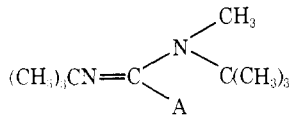
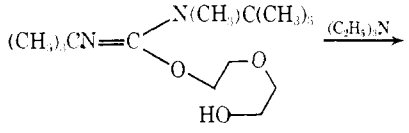
imidium ion (**2**), which, because of the quaternary nitrogen present, might act as an even more potent agent for such reactions. A preliminary survey reveals that *N*-methyl-*N,N'*-di-*tert*-butylcarbodiimidium tetrafluoroborate (**3**)[2] not only permits overall conversion of protected amino acids to peptide and nucleotide to pyrophosphate but also aliphatic glycol to cyclic ether, all reactions apparently involving initial rapid addition of alcohol or acid (AH) to the reagent, giving **4**, which is then transformed to final product.[3]



4

In the ether synthesis, 1.0 equiv of reagent **3** is added slowly to diethylene glycol in $CHCl_3$–$C_6H_5NO_2$ at room temperature. After addition of 1.2 equiv of triethylamine, the mixture is heated to 130° while the product, *p*-dioxane (55%), is collected by distillation over a 2-hr period. Under similar conditions, 1,4-butanediol generates tetrahydrofuran (64%), and 1.6-hexanediol provides oxepane (22%).[4] In our hands no dioxane is formed from equimolar amounts of glycol and tosylchloride in pyridine (with or without triethylamine), while 13% of this ether was detected when dicyclohexylcarbodiimide (DCC)-*p*-toluenesulfonic acid in $CHCl_3$ was employed. The rapid (<5 min), quantitative addition of methanol at 20° to **3** to give adduct **4** (A = OCH_3), mp 98.5–99.5° (ir (CH_2Cl_2) 3.4, 6.12 μ; nmr CD_3NO_2 δ 1.45 (s, 9 H), 1.50 (s, 9 H), 3.08 (3 H), 4.20 (3 H)), suggests that in the ether synthesis glycol addition initially provides **5**, which under the influence of the added amine undergoes internal displacement of trialkylurea by alkoxide ion.[5,6]



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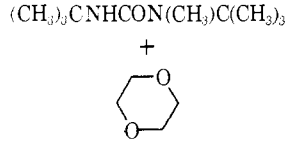
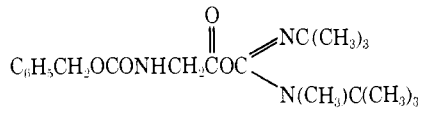


In the peptide synthesis experiments, equimolar amounts of *N*-acylamino acid and amino acid ester hydrochloride or amine were stirred in $C_2H_4Cl_2$ or CH_2Cl_2 at 0 or −78° under N_2 while salt **3** was added. During work-up, hexane–ether was used to remove urea by-product, and the desired amide was obtained by normal peptide isolation procedures. By such means, the expected amide was prepared from benzylamine and *N*-carbobenzoxyglycine (77%), and peptide was secured from *N*-benzoyl-L-leucine and ethyl glycinate (69%, product 86% optically pure), and from *N*-carbobenzoxy-L-valine and ethyl glycinate (69%). In the absence of amine, *N*-carbobenzoxyglycine is converted, apparently *via* O → N acyl migration of **6**, to the *N*-acylurea **7** (ir (CCl_4) 5.79, 5.93, 5.98 μ; nmr ($CDCl_3$) δ 1.43 (18 H), 3.03 (3 H), 3.86 (d, 2 H), 5.12 (2 H), 5.43–5.83 (m, 1 H), 7.31 (5 H)), which is inert to primary amines or glacial acetic acid for 3 hr at 70°.

