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REACTIONS OF ENYNES WITH ADSORBED METAL-CARBENES

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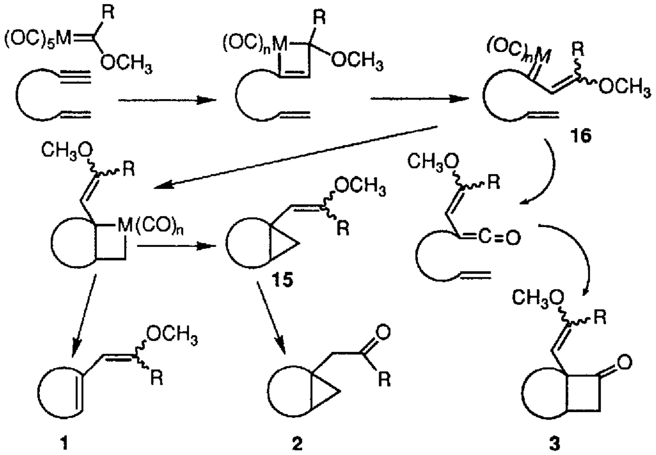
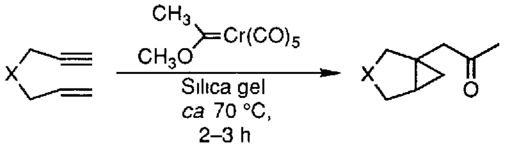
Summary Adsorbed on silica-gel or on other adsorbants ($MgSO_4$, Na_2SO_4, or Na_2CO_3), but not in homogeneous solution, pentacarbonyl(methoxyethylidene)chromium combines with simple enynes to give bicyclo[3 1 0]hexanes The method's usefulness is illustrated by the synthesis of a variety of previously unknown structures from simple hydrocarbons, ethers, and amines

Acetylenes, unlike unactivated olefins, combine with external metal-carbenes that are stabilized by heteroatoms [1] The resulting vinyl-metal-carbenes react with various olefins,[1] but most easily with those to which they are attached [2,3] These principles are the basis of a number of transformations, including three that cyclize enynes, shown in Scheme I [4,7]

Scheme I

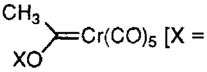


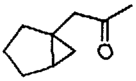
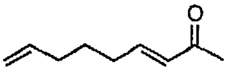
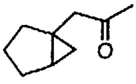
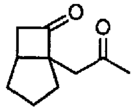
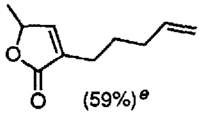
We report here a procedure (eq 1) that greatly improves the preparation of structures like **2**, whose synthesis from metal-carbenes was discovered and developed by Hoye [5] The process, tried because Smit found that adsorption on silica facilitates Pauson-Khand reactions,[8] is to adsorb the derivative of the metal-carbonyl on solids and use no solvent



(1)

Table I compares three methods for combining 1-hepten-6-yne with metal-carbenes The procedure in the third line is the one that Hoye and Rehberg discovered works best for enynes substituted by two carbomethoxyls at the fourth carbon from the acetylene-end,[5c] but with the unsubstituted enyne it forms no carbocy-

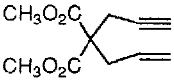
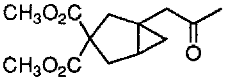
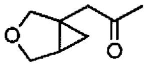
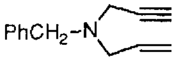
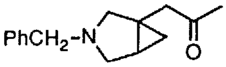
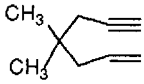
Table I Variation in Products when 1-Hepten-6-yne Reacts Under Different Conditions with 1 mole of  $(CH_3)(XO)C{=}Cr(CO)_5$ [X = CH_3 or $(CH_3)_4N^+$ −][a]

X	Conditions	Products and Yields	
CH_3	SiO_2 (4g/mmol), 70 °C, 3 h	 **4** (36%)[b]	 **5** (51%)[b]
CH_3	CH_3CN (0 05 M), 70 °C, 3 h	 **4** (8%)[c]	 **6** (41%)[c]
$(CH_3)_4N^+$ −	THF (0 33 M), 67 °C, 12 h	< 5 % **4**, **5**, or **6**,[d]	 (59%)[e]

[a]The yields were determined by ^{1}H NMR analysis (10 s relaxation delays, triethyl phosphate internal standard) [b]The products were isolated by extracting the silica gel with ethyl acetate (soxhlet extractor) Flash chromatography on silica then gave **5** preceded by a mixture of **4** and a small amount of **5** Pure **4** was obtained by preparative-GC [c]After reaction, the CH_3CN was stripped After refluxing in 0 125% HCl in aqueous acetone (1 3) and stripping solvent, product **6** was separated from **4** by flash chromatography Reference 6 reports a 31% yield of **6** [d]Aqueous workup The enyne's acetylene ^{1}H NMR at δ 1 93 was gone [e]Isolated by preparative GC NMR's at δ_H 1 37 (d, J = 6 8 Hz), 4 96 (dq, J = 1 5, 6 7 Hz), and 6 97 (br d, J = 1 3 Hz), and δ_C 77 4 ppm, and an IR peak ($CHCl_3$) at 1761 cm^{-1} match those of the butenolide in which the sidechain is butyl rather than pentenyl [5d]

cles The procedure in the second line is the one used by Wulff and Kaesler [6] It gives **6**, as they described, accompanied by another product, a small amount of **4** In contrast, our procedure, line 1, gives a large amount

