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L-MENTHYL ESTERS OF α-BROMOMERCURYPHENYLACETIC ACID: DIASTEREOISOMERIC PURITY, SYMMETRIZATION AND REVERSE REACTION. A STEREOCHEMICAL REINVESTIGATION *

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Summary

A new experimental procedure for isolation of L-menthyl esters of α-bromo mercuryphenylacetic acid as almost pure diastereoisomers I, $[\alpha]_D^{20}$ −132° and II, $[\alpha]_D^{20}$ −18° is reported. Related dialkylmercuries R_2Hg III, $[\alpha]_D^{20}$ −32°, and IV, $[\alpha]_D^{20}$ −5°, were prepared. Absolute configurations of benzylic chiral carbon are assigned from ORD curves (*R* for I, *S* for II). S_E2 type cleavage of III and IV with mercuric bromide affords I and II, respectively, with expected retention of configuration. ^1H NMR spectra (180 MHz) permit distinction between diastereomers I and II and quantitative evaluation of diastereomeric purity. A remarkable influence of solvent on the R_2Hg spectra was observed.

Introduction

For the stereochemical study of the platinum(0) carbenoid insertion into a carbon—mercury bond [1] optically active dialkylmercury compounds with the metal attached to a chiral centre were needed. To date, only a few appropriate organomercurials are known. The diastereomeric L-menthyl esters of α-bromomercuryphenylacetic acid were chosen. These compounds had served as useful models at the very beginning of the investigation of electrophilic substitution mechanisms [2—4]. At that time, however, no method was available to evaluate the purity of these diastereomeric organomercurials. In addition, the absolute configurations of the chiral benzylic carbons remained unknown. In this connection, we had to undertake the reinvestigation reported here.

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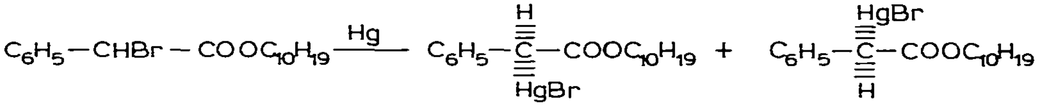
* Dedicated to Prof. G.A. Razuvaev on the occasion of his 85th birthday on August 23rd, 1980.

Results and discussion

Separation of diastereomeric organomercuric bromides

The mixture of diastereomeric organomercuric bromides I and II was obtained according to Reutov et al. [2] by shaking L-menthyl α-bromophenylacetates with metallic mercury. The crude product of this homolytic process exhibited, after the unreacted bromide was removed with hexane, specific rotation within the range $[\alpha]_D^{20}$ -- 72 to —76°, no matter which diastereomer of the α-bromoesters [5] or their mixture was reacted. The following new procedure for their separation gave good reproducibility. The more soluble diastereomer II was extracted from the crude solid with a hexane-benzene mixture wherefrom it crystallized. The diastereomer I could be obtained by the rapid crystallization of the residue from hot methanol avoiding the possible epimerization. In fact, we observed that the epimerization did occur in boiling methanol during several hours without any added base. Previously, McKenzie and Smith [6] had studied the epimerization of menthyl and bornyl esters of α-bromo- and α-chlorophenylacetic acids in methanol in the presence of alkali. The diastereomeric ratio attained in each case was 53 : 47.



$$C_6H_5{-}CHBr{-}COOC_{10}H_{19} \xrightarrow{Hg} C_6H_5{-}\overset{H}{\underset{HgBr}{C}}{-}COOC_{10}H_{19} + C_6H_5{-}\overset{HgBr}{\underset{H}{C}}{-}COOC_{10}H_{19}$$

In the work reported here we were able to obtain the specific rotation (in benzene) $[\alpha]_D^{20}$ —132° for diastereomer I (crystallized from isopropanol) and $[\alpha]_D^{20}$ — 18° for II which should be compared with the values of —95° and —49°, respectively, as reported previously [2]. Determination of the diastereomeric purity using ^{1}H NMR spectroscopy (vide infra) revealed that diastereomer I was nearly pure and diastereomer II was of about 94% purity. Hence the optical rotation $[\alpha]_D^{20}$ — 10° could be calculated for the pure II.

