Highly Functionalized Five-Membered Carbocycles from (3-Dialkylamino-1-ethoxyalkenylidene)pentacarbonylchromium Complexes and Alkynes: The Effects of Substituents, Solvents, Ligand Additives, and Reagent Concentrations on the Product Distribution

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The cocyclization reaction of pentacarbonyl(*β*-amino-1-ethoxyalkenylidene)chromium complexes **1** with alkynes has been studied with respect to the effects of substituents, solvents, ligand additives, and reagent concentrations upon the product distribution. This reaction proceeds either as a formal [2 + 2 + 1] cycloaddition to give 5-(1′-dialkylaminoalkylidene)-4-ethoxycyclopent-2-enones **8** or a formal [3 + 2] cycloaddition to give 5-dialkylamino-3-ethoxy-1,3-cyclopentadienes **9**. A working hypothesis for the mechanism of this reaction is proposed on the basis of that previously determined for the Dötz reaction. The effects of the aforementioned parameters upon the product distribution of this current reaction are explained in terms of this model. A pronounced ligand-induced allochemical effect has been observed. Conditions for the selective preparation of both classes of cycloadducts **8** and **9** have been determined.

Introduction

Recent years have witnessed many developments in the chemistry of Fischer carbene complexes, so that they have come to represent a valuable class of synthetic reagents.[1] The best known and most thoroughly studied reaction of these complexes is the so-called Dötz reaction, i.e., the reaction of a 1-alkenyl- or 1-aryl-1-alkoxy-substituted Fischer carbene complex of type **1** (X = OR) with an alkyne to form, in a chromium-mediated template cocyclization of the allyl- or benzylcarbene ligand with an alkyne and a carbonyl ligand, a 4-alkoxycyclohexadienone **3** (or the corresponding enol tautomer, a phenol/naphthol **2**, if possible).[1,2] The overall reaction is a formal [3 + 2 + 1] cycloaddition and complements the Diels−Alder reaction, among others, as an access to six-membered carbocycles. The Dötz reaction has been utilized in efficient syntheses of a number of natural products and bioactive compounds.[1,3] Intrinsically more difficult, however, is the formation of five-membered carbocycles by virtue of an umpoled (or dissonant) relationship of the carbon atoms in a linear arrangement.[4] Averting involvement of the carbonyl ligand in the Dötz reaction potentiates access to cyclopentadienes (or indenes) in a formal [3 + 2] cycloaddition of the allyl- or benzylcarbene and alkyne ligands. Such a process occurs upon reaction of 1-dialkylamino-1-arylcarbene chromium complexes **1** (X = NR_2) with alkynes to give indenes **4**, after 1,5-hydride shift, under forcing conditions (>110 °C), (Scheme 1).[5] The necessity of harsher reaction conditions and nonoccurrence of carbonyl inser-

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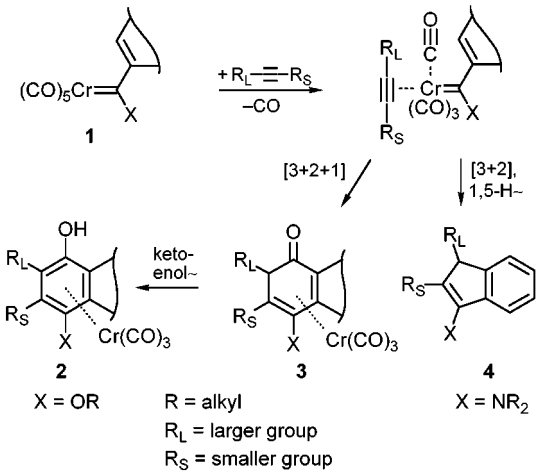
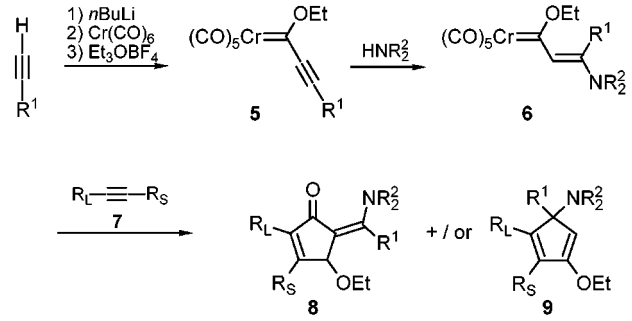
Scheme 1



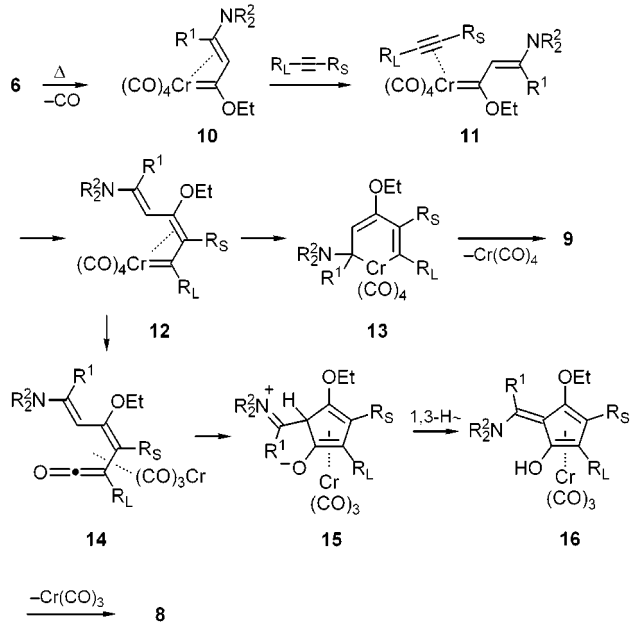
tion has been attributed to the higher donicity of the dialkylamino group stabilizing the Cr−CO bonds.[5d] Unlike their 1-aryl-substituted analogues, 1-dialkylamino-1-alkenylcarbene chromium complexes **1** (X = NR_2) are highly selective to form carbonyl-inserted formal [3 + 2 + 1] cycloadducts upon reaction with alkynes to give 4-dialkylaminocyclohexadienones **3** and the corresponding phenols **2**.[6]

The reactions of (1-alkoxy-3-dialkylamino-2-alken-1-ylidene)pentacarbonylchromium complexes **6** with alkynes that have only been uncovered in the last 10 years have also turned out to be particularly interesting and useful for organic synthesis.[1m,7−11] Complexes of type **6** are now most easily prepared in a simple four-step operation from terminal alkynes involving initial formation of the alkynylidene complex **5** followed by Michael addition of a secondary amine (Scheme 2).[12] All four operations can be performed in the same pot, giving ready access to the immediate precursors for many types of cocyclizations often in higher yields than can be achieved with intermediate isolation of **5**.[12] Unless group R^1 is very bulky, exclusive formation of the *E*-configurated complexes **6** is observed.[12] Except for complexes **6** and alkynes **7** in which R^1 and/or R_L are very large, the reactions invariably give 5-(1′-dialkylaminoalkylidene)-4-ethoxycyclopent-2-enones **8** via formal [2 + 2 + 1] cycloaddition and/or 5-dialkylamino-3-ethoxy-1,3-cyclopentadienes **9** via formal [3 + 2] cycloaddition.[1m,7−11]

