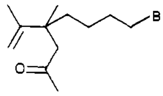
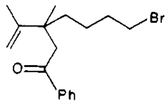
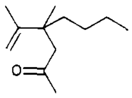
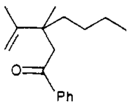
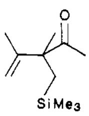
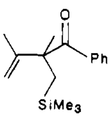
Table II. Stepwise Electrophilic Addition to (2,3-Dimethyl-2-butene-1,4-diyl)magnesium with Two Different Electrophiles

entry	first electrophile[a]	second electrophile[b]	product[c]	% iso. yield
1	$Br(CH_2)_4Br$	MeCOCl		62
2	$Br(CH_2)_4Br$	PhCOCl		60
3	$Me(CH_2)_3Br$	MeCOCl		61
4	$Me(CH_2)_3Br$	PhCOCl		82
5	Me_3SiCl	MeCOCl		73
6	Me_3SiCl	PhCOCl		79

[a] The first electrophile was added to the THF solution of (2,3-dimethyl-2-butene-1,4-diyl)magnesium at −78 °C. The reaction mixture was then allowed to warm to room temperature prior to the addition of the second electrophile. [b] The second electrophile was added at 0 °C. [c] All new compounds have satisfactory spectroscopic data including ^1H NMR, ^{13}C NMR, IR, and high-resolution mass spectral data.

with other electrophiles. For example, the addition of alkyl or aryl acid chlorides results in high yields of the corresponding ketones (Table II). The overall scheme yields a net "2,1-addition". The overall high isolated yields indicate that Grignard addition to the initially formed ketone was minimal.

Utilizing the reverse regioselectivity of harder electrophiles, one can effectively secure overall "1,2-addition". Treatment of **2** with chlorotrimethylsilane resulted in initial attack at the 1-position, yielding an allylic Grignard. While the structure of the allylic Grignard reagent has not been verified by spectroscopic studies, the most logical structure is with the magnesium on the primary carbon (Scheme III). Treatment of **4** with acid chloride results in addition to the γ-carbon, generating a quaternary center. The overall reaction is a formal addition of R_3Si-COR′ across a terminal double bond with the generation of a quaternary center and introduction of two functional groups.

In summary, we have demonstrated that highly reactive magnesium can efficiently prepare substituted 2-butene-1,4-diylmagnesium complexes. Furthermore, we have shown that these halide-free bis-Grignard reagents can be used for the formation of 6-, 5-, and 4-membered rings containing a quaternary center. Formal 1,4-additions, "2,1-additions", and 1,2-additions can be effected by proper choice of electrophiles. Current efforts have shown that this approach can be extended to unsymmetrical 1,3-dienes. Utilization of this technique for the synthesis of natural products is also currently under investigation.

Acknowledgment. We gratefully acknowledge the support of this work by the National Institutes of Health (Grant GM35153). We would also like to thank Dr. T.-C. Wu and Dr. K. P. Daruwala for their helpful suggestions.

Registry No. **1**, 117527-70-5; **2**, 95251-09-5; $Br(CH_2)_4Br$, 110-52-1; $Br(CH_2)_3Br$, 109-64-8; $Br(CH_2)_2Br$, 106-93-4; Me_2SiCl_2, 75-78-5; $Me(CH_2)_3Br$, 109-65-9; $MgCl_2$, 7786-30-3; *trans*-1-phenyl-2-((*E*)-2-phenylethenyl)cyclohexane, 120853-48-7; *trans*-1-phenyl-2-((*E*)-2-phenylethenyl)cyclopentane, 120853-49-8; (*E*,*E*)-1,4-diphenyl-1,3-butadiene, 538-81-8; 1,1-dimethyl-2,5-diphenylsilacyclopent-3-ene, 120881-25-6; 1-methyl-1-(1-methylethenyl)cyclohexane, 16580-19-1; 1-methyl-1-(1-methylethenyl)cyclopentane, 120853-50-1; 1-methyl-1-(1-methylethenyl)cyclobutane, 120853-51-2; 3,4-dimethyl-1,1-diphenylsilacyclopent-3-ene, 29163-98-2; 7-bromo-2,3,3-trimethyl-1-heptane, 120853-52-3; 6-bromo-2,3,3-trimethyl-1-hexene, 120853-53-4; 7-bromo-2,3-dimethyl-3-methylcarbonylmethyl-1-heptene, 120853-54-5; 7-bromo-2,3-dimethyl-3-phenylcarbonylmethyl-1-heptane, 120853-55-6; 2,3-dimethyl-3-methylcarbonylmethyl-1-heptene, 120853-56-7; 2,3-dimethyl-3-phenylcarbonylmethyl-1-heptene, 120853-57-8; 3,4-dimethyl-3-trimethylsilylmethyl-4-penten-2-one, 31397-76-9; 3-benzoyl-2,3-dimethyl-4-trimethylsilyl-1-butene, 55532-01-9; 2,3-dimethyl-1,3-butadiene, 513-81-5; 1,4-di-*n*-butyl-1,4-diphenylbut-2-ene, 120853-58-9; dichlorophenylsilane, 80-10-4.