Diastereomeric dialkylmercuries

Both organomercury bromides I and II were separately treated with ammonia in chloroform * as described previously [2]. The precipitate formed was probably a mixture of complexes $HgBr_2 \cdot (NH_3)_x$ and $RHgBr \cdot (NH_3)_y$; the reaction did not appear to reach completion even with an excess of ammonia.

$$2\ RHgBr + NH_3 \rightarrow R_2Hg + HgBr_2(NH_3)_2 + RHgBr(NH)_3)_2$$

According to thin-layer chromatography, the solid isolated from solution always contained both RHgBr and R_2Hg. Chromatographically homogeneous dialkylmercury which lacked any trace of halogen was obtained by means of crystallization from methanol. To evaluate its stereochemistry, dialkylmercury was reacted with 1 eq. of mercuric bromide in THF, i.e. under the conditions of S_E2 reaction with complete retention of configuration. During several hours RHgBr disappeared completely according to TLC. Dialkylmercury III, $[\alpha]_D^{20}$ —32°, afforded predominantly I, $[\alpha]_D$ —114°, and dialkylmercury, IV $[\alpha]_D$ —5°,

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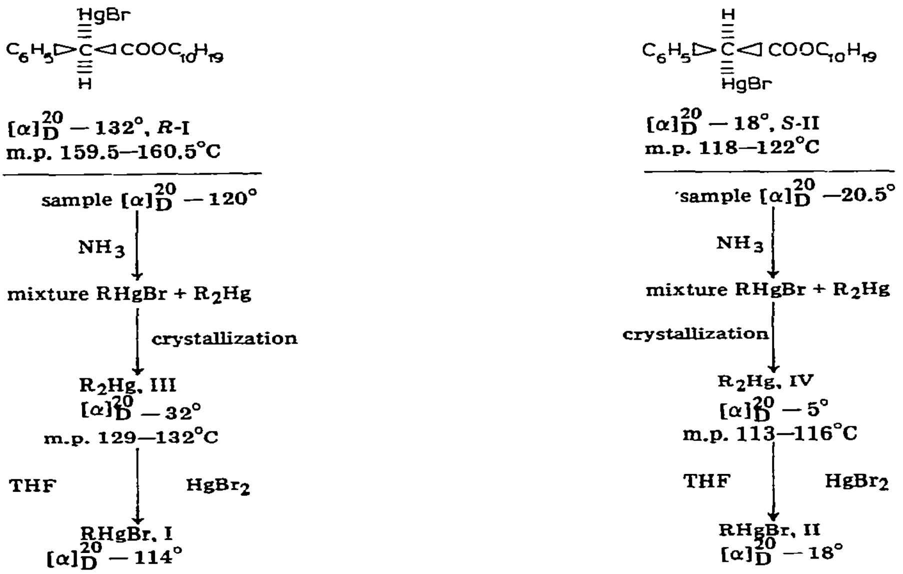
* The attempt to use $(C_6H_5)_3P$ as symmetrizing agent was unsuccessful because the reaction did not proceed after the stage of the mercuryphosphonium salt; similar behaviour is known [7].

SCHEME 1

ORGANOMERCURIAL DIASTEREOMERS OF L-MENTHYL α-PHENYLACETATE SPECIES



gave mainly II, $[\alpha]_D$ — 18°. The full picture of the conversion of these organomercurials is shown in Scheme 1. If one accepts that III is mainly the *R,R*-diastereomer admixed with some *R,S* *, so taking into account the full retention in the reaction with $HgBr_2$, one can deduce the diastereomeric composition as follows: III, 70%, *R,R*, and 30% *R,S*; IV, 88% *S,S*, and 12% *R,S*. **