Scheme 2



Scheme 3



A mechanistic rational for these reactions has been developed based on the mechanism proposed for the Dötz reaction (Scheme 3).[7,8,13] Thermally induced dissociation of a *cis*-carbonyl group from **6** and chelation of the tethered double bond gives rise to the allylidene chelate complex **10**,[14] which is intercepted by an alkyne to give **11**. Insertion of the alkyne into the chromium carbene bond in **11** gives the η^3-dienylcarbene **12**,[13] which is the branching point between carbonyl-inserted and non-carbonyl-inserted products **8** and **9**, respectively. This intermediate may either undergo 6π-electrocyclization to the chromacyclohexadiene **13**, followed by reductive elimination to give 5-dialkylamino-3-ethoxy-1,3-cyclopentadienes **9**,[7] or by carbonyl insertion to give the dienylketene complex **14**. Rather than undergo the usual 6π-electrocyclization to give 2,4-cyclohexadienones **3**, as in the Dötz reaction,[13] intermediate **14** prefers to undergo 1,5-cyclization, due to the 1,5-dipolarity imparted by the amino group, to give **15**.[8,15] Subsequent 1,3-proton migration in **15** gives rise to the fulvene complex **16**, which, after loss of the $Cr(CO)_3$ moiety and ketonization of the

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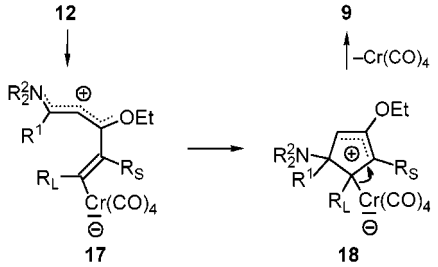
Scheme 4



endocyclic dienol gives 5-(1′-dialkylaminoalkylidene)-4-ethoxycyclopent-2-enones **8**.[8]

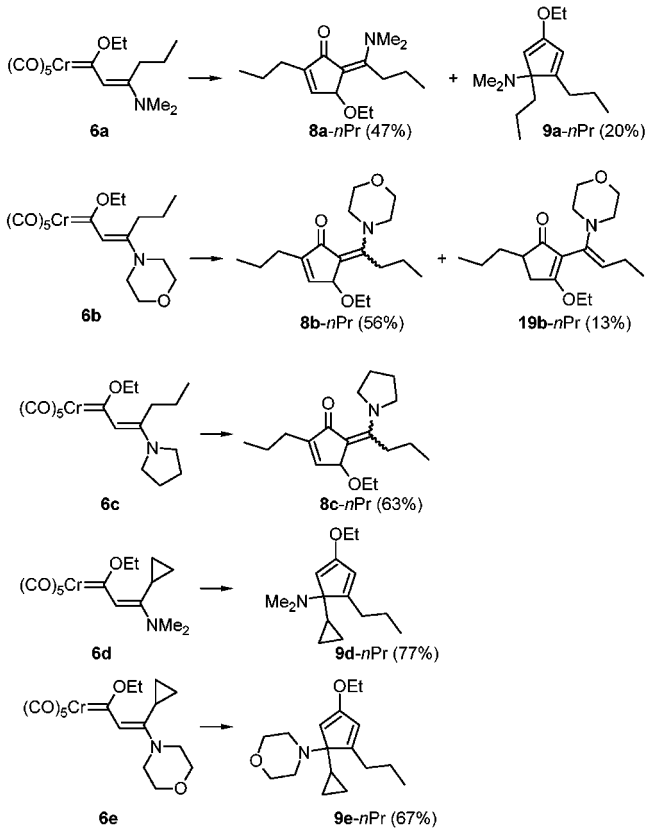
Unlike other intermediates represented in Scheme 3, the chromacyclohexadiene **13** is a coordinatively unsaturated 16-electron species, and it may be too high in its energy to be the most feasible intermediate en route from **12** to **9**. A better alternative to **13** may be a dechelated relative of **12**, the 18-electron zwitterionic **17**, which may give **18** by a Nazarov-type cyclization and then **9** after loss of $Cr(CO)_4$ (Scheme 4).[5b,c]

Here we report upon how each of these two classes of five-membered carbocycles **8** and **9** can be obtained selectively by altering simply the reaction conditions and/or the nature of the groups R^2 and R^1. These reactions appear to be very general and tolerant to a large variety of functional groups born by R^1, R_L, and R_S.[7,8]

Results and Discussion

Cocyclizations of Complexes 6 with Terminal Alkynes in THF: The Effect of Groups R^1 and R^2. The effect of altering the nature of the groups R^1 and R^2 in complexes of type **6** upon the product distribution in their reactions with a simple terminal alkyne, 1-pentyne, was investigated (Scheme 5). A series of complexes **6** bearing different dialkylamino and either an *n*-propyl or a cyclopropyl group were prepared and treated with 1-pentyne. The only products observed were the 5-(1′-dialkylaminoalkylidene)-4-ethoxycyclopent-2-enones **8** (usually as a thermodynamic mixture of *E*/*Z* stereoisomers) as well as their double-bond isomers **19** and 5-dialkylamino-3-ethoxy-1,3-cyclopentadienes **9**. Thus, when the complex **6a** was treated with 1-pentyne in THF solution both the carbonyl-inserted product **8a**-*n*Pr and the non-carbonyl-inserted product **9a**-*n*Pr were obtained in a ratio of approximately 2.5:1 (Scheme 5). As previously reported, complexes containing other secondary amino groups such as morpholinyl, pyrrolidinyl, and dibenzylamino exclusively form carbonyl-inserted products **8** (or some related derivative) upon reaction with alkynes.[8] For example, the reactions of complexes **6b** and **6c** with 1-pentyne gave only the carbonyl-inserted products **8b**-*n*Pr (and its double bond isomer **19b**-*n*Pr) and **8c**-*n*Pr. Since the dimethylamino group is intermediate between pyrrolidino and morpholino groups in its π-donicity, the difference in product selectivity is probably associated with the reduced steric bulk of the dimethylamino group relative to these other amino groups.[16] This can be understood in the context of both of the proposed mechanisms for cyclopentadiene formation (Schemes 3 and 4). Cyclization of **12** to give **13** (or of **17** to give **18**) both bring the amino substituent into close proximity

Scheme 5



with the bulky tetracarbonylchromium unit. Presumably, this process is inhibited with increasing bulk of the amino substituent leading to a preference for carbonyl insertion to give **14**.

