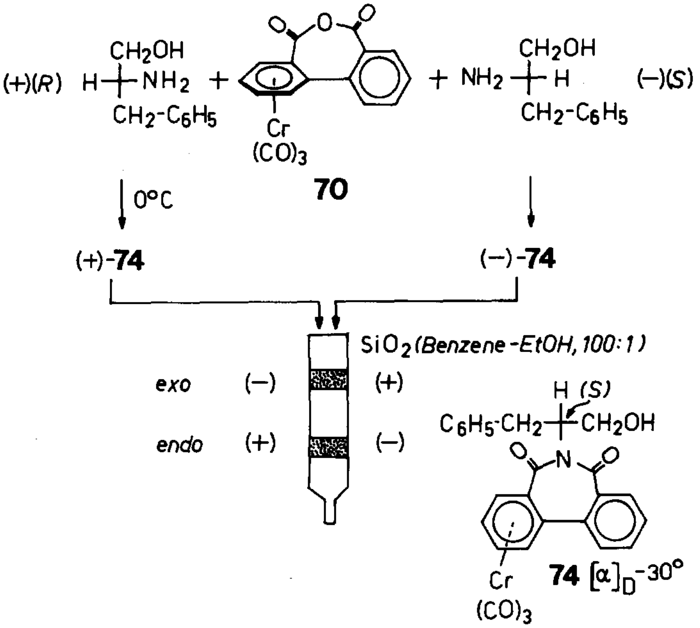
Fig. 7. Separation of four stereoisomers of the complex **65** on triacetylcellulose in ethanol (Ref. 75).

TABLE 3

COMPLEXATION OF BRIDGED BIPHENYLS [75,77,80]

Mono-complex		$-CH_2CH_2-$bridge						$-CH_2-CO-CH_2-$bridge					
No.	$Cr(CO)_2X$	R = H			R = CH_3			R = H			R = CH_3		
		exo/endo	$\Delta G^{\neq}$ [a]	ϕ [b]	*exo/endo*	$\Delta G^{\neq}$	ϕ	*exo/endo*	$\Delta G^{\neq}$	ϕ	*exo/endo*	$\Delta G^{\neq}$	ϕ
–	(Ligand)	–	~18	15°	–	98 $(+)\text{-}(S)_b$	30°	–	71	50°	–	150 $(-)(S)_b$	52°
58,59 **64,65**	$Cr(CO)_3$	~100/0 $(-)(R)_b(S)_m$ [c]	~18	15°	50/50 $(-)\text{-}(S)_b(R)_m$	90	30°	> 90/10 $(-)\text{-}(S)_b(R)_m$	64	50°	50/50 $(-)(S)_b(R)_m$	–	52°
60,61 **66,67**	$Cr(CO)_2CS$	–	–	–	50/50	92	–	88/12	92	–	–	–	–
62,63 **68,69**	$Cr(CO)_2PPh_3$	–	–	–	98/2	88 [d]	–	~ 90/10	–	–	50/50 [e]	–	–

[a] Torsional barrier (kJ mol^{-1}), round figures. [b] Torsional angle. [c] Chiralities for *exo*-isomers (for *endo* cf. Ref. 75). [d] For a possible mechanism see discussion on p. 242.
[e] No equilibrium attainable.



SCHEME 5. Ref. 78.

The absolute chiralities of the complexes **58**, **59**, **64**, **65** were established by decomplexation experiments (vide supra) and by optical comparison [75].

The previously mentioned monocomplex **70** of diphenic anhydride (made from diphenicacid-$Cr(CO)_3$ and cyclohexyl carbodiimide as the almost pure *exo*-isomer [78]) can be used for a rather surprising, highly stereoselective reaction (see Scheme 5 and Fig. 8).