Symmetrical pyrophosphate results from the action of **3** on nucleotide, for example, 2',3'-isopropylidineuridine 5'-phosphate (trimethylamine salt) (DMF at 20°; 73% yield, after cellulose chromatography and ion exchange). However, experiments designed to give a dinucleotide from suitably protected nucleotide and nucleoside provided only a



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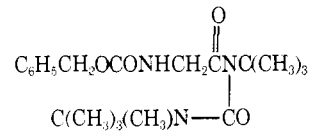

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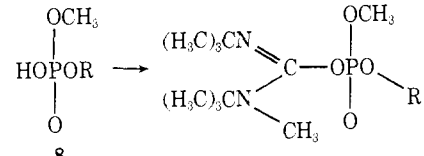
few per cent of the expected product after 2 days at 20°. Carbodiimidium reagent **3** converted methyluridine 5'-phosphate **8** to a product regarded as urea **10** (nmr (D_2O) δ



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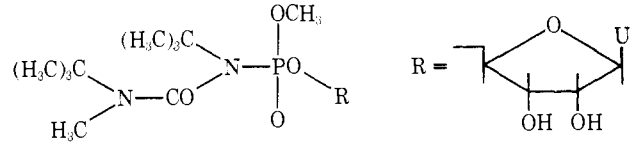

10

0.9–1.3 (m, 18 H), 2.45 (3 H), 3.40 (d(J = 11 Hz), 3 H), 3.8–4.3 (m, 5 H), 5.6–6.0 (m, 2 H); 7.73 (d(J = 8 Hz), 1 H)), arising by O → N migration of the phosphate unit in intermediate **9**. Similar behavior of nucleotide diesters with DCC has been reported by Khorana and coworkers.[7]

Acknowledgment. Financial support was provided by National Institutes of Health Grant GM20677.

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(2) K. Hartke, F. Rossbach, and M. Radau, *Justus Liebigs Ann. Chem.*, **762**, 167 (1972).
(3) The only other, previously reported reaction of trialkylcarbodiimidium ion involves use of the iodide salt for conversion of an alcohol to the corresponding iodide. See R. Scheffold and E. Saladin, *Angew. Chem., Int. Ed. Engl.*, **11**, 229 (1972).
(4) The sulfurane procedure of J. C. Martin, J. A. Franz, and R. J. Arhart, *J. Amer. Chem. Soc.*, **96**, 4605 (1974), gave 0% oxepane from 1,6-hexanediol, 40% *p*-dioxane from diethylene glycol, and 72% THF from 1,4-butanediol.
(5) On treatment of **3** with pyridine or trimethylamine in CH_2Cl_2 or anhydrous K_2CO_3 in $C_2H_4Cl_2$, isobutylene and methyl-*tert*-butylcyanamide are formed.
(6) The preparation of aryl alkyl ethers from phenols and primary alcohols through the agency of dicyclohexylcarbodiimide has been reported by E. Vorwinkel, *Ber. Deut. Chem. Ges.*, **99**, 42 (1966).
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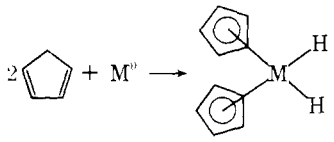
Syntheses with Tungsten and Molybdenum Atoms. Reactions with Cyclopentadiene and Cycloheptatriene

Sir:

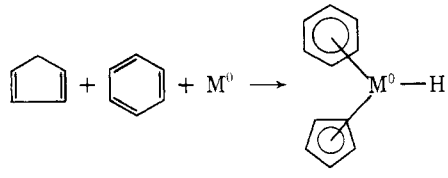
We report here syntheses of several organometallic compounds by reaction of free tungsten and molybdenum atoms with cyclopentadiene and cycloheptatriene. These one step reactions proceed in good yields offering convenient means for preparing several hundred milligrams of products.

Vacuum codeposition of thermally generated tungsten or molybdenum atoms[1] with a large excess of cyclopentadiene on a liquid nitrogen cooled surface produces a yellow matrix. Removal of cyclopentadiene from the melted matrix leaves a yellow-brown residue. Sublimation of this material gives the yellow crystalline bis(cyclopentadienyl)tungsten or molybdenum dihydrides in 40–50% yields based on metal reaching the reaction zone. The physical and spectral properties of these complexes are identical with those reported.[2,3] It is interesting that the tungsten product is also obtained from reaction of tungsten atoms with cyclopentene. The original codeposition mixture, in this case, is formed without release of hydrogen, and its color is orange-brown. The hydrogen lost in this reaction probably converts some cyclopentene to cyclopentane which is difficult to identify in high dilution. Sublimation of the residue produces the yellow bis(cyclopentadienyl)tungsten dihydride (~30% yield), contaminated by a trace of darker material.