Previous studies of the Dötz reaction of 1-alkoxy-1-aryl-substituted Fischer carbene complexes **1** with alkynes have revealed that increasing the donicity of the substituents on the carbene ligand increases the selectivity for the formation of non-carbonyl-inserted compounds.[5,17] To test this effect, the complex **6d** bearing a cyclopropyl group in the β-position was used in order to increase the donicity of the carbene tether while minimizing changes in steric bulk.[18] In this case, exclusive formation of the non-carbonyl-inserted product **9d**-*n*Pr was observed. Increasing the donicity of the carbene ligand is expected to retard carbonyl insertion by strengthening the chromium−carbonyl bonds in **12** (Scheme 3). It may also be that formation of non-carbonyl-inserted products becomes more favored due to the increased stabilization of the zwitterionic species **17** upon introduction of an additional donor group at the vinylic terminus. Even in the case of the morpholinyl-substituted complex, which usually exclusively gives carbonyl-inserted compounds upon reaction with alkynes, the introduction of the cyclopropyl group and its associated donicity in complex **6e** induces exclusive formation of the non-carbonyl-inserted product upon reaction with 1-pentyne to give cyclopentadiene **9e**-*n*Pr.

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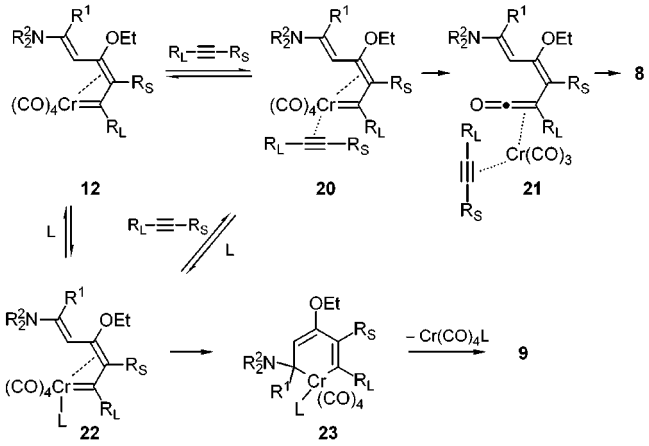
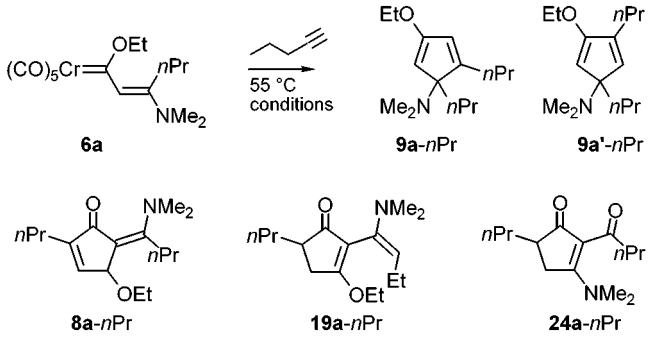
Scheme 6



Scheme 7



It is apparent from this study and previous ones that complexes of type **6** have an intrinsic preference for the formation of carbonyl-inserted products **8** upon reaction with alkynes. The scope of this reaction and some other in situ manipulated variants has previously been reported[8] including an application of this method to the synthesis of a cyclopentanoid natural product.[8b]

Cocyclization of Complex 6a ($R^1 = n$Pr, R^2 = Me) with 1-Pentyne: The Effect of Solvent, Ligand, and Additives, Water, as well as Reagent Concentration upon the Product Distribution. In an effort focused at improving the chemoselectivity in favor of cyclopentadiene formation, a systematic study of factors that might conceivably affect the product distribution was conducted for the reaction of complex **6a** ($R^1 = n$Pr, R^2 = Me) with 1-pentyne.

In the comprehensive studies conducted by Wulff et al. on the Dötz reaction of 1-alkoxy-1-aryl-substituted Fischer carbene complexes with alkynes, it was demonstrated that the chemoselectivity between carbonyl-inserted products (naphthols) and non-carbonyl-inserted products (indenes) could be affected by changes in solvent, ligand additives, reagent concentration, and temperature.[17] It was found that the Dötz reaction exhibited increasing selectivity for carbonyl-inserted compounds with increasing alkyne concentration due to the so-called allochemical effect and increasing selectivity for non-carbonyl-inserted products upon increasing coordinative ability of the solvent.[17] A mechanistic basis for these effects has been proposed by Wulff et al. and is contemplated here in the context of the related reaction between complexes **6** and alkynes to give either **8** or **9** (Scheme 6), where it would also be expected to operate in view of the close mechanistic relationship of this and the Dötz-type reaction. The allochemical effect arises when the intermediate chelate complex **12** is in some way intercepted by an alkyne to give complex **20** (Scheme 6).[17] The presence of the alkyne ligand at the chromium center in **20** induces carbonyl insertion to give **21**. This is thought to occur by virtue of the ability of the alkyne to act as a 4π-electron donor maintaining the chromium center in **21** as an 18-electron species, thus favoring the formation of carbonyl-inserted products.[17c] Other 2-electron coordinating agents (L) may intercept **12** to give **22**. Complex **22** is expected to be predisposed to form non-carbonyl-inserted products since the ligand L does not have a sufficient number of donor electrons in order to facilitate formation of an analogue of **21** in which the alkyne is replaced with a two-electron donor ligand L, but will be able to stabilize **23** as an 18-electron species relative to its 16-electron counterpart **13** (Scheme 3).[17]

To test these proposed effects, **6a** was treated with 1-pentyne (Scheme 7) at varying concentrations of pentyne in solvents of varying coordinating ability (entries 1−8, Table 1).[19] In each case, all the products that could be observed in the ^{1}H NMR spectrum of the crude product mixture were isolated (except where indicated, see Table 1). Despite the low overall mass balance in some cases, the ratio of isolated yields in most cases closely reflects the ratios of products observed in the ^{1}H NMR spectrum of the crude mixture. In the course of this study, five different products were observed in the reactions of **6a** with 1-pentyne including the cyclopentadiene **9a′**-*n*Pr, which is a regioisomer of the usually predominant **9a**-*n*Pr. At no point in this study was a regioisomer observed for any of the CO-inserted formal [2 + 2 + 1] cycloadducts (see below).[20] The carbonyl-inserted products **19a**-*n*Pr and **24a**-*n*Pr must have formed by double-bond migration in **8a**-*n*Pr or in the intermediate of type **16** en route to **8a**-*n*Pr and by enamine hydrolysis with subsequent reaction of the secondary amine to the resulting cyclopentenone, respectively.[8b,c] The mechanism for these transformations has been proposed in the context of the general selective access to these valuable variants that was developed for the related morpholinyl-substituted compounds of type **6**.[8b,c]