Treatment of **70** with either (+)-(*R*)- or (−)-(*S*)-phenylalaninol affords (in contrast to the ligand, even under mild conditions) a (+)- or (−)-imide ($[\alpha]_D$ $\pm 30°$), each of which was separated by medium-pressure chromatography into two stereoisomers (ratios ca. 1/1; $[\alpha]_D$ ca. + and $-145°$), with CD curves showing mirror image effects in the benchrotrene region, but identical effects in the biphenyl region (see Fig. 8). Photochemical decomplexation of each pair of these imide complexes (or of the mixture) gave the same optically stable (pure) ligand: Dextrorotatory (+18°) from the (+)-imide and vice versa. It follows that the (+)- and (−)-imide complexes have opposite biphenyl chiralities, and can be separated by chromatography into *exo*- and *endo*-isomers (with unlike metallocene chiralities). Thus (+)-(*R*)-aminoalcohol induces (*R*)-biphenyl chirality and vice versa. Application of the excitation model of coupled oscillators to the ligand established the biphenyl chirality as $(+)\text{-}(R)_b$ and $(-)\text{-}(S)_b$, resp. In connection with the known centro chirality of the aminoalcohol and on basis of chiroptical comparison the assignment of the imide complexes is $(+)\text{-}(R)_m\text{-}(S)_b\text{-}(S)_c$, and vice versa for (−)-**74** [78].

Photochemical decomplexation of the bis-complex **73** of the lactone **72** at ca. −60°C gave the optically active ligand; according to its low-temperature CD-spectrum (where it is optically stable for at least 1 h at −50°C) it has a half time of

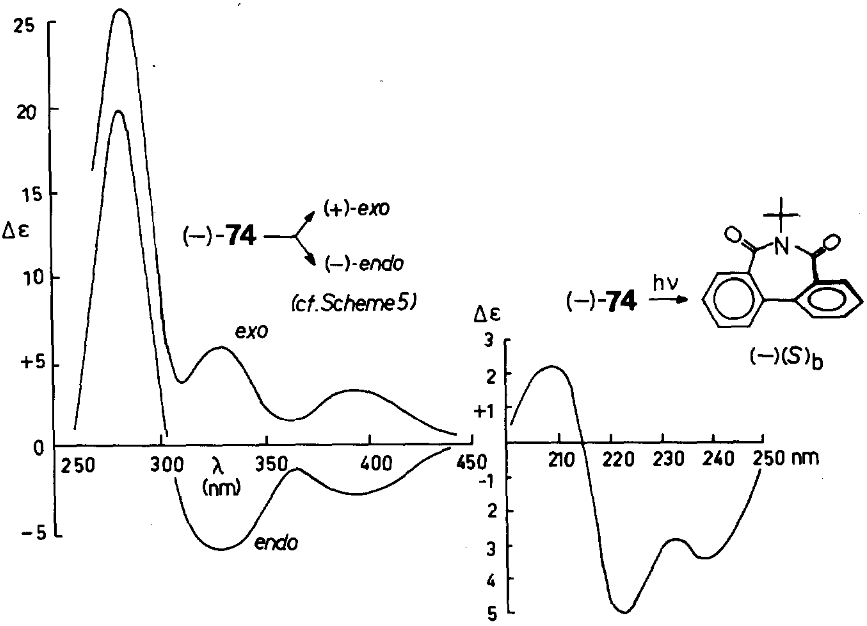


Fig. 8. CD spectra (in ethanol) of the stereoisomeric imide complexes **74** and of the (−)-ligand obtained from (−)-**74** (Ref. 78).

racemization of ca. 10 min at −20°C [78]. This is in good agreement with a recently determined rotational barrier for the lactone of $\Delta G^{\neq} = 65$ kJ mol^{-1} [79].

These results represent the first example of the preparation of an optically labile biphenyl via the tricarbonylchromium approach. Its extension to other arenes is being investigated (see also 2.3.3).

2.3.2. Biphenyl(dicarbonyl-triphenylphosphine and -thiocarbonylchromium) complexes

In order to study a possible influence on the rotational barriers and/or on the isomeric (*exo/endo*) ratios, one of the CO groups in the mono-$Cr(CO)_3$ complexes of bridged biphenyls (cf. the preceding section 2.3.1) was replaced by either CS or triphenylphosphine, by a photochemical reaction with CS_2 in the presence of *cis*-cyclooctene or THF or with PPh_3 in benzene. The PPh_3 complexes **62**, **63**, **68**, **69** are chemically rather labile, and therefore more difficult to investigate than the CS complexes **60**, **61**, **66**, **67** [80].

