[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF CINCINNATI, CINCINNATI 21, O.]

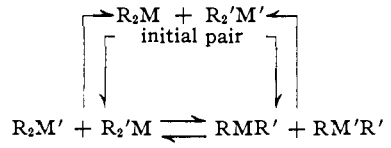
Exchange Reactions in Group II Organometallic Systems

BY RAYMOND E. DESSY,[1] FRED KAPLAN, GORDON R. COE[2] AND RUDOLF M. SALINGER[3]

RECEIVED SEPTEMBER 6, 1962

Exchange reactions in dialkylmetal–dialkylmetal systems (R_2M and $R_2'M'$) involving organometallic compounds derived from group II metals have been investigated. Exchange is rapid except when mercury is one of the metals. A pathway involving the transfer of one group at a time from the metal giving rise to unsymmetrical species RMR′ and RM′R′ must be present.

Exchange reactions involving disubstituted organometallic compounds derived from Group II metals (1)



(1)

have been investigated partially by McCoy and Allred,[4] and Reutov.[5] Using nuclear magnetic resonance (n.m.r.) as a tool, McCoy found that when M is zinc, M′ is cadmium and R and R′ are methyl in a series of solvents, the mean lifetime, τ_A, of a methyl group before exchange is less than 0.03 second. (In dilute solution the system was reported to give *two* methyl resonance peaks, indicating slow or no exchange.) In the systems where M is zinc and M′ is mercury, or M is cadmium and M′ is mercury, τ_A is greater than 0.08 and 0.14 second, respectively. Note that this tool, n.m.r., allows upper or lower limits to be set on the mean lifetime of the carbon–metal bond, but does not shed any light on the mechanism of the exchange reaction. Reutov, working with diphenylmercury–di-*p*-tolylmercury[203], has reported mercury–mercury exchange, involving *four* groups migrating simultaneously, since no RHgR′ was found.

Concern over the exact mechanistic pathways involved suggested that a more comprehensive investigation of this type of exchange was needed.

Experimental

Preparation of Compounds.—Dimethylzinc was purchased from Kahlbaum (Germany) and used without further purification.

Dimethylcadmium was purchased from Orgmet as a solution in heptane. The solvent was removed by distillation in an argon atmosphere and the residue collected.

Dimethylmercury was prepared in 30% yield by a variation of Koton's[6] method, using 62 ml. of iodomethane, 25 ml. of methyl acetate and 2500 g. of a 0.9% sodium amalgam.

Dimethylmagnesium was prepared from triply sublimed magnesium (Dow; 6 g.) and dimethylmercury (18 g.) by heating the mixture in a sealed Pyrex tube at 95–105° for 24 hours. The tube was allowed to cool, and opened in an argon-filled dry-box. The contents were extracted with tetrahydrofuran, and solids removed by filtration through a sintered-glass funnel. The filtrate was evaporated to dryness *in vacuo* and the residue baked at 130° (2 mm.) for 1 hour. It was finally dissolved in tetrahydrofuran, the resulting solution filtered, and standardized by acid titration and gasometric analysis.

Methylmagnesium bromide (0.69 *N*) was prepared from Mallinckrodt Grignard grade magnesium turnings (6 g.) and bromomethane (40 g.) in tetrahydrofuran (200 ml.). The resulting solution was filtered in an argon atmosphere through a sintered-glass funnel, and standardized by acid titration and gasometric analysis.

Perdeuteriodimethylmercury was purchased from Merck and Co., Ltd., and used without further purification.

Tetrahydrofuran was distilled from lithium aluminum hydride.

Nuclear Magnetic Resonance Spectra.—All samples were prepared in an argon-filled dry-box and then sealed. A small capillary tube containing chloroform was inserted in the n.m.r. tube for use as an external standard.

The n.m.r. spectra were observed at 32° and 60 Mc. with a Varian Associates model A-60 spectrometer. Chemical shifts are measured in cycles per second (c.p.s.) from chloroform.

Mass Spectrometer Measurements.—All samples were prepared in an argon atmosphere. Spectra for the rate of exchange study on the $(CD_3)_2Hg$–$(CH_3)_2Mg$ and $(CD_3)_2Hg$–"$(CH_3)MgBr$" systems were obtained on a General Electric analytical mass spectrometer, model G-6. All other spectra were obtained on a Bendix Time-of-Flight mass spectrometer.