The reaction of **6a** and 1-pentyne was first carried out in hexane, THF, DMF, and acetonitrile at varying concentrations of 1-pentyne and in neat 1-pentyne (entries 1−10). Only for reactions carried out in acetonitrile did the reaction exhibit a significant variation in the ratio of non-carbonyl-inserted (**9a**, **9a′**) versus carbonyl-inserted (**8a**, **19a**, **24a**) products as a function of alkyne concentration (compare entries 1−8 with 9 and 10). The reaction performed in acetonitrile at 0.4 M 1-pentyne (entry 9) demonstrates a pronounced preference for non-carbonyl-inserted products (54%) over carbonyl-inserted products (26%). This selectivity is reversed when the concentration of 1-pentyne is increased to 3.4 M (entry 10) giving an increased amount of carbonyl-inserted product (46%) at the expense of non-carbonyl-inserted product (29%). No such change in selectivity as a function of alkyne concentration is observed in hexane, DMF, or

(19) Reactions attempted at very low concentrations of the alkyne (0.015 M) in THF, DMF and acetonitrile, only gave back the unreacted starting material **6a** after 4 days, and are not included in Table 1.

(20) To the best of our knowledge, only one example of a reduction in the regioselectivity of the non-carbonyl-inserted, but not the carbonyl-inserted product in the Dötz reaction has previously been reported, though no explanation of this phenomenon has been offered (see ref 17b).

Table 1. Reaction of Carbene Complex 6a with 1-Pentyne under Various Conditions (Scheme 7)[a]

					yield (%)[c]						
entry	solvent	[pentyne][b]	ligand additive (M)	time (h)	**9a**-*n*Pr	**9a′**-*n*Pr	**8a**-*n*Pr	**19a**-*n*Pr[d]	**24a**-*n*Pr	mass balance (%)	ratio non-CO/ CO-insert.
1[e]	hexane	0.015[f]		90	11	0	10	0	0	21	1.1
2	hexane	0.4		20	26	t[g]	27	0	0	53	1.0
3	hexane	3.4		20	24	t[g]	25	0	0	49	1.0
4	1-pentyne	10.1		20	22	t[g]	24	0	0	46	0.9
5	THF	0.4		60	20	t[g]	47	0	0	67	0.4
6	THF	3.4		22	22	t[g]	37	0	0	59	0.6
7	DMF[h]	0.4		144	27	t[g]	0	0	28	55	1.0
8	DMF[h]	3.4		48	25	t[g]	0	0	27	52	0.9
9	MeCN	0.4		72	40	14	0	26	0	80	2.1
10	MeCN	3.4		14	13[i]	2[i]	1[i]	45	0	61	0.3
11	DMF[h]	0.4	PPh_3 (0.1)	90	42	10[i]	0	6	6	58	8.7
12	DMF[h]	0.4	PPh_3 (1.0)	72	50	12	0	0	0	62	>100[j]
13	DMF[h]	6.0	PPh_3 (0.1)	60	21	5[i]	0	0	24	50	1.1
14	pyridine	0.4		88	68	11	0	3[g]	0	82	26
15[k]	pyridine	0.15		7	78	15	0	0	0	93	>100[j]
16	hexane	0.4	MeCN (0.18)	7	6[i]	t[g]	13[i]	59	0	79	0.08

[a] All reactions were run between 55 and 60 °C at a starting concentration of 0.1 M of complex **6a**, unless otherwise stated. [b] Initial concentration. [c] Isolated yield, unless otherwise stated. [d] This product was only observed in the ^{1}H NMR spectrum of the crude reaction mixture and was isolated as **24a**-*n*Pr after rapid, efficient hydrolysis of the crude product in aqueous THF in the presence of alumina. [e] Starting concentration of complex **6a** was 0.01 M. [f] Another 3 equiv of pentyne was added after 72 h. [g] Trace quantities of this material could be observed in the ^{1}H NMR spectrum of the crude reaction mixture. [h] This solvent contained >1 equiv of water. [i] This material was not isolated, and its yield was estimated by comparison of the integration of signals in the ^{1}H NMR spectrum of the crude reaction mixture. [j] No carbonyl-inserted products could be observed in the ^{1}H NMR spectrum of the crude reaction mixture. [k] This reaction was performed at 80 °C and at a starting concentration of complex **6a** of 0.05 M.

THF (entries 1−8). These observations can be explained in terms of a *ligand-induced allochemical* effect analogous to that proposed by Wulff et al. for the Dötz reaction.[17,21]

The absence of an allochemical effect for reactions performed in hexane, THF, DMF, and neat 1-pentyne (entries 1−8) results from an inability of the alkyne, 1-pentyne, to intercept and dechelate complex **12** to give **20** directly (Scheme 6). This can be attributed to the presence of the strongly electron-donating amino group in **12**, which enhances the chelation relative to those systems studied by Wulff et al. which showed variation in the ratio of carbonyl-inserted to non-carbonyl-inserted products as a function of alkyne concentration irrespective of solvent type and in the absence of solvent.[17] Presumably, acetonitrile (but not hexane, THF, or DMF) is capable of dechelating **12** to give **22** (L = MeCN). Complex **22** is predisposed to give the chromacycle **23**. However, unlike **12**, **22** can also be intercepted by an alkyne, in a ligand-exchange reaction, to give **20**. As discussed above, complex **20** is predisposed to form carbonyl-inserted products via **21**.[17] Consequently, the ratio of carbonyl-inserted and non-carbonyl-inserted products will be dependent upon the relative ratios of **22** and **20**, which, in turn, depend on the relative concentrations of ligand (L) and alkyne.

To further test this hypothesis, the reaction was performed in a solvent for which variation in alkyne concentration does not affect product distribution (DMF), in the absence or presence of a ligand additive (L = triphenylphosphine) and with variation of the relative concentrations of the ligand additive and the alkyne (entries 11−13, Table 1). At a ratio of 1-pentyne to triphenylphosphine of 4:1, the product distribution showed a marked shift in favor of the non-carbonyl-inserted product relative to that of the same reaction performed without added triphenylphosphine (compare entries 7−11, Table 1). When this ratio was adjusted to 4:10 in favor of the triphenylphosphine, exclusive formation of the non-carbonyl-inserted product **9** was observed (entry 12, Table 1). These results are consistent with the ability of the 2-electron donor (L = triphenylphosphine) to induce chromacycle formation and reductive elimination to give cyclopentadiene **9**. Increasing this ratio of the alkyne to triphenylphosphine concentration to 60:1 in favor of the alkyne led to a dramatic reduction in the preference for non-carbonyl-inserted products (compare entries 12 and 13, Table 1). Presumably, the larger alkyne concentration favors interception of **22** to give **20** and resultant induction of carbonyl insertion (a ligand-induced allochemical effect).