It may be noted that the influence on the activation energy in an alkylation reaction of the arene moiety decreases in the order [50]: $Cr(CO)_2CS > Cr(CO)_3 >$ (arene) $> Cr(CO)_2PPh_3$

Like the $Cr(CO)_3$ complexes of bridged biphenyls (see 2.3.1), these modified complexes were also separated into their stereoisomers first by chromatography on TAC in ethanol (into stable enantiomers) and subsequently by (low temperature) chromatography on silica gel [80]. The isomeric ratios were established from both chromatographic and spectroscopic data, and the rotational (*exo/endo*) barriers deduced from kinetic studies by ^{1}H NMR spectroscopy and/or circular dichroism. NMR spectroscopy was also employed for assigning the *exo*- or *endo*-conformations

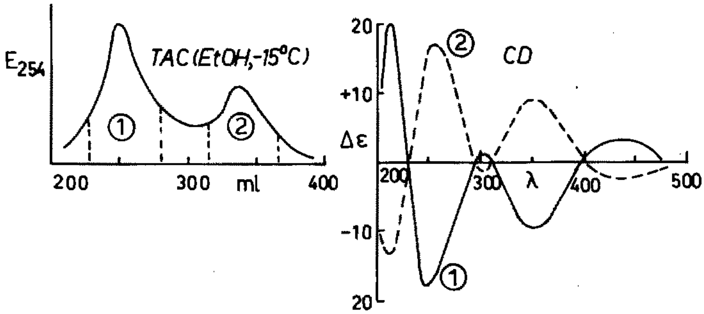


Fig. 9. Optical resolution on triacetylcellulose and CD spectra (in ethanol) of the dicarbonyl-triphenylphosphine complex **63** (Ref. 80).

(configurations). The results obtained so far, together with those for the $Cr(CO)_3$ complexes of bridged biphenyls are summarized in Table 3. (Blanks mean that the values have not yet been determined) [80].

Whereas the $\Delta G^{\neq}$-values differ only slightly (if at all) from those of the unmodified complexes, there is a significant difference for the *exo/endo* ratio of the dimethyldihydrophenanthrene complexes, probably due to the bulky PPh_3 moiety. This complex **63** exhibits some remarkable features. Thus according to ^1H NMR and chromatography (on silica gel, even at $-20°C$) it is an almost pure ($>98\%$) *exo*-isomer. (It should be noted that the *exo/endo* mixture of the corresponding tricarbonylchromium complex is easily separable! [77]). However, **63** can be separated on TAC into two enantiomers (for their CD-curves see Fig. 9, in which the Cotton effect around 350 nm can be attributed to the new type of chirality - vide infra). These enantiomers racemize, with a $\Delta G^{\neq}$ of ca. 87 kJ mol^{-1}, thereby excluding the possibility that they are metallocene enantiomers (cf. section 2.3.1. for the stability of "benchrotrene chirality"). It may be assumed, however, that we are dealing with a novel type of "propeller chirality" [81] (designated as "x"), in which the PPh_3 moiety may play an important role.

However, all the known (similar) propellers have significantly lower barriers. In our case, the rotation may be influenced (with an increased barrier) by the inversion barrier of the biphenyl system. This situation may be tentatively represented as follows [80]:

$$(R)_m\text{-}(S)_b\text{-}(R)_x \rightleftharpoons (R)_m\text{-}(S)_b\text{-}(S)_x$$

$$(S)_m\text{-}(R)_b\text{-}(S)_x \rightleftharpoons (S)_m\text{-}(R)_b\text{-}(R)_x$$

This phenomenon is now under investigation.

2.3.3. Tricarbonylchromium complexes of diarylmethanes and related compounds

Hindered rotation in mono-$Cr(CO)_3$ complexes of *ortho*-methylated diphenylmethanes and diphenyl ketones was first studied by Trahanovsky et al. [82] and the barriers for the methanes found by NMR spectroscopy to be $\Delta G^{\neq}$ 60 kJ and those for the ketones ca. 81 kJ mol^{-1}. The authors explained these results in terms of a cogwheel mechanism (for similar, more recent results see Refs. 83, 84).

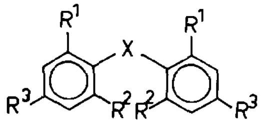
We extended these investigations to a systematic study of several (higher) *o,o'*-dialkylated diarylmethanes, 1,1'-diarylethanes and -ketones and their mono- and