Absolute configurations of benzylic chiral centres and optical rotation of diastereomers I and II, III and IV

The absolute configurations of the chiral carbons bearing the mercury atom (C(12)) in both I and II can be readily assigned using ORD curves, which are shown in Fig. 1. Curve I decreases down to the region of negative rotation while curve II increases up through the absciss axes at λ = 480 nm (in THF) into the region of positive rotation angles. This indicates the presence of near Cotton effects of opposite signs which are evidently related to the homoconjugated aromatic chromophore. The UV spectra of I and II exhibit maxima near 254 nm. Since this chromophore incorporates the C(12)—HgBr moiety and is removed from the menthyl group which possesses Cotton effects in the far UV region, it is quite possible to assign unambiguously an absolute configuration to the C(12) centre.

In terms of Brewster's theory [8,9], this moiety may contribute a molecular rotation due to the atomic asymmetry only. This contribution is positive for

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* Here only the absolute configurations of benzylic carbon centres are indicated.

** One should emphasize that the present result does not give any information concerning the stereochemistry of symmetrization because the pure diastereomeric dialkylmercuries were obtained after crystallization.

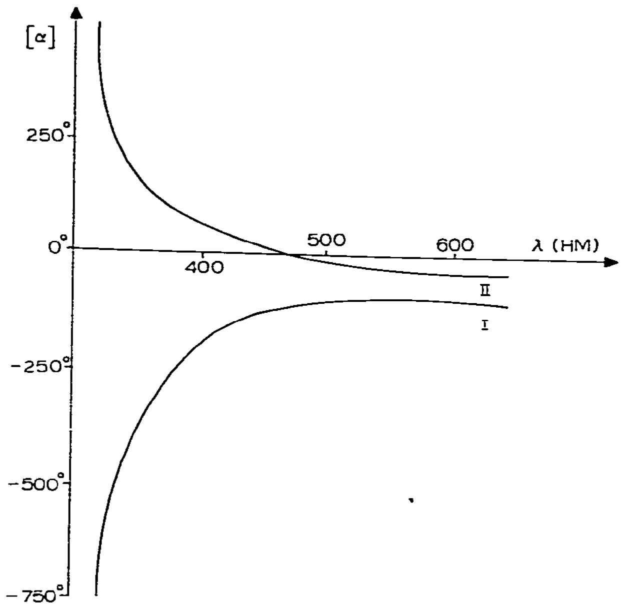
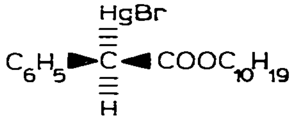
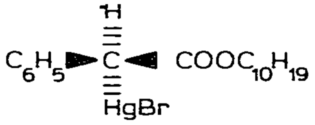


Fig. 1. ORD curves in THF for diastereomer I and II.

diastereomer II which therefore has *S* configuration and negative for diastereomer I having *R* configuration as shown below. The conventional polarizability order for the groups involved here is accepted: HgBr > C_6H_5 > COOR.


$$\begin{array}{c} \mathrm{HgBr} \\ \mathrm{C_6H_5} \blacktriangleright \mathrm{C} \blacktriangleleft \mathrm{COOC_{10}H_{19}} \\ \mathrm{H} \end{array}$$

(*R* (−) I)


$$\begin{array}{c} \mathrm{H} \\ \mathrm{C_6H_5} \blacktriangleright \mathrm{C} \blacktriangleleft \mathrm{COOC_{10}H_{19}} \\ \mathrm{HgBr} \end{array}$$

(*S* (+) II)

This conclusion has been confirmed by an X-ray study of a single crystal of diastereomer II [10].