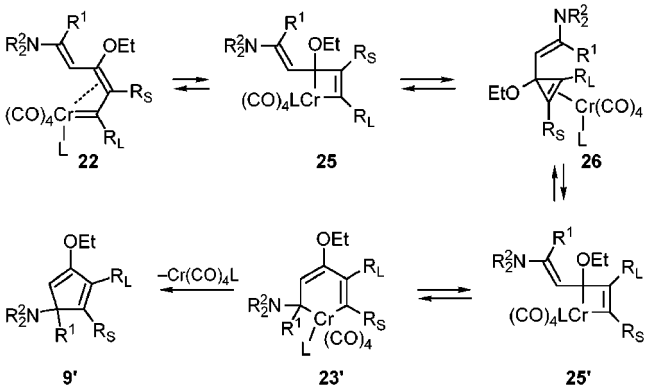
In the presence of ligating agents L, a significant decrease in the regioselectivity for the formation of cyclopentadienes **9a**-*n*Pr and **9a′**-*n*Pr, but not for the carbonyl-inserted products **8a**-*n*Pr, **19a**-*n*Pr, and **24a**-*n*Pr was observed (compare entries 1−8 and 9−16). In fact, no equivalent *n*Pr/H regioisomer was observed for any of the carbonyl-inserted products in the course of this study. This may be rationalized by assuming that donating ligands L do not only induce formation of chromacyclohexadienes **23** and reductive elimination to give cyclopentadienes **9** (Scheme 6), but also formation of chromacyclobutenes **25** and subsequent reductive elimination to give cyclopropene complexes **26** (Scheme 8).[22] The carbonyl chromium group in **26** would be expected to reinsert into the least sterically congested carbon−carbon single bond to give the regioisomeric chromacyclobutene **25′** which can undergo ring enlargement to chromacyclohexadiene **23′** and subsequently reductive elimination to give **9′**.[23]

While complete selectivity for non-carbonyl-inserted products has been achieved using a ratio of alkyne to

(21) Wulff et al. have previously reported that the product distribution of the reaction of some electron-rich 1-alkoxy-1-aryl-substituted Fischer carbene complexes with alkynes is unaffected by variations in alkyne concentration in noncoordinating solvents, but is affected in coordinating solvents; see ref 17c.

(22) Reissig et al. have demonstrated that coordinating agents, such as acetonitrile, promote vinylcyclopropane formation. Presumably, acetonitrile promotes chromacyclobutane formation from which the cyclopropane is derived by reductive elimination: Reissig, H.-U.; Hoffmann, M. *Synlett* **1995**, 623.

Scheme 8



triphenylphosphine of 4:10 in DMF (entry 12, Table 1), the isolated yield of **9a**-*n*Pr (50%) suffered from poor recovery mass balance and poor regioselectivity. It was noticed that the mass balance and regioselectivity are higher in acetonitrile than in other solvents especially at moderate concentrations of alkyne (entry 9, Table 1). Accordingly, it was considered that a more highly coordinating solvent such as pyridine might show even higher selectivity for non-carbonyl-inserted compounds than acetonitrile and also retain a high mass balance. Indeed, when run at the standard concentration of alkyne (0.4 M), the reaction of **6a** with 1-pentyne highly selectively and in a reasonable yield (68%) gives the cyclopentadiene **9a**-*n*Pr. Fortuitously, the reaction performed in pyridine also exhibited a slightly improved regioselectivity for **9a**-*n*Pr compared to that found with acetonitrile or triphenylphosphine as the coordinating agents. Further optimization of the reaction between **6a** and 1-pentyne in pyridine was accomplished by reducing the alkyne concentration from 0.4 to 0.15 M (entry 15, Table 1). It was necessary under these conditions to increase the reaction temperature from 60 to 80 °C in order to achieve a reasonably short reaction time (7 h). It is noteworthy that selectivity for non-carbonyl-inserted compounds is expected to increase with elevating temperatures for reactions conducted in coordinating media.[17] Under the optimized conditions (entry 15, Table 1) the reaction of **6a** with 1-pentyne gives exclusively the non-carbonyl-inserted product **9a**-*n*Pr in a good isolated yield (78%).

While exclusive formation of carbonyl-inserted products of type **8** can be achieved simply by appropriate choice of the amino group in **6** (any dialkylamino group larger than the dimethylamino group) it was also considered interesting to investigate whether improved selectivity for such cycloadducts could be achieved for the dimethylamino-substituted complex **6a** by varying reaction conditions alone. This ought to be possible by taking advantage of the ligand-induced allochemical effect and employing a high ratio of alkyne to ligand (L) concentration, with a ligand fulfilling the minimum required coordinating ability in order to expedite formation of **20** from **22** (Scheme 6). Indeed, when the reaction of **6a** with 1-pentyne (concentration = 0.4 M), which in hexane gives non-carbonyl- and carbonyl-inserted products in a ratio of about 1:1 (entry 2, Table 1), was repeated in the presence of a small amount of acetonitrile (L) (ratio pentyne/MeCN 5:2), giving highly selectively the carbonyl-inserted product **19a**-*n*Pr, as observed in the ^{1}H NMR spectrum. Due to the workup conditions, **19a**-*n*Pr was not isolated as such, but only as its hydrolysis product **24a**-*n*Pr in 59% yield (entry 16, Table 1).[24]

The above explanation of the effects of coordinating agents upon the product distribution and variation in regioselectivity in the formation of non-carbonyl-inserted products, i.e., cyclopentadienes **9**, is inconsistent with a Nazarov-type mechanism. It may well be that such a mechanism is operative for the reaction performed in the absence of coordinating agents but the anticipation[5] that cyclopentadiene formation should be favored in more polar solvents as a result of better solvation of **12** with its zwitterionic feature, as expressed by the mesomeric structure **17**, was not found. In fact, the highest yields of the cyclopropyl-substituted cyclopentadienes of type **9d** from the corresponding cyclopropyl-substituted complexes **6d** were obtained in the noncoordinating solvent hexane.[7b,9]

