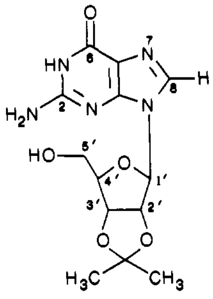
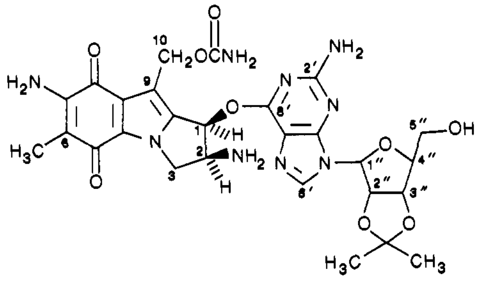


9



10

supported the proposed *cis*-O^6-guanosyl-1-mitosene assignment. First, the mitosene chemical shift values agreed with expectation.[5,24] The resonance noted for the carbon-1 mitosene proton (δ 5.32) was notably downfield from that recorded for *cis*-1-methoxy-2,7-diaminomitosene[5] (δ 4.42) and is consistent with the proposed O^6-guanosyl substitution. A similar deshielding effect was noted in comparing the methoxy chemical shift value for dimethyl ether (δ 3.24) vs. 2-*N*-acetyl-O^6-methyl-2′-deoxyguanosine (δ 4.10).[25,26] Second, three broad singlets were observed in the ^{1}H NMR spectrum of **10** between δ 6.23 and 6.60 and have been attributed to the N–H protons at the C_{10}-carbamate, C_7-amino, and 2′-amino groups.[4] In agreement with this assignment, no signals were detected between δ 10 and 11, a region considered diagnostic for the guanosyl N-1 proton.[27]

Information concerning the generality of the mitomycin C alkylation process was secured by examining the reactivity of **1** with the 2′,3′-*O*-isopropylidene derivatives of adenosine, cytidine, and uridine in the presence of hydrazine (50 equiv). In each case, no noticeable amounts of nucleoside–mitomycin C products were detected (HPLC analysis).[28] Significantly, the base preference noted in this preliminary study mirrors the high guanine specificity reported for the treatment of polynucleotides with mitomycin C under reductive conditions.[8] This suggests that the observed selectivity is a reflection of the reactivity differences which exist at the monomeric nucleoside level for reductively activated mitomycin C. These results imply that prior association (i.e., intercalation) of **1** with DNA may not necessarily be a prerequisite for covalent binding. We note that both the base specificity and the proposed guanosine alkylation site are in agreement with the prescient thesis by Szybalski and Iyer concerning the primary drug binding site on DNA.[2f]

The beneficial properties observed for the hydrazine-mediated reduction of mitomycin C strongly argue for the implementation of this technique in future mitomycin C studies. Moreover, the elucidation of the mode of interaction of the drug with simple nucleosides should serve as a touchstone for understanding the antineoplastic activity of mitomycin C. Additional studies in progress are aimed at determining the generality of this reaction and the structures of the adducts, as well as factors that govern the selectivity of the alkylation process.

Acknowledgment. We thank the National Institutes of Health (R01CA29756) and the Robert A. Welch Foundation for their generous support of our work. We express our sincere appreciation to Dr. Gary Martin (College of Pharmacy, University of Houston) and Drs. Laurence Hurley and Steve Cheatham (College of Pharmacy, University of Texas at Austin) for securing the high-field NMR spectra. Grateful acknowledgment is made to Drs. Larry Kevan and Ichiro Hiromitsu (University of Houston) for running the ESR spectra and to Drs. Marvin Vestal (University of Houston), John Chinn (University of Texas at Austin), and P. V. Fennessey (University of Colorado Health Sciences Center; N.I.H. Clinical Mass Spectrometry Research Resource Grant RR01152) for securing the mass spectral data. We thank Dr. W. T. Bradner (Bristol-Myers Laboratories, Syracuse, NY) for gifts of mitomycin C.

Supplementary Material Available: Experimental section and table of spectral data for compounds **2–4**, **8**, and **10** and a ^{1}H NMR spectrum of **10** (3 pages). Ordering information is given on any current masthead page.

