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Reduction of Cyclic Group 6 Fischer Carbene Complexes: A Case of Exquisite Regioselectivity

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The reduction of α,β-unsaturated cyclic group 6 metal−carbene complexes strongly depends on the electronic profile of the groups attached both to the carbene and the β-carbon and occurs with exquisite regioselectivity. Thus, for complexes **8** the reduction does not take place at the carbene carbon but exclusively at the γ-carbonyl group. The resulting alkoxide **20** evolves to a tricyclic epoxide structure **21**, which precludes additional hydride transfers. Complex **9** experiences the exclusive 1,4-reduction because of the imino character of the β-carbon (due to the participation of the aromatic resonance form **22**). In contrast, monocyclic carbene complexes **10** behave as their acyclic congeners and experience 1,2-hydride addition followed by the 1,3-migration of the metal center. In this case, the participation of η^3-Cr(CO)$_5$ species **31** allows us to understand the labeling pattern found in the final products.

Introduction

α,β-Unsaturated group 6 metal−carbene complexes[1] behave in their reactions with nucleophiles as their organic esters analogues. In this regard, these otherwise extremely versatile reagents[2] are a special type of conjugated acceptors in agreement with the isolobal relationship.[3] The competition between 1,2- and 1,4-additions is a fact well established since the original report by Fischer[4] on the addition of dimethylamine to alkynylcarbene complexes of chromium and tungsten 30 years ago.[5] Nevertheless, very little is still known about the factors that control the regioselectivity of these reactions. In fact, steric control was claimed to be responsible for the selectivity obtained by Casey in the conjugate addition of enolates to vinylcarbene complexes,[6] a pattern that is usually followed by carbon nucleophiles.[7] However, this general trend is broken by organo-Zn and organo-Li reagents which form exclusively 1,2-adducts in their reactions with alkynyl group 6 carbene complexes.[8] In contrast, the regioselectivity obtained in the reaction of α,β-unsaturated group 6 metal−carbene complexes and sulfur and phosphorus ylides[9] showed a

(1) Reviews on the chemistry of α,β-unsaturated group 6 carbene complexes: (a) Barluenga, J.; Flórez, J.; Fañanás, F. J. *J. Organomet. Chem.* **2001**, *624*, 5. (b) de Meijere, A.; Schirmer, H.; Duetsch, M. *Angew. Chem., Int. Ed.* **2000**, *39*, 3964. (c) Aumann, R.; Nienaber, H. *Adv. Organomet. Chem.* **1997**, *41*, 163.

(2) Reviews: (a) Dötz, K. H.; Fischer, H.; Hofmann, P.; Kreissel, R.; Schubert, U.; Weiss, K. *Transition Metal Carbene Complexes*; Verlag Chemie: Deerfield Beach, FL, 1983. (b) Dötz, K. H. *Angew. Chem., Int. Ed. Eng.* **1984**, *23*, 587. (c) Wulff, W. D. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, 1991; Vol. 5, p 1065. (d) Schwindt, M. A.; Miller, J. R.; Hegedus, L. S. *J. Organomet. Chem.* **1991**, *413*, 143. (e) Rudler, H.; Audouin, M.; Chelain, E.; Denise, B.; Goumont, R.; Massoud, A.; Parlier, A.; Pacreau, A.; Rudler, M.; Yefsah, R.; Alvarez, C.; Delgado-Reyes, F. *Chem. Soc. Rev.* **1991**, *20*, 503. (f) Grotjahn, D. B.; Dötz, K. H. *Synlett.* **1991**, 381. (g) Wulff, W. D. In *Comprehensive Organometallic Chemistry II*; Abel, E. W., Stone, F. G. A., Wilkinson, G., Eds.; Pergamon: Oxford, 1995; Vol. 12, p 470. (h) Hegedus, L. S. In *Comprehensive Organometallic Chemistry II*; Abel, E. W., Stone, F. G. A., Wilkinson, G., Eds.; Pergamon: Oxford, 1995; Vol. 12, p 549. (i) Harvey, D. F.; Sigano, D. M. *Chem. Rev.* **1996**, *96*, 271. (j) Hegedus, L. S. *Tetrahedron* **1997**, *53*, 4105. (k) Aumann, R.; Nienaber, H. *Adv. Organomet. Chem.* **1997**, *41*, 163. (l) Sierra, M. A. *Chem. Rev.* **2000**, *100*, 3591.

(3) This is in agreement with the statement of the isolobal analogy principle. See: (a) Hoffmann, R. *Science* **1981**, *211*, 995. (b) Hoffmann, R. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 711.

(4) (a) Fischer, E. O.; Kreissl, F. R. *J. Organomet. Chem.* **1972**, *35* C47. (b) Fischer, E. O.; Kalder, H. J. *J. Organomet. Chem.* **1977**, *131*, 57.