Cyclohexadienone Annulations of Aryl Carbene Complexes of Chromium: New Strategies for the Synthesis of Indole Alkaloids

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Summary: The first examples of the reactions of indolyl carbene complexes with acetylenes are reported. These reactions have potential for the development of a totally new approach to the synthesis of *aspidosperma* alkaloids.

Sir: The reactions of alkenyl- and arylchromium carbene complexes with acetylenes have become useful annulation processes for the construction of 4-alkoxyphenols and 4-alkoxynaphthols.[2] One of the synthetic advantages of

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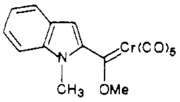
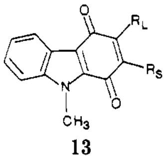
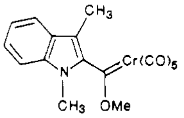
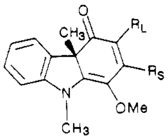
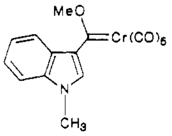
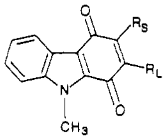
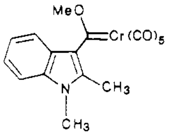
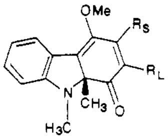
(1) (a) National Science Foundation Predoctoral Fellow, 1984–87; American Chemical Society Organic Division Monsanto Fellow, 1987–1988. (b) Eli Lilly Young Scholar, 1986–87.

Table I. Annulations of Indole Carbene Complexes with Alkynes[a]

carbene complex	R_L	R_S	annulated indole	% yield
 **10a**	Et	Et	 **13**	79[b]
	Et	Et	**13**	79[c]
	Et	Et	**13**	81[d]
	Et	Et	**13**	29[e]
	n-Pr	H	**14**	68[f]
	Ph	H	**15**	61[c]
	$SiMe_3$	OEt	**16**	78[d,g]
 **10b**	Et	Et	 **18**	95[b,h]
	n-Pr	H	**20**	85
	Ph	H	**21**	80[b]
	n-Pr	OEt	**22**	49[b,i]
 **11a**	Et	Et	 **13**	78[j]
	n-Pr	H	**23**	73[b,j,k]
	Ph	Ph	**24**	52
 **11b**	Et	Et	 **25**	76[l]
	n-Pr	H	**26**	48[b]

[a] Unless otherwise specified all reactions were run in hexane at 0.01 M in carbene complex with 1.1–1.5 equiv of alkyne at 50 °C for 24 h. The reaction mixtures were oxidized by excess (>7 equiv) of aqueous ceric ammonium nitrate at 25 °C for 30 min to give the quinones and simply chromatographed on silica gel in air to give the dienones. [b] Average of duplicate runs. [c] 0.20 M in benzene, 2.5 equiv of alkyne. [d] 0.17–0.20 M in THF, 2.5 equiv of alkyne. [e] 0.01 M in acetonitrile; **13** was obtained in ~90% purity from SGC, crystallization (2 crops) gave a 17% yield of **13**. [f] Ratio of **14**:**23** ≥ 350:1 by capillary GC. [g] As a 36:42 isolable mixture of the desilylated to silylated quinones **17**:**16**. [h] 3.8:1 mixture of **18**:**19**. [i] 3.2 equiv of alkyne. [j] 80 °C, 9–20 h, 2.0 equiv of alkyne. [k] Ratio of **23**:**14** ≥ 110:1 by capillary GC. [l] Can be purified and characterized but not stored.

alkenyl complexes is that cyclohexa-2,4-dienones **2** containing a new chiral center can be obtained from β,β-disubstituted complexes **1**.[2c,d,3] In contrast, aryl complexes **4** that are 2,6-disubstituted have never been observed to give cyclohexadienones but rather typically give indenes of the type **5** (Scheme I) that differ from the outcome in the reactions of the alkenyl complexes by the failure of a carbon monoxide ligand to be incorporated.[2,3a,4]

The annulations of a number of heteroaryl complexes have been examined including furan,[5] thiophene,[5a,h,k] and pyrrole[5c,d] carbene complexes. In all cases of complexes of the type **7** the substituent R_1 was hydrogen and thus the question as to whether "ortho"-substituted heteroaryl complexes would give cyclohexadienones **9** or cyclopentadienes **8** has not been experimentally addressed. We report here that the annulations of "ortho"-substituted indolyl carbene complexes **10b** and **11b** give cyclohexa-2,4-dienone annulated products of the type **9** and thus, unexpectedly, their reactivity parallels most closely the alkenyl complexes **1** rather than the aryl complexes **4**.