---

(20) Pan, S.-S.; Iracki, T.; Bachur, N. R. *Mol. Pharmacol.* **1986**, *29*, 622–628.

(21) Tomasz, M.; Lipman, R.; Verdine, G. L.; Nakanishi, K. *Biochemistry* **1986**, *25*, 4337–4344.

(22) Tomasz, M.; Chowdary, D.; Lipman, R.; Shimotakahara, S.; Veiro, D.; Walker, V.; Verdine, G. L. *Proc. Natl. Acad. Sci. U.S.A.* **1986**, *83*, 6702–6707.

(23) The following ^{1}H NMR spectral properties have been secured for the second guanosyl–mitomycin C adduct: ^{1}H NMR (300.1 MHz, Me_2SO-d_6) δ 1.27 (s, 3 H), 1.44 (s, 3 H), 1.74 (s, 3 H), 3.66 (m, 2 H), 4.12–4.21 (m, 2 H), 4.41–4.43 (m, 1 H), 4.73 (dd, 1 H, J = 8.8, 13.0 Hz), 4.88 (dd, 1 H, J = 3.0, 6.2 Hz), 4.98 (s, 1 H), 5.01 (d, AB_q, 1 H, J = 12.0 Hz), 5.08 (d, AB_q, 1 H, J = 12.0 Hz), 5.17 (dd, 1 H, J = 3.3, 6.2 Hz), 5.73 (br s, 1 H), 6.39 (br s, 2 H), 6.66 (br s, 2 H), 6.68 (br s, 2 H), 8.01 (s, 1 H).

(24) Bean, M.; Kohn, H. *J. Org. Chem.* **1983**, *48*, 5033–5041. Bean, M.; Kohn, H. *Ibid.* **1985**, *50*, 293–298.

(25) Gaffney, B. L.; Marky, L. A.; Jones, R. A. *Biochemistry* **1984**, *23*, 5686–5691.

(26) The NMR chemical shift analysis predicts that the C-1 methine hydrogen resonance in both the isomeric N(1)- and the N(2)-guanosyl substituted adducts would appear upfield from the observed signal (δ 5.32).[27]

(27) Reese, C. B.; Saffhill, R. *J. Chem. Soc., Perkin Trans. 1* **1972**, 2937–2940.

(28) No significant losses of the nucleosides were noted (HPLC analyses). For the relative rates of hydrazinolysis of purine and pyrimidine nucleosides, see: Hayes, D. H.; Hayes-Baron, F. *J. Chem. Soc. C* **1967**, 1528–1533. Budovskii, E. I.; Hines, J. A.; Kochetkov, N. K. *Dokl. Akad. Nauk SSSR* **1964**, *158*, 379–381 and references therein.

Photoinduced Electrocyclic Rearrangements of Allyl Phosphites via Possible Phosphoranyl 1,3-Biradicals

Wesley G. Bentrude,* Sueg-Geun Lee, Kunihiko Akutagawa, Wei-zhen Ye, and Yves Charbonnel

Department of Chemistry, University of Utah
Salt Lake City, Utah 84112

Received April 14, 1986

Both singlet and triplet excited states of alkenes participate in H-abstraction reactions (eq 1) which are analogous to those of

$$>C{=}CH_2 \xrightarrow{h\nu} \underset{S_1 \text{ or } T_1}{[>C{=}CH_2]^*} \xrightarrow{RH} >\dot{C}{-}CH_2{-}H + R^\bullet \qquad (1)$$

alkyl radicals.[1,2] It is known that methyl and ethyl radicals react with trialkyl phosphites to yield the product of a free radical Arbuzov process when the radical formed on β-scission (eq 2) is