Conclusion

In general, complexes of type **6** react with alkynes with high selectivity toward carbonyl-inserted products to give 5-(1′-dialkylaminoalkylidene)-4-ethoxycyclopent-2-enones **8**.[8] Only in cases in which the amino group is quite small (such as a dimethylamino group) and the group R^1 is also strongly electron donating are non-carbonyl-inserted products 5-dialkylamino-3-ethoxy-1,3-cyclopentadienes **9** observed.[7] The distribution between carbonyl-inserted and non-carbonyl-inserted products in the reaction of complexes **6** and alkynes can be controlled by the use of appropriate ligand additives. The dependence of this reaction on the presence of such agents is consistent with the mode of action proposed by Wulff et al. for the related Dötz reaction.[17c] Ligand additives or highly coordinating solvents (L) dechelate **12** to give **22** and facilitate formation of chromacycles **23** as well as subsequent reductive elimination to give cyclopentadienes **9** (Scheme 6). Interception of the chelate **12** by alkynes gives **20**, which is predisposed to carbonyl insertion to give carbonyl-inserted cocyclization products via intermediate **21** (allochemical effect). However, direct interception of chelate **12** by an alkyne to give **20** is not possible, but formation of **20** can only occur by exchange of the ligand L in **22** with an alkyne (a ligand-induced allochemical effect). By appropriate choice of the ligand L, and ratio of ligand L to alkyne, the reaction of **6a** with 1-pentyne can be tuned to be highly selective for either carbonyl-inserted products (**8a**-*n*Pr, **19a**-*n*Pr, and **24a**-*n*Pr) or non-carbonyl-inserted products (**9a**-*n*Pr, **9a′**-*n*Pr). The full scope of the synthetically useful selective preparation of 5-(dimethylamino)-3-ethoxy-1,3-cyclopentadienes **9** will be reported separately.[25]

Experimental Section

All operations were performed under an atmosphere of argon unless otherwise stated. Tetrahydrofuran (THF) and diethyl ether were freshly distilled from sodium/benzophenone.

(23) For examples of carbonylchromium insertion into cyclopropene single bonds to give chromacyclobutenes, see: Semmelhack, M. F.; Suzzy, H.; Cohen, D.; Steigerwald, M.; Lee, M. C.; Lee, G.; Gilbert, A. M.; Wulff, W. D.; Ball, R. G. *J. Am. Chem. Soc.* **1994**, *116*, 7108.

(24) The structure of **19a**-*n*Pr was assigned on the basis of definitive resonances in the ^{1}H NMR spectrum of the crude reaction mixture which were consistent with those observed for the isolated morpholinyl-substituted analogue **19b**-*n*Pr that hydrolyzes to **24b**-*n*Pr upon treatment with moist alumina, see ref 8b,c.

(25) For a preliminary communication of our studies in this area see ref 7b.

Acetonitrile and pyridine were distilled from calcium hydride. Column chromatography was carried out using silica gel (230−400 mesh) or neutral alumina (ICN Alumina N − Super I, deactivated to activity grade Super II). Melting points were obtained on a Büchi 510 apparatus and are uncorrected. ^{1}H NMR, ^{13}C NMR and DEPT (distortionless enhancement by polarization transfer) spectra were recorded using a Bruker AM 250 spectrometer (^{1}H NMR at 250 MHz, ^{13}C NMR and DEPT at 62.9 MHz). Chemical shifts refer to $\delta_{TMS} = 0.00$ relative to residual solvent signals. Infrared spectra were obtained using a Bruker IFS 66 spectrometer. Low resolution mass spectra were recorded on a Varian MAT CH 7, MAT 731. High-resolution mass spectra were recorded on a Varian MAT 311 A with preselected ion peak matching $R \gg 10\,000$ to be within ±2 ppm of the exact mass. Elemental analyses were performed by Mikroanalytisches Laboratorium des Instituts für Organische Chemie der Universität Göttingen. The synthesis of the compounds **6a**,[12a] **6b**,[8c] **6e**,[12a] **6d**,[12a] **8b**-*n*Pr,[8c] **9b**-*n*Pr,[8c] **9d**-*n*Pr,[7a] **19b**-*n*Pr[8c] has previously been reported.

Pentacarbonyl[(2*E*)-1-ethoxy-3-pyrrolidinyl-2-hexen-1-ylidene]chromium (6c). Pyrrolidine (160 mg, 2.25 mmol) was added slowly to a solution of pentacarbonyl-(1-ethoxy-2-hexyn-1-ylidene)chromium (386 mg, 1.22 mmol) in diethyl ether (15 mL) at 20 °C. After the addition was complete, the reaction mixture was concentrated under reduced pressure, and the residue subjected to flash chromatography on silica gel (30 g), eluting with pentane/diethyl ether (3:1) to give **6c** (434 mg, 92%) as yellow crystals: mp 113 °C; ^{1}H NMR (250 MHz, $CDCl_3$) δ 0.79 (t, $^3J = 7.0$ Hz, 3 H), 0.85−1.03 (m, 4 H), 1.23 (t, $^3J = 7.0$ Hz, 3 H), 1.63 (tq, $^3J = 7.0$ Hz, $^3J = 7.0$ Hz, 2 H), 2.31 (t, $^3J = 7.0$ Hz, 2 H), 2.44 (t, $^3J = 5.3$ Hz, 2 H), 2.81 (t, $^3J = 5.3$ Hz, 2 H), 4.68 (q, $^3J = 7.0$ Hz, 2 H), 6.35 (s, 1 H); ^{13}C NMR (250 MHz, $CDCl_3$) δ 14.30, 15.54, 21.06, 24.30, 24.59, 35.35, 47.81, 49.57, 73.84, 118.59, 157.02, 220.60, 224.92, 283.39; IR (KBr) $\tilde{\nu}$ 2998 cm^{-1}, 2873, 2045, 1943, 1520, 1250, 1094; MS (70 eV) *m*/*z* 387 (2) [M$^+$], 359 (1), 331 (1), 303 (2), 275 (3), 247 (27), 165 (34), 137 (100); calcd for $C_{17}H_{21}CrNO_6$ 387.0774 (correct HRMS).

General Procedure (GP) for Cocyclization Reactions of Complexes 6 with Alkynes. In a thick-walled Pyrex bottle equipped with a magnetic stirring bar were placed the solvent, the complex **6**, and the ligand additive (where used). A stream of argon was bubbled through the solution for 1 min, and then the alkyne was added. The sealed reaction vessel was placed in an oil bath preheated to the desired temperature. The reaction vessel was removed from the oil bath when consumption of the complex **6** was complete (TLC). After being cooled to room temperature, the mixture was transferred to a round-bottom flask, and the solvents were removed under reduced pressure (an efficient oil pump was used in the case of DMF). The residue was diluted with pentane/diethyl ether (2:1) and then stirred, open to the air, for 20 min. The reaction mixture was then filtered through Celite, and the filtrate concentrated under reduced pressure. An ^{1}H NMR spectrum was recorded for this crude reaction mixture before it was chromatographed. Toward that, the residue was dissolved in diethyl ether, and alumina (activity grade II) (4 g/mmol based on starting complex **6**) was added, and the slurry concentrated under reduced pressure. The resultant powder was added onto a column of alumina (II), and the products eluted sequentially with pentane, pentane/CH_2Cl_2 (4:1), pentane/diethyl ether (9:1), (5:1), (1:1), diethyl ether, diethyl ether/methanol (20:1).