Correspondingly, the main component of dialkylmercury III is the *R,R* diastereomer and of dialkylmercury IV the *S,S* diastereomer, as mentioned above. Taking into account the diastereomeric composition as derived above and assuming the additivity of molecular rotations one can calculate $[A]_D$ for pure diastereomers of dialkylmercuries to be —37° for *R,R*; —3° for *S,S* and —20° for *R,S*. In the *R,S* diastereomer the contributions of the chiral centres of opposite configurations should be eliminated, so $[M]_D$ has to represent the double contribution of the L-menthyl moiety which should therefore be —75° which is in a fair agreement with $[M]_D$ of L-menthol itself, —66°. This demonstrates that the additivity is maintained for the optical rotation of dialkylmercuries and that the low values obtained are not abnormal. There is no similar additivity for the diastereomeric bromides I and II, however. The possible reason for this may be the preference for conformations in which there is intra- or intermolecular coordination as was seen in crystals of diastereomer II [10].

Diastereomeric purity of organomercurials as determined using NMR spectroscopy

To evaluate quantitatively the diastereomeric purity of I and II we used ^{13}C and ^{1}H NMR spectroscopy *. The assignment of chemical shifts in ^{13}C spectra was made by comparison with the spectra of L-menthol in $CHCl_3$ [12] and L-menthyl phenylacetate, specially prepared, in pyridine. The ^{13}C spectra of II, $[\alpha]_D - 18°$, in dichloromethane, pyridine and quinoline appeared to contain only one signal per carbon atom (Table 1). There were no complications in the spectrum of a mixture I + II, $[\alpha]_D - 76°$, in CH_2Cl_2. However, the same sample in pyridine or quinoline exhibited diastereomeric splitting of some resonances. Chemical shifts of less intense components corresponded strictly to those in the spectrum of II, $[\alpha]_D - 18°$. In the spectrum of impure I, $[\alpha]_D - 120°$, some peaks were also split, indicating the presence of not more than 10% of an admixture of I. It is impossible to use shift reagents in pyridine while the addition of $Eu(dpm)_2$ to a mixture I + II in CH_2Cl_2 did not have the desired effect, presumably owing to the low complexing capacity of both oxygen and bromine atoms in these organomercurials.

The more interesting and promising results were obtained by using ^{1}H spectroscopy at 180 MHz. In Fig. 2 is shown part of the spectrum of I + II, $[\alpha]_D$ —53°, with two singlets of the H—C—HgBr moiety at 3.56 (II) and 3.59 ppm (I) with the corresponding spin-spin coupling constants, $^{2}J(^{1}H—^{199}Hg)$, of 309 and 278 Hz respectively. These values of δ and J are characteristic of arylalkyl organomercurials [13,14]. The detailed analysis of the proton NMR spectra of different mixtures revealed that diastereomer I, $[\alpha]_D - 132°$, had a diastereomeric purity of ca. 99% and diastereomer II, $[\alpha]_D - 18°$, was 94 ± 2% pure indicating —10° for pure II.

Apart from the organomercurial bromides the corresponding dialkylmercuries III and IV were also studied by ^{1}H spectroscopy.

Dependence of the number of singlet in the R_2Hg proton spectra on the solvent nature

Three singlets, δ 4.08, 4.11 and 4.17 ppm, were observed in pyridine for —HC—Hg—CH— protons for IV which is in agreement with the number of diastereomers: RRL_2, RSL_2 and SSL_2 (L represents menthyl group). Surprisingly, the same sample of IV in C_6D_6 exhibited six singlets in the region 3.2—3.6 ppm with all related coupling constants ranging from 170 to 190 Hz (Fig. 3). A similar decrease of $^{2}J(^{1}H—^{199}Hg)$ magnitudes on going from RHgX to R_2Hg is common for organomercurials [13]. The reason for the above-mentioned increase of the singlet number could be either enhanced stability of the conformational isomers or the specific diastereomeric interactions like those investigated by Kabachnik et al. [15]. To elucidate this point, we studied the related ethyl esters $(C_6H_5CHCOOC_2H_5)_2Hg$ as a mixture of both diastereomers. This substance exhibited in C_6D_6 the two expected singlets, δ 3.37 and 3.41 ppm, $^{2}J(^{1}H—^{199}Hg)$ 185 and 187 Hz, respectively, while $C_6H_5CH(HgBr)COOC_2H_5$ showed one singlet, δ 3.55 ppm, ^{2}J 296 Hz. Hence the presence in the molecule of a bulky menthyl group seems to be a necessary requirement for the obser-