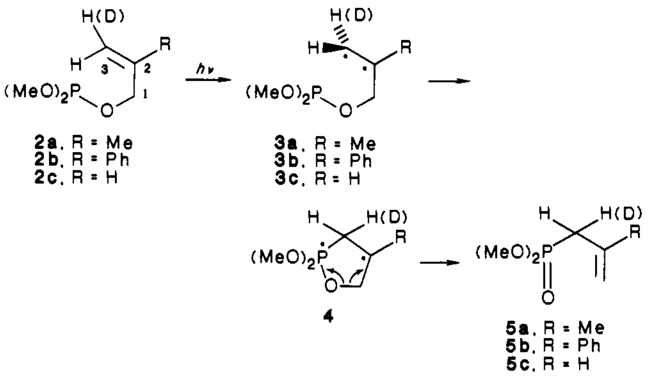
$$Et^\bullet + PhCH_2OP(OEt)_2 \rightleftarrows \underset{\mathbf{1}}{Et\dot{P}(OEt)_2(OCH_2Ph)} \xrightarrow{\beta\text{-scission}} EtP(O)(OEt)_2 + PhCH_2^\bullet \qquad (2)$$

---

(1) For reviews of the photochemistry of alkenes, see: Kropp, P. J. *Org. Photochem.* **1979**, *4*, 1. Kropp, P. J. *Mol. Photochem.* **1978/1979**, *9*, 39.

(2) Indeed, intramolecular hydrogen abstraction to give a 1,4-biradical leading to a Norrish II like cleavage occurs on triplet-sensitized photoreaction of $PhCHOHCHCH_2CPh{=}CH_2$. (Hornback, J. M.; Proehl, G. S. *J. Am. Chem. Soc.* **1979**, *101*, 7367.) Both singlet and triplet excited states of alkenes are capable of H-abstraction, see: Kropp, P. J. *J. Am. Chem. Soc.* **1969**, *91*, 5783. Scully, F.; Morrison, H. *J. Chem. Soc., Chem. Commun.* **1973**, 529. Kropp, P. J.; Tise, F. P. *J. Am. Chem. Soc.* **1981**, *103*, 7293.

Scheme I

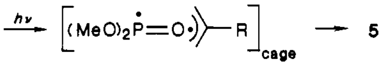


sufficiently stable ($PhCH_2^{\bullet}$), thereby trapping the reversibly formed phosphoranyl radical, **1**.[3] It seemed possible, therefore, that the reaction sequence of Scheme I might be induced photochemically. In this process, biradical excited state **3** acts like a primary carbon radical, and **4** → **5** represents a potentially very rapid β-scission step (two π bonds are formed) which traps phosphoranyl 1,3-biradical **4** in a reaction analogous to that of intermediate **1** of reaction sequence 2. (This process is also very similar to the cleavage of Norrish type-II 1,4-biradicals.[4]) Indeed, we report here that 0.1 M **2a** in benzene photorearranges cleanly to **5a** on irradiation through quartz at 254 nm. Yields are 60–70% at low conversions (10–30%). In cyclopentane the reaction is slower. The yield of **5a** is reduced to 25–30% and accompanied by minor side products.

The reaction of **2a** in benzene is quite probably triplet sensitized since the solvent undoubtedly absorbs all of the incident light at 254 nm, and benzene and xylene are known triplet sensitizers of alkenes.[1,5] Indeed, addition of *p*-xylene (0.6 M) to a 0.1 M solution of **2a** in cyclopentane leads to a 4-fold acceleration of the consumption of **2a** on 254-nm irradiation through quartz. The yield of **5a** at 40% conversion is increased by the addition of *p*-xylene from 25% to 70%.

Moreover, phosphite **2b**, which will have a lower E_T than **2a**,[6] undergoes rapid, clean benzophenone-sensitized rearrangement to **5b** in benzene (medium-pressure 450-W Hg lamp, Pyrex filter) in >95% yield at 95% conversion.[7] Rearrangement of **2b** on direct irradiation in the absence of benzophenone (Pyrex filter, benzene) is approximately 10-fold slower. (Yield 54% at 59% conversion, quartz, benzene.) The quantum yield for **2b** → **5b**, $\Phi_{2b\to 5b}$, on direct irradiation at 254 nm in cyclohexane is 0.71. On benzophenone sensitization (350 nm, benzene, Pyrex) $\Phi_{2b\to 5b}$ is 0.82.[8] The apparent S_1 and T_1 processes are both reasonably efficient.