Earlier we reported the syntheses of bisarenetungsten compounds by similar methods.[1b] If tungsten atoms are cocondensed with a mixture of arene and cyclopentadiene, a mixed product is obtained. These are cyclopentadienylarenetungsten monohydrides, compounds which may not yet have been prepared by other methods.

Cocondensation of tungsten atoms with a 5:1 mixture of benzene and cyclopentadiene produces a yellow-brown matrix. On warming to room temperature a dark solution is obtained. Removal of excess reactants *in vacuo* and sublimation of the residue (65° (10^{-3} Torr)) yields a reddish brown sublimate. A 12-eV mass spectrum shows 40% intensity at *m/e* 328 (^{184}W), $(C_5H_5)(C_6H_6)WH^+$, 60% at *m/e* 314, $(C_5H_5)_2W^+$, and only a trace at 340, $(C_6H_6)_2W^+$. The ion at 314 corresponds to the base peak for pure bis(cyclopentadienyl)tungsten (−2H),[4] while 328 corresponds to the mixed product. With a 1:1 mixture of reactants the product percentages are 30, 70%, and trace, respectively. The proton nmr spectrum remaining after removal of all the features of the bis(cyclopentadienyl)tungsten dihydride is consistent with the proposed structure of the monohydride product: C_5H_5, τ 5.42, doublet (J = 1.2 Hz); C_6H_6, 6.20, doublet (J = 3.0 Hz); W–H 12.2, broad multiplet.

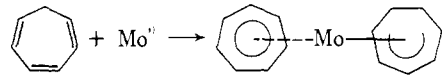


An earlier tentative report,[4] of a preparation (0.5% yield) of cyclopentadienylbenzenetungsten monohydride, does not agree with the nmr data reported above.

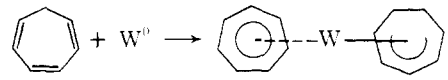
Similarly the cyclopentadienyltoluenetungsten monohydride was prepared. From a 1:1 mixture of reactants the sublimate was a dark red oily material. The 12-eV mass spectrum indicated relative ion intensities: monohydride 55%, dihydride 25%, and bistoluenetungsten 20%. The nmr spectrum shows only the features of these three compounds and gives a similar composition. Clearly toluene is more reactive than benzene. By liquid chromatography over acid Alumina (activity 1), the dihydride is eluted with 50:50 pentane:toluene, the monohydride 50:50 THF:toluene. This sample was not completely free of dihydride; it consisted mainly of dark red crystals and a small amount of oil. The nmr spectrum showed 16% contamination by dihydride and 11% bistoluenetungsten. The remainder of the spectrum can be attributed to the cyclopentadienyltoluenetungsten monohydride: CH_3, τ 7.80, singlet, area 3.3; C_6H_5, 6.10, multiplet, area (5.0); C_5H_5, 5.42, doublet (J = 1.2 Hz), area 5.0; W–H, 12.3, broad multiplet, area 0.7.

Presently we are investigating the reactions of tungsten and molybdenum atoms with indene. Preliminary results indicate that a mixture of at least three components is formed with each metal. These products have been tentatively identified as the bisindene species, the bisindenyl dihydride species, and the mixed indenylindene hydride species.