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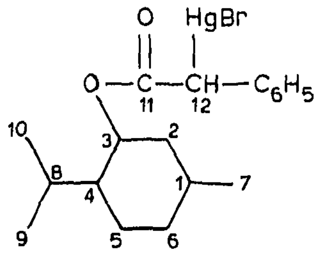
* For preliminary communication, see ref. 11.

TABLE 1



carbon atoms numbering

^{13}C CHEMICAL SHIFTS (46.64 MHz) OF L-MENTHYL α-BROMOMERCURYPHENYLACETATES I AND II IN PYRIDINE (WITH NO ARYL RESONANCES)

diastereomer and rotation	Chemical shift (ppm)									
	C(1)	C(2) and C(12)	C(3)	C(4)	C(5)	C(6)	C(7)	C(8)	C(9)	C(10)
I −120°C	31.62	41.15 41.45 41.74	74.16	47.63	23.76 24.15	34.61	22.08	27.01	16.59 15.85	20.93
II −20.5°	31.67	41.80	74.03	47.85	23.84	34.66	22.19	26.96	16.54	21.15
I + II −76.2°	31.64	41.13 41.30 41.81	74.03 74.13	47.65 47.88	23.78 24.11	34.60	22.06	27.00	16.83	20.92 21.09
L-menthyl phenylacetate	31.58	41.97 41.22	74.68	47.43	23.99	34.51	22.08	26.68	16.66	20.76

The α-carbon of pyridine was taken as internal standard, δ 124.00 ppm from tetramethylsilane.

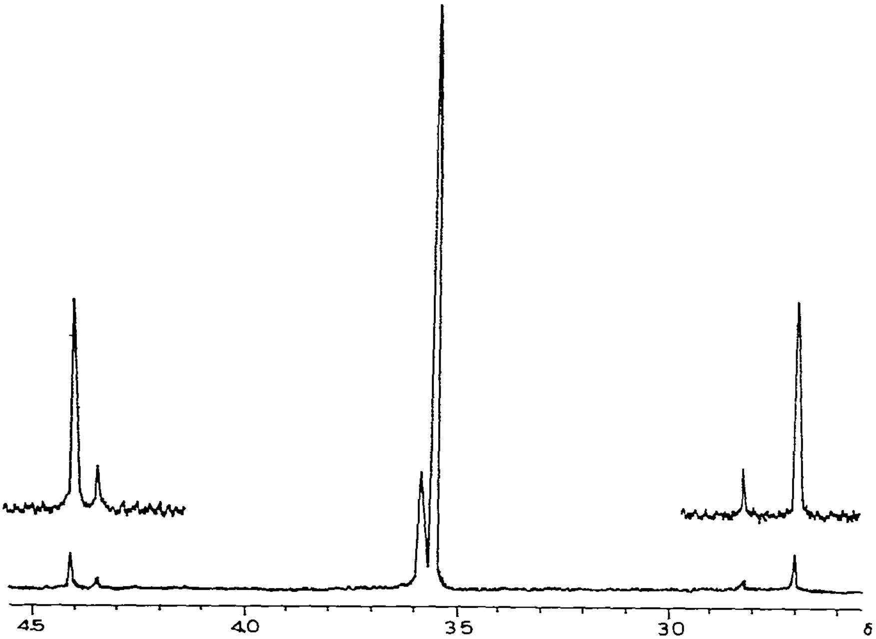


Fig. 2. Part of ^1H spectrum (180 MHz) of the I + II mixture, $[\alpha]_D^{20}$ — 53°, in C_6D_6 which represents the methine proton H—C—HgBr region.