Allyl phosphite **2c**, monodeuterated at C(3), yielded **5c** with deuterium at the -P(O)CHD- position, as indicated in Scheme I, with a regioselectivity of at least 95% on irradiation in benzene through quartz (yield 89% at 73% conversion). The regiochemistry was readily followed by ^2H NMR at 46 MHz. The same result was obtained by ^1H NMR on product phosphonate. In both cases, **5c** was isolated in >99% purity prior to NMR study. The benzophenone-sensitized photorearrangement of **2b** (deuterium-labeled at C(1)) showed the same regiospecificity. The deuterium labeling experiments exclude the potential rearrangement shown in sequence 3, which involves the discrete radical pair **6**. However,



$$2 \xrightarrow{h\nu} \left[(MeO)_2\dot{P}{=}O\cdot)\rangle\!-\!R\right]_{cage} \longrightarrow 5 \qquad (3)$$

6

a radical *chain process* (eq 4 and 5) which utilizes $(MeO)_2\dot{P}(O)$

$$\underset{\mathbf{2c}}{(MeO)_2\dot{P}(O) + CH_2{=}CHCH_2OP(OMe)_2} \rightarrow (MeO)_2P(O)CH_2\dot{C}HCH_2OP(OMe)_2 \quad (4)$$

$$(MeO)_2P(O)CH_2\dot{C}H{-}CH_2{-}OP(OMe)_2 \rightarrow \mathbf{5c} + (MeO)_2\dot{P}(O) \quad (5)$$

$$\mathbf{2c} \rightarrow \mathbf{5c}$$

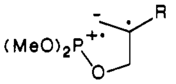
as a chain-carrying species and would give the same regiochemistry as Scheme I, though ruled out by the quantum yield for **2b** → **5b**, is a potential alternative for **2c** → **5c**.[9] Phosphites **7** and **8**

$$\underset{\mathbf{7}}{(MeO)_2POCH_2CCH_3{=}CH_2} \qquad \underset{\mathbf{8}}{(EtO)_2POCH_2CH{=}CH_2}$$

photorearrange in benzene at comparable rates but on reaction at 0.1 M concentration in the same tube do not give so much as 1% of the crossover products required if chain steps 4 and 5 were operative. This result excludes any *intermolecular* process for **2c** → **5c**.

It is reasonable to propose that the reactions of **2a** and **2c** in benzene, and those sensitized by *p*-xylene (**2a**) or benzophenone (**2b**), involve triplet **3** which reacts by way of cyclic intermediate, **4**. Biradical **4** would also be a triplet species at least initially.[10,11]

Although other processes prior to formation of **4** could be envisaged, such as internal electron transfer (eq 6)[12] or electron

2 $\xrightarrow{h\nu}$  → **4** (6)

transfer to excited benzene,[13] Scheme I most simply correlates the current facts concerning the sensitized photorearrangements of **2** to **5**.[14] This reaction bears similarity to the xanthone-sensitized reaction of 1,1-diphenylethylene with $Ph_2P{-}PPh_2$ which yields $Ph_2PCH{=}CPh_2$.[15] That system apparently relies on the ease of cleavage of the weak phosphorus–phosphorus bond (an α-scission) concerted with or subsequent to attack of triplet $Ph_2\dot{C}{-}\dot{C}H_2$ on phosphorus.[16]

---

(3) Davies, A. G.; Griller, D.; Roberts, B. P. *J. Chem. Soc., Perkin Trans 2* **1972**, 2224. Hansen, E. R.; Rogers, P. E., unpublished results from this laboratory. Reversible reactions of $Me_2N^{\bullet}$ with $PhCH_2OP(OEt)_2$ are described in: Bentrude, W. G.; Alley, W. D.; Johnson, N. A.; Murakami, M.; Nishikida, K.; Tan, H. W. *J. Am. Chem. Soc.* **1977**, *99*, 4383.

(4) Wagner, P. J. *Acc. Chem. Res.* **1971**, *4*, 168.

(5) Haninger, Jr., G. A.; Lee, E. K. C. *J. Phys. Chem.* **1967**, *71*, 3104.