Vacuum codeposition of 500 mg of thermally generated molybdenum atoms with 30 g of cycloheptatriene produces a yellow-brown matrix. On melting the matrix a brown solution was obtained, from which excess substrate was removed *in vacuo* and the residue was sublimed (65–85° (10^{-3} Torr)) to give the pure product as a red crystalline solid in 52% yield, based on molybdenum deposited in the reaction zone. The solid is soluble in all hydrocarbon solvents; it reacts with chloroform. The major electron impact product (70 eV) is the parent peak, $C_{14}H_{16}Mo^+$, with proper isotope pattern for one Mo; the only other major fragment is $C_7H_7^+$; a minor fragment is $C_{12}H_{12}Mo^+$. The proton nmr spectrum in C_6D_6 (TMS) shows a prominent singlet of 7 H at τ 5.35; the remainder of the spectrum consists of three complex multiplets centered at 5.1, 5.8, and 8.5 with relative areas of 3.0, 1.9, and 3.9, respectively. This spectrum is interpreted as a C_7H_7 unit with equivalent hydrogens and the remainder as C_7H_9.[5] The ^{13}C nmr spectrum (C_6D_6) is wholly consistent with this interpretation, showing a larger peak at 83.9 ppm (7.01 C) and smaller ones at 102.6 (1.89 C), 91.3 (0.83 C), 82.5 (2.10 C), and 37.4 ppm (2.16 C). The absorption at 102.6 is assigned to C-1 and C-5 (possibly C-2 and C-4) of the cycloheptadienyl portion, 91.3 to C-3, and 37.4 to C-6 and C-7.

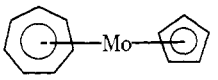


The preparation of the corresponding tungsten compound is identical, except that the yield is ~20%; the gross appearances of the tungsten and molybdenum products are the same. The mass spectrum of the tungsten product is similar, with $C_{14}H_{16}W^+$ the most prominent feature, followed by $C_7H_7^+$ and $C_{12}H_{12}W^+$ (25%). The proton nmr spectrum in C_6D_6 (TMS) consists of a sharp singlet at τ 5.18 (7 protons) and three multiplets, 4.6 (3.15 H), 6.0 (1.95 H), and 8.3 (3.9 H). There is a close similarity to the corresponding molybdenum spectrum above, and the analogous structure is assigned.



The 7–7 molybdenum compound was converted to the 7–5 sandwich compound by refluxing 18 hr with a 15-fold excess of sodium cyclopentadienide in THF. The solvent was stripped off *in vacuo* and the crude residue was sublimed to obtain a dark brown crystalline solid which was purified further by recrystallization from a heptane–toluene mixture. The mass spectrum (70 eV) shows a prominent parent peak for $C_{12}H_{12}Mo^+$, with $C_7H_7^+$ the only other noteworthy feature. The proton nmr spectrum in toluene-d_8 (TMS) consisted of two sharp singlets, τ 5.08 (7.3 H) and 5.27 (4.7 H). The ^{13}C spectrum in THF also showed two

absorptions, 84.4 (5.03 C) and 80.4 ppm (6.97 C). These data strongly support the assignment of the 7-5 sandwich structure, cycloheptatrienylcyclopentadienylmolybdenum.



The analogous reaction to prepare the 7-5 tungsten sandwich compound is not as readily affected. Despite efforts, employing a variety of conditions, it was not possible to obtain a pure product; only mass spectral evidence could be obtained for its presence.

Both of these 7-5 sandwich compounds were described earlier.[4] While we have full accord in mass spectral features for the molybdenum compounds, there is an apparent disagreement in the proton nmr spectrum, probably in the reporting of the data.

Acknowledgment. The financial support of the Air Force Office of Scientific Research (Grant No. 71-1983) is acknowledged with gratitude.

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Book Reviews

Structure and Bonding. Volume 16. Edited by J. D. DUNITZ (Eidgenössischen Hochschule, Zürich). Springer-Verlag, New York-Heidelberg-Berlin. 1973. 189 pp. $23.00.

The topic of this volume of "Structure and Bonding" is Alkali Metal Complexes with Organic Ligands. The chapter titles and authors are: (1) Design of Organic Complexing Agents. Strategy towards Properties (J.-M. Lehn); (2) Structures of Organic Complexes with Alkali Metal Ions (M. R. Truter); (3) Specificity for Alkali and Alkaline Earth Cations of Synthetic and Natural Organic Complexing Agents in Membranes (W. Simon, W. E. Morf, and P. Ch. Meir); and (4) Thermodynamics of Cation-Macrocyclic Compound Interaction (R. M. Izatt, D. J. Eatough, and J. J. Christensen).