Table II Examples of Equation 1[a]

Enyne	Conditions	Product (yield)	
 **7**	63 °C, 3 h	 **11**	(94%)[b]
 **8**	63 °C, 3 h	 **12**	(85%)[c]
 **9**	80 °C, 2 h	 **13**	(51%)[d]
 **10**	70 °C, 2 h	 **14**	(50-54%)[e]

[a]Reactions were performed using equivalent amounts (1–2 mmol) of enyne and metal-carbene and 4–5 g of silica gel per millimole Products were isolated by soxhleting with ethyl acetate or ether (20 mL) [b]After concentration and filtration with EtOAc through a small amount of silica gel, the product was essentially pure (^{1}H NMR) [c]The yield according to ^{1}H NMR analysis using *n*-decane as the internal standard Isolated by preparative-GC [d]Obtained by flash chromatography [e]The yield according to ^{1}H NMR analysis using triethyl phosphate as the internal standard Isolated by preparative-GC

of **4**, along with a dienone that may arise by a process similar to one discovered by Macomber [9]

Table II indicates the generality of the procedure and its potential, for with the exception of **11**,[5b] all the products were previously unknown Some of these—**4**, **5**, and **14**—were identified by synthesizing them in other ways,[10] while **12** and **13** were identified on the basis of their spectra [12] With the exception of **9**,[13] all the starting enynes—1-hepten-6-yne,[14] **7**,[15] **8**,[16] and **10**[17]—are known compounds

Experiments were also performed to see whether adsorbants other than silica would be effective, and Table III records the yields obtained in studies that started with **10** The observation is that $MgSO_4$ and Na_2SO_4 are very effective, that alumina is not, and that whereas the more acidic adsorbants give **14**, Na_2SO_4 and Na_2CO_3 give the enol-ethers (**15** in Scheme I)

Table III Yields Obtained in the Reactions of **10** with Pentacarbonyl(methoxyethylidene)chromium on Different Adsorbants[a]

Adsorbant	Product (yield)	Adsorbant	Product (yield)
silica gel	**14** (50–54%)	$MgSO_4$	**14** (86%)
acidic alumina	**any** (<10%)	Na_2SO_4	**15** (48%)
neutral alumina	**any** (<10%)	Na_2CO_3	**15** (25%)
basic alumina	**any** (<10%)		

[a] Reactions were carried out at 75–80 °C using 1 equiv of metal-carbene and 10 mL of adsorbant per mmol of enyne After extracting with 20 mL of EtOAc and spiking with 1/6 equiv of $(EtO)_3PO$, the yields were determined by ^1H NMR analysis (20 s relaxation delays) Structure **15** (see Scheme I) signifies the enol-ethers of **14**, determined to be a 5 1 mixture of *Z* and *E* isomers (see footnote 18) It was isolated by flash chromatography on silica gel, eluting with 1 9 ethyl acetate/hexane (1% triethylamine), and gas chromatographed

How do the adsorbants exert their effect? Simple removal of CO from the metal does not seem to be the key, for *N*-methylmorpholine oxide, which does remove such CO's[19] and induces Pauson-Khand reactions,[20] does not bring about the transformation in eq 1 [21] A possible mechanism, analogous to previous proposals,[8b,c] is that anchoring constrains the conformation to promote the availability of the olefin to the metal-carbene, increasing the likelihood that this olefin will react rather than the acetylene of another molecule While we do not know what happens to the metal-carbene when it is warmed on the adsorbants, our alternative hypothesis is that when an oxygen in **16** coordinates a cation on the surface, the electrophilicity of the carbene increases, and with it the selectivity for reaction with alkene rather than alkyne [22]

Experimental Procedure The conversion of **8** to **12** illustrates the methodology Silica gel (Woelm 32–63 µm, 8 g) was combined with the metal-carbene (500 mg, 2 mmol) in hexane (40 mL), and the solvent was removed at reduced pressure The yellow, coated silica gel under nitrogen (note not oxygen as in ref 8) in a 100 mL round-bottomed flask was shaken while immersed in an oil bath at 63 °C with enyne **8** (2 mmol) and *n*-decane (0 33 mmol) The shaker was a VIBRAX-VXR from IKA Works (Cincinnati, Ohio) After 3 h, soxhlet extraction with 20 mL ether gave material, which ^1H NMR analysis (using the intensity of the decane resonance at δ 0 88 as a reference) showed to contain an 85% yield of **12** It was isolated by preparative GC on 5% SE30 on Chromosorb W-HP

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References and Notes

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(2) Katz, T J , Sivavec, T M *J Am Chem Soc* **1985**, *107*, 737