The reaction of the 1,3-dimethyl-2-indolyl carbene complex **10b**[6] with diethylacetylene occurred to give carbon

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(2) (a) Dötz, K. H.; Fischer, H.; Hofmann, P.; Kreissel, F. R.; Schubert, U.; Weiss, K. *Transition Metal Carbene Complexes*; Verlag Chemie: Deerfield Beach, FL, 1984. (b) Dötz, K. H. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 587. (c) Wulff, W. D.; Tang, P. C.; Chan, K. S.; McCallum, J. S.; Yang, D. C.; Gilbertson, S. R. *Tetrahedron* **1985**, *41*, 5813. (d) Wulff, W. D. In *Advances in Metal-Organic Chemistry*; Liebeskind, L. S., Ed.; JAI Press Inc.: Greenwich, CT, 1989; Vol. 1.

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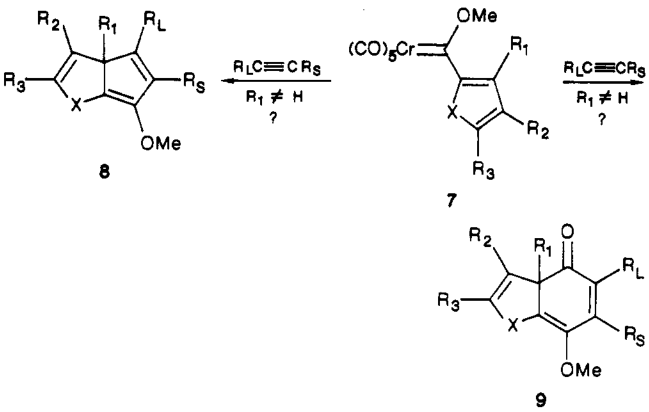
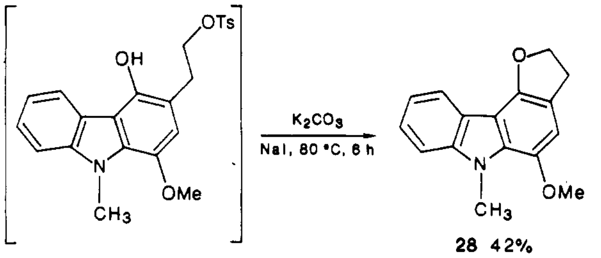
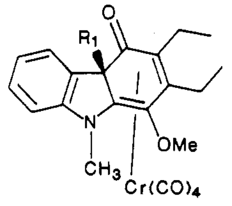


monoxide inserted cyclohexa-2,4-dienone **18** (Table I) in 95% total yield with no evidence for the formation of a five-membered ring annulated product. The formation of the 6-membered ring product was unexpected, not only because of the precedent discussed above, but also because it has been observed that electron-rich carbene complexes have a greater tendency to give indene products.[2c,8] The dienone chromium tetracarbonyl complex **19** can be isolated as a minor product from this reaction and is the first such metal complex that has been reported from a cyclohexadienone annulation.[3] The ^{13}C NMR spectra reveals that **19** is fluxional with only a single absorption for the carbonyl ligands (δ 228.16 ppm).[9] The structure of **19** was confirmed by X-ray diffraction, and the details of the structure study have been published elsewhere.[10]