5-[1′-(Dimethylamino)butylidene]-4-ethoxy-2-propylcyclopent-2-enone (8a-*n*Pr) and 5-(Dimethylamino)-3-ethoxy-1,5-(di-*n*-propyl)-1,3-cyclopentadiene (9a-*n*Pr). A solution of **6a** (150 mg, 0.42 mmol) in THF (4.0 mL) was treated with 1-pentyne (113 mg, 1.66 mmol) at 55 °C according to GP. The crude product was purified by chromatography on alumina (II) giving **8a**-*n*Pr (1.2:1 mixture of two inseparable *E*/*Z* stereoisomers, 52 mg, 47%) and **9a**-*n*Pr (20 mg, 20%) as colorless oils. **8a**-*n*Pr: ^{1}H NMR (250 MHz, $CDCl_3$) δ 0.98−1.29 (m, 9 H), 1.59 (quintet, $^3J = 7.0$ Hz, 2 H), 2.41, 2.65 (2 × m, 2 H), 3.16 (s, 6 H), 3.27−3.60 (m, 2 H), 5.05, 5.27 (2 × dt, $^3J = {}^4J = 1.0$ Hz, $^3J = {}^4J = 2.0$ Hz, 2 H); ^{13}C NMR (250 MHz, $CDCl_3$) δ 13.99, 14.00, 14.23, 14.45, 15.22, 15.96, 20.81, 20.86, 21.47, 22.30, 27.40, 27.67, 30.97, 34.48, 41.25, 43.34, 57.99, 60.46, 77.51, 79.70, 104.60, 105.30, 139.41, 140.44, 150.43, 150.59, 162.00, 162.48, 187.87, 193.25; IR (film) $\tilde{\nu}$ 2960 cm^{-1}, 2930, 2870, 1733, 1717, 1699, 1652, 1635, 1549, 1456, 1058; MS (70 eV) *m*/*z* 265 (24) [M$^+$], 236 (100), 220 (95), 190 (31). Anal. Calcd $C_{16}H_{27}NO_2$: C, 72.41; H, 10.26. Found: C, 72.27; H, 10.31. **9a**-*n*Pr: ^{1}H NMR (250 MHz, $CDCl_3$) δ 0.8−0.98 (m, 3 H), 0.92 (t, $^3J = 7.0$ Hz, 3 H), 0.99 (t, $^3J = 7.0$ Hz, 3 H), 1.40−1.65 (m, 4 H), 1.75−2.10 (m, 4 H), 2.18 (s, 6 H), 3.88 (q, $^3J = 7.0$ Hz, 2 H), 4.70 (d, $^4J = 1.8$ Hz, 1 H), 5.69 (dd, $^4J = 1.8$ Hz, $^4J = 1.0$ Hz, 1 H); ^{13}C NMR (250 MHz, $CDCl_3$) δ 14.23, 14.50, 14.76, 16.60, 19.67, 29.04, 36.75, 39.86, 64.45, 68.15, 94.65, 122.07, 156.11, 160.30; IR (film) $\tilde{\nu}$ 2958 cm^{-1}, 2872, 2821, 1729, 1635, 1584, 1462, 1340, 1272, 1121, 1044; MS (70 eV) *m*/*z* 237 (35) [M$^+$], 208 (100), 194 (22), 166 (24). Anal. Calcd $C_{15}H_{27}NO$: C, 75.90; H, 11.46. Found: C, 75.99; H, 11.45.

4-Ethoxy-2-propyl-5-[1′-(pyrrolidinyl)butylidene]cyclopent-2-enone (8c-*n*Pr). A solution of **6c** (194 mg, 0.50 mmol) in THF (5.0 mL) was treated with 1-pentyne (136 mg, 2.0 mmol) at 55 °C according to GP. The crude product was purified by chromatography on alumina (II) eluting sequentially with pentane/CH_2Cl_2 (4:1), pentane/diethyl ether (9:1), (5:1), (1:1), and diethyl ether giving **8c**-*n*Pr (2:1 mixture of inseparable *E*/*Z* stereoisomers, 92 mg, 63%) as a colorless oil: ^{1}H NMR (250 MHz, $CDCl_3$) δ 0.90 (m, 9 H), 1.51 (m, 4 H), 1.80 (m, 2 H), 1.92 (m, 2 H), 2.17 (m, 2 H), 2.55, 2.85, 2.65−3.15 (3 × m, 2 H), 3.18−3.40 (m, 2 H), 3.80 (m, 2 H), 3.97 (m, 2 H), 4.96, 5.72 (2 × s, 1 H), 6.52, 7.11 (2 × s, 1 H); ^{13}C NMR (250 MHz, $CDCl_3$) δ 13.89, 14.33, 14.40, 15.72, 15.93, 20.83, 21.40, 22.19, 25.22, 27.34, 27.61, 32.38, 34.73, 49.32, 57.53, 60.36, 77.77, 79.14, 102.88, 104.87, 138.60, 139.73, 150.34, 150.64, 159.03, 160.12, 187.67, 192.77; IR (film) $\tilde{\nu}$ 2962 cm^{-1}, 2870, 1694, 1653, 1539, 1447, 1336; MS (70 eV) *m*/*z* 291 (21) [M$^+$], 262 (100), 246 (49), 234 (42), 216 (18), 190 (15), 172 (9), 136 (10), 70 (30); calcd for $C_{18}H_{29}NO_2$ 291.2220 (correct HRMS).