Discussion and Results

The basic principles involved in an n.m.r. study of exchange reactions illustrated by eq. 1, developed by Gutowsky,[7] have been discussed by McCoy and Allred.[4] For methyl groups exchanging between two sites, the mean lifetime before exchange, τ_A, is given by the equation

$$\tau_A \leqq \sqrt{2}/\pi(\nu_a - \nu_b) \qquad (2)$$

where $(\nu_a - \nu_b)$ is the difference in chemical shifts in c.p.s. between the methyl resonances of non-exchanging species. When the two resonance components occur with the sharpness and separation comparable to that in the pure compounds, one may calculate the mean lifetime by the formula

$$\tau_A \geqq \frac{10\sqrt{2}}{\pi(\nu_a - \nu_b)} \qquad (3)$$

Using essentially the technique of McCoy and Allred, who examined group IIb–group IIb interchanges, the present work extended this investigation to include group IIa–group IIb interchanges. Table I indicates the results obtained in THF. It may be concluded that within group II derivatives, exchange occurs in THF with a mean pre-exchange lifetime of <0.04 sec., except when mercury is one of the metals involved.

Information about exchange reactions when M is equal to M′ may also be obtained from n.m.r. spectra. Naturally occurring cadmium contains two isotopes with spin one-half, Cd^{111} and Cd^{113}. If the C–Cd pre-exchange lifetime is long, Cd^{111} and/or Cd^{113}–H^1 spin–spin coupling peaks should appear in the n.m.r. spectra. Spectra of neat dimethylcadmium samples, or samples dissolved in heptane, show such satellites (J_{Cd-H^1} = 48 c.p.s.). When THF is added, however, these satellites *disappear*.

It is reasonable to conclude that coördinating solvents will aid the exchange process. Brownstein[8] has shown that coördinating ligands do indeed weaken the carbon–metal bond in triethylaluminum and gallium. The concepts involved are discussed by Dessy and Paulik.[9] However, the important observation is

(1) Alfred P. Sloan Fellow.

(2) Predoctoral Fellow under Air Force Office of Scientific Research Grant USAF-49-638-824.

(3) National Science Foundation Coöperative Graduate Fellow.

(4) C. R. McCoy and A. L. Allred, *J. Am. Chem. Soc.*, **84**, 912 (1962). At the time of preparation of this manuscript only McCoy and Allred's preliminary communication had been published. It discussed only $(CH_3)_2Cd$, $(CH_3)_2Zn$ exchanges. The present work duplicated their efforts in the $(CH_3)_2Zn$, $(CH_3)_2Hg$ and $(CH_3)_2Cd$, $(CH_3)_2Hg$ systems. The findings in both investigations were in complete agreement.

(5) O. A. Reutov, *Rec. Chem. Prog.*, **22**, 1 (1961).

(6) M. M. Koton, *Zhur. Obshchei Khim.*, **22**, 1136 (1952); *Chem. Abstr.*, **47**, 6341 (1953).

(7) H. S. Gutowsky and C. H. Holm, *J. Chem. Phys.*, **25**, 1228 (1956).

(8) S. Brownstein, B. C. Smith, G. Ehrlich and A. W. Laubengayer, *J. Am. Chem. Soc.*, **81**, 3826 (1959).

(9) R. E. Dessy and F. E. Paulik, *ibid.*, in press.

TABLE I

NUCLEAR MAGNETIC RESONANCE DATA AND RESULTS OF GROUP II DERIVED ORGANOMETAL SYSTEMS $(CH_3)_2M$ AND $(CH_3)_2M'$ IN TETRAHYDROFURAN AT 28°

$(CH_3)_2M$	Approx. concn., mole/liter	$(CH_3)_2M'$	Approx. concn., mole/liter	δ[a]	τ_A[b]
$(CH_3)_2Mg$	0.20	.....	..	557	
$(CH_3)_2Mg$	.50	.....	..	556	
$(CH_3)_2Mg$	.40	$(CH_3)_2Zn$	0.20	538	
$(CH_3)_2Mg$	.33	$(CH_3)_2Zn$	.33	526	<0.009
$(CH_3)_2Mg$	.25	$(CH_3)_2Zn$	.50	520	
.....	..	$(CH_3)_2Zn$	.33	507	
$(CH_3)_2Mg$	.60	$(CH_3)_2Cd$	.60	517	< .007
.....	..	$(CH_3)_2Cd$	.60	490	
$(CH_3)_2Mg$	.60	$(CH_3)_2Hg$	.60	540, 428	> .040
.....	..	$(CH_3)_2Hg$	.60	429	
$(CH_3)_2Hg$	.60	$(CH_3)_2Zn$	.60	507, 429	> .058[c]
$(CH_3)_2Hg$	.60	$(CH_3)_2Cd$	.60	490, 429	> .073[c]