(6) $E_T \lesssim 60$ kcal/mol for styrenes. (a) Crosby, P. M.; Dyke, J. M.; Metcalfe, J.; Rest, A. J.; Salisbury, K.; Sodeau, J. R. *J. Chem. Soc., Perkin Trans. 2* **1977**, 182. (b) Lamola, A. A.; Hammond, G. S. *J. Chem. Phys.* **1965**, *43*, 2129.

(7) Styrenes readily undergo energy transfer with triplet benzophenone. Caldwell, R. A.; Cao, C. V. *J. Am. Chem. Soc.* **1982**, *104*, 6174 and refs 1 and 6.

(8) Actinometer system at 254 nm was the benzene-sensitized cis–trans isomerization of *trans*-2-octene (Hentz, R. R.; Thibault, R. M. *J. Phys. Chem.* **1973**, *77*, 1105). The sensitized cis–trans isomerization of *trans*-β-methylstyrene provided the actinometer for Ph_2CO-sensitized **2b** → **5b** (0.2 M **2b**, 0.05 M Ph_2CO; 0.05 M *trans*-β-methylstyrene, 0.05 M PH_2CO), ref 6b.

(9) The free-radical additions of dialkyl phosphites, $(RO)_2P(O)H$, to alkenes involve eq 4 as one of two chain-propagating steps. Sosnovsky, G. *Free Radical Reactions in Preparative Organic Chemistry*; MacMillan: New York, 1964, Chapter 5.

(10) Although $T_1 \rightarrow S_0$ crossings of the twisted triplets of alkenes occur readily (Caldwell, R. A. *Pure Appl. Chem.* **1984**, *56*, 1167), it is unlikely that S_0 **3** would be the reactive species.

(11) Interestingly, the thermal Arbuzov rearrangement of $Ph_2POCH_2CH{=}CH_2$ at 200 °C has the same regiospecificity as the photoprocess **2** → **5**.[12] (Herriott, A. W.; Mislow, K. *Tetrahedron Lett.* **1968**, 3013.) The presumably S_1 direct irradiations of **2b** and **2c** proceed with scrambling of deuterium labeling. (Label of unreacted **2c** unscrambled.)

(12) A similar process has been proposed for aromatic aminoalkenes. Trinquier, G.; Paillous, N.; Lattes, A.; Malrieu *Nouv. J. Chem.* **1977**, *1*, 403.

(13) Maroulis, A. J.; Shigemitsu, Y.; Arnold, D. R. *J. Am. Chem. Soc.* **1978**, *100*, 535.

(14) A completely concerted, direct rearrangement of **2** to **5**, on direct irradiation in cyclic alkanes, cannot be excluded. We are not aware of a definitive theory for electrocyclic photorearrangements of such heteroatom systems which would predict the relative allowedness of concerted and stepwise processes. However, a stepwise process in reactions of *triplet* **3** is consistent with the need for spin inversion at some stage prior to formation of **5**.

(15) Okazaki, R.; Hirabayashi, Y.; Tamura, K.; Inamoto, N. *J. Chem. Soc., Perkin Trans 1* **1976**, 1034.

(16) Benzophenone triplets also are reactive with Ph_2PPPh_2, $(EtO)_2POP(OEt)_2$ (Alberti, A.; Griller, D.; Nazran, A. S.; Pedulli, G. F. *J. Org. Chem.* **1986**, *51*, 3959) (Okazaki, R.; Tamura, K.; Hirabayashi, Y.; Inamoto, N. *J. Chem. Soc., Perkin Trans 1* **1976**, 1924) and other tricovalent phosphorus compounds (Fox, M. A. *J. Am. Chem. Soc.* **1979**, *101*, 5339). A possible 1,3-biradical intermediate was proposed for the electrocyclic photorearrangement of $(CH_3O)_2POCH_2COR$ to $(CH_3O)_2P(O)OCHR{=}CH_2$ (Griffin, C. E.; Bentrude, W. G.; Johnson, G. M. *Tetrahedron Lett.* **1969**, **969**).