5-Cyclopropyl-3-ethoxy-5-(dimethylamino)-1-propyl-1,3-cyclopentadiene (9d-*n*Pr). A solution of **6d** (300 mg, 0.84 mmol) in THF (6.0 mL) was treated with 1-pentyne (460 mg, 6.8 mmol) at 52 °C according to GP. The crude product was chromatographed on silica gel (pentane/diethyl ether 1:1) giving **9d**-*n*Pr (152 mg, 77%), the spectral data of which have been reported previously.[7a]

5-Cyclopropyl-3-ethoxy-5-(morpholinyl)-1-propyl-1,3-cyclopentadiene (9e-*n*Pr). A solution of **6e** (330 mg, 0.82 mmol) and 1-pentyne (252 mg, 3.7 mmol) in THF (15 mL) was heated at 55 °C according to GP. The crude product was chromatographed on silica gel (pentane/diethyl ether 4:1), giving **9e**-*n*Pr (151 mg, 67%) as colorless crystals: mp 64 °C; ^{1}H NMR (250 MHz, $CDCl_3$) δ −0.52 to −0.39 (m, 1 H), −0.05−0.08 (m, 1 H), 0.13−0.23 (m, 1 H), 0.35−0.48 (m, 1 H), 0.69−0.80 (m, 1 H), 0.86 (t, $^3J = 7.0$ Hz, 3 H), 1.20 (t, $^3J = 7.0$ Hz, 3 H), 1.45 (m, 2 H), 2.04 (m, 2 H), 2.14−2.27 (m, 2 H), 2.72−2.85 (m, 2 H), 3.47−3.74 (m, 6 H), 4.30 (d, $^4J = 2.0$ Hz, 1 H), 5.45 (d, $^4J = 2.0$ Hz, 1 H); ^{13}C NMR (250 MHz, $CDCl_3$, DEPT) δ −1.77 (−), 7.28 (−), 14.23 (+), 14.39 (+), 14.83 (+), 20.06 (−), 28.50 (−), 48.20 (−), 64.52 (−), 67.75 (−), 77.52 (C_{quat}), 84.37 (C_{quat}), 120.45 (+), 157.64 (C_{quat}), 162.09 (C_{quat}); IR (film) $\tilde{\nu}$ 2963 cm^{-1}, 2847, 2806, 2639, 1587, 1456, 1372, 1338, 1303, 1117, 1020; MS (70 eV) *m*/*z* 277 (3) [M$^+$], 248 (71), 190 (51), 163 (70), 100 (100); calcd for $C_{17}H_{27}NO_2$ 277.2050 (correct HRMS).

Reaction of Complex 6a with 1-Pentyne under Optimized Conditions (in Pyridine) To Give 9a-*n*Pr (Table 1, Entry 15). A solution of **6a** (150 mg, 0.42 mmol) and 1-pentyne (85 mg, 1.25 mmol) in pyridine (8.3 mL) was heated at 80 °C according to GP. The crude product was purified by chromatography, eluting sequentially with pentane, pentane/CH_2Cl_2 (4:1), pentane/diethyl ether (9:1), (5:1), (1:1), and diethyl ether, to give **9a**-*n*Pr (77 mg, 78%) and **9a′**-*n*Pr (15 mg, 15%) as slightly tan oils. **9a**-*n*Pr: Spectroscopic data see above. **9a′**-*n*Pr: ^{1}H NMR (250 MHz, $CDCl_3$) δ 0.89 (t, $^3J = 7.1$ Hz, 3 H), 0.92 (t, $^3J = 7.1$ Hz, 3 H), 1.24 (m, 2 H), 1.33 (t, $^3J = 7.1$ Hz, 3 H), 1.46−1.63 (m, 4 H), 2.14 (m, 2 H), 2.28 (s, 6 H), 3.84 (q, $^3J = 7.1$ Hz, 2 H), 4.80 (t, $^4J = 1.7$ Hz, 1 H), 5.87 (s, 1 H); ^{13}C NMR (250 MHz, $CDCl_3$) δ 13.91, 14.48, 14.83,

18.51, 21.11, 29.68, 37.42, 40.16, 64.56, 73.41, 100.59, 133.82, 159.19, 171.48; IR (film) $\tilde{\nu}$ 2958 cm^{-1}, 2931, 2871, 1634, 1571, 1445, 1412; MS (70 eV) *m*/*z* 237 (20) [M^+], 208 (58), 194 (100), 166 (42). Anal. Calcd for $C_{15}H_{27}NO$: C, 75.90; H, 11.46. Found: C, 76.08; H, 11.38.

Reaction of Complex 6a with 1-Pentyne under Conditions Optimized for the Formation of 2-[1′-(Dimethylamino)-1′-butenyl)]-3-ethoxy-5-*n*-propylcyclopent-2-enone (19a-*n*Pr) and Its Hydrolysis to 2-Butyryl-3-(dimethylamino)-5-*n*-propylcyclopent-2-enone (24a-*n*Pr) (Table 1, Entry 16). A solution of **6a** (150 mg, 0.42 mmol) and acetonitrile (37.0 μL, 0.71 mmol) in *n*-hexane (4.0 mL) was treated with 1-pentyne (113 mg, 1.66 mmol) at 55 °C according to GP. This reaction gave products **9a**-*n*Pr, **9a′**-*n*Pr, **8a**-*n*Pr, and **19a**-*n*Pr in a ratio of 12:1:26:120 according to a ^{1}H NMR spectrum of the crude reaction mixture.[24] A suspension of neutral alumina (I) (150 mg) in THF/H_2O (4:1) (10 mL) was added to the crude reaction residue and the resultant slurry stirred at 18 °C for 5 h. After this time neutral alumina (activity grade I) (1.0 g) was added, and the reaction mixture concentrated under reduced pressure, and the resultant powder was subjected to flash chromatography on neutral alumina (II) eluting sequentially with pentane, pentane/CH_2Cl_2 (4:1), pentane/diethyl ether (9:1), (5:1), (1:1), diethyl ether, diethyl ether/methanol (20:1). Consequently, the major isolated product was not **19a**-*n*Pr, but **24a**-*n*Pr (58 mg, 59%): a colorless oil;[24] ^{1}H NMR (250 MHz, $CDCl_3$) δ 0.92 (bt, 2 × ^3J = 7.0 Hz, 6 H), 1.34 (m, 4 H), 1.58 (sextet, ^3J = 7.3 Hz, 2 H), 1.83 (m, 1 H), 2.26 (dd, ^2J = 16.6 Hz, ^3J = 3.6 Hz, 1 H), 2.35 (m, 1 H), 2.79 (dd, ^2J = 16.6 Hz, ^3J = 7.9 Hz, 1 H), 2.93 (m, 1 H), 2.94 (bs, 3 H), 3.16 (bs, 3 H); ^{13}C NMR (250 MHz, $CDCl_3$, DEPT) δ 13.99 (−), 14.03 (−), 18.17 (+), 20.31 (+), 34.08 (+), 34.63 (+), 41.41 (−), 44.64 (−), 44.77 (+), 45.31 (−), 113.30 (C_{quat}), 177.07 (C_{quat}), 199.73 (C_{quat}), 202.34 (C_{quat}); IR (film) $\tilde{\nu}$ 2960 cm^{-1}, 2937, 1701, 1694, 1652, 1635, 1552, 1456, 1100; MS (70 eV) *m*/*z* 237 (29) [M^+], 222 (15), 208 (10), 194 (100). Anal. Calcd for $C_{14}H_{23}NO_2$: C, 70.85; H, 9.77. Found: C, 70.68; H, 9.71.

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