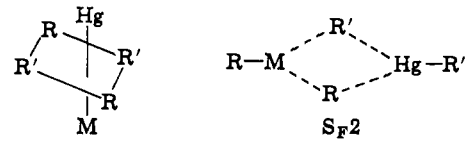
[a] Chemical shift(s) of observed methyl resonance(s) in cycles per second from $CHCl_3$ which was used as an external reference. [b] Obtained from the equations $\tau_A \leqq \sqrt{2}/\pi(\nu_A - \nu_B)$ for rapidly exchanging methyl groups or $\tau_A \geqslant 10\sqrt{2}/\pi(\nu_A - \nu_B)$ for non-exchanging methyl groups. [c] McCoy and Allred have measured τ_A for these systems under slightly different conditions: $(CH_3)_2Zn$–$(CH_3)_2Hg$, $\tau_A > 0.08$; $(CH_3)_2Cd$–$(CH_3)_2Hg$, $\tau_A > 0.14$.

that in ether solvents the pre-exchange lifetime of a methyl–cadmium linkage is <0.009 sec. (*vide infra*).

Optically active Grignard reagents involving an asymmetric center attached directly to the magnesium atom have not been prepared, except in small ring systems where inversion of the carbanion would be restricted.[10] This suggests that the carbon–magnesium linkage is rapidly breaking and re-forming. Unpublished results by Kaplan and Roberts,[11] where equivalent methylene protons are observed adjacent to a magnetically asymmetric center in the Grignard reagent prepared from $C_6H_5CH(CH_3)CH_2Br$, suggest this also. In addition, no Mg^{25}–H^1 spin–spin coupling satellites are observed in the n.m.r. spectra of dimethylmagnesium. The pre-exchange lifetime of carbon–magnesium linkages is therefore very short. Dimethylmercury, which contains naturally some Hg^{199} (spin $^1/_2$), shows Hg^{199}–H^1 spin–spin coupling satellites ($J_{Hg^{199}-H^1}$ = 103 c.p.s.) in the neat liquid.[12] The addition of THF does not affect the appearance of these peaks, suggesting that methyl–mercury linkages possess long pre-exchange lifetimes. This is consistent with the fact that optically active organomercury compounds are known.

It is again apparent that in the exchange reactions between group II organometallic compounds pre-exchange lifetimes are very short in THF (<0.04 sec.) except when mercury is one of the metal atoms involved.

The large pre-exchange lifetimes of mercury compounds presumably are due to the large size of mercury, which prevents the metal–metal approach necessary for exchange; alternatively, the tendency for mercury to utilize ds-hybrid orbital contributions[13] in its bonding may prevent distortion from the expected 180° bond angle. Both effects would hinder good overlap in the three-centered molecular orbital bonding necessary for the non-ionic exchange pathways. One may picture such transition states as



octahedral S_F2

The octahedral form would probably require the transfer of two groups from each metal during one interchange, thus providing no RMR′ species while the S_F2 transition state[14] would give rise to RMR′.

It was of interest therefore to attempt to devise a metal–metal interchange experiment in a group II derived system in which one could possibly detect RMR′ species as they were produced so as to make possible a decision between octahedral and S_F2 transition states.

In order to minimize equilibrium factors and isolation procedures, the logical choice of a system was $(CH_3)_2M$ and $(CD_3)_2M'$. The analytical tool of choice is of course mass spectrometry. Since there should be no selectivity of M and M′ for CH_3 or CD_3, the resulting equilibrium mixture would obey the redistribution laws formulated by Calingaert.[15] Dimethylmagnesium and dimethylberyllium do not give an easily obtainable parent peak in the mass spectrometer and the parent peak for dimethylzinc falls in the Hg^{2+} area. Thermal instability of dimethylcadmium renders it an unfavorable material. In addition, exchanges where M is equal to M′ must be considered, since obviously those systems which exchange rapidly will not lend themselves to this investigation as they will exhibit random exchange long before the time of analysis. As the above development on these exchanges indicated, only Hg–Hg exchange appeared to be slow. Dimethylmercury also provides a stable reference system with strong parent peaks in a mass region free of contribution by other fragments.