TABLE 4

ROTATIONAL BARRIERS (kJ mol^{-1}; IN ROUND FIGURES) FOR *o*,*o*′-DISUBSTITUTED DIARYL-METHANES, -KETONES AND -ETHANES AND THEIR MONO- AND BIS-Cr(CO)$_3$ COMPLEXES

o-Substituents	Barriers								
	Methane			Ketone			Ethane		
	Ligand	Mono	Bis	Ligand	Mono	Bis	Ligand	Mono	Bis
CH_3, CH_3	**75** 55	60		**76** ~ 50	83	81	**77** 60	65	63
CH_3, C_2H_5	**78** 69	66	63	**79** 51	84	82	**80** 69	65	63
CH_3, $C(CH_3)_3$	**81**			**82** ~ 80	> 100		**83**		

bis-complexes [85]. NMR kinetics (supported by force field calculations) revealed that for the Me-Et derivatives mono-complexation lowers the rotational barriers in the methanes and ethanes (**78**, **80**) by about 4 kJ, whereas in the ketone **79** the barrier is raised by as much as ca. 30 kJ. The barriers of the bis-complexes are 2–3 kJ lower than those of the mono-complexes. The results are summarized in Table 4.

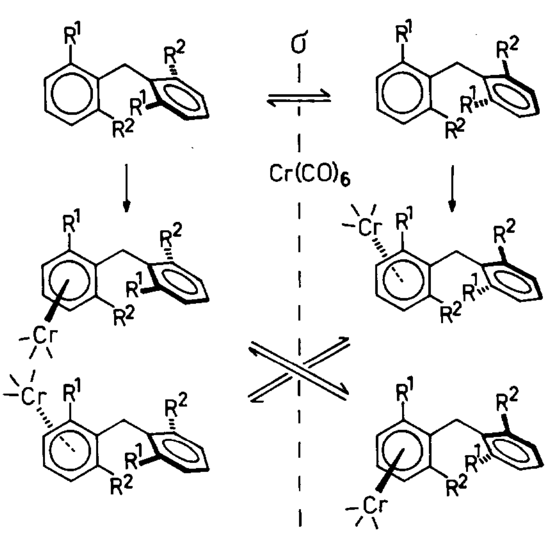


	R^1	R^2	R^3	X
75	CH_3	CH_3	CH_3O	CH_2
76	CH_3	CH_3	CH_3O	C=O
77	CH_3	CH_3	CH_3O	CH-CH_3
78	CH_3	C_2H_5	H	CH_2
79	CH_3	C_2H_5	H	C=O
80	CH_3	C_2H_5	H	CH-CH_3
81	CH_3	*t-Bu*	CH_3	CH_2
82	CH_3	*t-Bu*	CH_3	C=O
83	CH_3	*t-Bu*	CH_3	CH-CH_3

and Mono-and Bis- Cr(CO)$_3$ Complexes

As shown schematically in Scheme 6, complexation of chiral diaryls leads to diastereomers which are interconverted by internal rotation. When for instance, a diarylmethane (Scheme 6, $R^1 \neq R^2$) reacts with $Cr(CO)_6$, two pairs of diastereomers are feasible, two of which are interconvertible by rotation. This equilibrium as well as the height of the barrier for interconversion determine whether tricarbonylchromium can be used as a auxiliary group for optical resolution (see also p. 233 and Ref. 65). In such unsymmetrically *o*,*o*′-disubstituted diaryls, correlated rotation gives rise to two chiral isomers with C_2 symmetry, whereas uncorrelated movement gives only one, an achiral, isomer.

It should be noted that so far only a few such optically active propellers have been described, e.g. diarylacetic acids [86], tris(pentachlorophenyl)amine [87] or a 1,1,2,2-tetrakisarylethane [88].



SCHEME 6. Ref. 85.

The results with bis(2-t-butyl-4,6-dimethylphenyl)ketone (**82**) are especially remarkable [85]. Monocomplexation of this ketone (which shows a very simple NMR spectrum due to a low rotational barrier of ca. 80 kJ mol^{-1}, see Fig. 10) leads to a mixture which can be separated (by chromatography on silica gel in ligroin/ethylacetate) into **a** and **b** in the ratio ~ 4/1; these isomers are stable at room temperature. The configurational (= conformational) assignment shown in Fig. 10 is based on the very strong splitting of the t-butyl signal in the ^1H NMR spectrum of isomer **b** (which must therefore have the t-butyl group on the same side as $Cr(CO)_3$ and is thus thermodynamically less stable than **a**, which is formed in excess). Both isomers **a** and **b** can be decomplexed by irradiation (**a** faster than **b**!) to a single compound, namely the original ligand, as shown by its NMR spectrum (cf. Fig. 10). These results represent an interesting example of stable torsional-isomers = diastereomers.