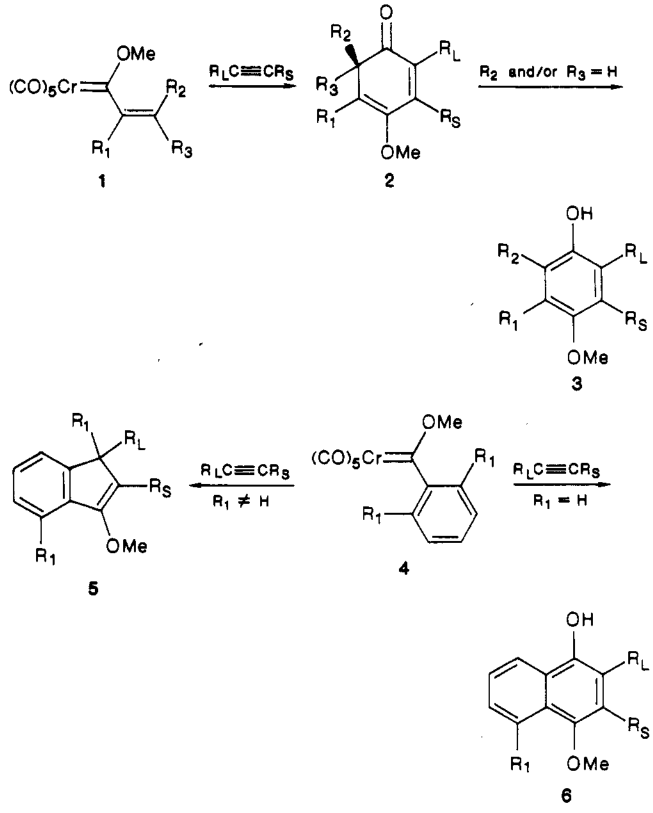
27

28 42%



19

Scheme I



Since the annulations of indole carbene complexes have not been previously reported, we surveyed these reactions with the substituted complexes **10b** and **11b** as well as the unsubstituted complexes **10a** and **11b**, which were found to give hydroxy carbazoles.[6] The hydroxy carbazole products (of the type **27**) initially obtained from the reactions of complexes **10a** and **11a** were not isolated: rather, the crude reaction mixtures were oxidized with ceric ammonium nitrate to provide the corresponding carbazole quinones.[13] As indicated by the first four entries in the Table, these reactions are less efficient in polar solvents such as acetonitrile, which is in line with observations for the reactions of other aryl complexes where selectivity for benzannulated products is highest in nonpolar noncoordinating solvents.[8b]

The direction of the alkyne incorporation was determined from the reaction of the 2-indolyl complex **10a** with 3-butynyl tosylate,[14] and the initial hydroxy carbazole **27** was cyclized to **28** in 42% yield from **10a**. Thus, the direction of alkyne incorporation is the same as has been established for other aryl complexes.[15] The degree of regioselectivity of these reactions was conveniently measured from the reactions of the complexes **10a** and **11a** with 1-pentyne since the pair of quinones **14** and **23** are mutually shared as the two possible regioisomers that would be produced from each reaction. Analysis of the crude mixture, obtained from an oxidative workup of the reaction of the 2-indolyl complex **10a** with 1-pentyne by capillary GC, revealed that the selectivity for the formation of **14**

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(6) The carbene complexes **10a**, **10b**, **11a**, **11b**, and **29** were prepared from the corresponding indolyllithium and chromium hexacarbonyl according to the standard Fischer procedure.[7d] The yields for these complexes are not optimized in all cases and are as follows: **10a**, 50% from *N*-methylindole; **10b**, 40% from 2-bromo-*N*-methylskatole;[7b] **11a**, 42% from 3-bromo-*N*-methylindole;[7a] **11b**, 22% from 3-bromo-1,2-dimethylindole;[7c] **29**, 65% from the MOM ether of *N*-methyltryptophol.

(7) (a) Piers, K.; Meimaroglou, C.; Jardine, R. V.; Brown, R. K. *Can. J. Chem.* **1963**, *41*, 2399. (b) Hino, T.; Nakagawa, M. *Chem. Pharm. Bull.* **1975**, *23*, 2997. (c) Bocchi, V.; Palla, G. *Synthesis* **1982**, 1096. (d) Fischer, E. O.; Heckl, B.; Dötz, K. H.; Müller, J.; Werner, H. *J. Organomet. Chem.* **1969**, *16*, P29.

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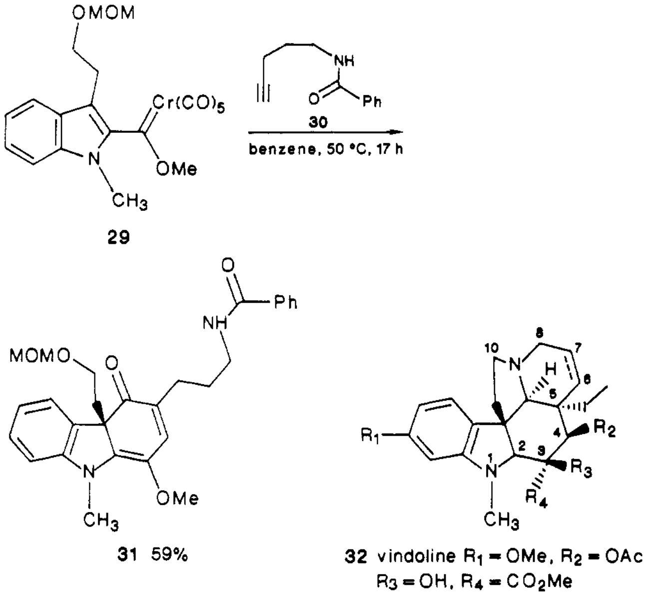
is greater than 350:1. In a similar manner, it was determined that the selectivity for the formation of **23** from the reaction of the complex **11a** was greater than 110:1.