The editor could not have chosen better authors or subject matter in trying to present the status of organic complexes of alkali metal cations. The authors are among the major contributors and the topics are representative of the recent efforts in this "new area of chemistry." The first article begins with Professor Lehn's thoughts on the necessary features for synthetic organic ligands and reports in a concise and thorough manner the state of the art for their synthesis, properties, and complexes up to 1973. A comprehensive bibliography of 165 references which covers the significant contributions to this area is given. Professor Truter's chapter concerns the structures of a variety of alkali metal complexes, from chelating anions through naturally occurring compounds to synthetic macrocycles like the crown ethers and cryptates. None is discussed at length, but many structures and interesting information are given. The third chapter is a more physical presentation of cation selectivity and permeability through biological and artificial membranes. Theoretical considerations and factors which influence these processes are given. In the last chapter, the Brigham Young group discusses in detail stability constants of complexation of the Pedersen crown ethers and factors which affect these, *e.g.*, cation size, type, and charge, ligand parameters, and the role of solvent.

Because the chapters cover different scientific disciplines, few readers will find all chapters equally interesting. Also applications and use discussion are brief because of the very nature of the studies investigated thus far. In total, though, this is a well-written and concise summary of alkali metal complexation. Coupled with some supplemental literature study, this is a good book for those who would like to learn about the recent state of affairs dealing with alkali metal complexes, and it is helpful even to those currently working in this area.

Donnie J. Sam, *E. I. du Pont de Nemours and Company*

Methods in Membrane Biology. Volumes 1 and 2. Edited by E. D. KORN (National Heart and Lung Institute). Plenum Press, New York, N.Y. 1974. xv + 277 and xiii + 363 pp. $17.50 and $22.50.

These volumes are intended for the membrane researcher who wants to develop an appreciation and understanding of new techniques sufficient to permit critical evaluation of the data obtained.

Each volume has five chapters. The first chapter, by Bangham, Hill, and Miller on liposomes, gives a complete and interesting account of phospholipid vesicles as membrane models. Next Gershfeld describes the use of lipid monolayers and renders a readable treatment of the thermodynamics of films in equilibrium with aqueous phases. The methodology of forming monolayers is treated thoroughly and pitfalls are emphasized. The third chapter concerns spectroscopy of membranes: Urry and Long present seemingly rigorous mathematics to prove the dangers of applying the circular dichroism technique to particulate materials. In a chapter on HL-A antigens, by Reisfeld, Ferrone, and Pellegrino, the difficulties encountered in solubilizing, without denaturing, membrane proteins are presented. Finally, Volume 1 contains a chapter by Kagawa on the reconstitution of mitochondrial membranes. His section on the use of detergents is particularly good.

Volume 2 begins with a long chapter (156 pp) by Lee, Birdsall, and Metcalfe on the application of nmr to membranes. Relaxation times are thoroughly explained and the nmr approach is compared with others, *e.g.*, fluorescent antibody. The evidence for our current concept of the membrane is lucidly presented. The second chapter is by Glick concerning membrane glycoproteins. Assays and methodology are concisely stated with descriptions of advantages and disadvantages. Next comes glycosphingolipids by Laine, Stellner, and Hakomori, in which methodology is stressed. The fourth chapter, written by Steck, is about inside-out and right-side-out vesicles of erythrocytes. The facts are laid bare as the author is delightfully candid about the difficulties encountered in reproducibly generating these vesicles. Surprisingly this is one of the few places where the use of marker enzymes was discussed. The final chapter, by Eilam and Stein, is a mathematical treatment of transport across the erythrocyte membrane.

To conclude, I feel that the methods presented are described so as to reveal their powers and their limitations. On the other hand, this collection of methods does not represent a how-to-do-it book. Also, I feel that the authors could have made greater attempts to relate one method to another. Several topics have not been covered which might have been, including preparation of cell organelles by differential and gradient centrifugation, use of marker enzymes, analysis of membrane lipids, analysis of membrane proteins by