2.4. The tricarbonylchromium and related carousels

This interesting phenomenon of hindered rotation around the (formal) arene–Cr bond with further ligands, such as CO, CS or PPh_3 attached to chromium was investigated in some detail, mainly by two research groups (those of K. Mislow and M.J. McGlinchey). Only some of the more important results are briefly mentioned here.

Hexaethylbenzene (HEB) proved to be an excellent model for studying the static and dynamic stereochemistry of chromium (and related) complexes. Depending on the type of ligands attached to Cr (vide supra), different arrangements of the ethyl groups are feasible; they are schematically depicted in Fig. 11.

According to X-ray studies, in HEB and in its $Cr(CO)_3$ complex, the methyl groups project alternatively above and below the benzene plane (stereoisomer **a** in Fig. 11 with D_{3d} and C_3 symmetry, respectively [89]). In the complex, three of the ethyl groups are eclipsed by three CO groups. The triphenylphosphine derivative, however, in the solid state adopts structure **b**, with 4 methyl groups "up" and 2

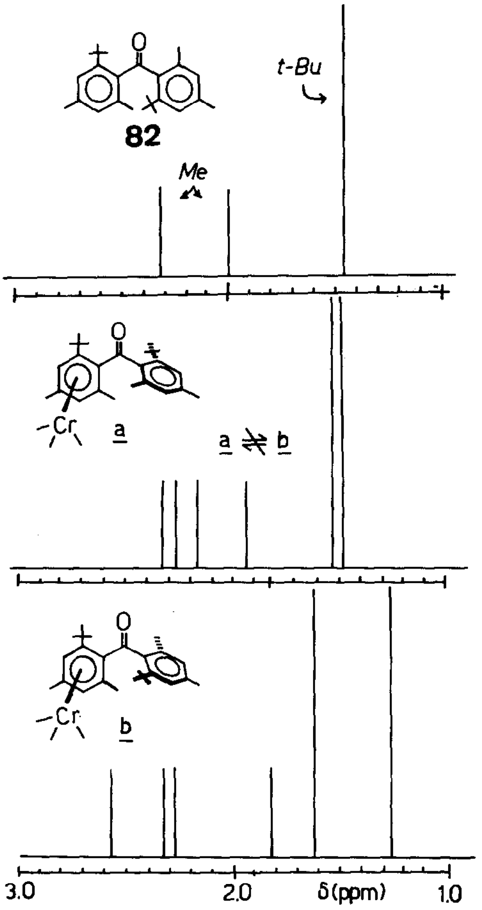


Fig. 10. 250 MHz-^{1}NMR-spectrum of the diarylketone **82** and its mono(tricarbonylchromium)complex (in $CDCl_3$) (Ref. 85).

"down". In solution, according to NMR studies, there is an equilibrium between the four favoured stereoisomers **a–d** [90]; it is not necessary to assume that rotation about the Cr–HEB is slowed down.

This problem of the chromium carousel is the subject of some controversy between the two research groups mentioned above, especially in the case of the

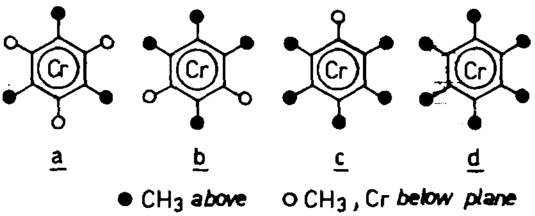


Fig. 11. Schematic representation of preferred stereoisomers **a–d** of hexaethylbenzene (HEB) complexes (Ref. 90).

$Cr(CO)_2CS$ complex. In the crystal this compound has structure **a** (Fig. 11). The results of variable temperature ^1H and ^{13}C NMR studies were interpreted by Mislow and Hunter [91] in terms of restricted ethyl rotation, with the stereoisomer **b** predominant in solution, and so a tripodal rotation would not be required to explain these results. McGlinchey et al., however, postulate such a slowed tripodal rotation (i.e. a chromium carousel - on the NMR timescale) with **a** (having C_3 symmetry) being the predominant stereoisomer both in the solid state and in solution [92]. For the effect of complexation on the stereodynamics of higher substituted benzenes see Ref. 83.

Acknowledgements

Since the beginning of our work on the stereochemistry of metallocenes (inspired in part by the tenure of a British Council fellowship at the University of Manchester 1954/55) I had the good fortune to have many enthusiastic and very able collaborators who shared my fascination with this field of research. Their names are to be found in the list of references. Without them the work outlined in this survey would not have been possible.

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