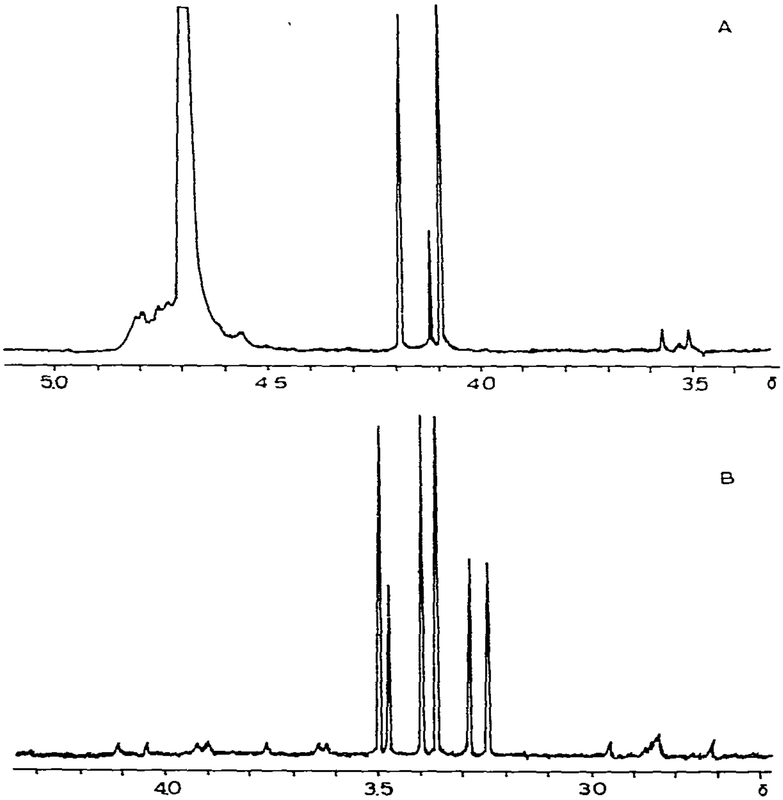


Fig. 3. Part of ^1H spectrum (180 MHz) of IV, $[\alpha]_D^{20}$ — 5° which represents the methine proton H—C—Hg—C—H region; A in C_5H_5N; V, in C_6D_6.

vation of the above-mentioned abnormal ^1H spectra in C_6D_6. This probably suggests the conformational nature of the effect.

Experimental

NMR spectra were recorded using Bruker instruments WH-180 (^1H) and HX-90 (^{13}C) at 30°C. Optical rotations were measured in benzene at 20°C with a Perkin-Elmer 241 polarimeter, the length of the tube being 1 or 2 cm.

Synthesis and separation of diastereomers I and II of L-menthyl esters of α-bromomercuryphenylacetic acid

49.0 g of the diastereomers mixture of L-menthyl α-bromophenylacetates as an oil [5], n_D^{22} 1.5005, $[\alpha]_D - 64°$ (c 4,9), ν(C=O) 1742 cm^{-1} (CH_2Cl_2), ^1H NMR: δ 5.33 ppm (—CHBr— singlet, 60 MHz, $CDCl_3$), were shaken with 50 ml of metallic mercury until a thick mass was formed [2]. This was extracted with dichloromethane (80 ml). The solution was decanted from the solid through a filter paper, then evaporated and residue was treated with hexane (200 ml). After 24 h a light yellow solid was separated and washed thoroughly with cold hexane (3 × 40 ml). The weight of dried product was 17.6 g (22.5%), $[\alpha]_D$ in the range —72 to —76°, ν(C=O) 1735 cm^{-1} (CH_2Cl_2), ^1H NMR: δ 4.38 ppm (—CHHgBr—singlet, 60 MHz, $CDCl_3$).