Therefore a study of the system

$$(CD_3)_2Hg + (CH_3)_2M \xrightarrow[t,\ \text{time}]{\text{THF}} \qquad (4)$$

was made, employing mass spectrometry to detect CH_3HgCD_3 and $(CH_3)_2Hg$ species derived from the parent $(CD_3)_2Hg$ by exchange. Table II shows how this may conveniently be done, using a specific mercury isotope which gives rise to the bracketed mass numbers.

TABLE II

MASS NUMBERS IN $(CH_3)_2Hg$–$(CD_3)_2Hg$ SYSTEMS

Hg	198	199	200	201	202	204
$(CH_3)_2Hg$	228	229	[230]	231	232	234
CH_3HgCD_3	231	232	[233]	234	235	237
$(CD_3)_2Hg$	234	235	[236]	237	238	240

Table IIIa shows the results for $(CH_3)_2Mg$–$(CD_3)_2Hg$ system. In more controlled experiments (Tables IIIb and IIIc) an idea of the rate of mercury–magnesium exchange was obtained. Note that both $(CH_3)_2Hg$ and CH_3HgCD_3 were observed. When the $(CH_3)_2Hg$, $(CD_3)_2Hg$ system was heated to 65° for 78 hours exchange was noted, *both $(CH_3)_2Hg$ and CD_3HgCH_3 species being present.* The rate of exchange in the system "CH_3MgBr"–$(CD_3)_2Hg$ was only slightly faster than in the system $(CH_3)_2Mg$–$(CD_3)_2Hg$. The presence of magnesium bromide does not drastically alter the exchange rate.

McCoy and Allred[4] have shown that exchanges involving Zn and Cd do not seem to involve ionic

(10) (a) H. Walborsky, *Rec. Chem. Progr.*, **23**, 75 (1962). (b) Prof. O. Reutov has, however, claimed the preparation of R_3C^*Mg compounds from R_3C^*Hg + R′Mg → exchange; Symposium on Organometalliques, Problèmes de Structure et Reactions Nouvelles, Paris, September, 1963.

(11) F. Kaplan and J. D. Roberts, personal communication.

(12) R. E. Dessy, T. J. Flautt, H. H. Jaffé and G. F. Reynolds, *J. Chem. Phys.*, **30**, 1422 (1960).

(13) L. E. Orgel, *J. Chem. Soc.*, 4186 (1958).

(14) R. E. Dessy, W. L. Budde and C. Woodruff, *J. Am. Chem. Soc.*, **84**, 1172 (1962); S_F2 = substitution, four-center, bimolecular.

(15) G. Calingaert, *ibid.*, **61**, 2748 (1939).

TABLE IIIa

EXCHANGE STUDIES OF $(CD_3)Hg$–$(CH_3)_2M$ SYSTEMS ANALYZED BY MASS SPECTROMETRY

$$\underset{X\,M}{(CH_3)_2M} + \underset{M\,X}{(CD_3)_2Hg} \xrightarrow[28^\circ]{THF}$$

$(CH_3)_2M$	Concn., m./l.	Results
$(CH_3)_2Mg$	0.6	Exchange
$(CH_3)_2Zn$	2.0	Slight or no exch., 8 days
$(CH_3)_2Cd$	2.0	Slight or no exch., 8 days
$(CH_3)_2Hg$	2.0	Slight or no exch., 8 days

TABLE IIIb

$$\underset{0.56\,M}{(CH_3)_2Mg} + \underset{0.87\,M}{(CD_3)_2Hg} \xrightarrow{THF}$$

t, hours	Mole fraction $(CH_3)_2Hg$	CH_3HgCD_3	$(CH_3)_2Hg$	Exch., %
0	1.00	0	0	0
1	0.94	0.06	0	9.8
6	.77	.21	0.02	48
30	.44	.44	.12	91
175	.39	.46	.15	100