Acknowledgment. This research was supported by a grant from the National Science Foundation. We thank Professor Paul J. Kropp for suggesting the *trans*-2-octene actinometer system and for advice concerning its use.

Registry No. 2a, 7446-89-1; **2b**, 51875-99-1; **2c**, 757-54-0; **5a**, 106319-59-9; **5b**, 106319-60-2; **5c**, 106319-61-3.

Organometallic Route to the Chemical Vapor Deposition of Titanium Carbide Films at Exceptionally Low Temperatures

Gregory S. Girolami,* James A. Jensen, and
Deborah M. Pollina

School of Chemical Sciences
University of Illinois at Urbana—Champaign
Urbana, Illinois 61801

Wendell S. Williams,* Alain E. Kaloyeros, and
Clare M. Allocca

Department of Physics, Department of Ceramic Engineering
and Materials Research Laboratory
University of Illinois at Urbana—Champaign
Urbana, Illinois 61801

Received September 26, 1986

Titanium carbide, TiC, is one of the hardest materials known[1] (9–10 Mohs), possesses remarkable thermal stability (mp 3067 °C), and is essentially unaffected by acids and aqueous alkali.[2] These properties make TiC a very useful material for such diverse applications as first-wall coatings for fusion reactors, protective coatings for cutting tools,[3] and low-friction coatings for bearings.[4] Unfortunately, crystalline TiC is also brittle, and this limits its structural applications at low temperatures.[5] With present industrial technology, only crystalline TiC coatings can be deposited on complex shapes; the commercial process involves chemical vapor deposition from hydrogen, methane, and titanium tetrachloride at 1000 °C.[6] More recently, plasma-assisted chemical vapor deposition[7] techniques have been applied to the synthesis of TiC coatings, but these methods also require high temperatures, in excess of 1200 °C.

We now report a simple and powerful chemical vapor deposition (CVD) method for preparing thin films of TiC using an organometallic precursor at exceptionally low temperatures (~150 °C). Tetraneopentyltitanium, $Ti[CH_2C(CH_3)_3]_4$,[8,9] was chosen for metal–organic chemical vapor deposition (MOCVD) studies since it volatilizes easily and has been reported to thermolyze at low temperature.[9,10] We have devised an improved synthesis of $Ti[CH_2C(CH_3)_3]_4$: interaction of $Ti(OCH_2CH_3)_4$ with 4 equiv of $LiCH_2C(CH_3)_3$ in pentane followed by sublimation at 50 °C (10^{-3} torr) gives yellow crystals of the titanium alkyl. The use of titanium tetraethoxide as a starting material prevents reduction of the titanium center that occurs upon alkylation of titanium tetrachloride,[9] thereby doubling the yield from 25% to over 50%.

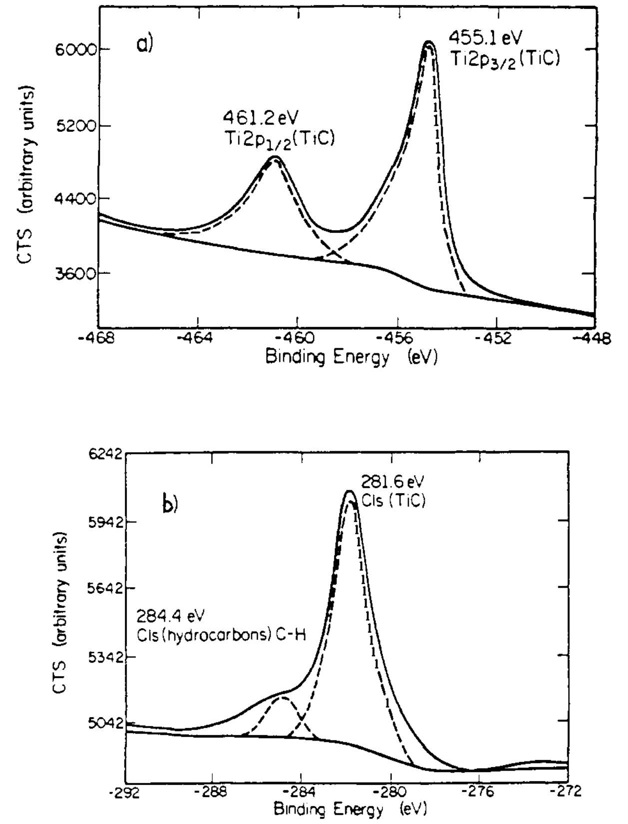


Figure 1. XPS spectra from titanium carbide films prepared by MOCVD from $Ti[CH_2C(CH_3)_3]_4$: (a) Ti 2p spectrum showing that TiC is the only titanium-containing species present; (b) C 1s spectrum showing that TiC and small amounts of hydrocarbons are the only carbon-containing species present.