The unexpected finding that the annulations of "ortho"-substituted indolyl carbene complexes give cyclohexadienones of the type **9** rather than the cyclopentadiene **8** permits a consideration of a carbene complex based strategy for entry into a variety of indole alkaloids that would not have been considered in any retroanalysis. The reaction of the carbene complex **29**[6] and the alkyne **30** revealed that these reactions are tolerant of functionality at a level sufficient to prompt our further attention with regard to their development for a totally new approach to the synthesis of *aspidosperma* family of alkaloids of which vindoline **32** is an important member.[16] These findings should also serve to stimulate the investigation of the annulations of other "ortho"-substituted heteroaryl carbene complexes.



29

30

31 59%

32 vindoline $R_1 = OMe$, $R_2 = OAc$, $R_3 = OH$, $R_4 = CO_2Me$

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Supplementary Material Available: Spectral data for all new compounds (9 pages). Ordering information is given on any current masthead page.

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A New Oxidizing Reagent: Triethylsilyl Hydrotrioxide

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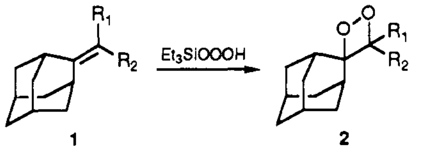
Summary: Triethylsilyl hydrotrioxide ($Et_3SiOOOH$) is a new, short-lived oxidizing agent that can react at −78 °C directly and rapidly with olefins to form 1,2-dioxetanes and oxidatively cleaved carbonyl products.

Sir: Triethylsilyl hydrotrioxide ($Et_3SiOOOH$), prepared in situ at −78 °C in CH_2Cl_2 from triethylsilane plus ozone, was reported in 1986 to be a new chemical source of the powerful oxidant singlet molecular oxygen ($^1O_2$).[1] Shortly thereafter we showed for the first time (1) a *direct* reaction of $Et_3SiOOOH$ (i.e., not via free $^1O_2$) with some electron-rich arylalkenes and (2) the superiority of $Et_3SiOOOH$ over free $^1O_2$ for preparation of an aryldioxetane.[2] Herein (1) $Et_3SiOOOH$ is shown to react within seconds at −78 °C directly also with *unactivated olefins* to form oxidatively cleaved carbonyl products, and (2) a dioxetane is isolated for the first time from direct reaction of $Et_3SiOOOH$ with an *electron-rich olefin.*

A precooled (−78 °C) methylene chloride solution of the electron-rich tetrasubstituted enol ether **1a**[3] was added immediately and rapidly via cannula to a large excess of very freshly prepared $Et_3SiOOOH$ in methylene chloride at −78 °C.[1] After a few minutes, product isolation by preparative TLC gave dioxetane **2a** in 47% yield, having ^1H NMR signals at δ 3.05 and 2.22 and a mass spectrum characteristic of an authentic sample of dioxetane **2a**.[3] In



(1)

	R_1	R_2	yield, %
a	OMe	m-HOC_6H_4	47
b	OMe	H	34
c	H	C_6H_5	–

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(1) Corey, E. J.; Mehrotra, M. M.; Khan, A. U. *J. Am. Chem. Soc.* **1986**, *108*, 2472.

(2) Posner, G. H.; Weitzberg, M.; Nelson, W. M.; Murr, B. L.; Seliger, H. H. *J. Am. Chem. Soc.* **1987**, *109*, 278.

(3) We thank Drs. Brooks Edwards and Irena Bronstein of Quest Systems Inc. for a generous gift of enol ether **1a** and for the ^1H NMR spectrum of authentic dioxetane **1c**. See: Bronstein, I.; Edwards, B.; Voyta, J. C. *J. Bioluminescence Chemiluminescence* **1988**, *2*, 186. See also: Bronstein, I.; McGrath, P. *Nature* **1989**, *338*, 599.