TABLE IIIc

$$\underset{0.64\,M}{\text{"}CH_3MgBr\text{"}} + \underset{0.59\,M}{(CD_3)_2Hg} \xrightarrow[28^\circ]{THF}$$

t, hours	Mole fraction $(CD_3)_2Hg$	CH_3HgCD_3	$(CH_3)_2Hg$	Exch., %
0	1.00	0	0	0
1	0.92	0.07	0.01	13
7	.68	.28	.04	55
31	.44	.44	.12	97
199	.42	.45	.13	100

pathways. If this conclusion can be extrapolated to the systems described above, which seems certain in the Hg–Hg case and likely in the Mg–Hg case, since R_3HgLi complexes are unknown[16] it would appear that the exchanges studied thus far occur by a mechanism which entails interchange of one group from each metal at a time. The present results suggest that an S_F2 exchange transition state is involved. It should be noted that an interchange involving migration of all four groups simultaneously is not strictly forbidden by this work; but it must be recognized that this type of exchange would not give rise to RHgR′. Reutov's surprising results[5] may possibly be explained by the thermodynamic instability of *p*-tolylphenylmercury under his isolation conditions or to distinct differences in the mechanistic pathways available to alkyl and arylmercury compounds in exchange reactions. The possibility of an ionic exchange mechanism in the group IIb–group IIa systems cannot be completely disregarded of course.

Acknowledgment.—This work was supported in part by grants from the Petroleum Research Fund, American Chemical Society PRF-1086-A4, the Air Force Office of Scientific Research (USAF-49-638-824), the National Science Foundation (NSF G14182), and an F. G. Cottrell Research Grant from Research Corp. The purchase of the nuclear magnetic resonance spectrometer used in these studies was assisted by a grant from the National Science Foundation, and the mass spectrometer was purchased from funds provided by the Advanced Research Projects Agency. The aid of Professor J. Todd of this Department, and Mr. R. Vordenberg and Mr. Don Hinshaw of the United States Industrial Chemicals Company in obtaining the mass spectral data is gratefully acknowledged.

(16) G. Wittig, *Ann.*, **571**, 167 (1951).

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, HARVARD UNIVERSITY, CAMBRIDGE 38, MASS.]

A Conformation Examination of Poly-L-alanine and Poly-D,L-alanine in Aqueous Solution

BY WALTER B. GRATZER AND PAUL DOTY

RECEIVED NOVEMBER 24, 1962

A block polymer consisting of a central block of poly-L-alanine and two flanking blocks of poly-D,L-glutamic acid has been synthesized. Its water solubility permits the examination of the conformation of the poly-L-alanine in aqueous media: optical rotatory dispersion serves to establish the form of the poly-L-alanine since the glutamic acid blocks are optically inactive. It is found that this hydrophobic chain is in the form of an α-helix of extraordinary stability, although it lacks any basis of helix stabilization through interaction between side chains. Morever, the helical form is stable at 95°, and in detergent or 8 *M* urea solution. A random copolymer of similar composition is shown to have no helical conformation. Low molecular weight water-soluble poly-D,L-alanine was also examined. The far ultraviolet spectrum revealed a substantial hypochromicity in the band associated with the peptide chromophore, indicating the presence of some helical form. This too was resistant to heat, organic solvents and detergent. The relation of these results to the sources of the α-helix stability in proteins is discussed.

If synthetic polypeptides are to serve as valid models for understanding the complex structures of proteins, it is necessary to establish the conformational preferences of their chains in neutral aqueous solution, which approximates the native environment of most proteins. The fact is, however, that only a few polymers of the naturally occurring amino acids are soluble under these conditions; those that are, *viz.*, poly-L-glutamic acid,[1] poly-L-lysine[2] and poly-L-serine,[3] exhibit the randomly coiled, or disordered, form. The instability of the helical conformation in these cases may be explicable in terms of electrostatic repulsions between charged groups or the presence of bulky or polar groups in the immediate proximity of the peptide bond. The question of the inherent stability in aqueous solution of the α-helix *per se* is thus left unanswered. The possibility must be considered then that other polyamino acids, particularly those made up of uncharged residues with small β-carbon substituents, might normally exist in the helical state in water solution. We have approached this problem, which is essentially one of bringing such insoluble polymers into solution, by synthesizing a three-component block copolymer in which the middle block is poly-L-alanine and the two flanking blocks poly-D,L-glutamic acid. Since the

(1) M. Idelson and E. R. Blout, *J. Am. Chem. Soc.*, **80**, 4631 (1958).

(2) J. Applequist and P. Doty, "Polyamino Acids, Polypeptides and Proteins," 1st International Symposium, Madison, 1961, Univ. of Wisconsin Press, Madison, Wis., 1962, p. 161.

(3) G. D. Fasman and E. R. Blout, *J. Am. Chem. Soc.*, **82**, 2262 (1960).