(3) That appropriate attachment notably facilitates such reactions is demonstrated in the work of Casey [Casey, C P , Hornung, N L , Kosar, W P *J Am Chem Soc* **1987**, *109*, 4908 and references therein] and Hegedus [Soderberg, B C Hegedus, L S *Organometallics* **1990**, *9*, 3113]

(4) **1** reference 2, **2** reference 5, **3** reference 6

(5) (a) Korkowski, P F , Hoye, T R , Rydberg, D B *J Am Chem Soc* **1988**, *110*, 2676 (b) Hoye, T R , Rehberg, G M *Organometallics* **1989**, *8*, 2070 (c) Hoye, T R , Rehberg, G M *J Am Chem Soc* **1990**, *112*, 2841 (d) Hoye, T R , Rehberg, G M *Organometallics* **1990**, *9*, 3014

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(7) Other such reactions (a) Parlier, A , Rudler, H , Platzer, N Fontanille, M , Soum, A *J Chem Soc , Dalton Trans* **1987**, 1041 (b) Alvarez, C , Parlier, A , Rudler, H , Yefsah, R , Daran, J C , Knobler, C *Organometallics* **1989**, *8*, 2253 (c) Parlier, A , Yefsah, R , Rudler, M , Rudler, H , Daran, J C , Vaissermann, J *J Organomet Chem* **1990**, *381*, 191 (d) Harvey, D F , Brown, M F *J Am Chem Soc* **1990**, *112*, 7806

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(9) Macomber, D W *Organometallics* **1984**, *3*, 1589

(10) **4** Ethyl-1-cyclopentene-1-acetate was cyclopropanated,[11a] hydrolyzed, and converted to the methyl ketone [11b]
5 5-Hexen-1-ol was oxidized with pyridinium chlorochromate[11c] and combined with acetonyl diethyl phosphonate [11d]
14 3,3-Dimethyl cyclopentene-1-carboxaldehyde, prepared from 5,5-dimethyl-1,3-cyclohexanedione,[11e] was reduced to the alcohol,[11f] cyclopropanated,[11g] and reoxidized to the aldehyde [11h] A Wittig reaction gave a mixture of enol ethers (1 1), which was hydrolyzed with aqueous HCl in MeOH [11i]

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(12) **12** ^{1}H NMR ($CDCl_3$) δ 3 89 (d, J = 9 9 Hz, 1H, OCH_2C), 3 78 (s, 2H, OCH_2), 3 51 (d, J = 9 9 Hz, 1H, OCH_2C), 2 76 (d, J = 16 8 Hz, 1H, $COCH_2$), 2 58 (d, J = 16 8 Hz, 1H, $COCH_2$), 2 15 (s, 3H, CH_3CO), 1 38 (m, 1H, CH in 3-ring), 0 70 (t, J = 4 7 Hz, 1H, CH_2 in 3-ring), 0 60 (dd, J = 2 0, 4 7 Hz, 1H, CH_2 in 3-ring), ^{13}C NMR ($CDCl_3$) δ 207 24, 72 49, 69 54, 46 10, 30 12, 24 68, 22 80, 13 03 MS (CI, NH3) 141 (M + 1), 158 (M + 18) I R ($CDCl_3$) 1731 (s) cm^{-1}
13 ^{1}H NMR ($CDCl_3$) δ 7 20–7 29 (m, 5H, C_6H_5), 3 58 (s, 2H, $PhCH_2N$), 2 97 (d, J = 8 6 Hz, 1H, NCH_2C), 2 93 (d, J = 8 6 Hz, 1H, NCH_2C), 2 68 (d, J = 15 6 Hz, 1H, $COCH_2$), [2 44 (m, NCH_2CH), 2 41 (d, J = 15 6 Hz, $COCH_2$), 2H], 2 19 (d, J = 8 4 Hz, 1H, NCH_2CH), 2 14 (s, 3H, $COCH_3$), 1 19 (m, 2H, cyclo-$CHCH_2C$), 0 40 (m, 1H, $CHCH_2C$ in 3-ring) ^{13}C NMR ($CDCl_3$) δ 208 24, 128 47, 128 12, 126 77, 58 98, 58 18, 54 59, 48 46, 30 05, 23 48, 21 85, 13 26 MS (CI, NH_3) 230 (M + 1) IR ($CHCl_3$) 1706 (s) cm^{-1}

(13) Prepared in 46% yield from allylpropargylamine (made in 90% yield by refluxing propargyl bromide and excess allylamine—see Ben-Efraim D A *Tetrahedron* **1973**, *29*, 4111) by heating it overnight at 95 °C in 10 volumes of triethylamine and 0 5 eq benzyl bromide, then quenching with benzoyl chloride

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(15) (a) Atkinson, R S , Grimshire, M J *J Chem Soc , Perkin Trans 1* **1986**, 1215 (b) R Mook, Ph D Dissertation, Columbia University (1985)

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(18) The NOE's between the methoxyl and vinyl protons in the mixture were used to assign the stereochemistries

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(21) The *N*-oxide (6 eq)[20] plus **7** in CH_2Cl_2, −78 °C → 25 °C, returned enyne **7**

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