12.8 g of this I + II mixture were triturated with hexane (250 ml) during several minutes, then with benzene-hexane 1 : 1 (5 × 50 ml). Upon standing at ambient temperature for several days white crystals of diastereomer II (5.2 g) separated, m.p. 118—122°C, $[\alpha]_D - 20.5°$ (c 2,5). Analytical data were obtained for a sample having $[\alpha]_D - 23.3°$. Found: C, 39.00; H, 4.69; Br, 14.25; Hg, 36.28. $C_{18}H_{25}BrHgO_2$ calcd.: C, 39.23; H, 4.25; Br, 14.46; Hg, 36.15%.

The residue after extraction (6.5 g, m.p. 142—154°C, $[\alpha]_D - 70.3°$) was recrystallized from hot methanol (700 ml). After 1 hour 3.2 g of crystals were obtained, m.p. 159.5—160.5°C, $[\alpha]_D - 92°$, which were recrystallized from another 700 ml of methanol. Crystals were separated immediately after formation from hot filtrate, the yield of diastereomer I was 2.7 g, m.p. 159.5—161.5°C, $[\alpha]_D - 120°$ (c 0,23). Elemental analysis was obtained for a sample which had $[\alpha]_D - 104°$. Found: C, 39.10; H, 4.73; Br, 14.16; Hg, 35.97. $C_{18}H_{25}BrHgO_2$ calcd.: C, 39.23; H, 4.52; Br, 14.46; Hg, 36.15%.

Further crystallization from isopropanol (100 ml for 0.25 g) afforded pure I, m.p. 157.5—158.5°C, $[\alpha]_D - 132°$ (c 1,35). ^1H NMR: only one singlet for methine proton H—C—HgBr δ 3.59 ppm (C_6D_6), $^2J(^1H—^{199}Hg)$ 278 Hz.

Epimerisation of I and II in absolute methanol

0.2 g of I, m.p. 157.0—159.5°C, $[\alpha]_D - 114°$ were boiled in 8 ml of CH_3OH during 18 h. The recovered organomercurial had m.p. 149—150°C, $[\alpha]_D$ —66.4°.

0.12 g of II, m.p. 118—126°C, $[\alpha]_D - 26.8°$ were boiled in 5 ml of CH_3OH during 4 h. The recovered organomercurial had m.p. 140—146°C, $[\alpha]_D - 58.2°$.

Symmetrization of diastereomer I

Dry ammonia gas was bubbled through a solution of I (0.5 g), m.p. 157—

161°C, $[\alpha]_D$ — 120°, in chloroform (30 ml) during 3 h with intensive stirring. After standing the procedure was repeated and the reaction mixture was left overnight. The precipitate was separated, washed with $CHCl_3$ and the combined chloroform solution evaporated. The oily product solidified on cooling. It contained, according to TLC, two substances: starting RHgBr, R_f 0.28, and formed R_2Hg, R_f 0.39 (silufol, eluent C_6H_6-CH_2Cl_2 2 : 1). The solid was extracted with CH_3OH (10 ml) and at —15°C 0.18 g (53%) of chromatrographically pure III was obtained, m.p. 129—132°C, $[\alpha]_D$ — 32° (c 2.4), ν(C=O) 1735 cm^{-1} (CH_2Cl_2). ^1H NMR: δ 3.28; 3.32; 3.40; 3.42; 3.53; 3.57 ppm (C_6D_6). Found: C, 57.71; H, 6.98; Hg, 26.52. $C_{36}H_{50}HgO_4$ calcd.: C, 57.83; H, 6.74; Hg, 26.85%.