Low-temperature (150 °C) and low-pressure ($<10^{-5}$ torr) chemical vapor deposition of $Ti[CH_2C(CH_3)_3]_4$ was achieved by using a Pyrex high-vacuum apparatus containing an externally heated reaction zone. Passage of $Ti[CH_2C(CH_3)_3]_4$ through the apparatus resulted in the deposition of adhesive thin films of TiC on Pyrex glass slides mounted in the hot zone. Electron diffraction studies of the silvery metallic films showed only broad diffuse rings characteristic of an amorphous solid, while Auger electron spectroscopy (AES) revealed the presence of titanium and carbon in a Ti/C ratio of ca. 1:0.93. The carbon AES signature from the films was qualitatively different from that characteristic of crystalline titanium carbide, indicating a difference in the local atomic environment. X-ray photoelectron spectroscopy (XPS) results indicated that the Ti $2p_{3/2}$ peak at 455.1 eV and the C 1s peak at 281.6 eV (Figure 1) do in fact correspond to a TiC phase.[11,12] Furthermore, small amounts of organic fragments were detected in the coatings, as shown by the C 1s shoulder at 284.4 eV.[13] No oxygen (<2%) or other elements were present in the interior of the films, but some surface oxidation was apparent that resulted in an oxygen atomic concentration of 10% that fell to <2% within 0.2 μm of the surface. Below this level, there were no changes in the relative elemental amounts or shapes of the XPS peaks as a function of depth within the films.

The thickness of the films can be quite easily tailored by varying the deposition time and temperature. For example, films of 2 μm

---

(1) Storms, E. K. *The Refractory Carbides*; Academic: New York, 1967; p 3.

(2) Toth, L. E. *Transition Metal Carbides and Nitrides*; Academic: New York, 1971; p 141.

(3) Schwarzkopf, P.; Kieffer, P.; Leszynski, W.; Benesovsky, F. *Refractory Hard Metals*; Macmillan: New York, 1953; p 67.

(4) *Refractory Carbides*; Samsonov, G. V., Ed.; Consultants Bureau: New York, 1974.

(5) Williams, W. S. *Prog. Solid State Chem.* **1971**, *6*, 57–118.

(6) Hintermann, H. E.; Gass, H. *Schweiz. Arch. Angew. Wiss. Tech.* **1967**, *33*, 3–10.

(7) Takahashi, T.; Sugimaya, K.; Itoh, H. *J. Electrochem. Soc.* **1970**, *117*, 541–545.

(8) Mowat, W.; Wilkinson, G. *J. Chem.* Soc., *Dalton Trans.* **1973**, 1120–1124.

(9) Davidson, P. J.; Lappert, M. F.; Pearce, R. *J. Organomet. Chem.* **1973**, *57*, 269–277.

(10) Davidson, P. J.; Lappert, M. F.; Pearce, R. *Chem. Rev.* **1976**, *76*, 219–242.

(11) Ramquist, L.; Ekstig, B.; Kallne, E.; Noreland, E.; Manne, R. *J. Phys. Chem. Solids* **1969**, *30*, 1849–1860.

(12) Ramquist, L.; Hamrin, K.; Johannson, G.; Gelius, V.; Nordling, C. *J. Phys. Chem. Solids* **1970**, *31*, 2669–2672.

(13) Johannson, L. I.; Hagstrom, A. L.; Jacobson, B. E.; Hagstrom, S. B. M. *J. Electron. Spectrosc. Relat. Phenom.* **1977**, *10*, 259–271.