Symmetrization of diastereomer II

This was performed as described above starting from 4.0 g of II, m.p. 118—122°C, $[\alpha]_D$ — 20.5°, in 50 ml of $CHCl_3$. Ammonia gas was introduced during 5 h. The crude oily product exhibited the presence of both intial RHgBr, R_f 0.29, and formed R_2Hg, IV, R_f 0.19 (silufol, eluent C_6H_6-CH_2Cl_2 2 : 1). Hexane (10 ml) was added to the oil (2.55 g). After 24 h the precipitate was removed, the filtrate was evaporated and the residue taken in benzene (25 ml). The addition of hexane (10 ml) gave a solid (mainly RHgBr). The oil from the filtrate was dissolved in methanol (10 ml) which afforded on cooling 0.36 g (13%) of chromatogaphically pure IV, m.p. 113—116°C, $[\alpha]_D$ — 8.2° (c 3.14), ν(C=O) 1735 cm^{-1} (CH_2Cl_2). ^1H NMR: δ 3.26; 3.31; 3.39; 3.42; 3.49; 3.52 ppm (C_6D_6). Found: C, 57.68; H, 6.93; Hg, 26.66. $C_{36}H_{50}HgO_4$ calcd.: C, 57.83; H, 6.74; Hg, 26.85%. In some experiments IV, having $[\alpha]_D$ —5°, were obtained.

Reaction between dialkylmercuries and mercuric bromide

To a solution of 0.075 g of III, $[\alpha]_D$ — 32° (prepared from I, $[\alpha]_D$ — 120°) in absolute THF (3 ml) under argon 0.036 g of $HgBr_2$ was added. After 5 h TLC indicated the absence of R_2Hg. Evaporation to dryness afforded RHgBr, m.p. 157.5—159.5°C, $[\alpha]_D$ — 114° (85% I and 15% II, according to PMR). Similar reaction of IV, $[\alpha]_D$ — 5° (prepared from II, $[\alpha]_D$ — 20.5°) gave RHgBr, m.p. 118—122°C, $[\alpha]_D$ — 18° (6% I and 94% II, according to PMR).

Acknowledgement

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References

1 O.A. Reutov, V.I. Sokolov, G.Z. Suleimanov and V.V. Bashilov, J. Organometal. Chem., 160 (1978) 7.

2 A.N. Nesmeyanov, O.A. Reutov and S.S. Poddubnaya, Dokl. Akad. Nauk SSSR, 88 (1953) 479; Izv. Akad. Nauk SSSR, Ser. Khim., (1953) 649, 850.

3 A.N. Nesmeyanov, O.A. Reutov, U. Yang Tsay and Lu Tsing Chzhu, Izv. Akad. Nauk SSSR. Ser. Khim., (1958) 1328.

4 O.A. Reutov, I.P. Beleskaya and V.I. Sokolov, Mechanisms of Organometallic Reactions (in Russian), Khimia, Moscow, 1972.

5 A. McKenzie and I.A. Smith, J. Chem. Soc., 125 (1925) 1586.

6 A. McKenzie and I.A. Smith, Ber., 58 (1925) 894.
7 G.E. Coates and A. Lauder, J. Chem. Soc., (1965) 1857.
8 J.H. Brewster, J. Amer. Chem. Soc., 81 (1959) 5475.
9 J.H. Brewster, Topics in Stereochemistry, vol. 2, Interscience, N.-Y., 1967.
10 G.Z. Suleimamov, V.V. Bashilov, A.A. Musaev, V.I. Sokolov and O.A. Reutov, J. Organometal. Chem., in press.
11 O.A. Reutov, G.Z. Suleimanov, V.I. Rozenberg, A.I. Lutsenko, E.I. Fedin and V.I. Sokolov, Izv. Akad. Nauk SSSR, Khim., (1979) 470.
12 V. Formacek, Z. Desnoyer, H.P. Kellerhals, T. Keller and J.T. Clerc, ^{13}C Data Bank, vol. 1, Bruker Physik, Karlsruhe, 1976.
13 M.L. Maddox, S.L. Stafford and H.D. Kaesz, Adv. Organometal. Chem., 3 (1965) 1.
14 V.S. Petrosyan, V.I. Bakhmutov and O.A. Reutov, Izv. Akad. Nauk SSSR, Ser. Khim., (1974) 1428.
15 M.I. Kabachnik, T.A. Mastryukova, E.I. Fedin, M.S. Vaisberg, L.L. Morosov, P.V. Petrovsky and A.E Shipov, Tetrahedron, 32 (1976) 1719.