(5) Selected references dealing with mechanistic aspects of the conjugate addition to α,β-unsaturated Fischer carbenes: (a) Aumann, R.; Jasper, B.; Fröhlich, R. *Organometallics* **1995**, *14*, 3173. (b) Aumann, R.; Jasper, B.; Läge, M.; Krebs, B. *Organometallics* **1994**, *13*, 3502. (c) Pipoh, R.; van Eldik, R. *Organometallics* **1993**, *12*, 2668. (d) Pipoh, R.; van Eldik, R.; Henkel, G. *Organometallics* **1993**, *12*, 2236.

(6) (a) Casey, C. P.; Brunsvold, W. R. *Inorg. Chem.* **1977**, *16*, 391. Other examples: (b) Aoki, S.; Fujimura, T.; Nakamura, E. *J. Am. Chem. Soc.* **1992**, *114*, 2985. (c) Nakamura, E.; Tanoka, K.; Fujimura, T.; Aoki, S.; Williard, P. G. *J. Am. Chem. Soc.* **1993**, *115*, 9015. The 1,2-addition of methyl ketone enolates to α,β-unsaturated carbene complexes has been also reported: (d) Barluenga, J.; Alonso, J.; Rodríguez, F.; Fañanás, F. J. *Angew. Chem., Int. Ed.* **2000**, *39*, 2460.

(7) (a) Merino, I.; Laxmi, S.; Flórez, J.; Barluenga, J.; Ezquerra, J.; Pedregal, C. *J. Org. Chem.* **2002**, *67*, 648. (b) Aumann, R.; Göttker-Schnetmann, I.; Fröhlich, R.; Saarenketo, P.; Holst, C. *Chem. Eur. J.* **2001**, *7*, 711.

(8) Dötz, K. H.; Christoffers, C.; Knochel, P. *J. Organomet. Chem.* **1995**, *489*, C84.

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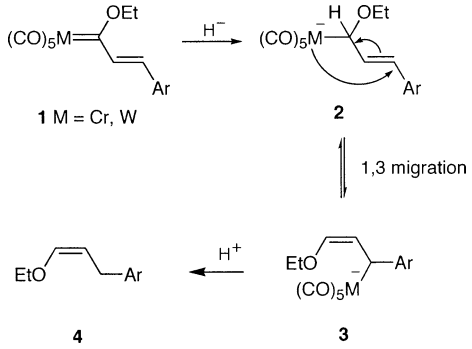
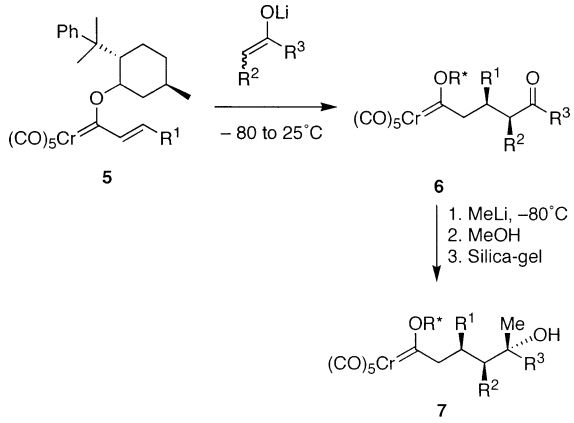
strong dependence with the reactivity of the ylide. More stable ylides added preferentially in 1,4-mode independently of the steric hindrance at the β-position, while the steric hindrance of this position was decisive to determine the regioselectivity for less stable ylides. Meanwhile, heteronucleophiles may form either 1,4- or 1,2-adducts depending on the case, with the reaction conditions, especially temperature, playing an exceptional role in the regioselectivity of the reaction.[10] The situation has been recently exacerbated by the recent reports by us[11] and others[12] describing the participation of the metal center in the addition of simple nucleophiles to α,β-unsaturated group 6 carbene complexes. Thus, the addition of simple hydrides to either alkynyl- or alkenyl-substituted carbene complexes **1** occurs by the initial 1,2-addition of hydride to form **2**, and this is followed by a 1,3-metal rearrangement yielding an anionic σ-complex **3** that finally leads to vinyl ethers **4**. The existence of **3** was demonstrated by diverse labeling experiments (Scheme 1).

SCHEME 1



The reactivity toward nucleophiles of group 6 carbene complexes having additional electrophile centers conjugated with the carbene carbon through a double or triple bond is unknown, probably due to the limited number of such complexes available. Furthermore, except for the addition of organolithium reagents to the keto-group of the in situ generated δ-keto carbene complexes **6**,[13] there are no other examples in which a nucleophile is intermolecularly added to a metal−carbene possessing an additional electrophile center. It should be noted that complexes **6** reacted exclusive and efficiently at the ketone group to yield **7**, leaving the electrophile carbene carbon unchanged (Scheme 2).

SCHEME 2



In connection with our ongoing project directed toward the study of diverse addition reactions to α,β-unsaturated complexes,[9,10e,11] including the addition of radicals[14] and SET processes,[15] complexes **8**, **9**, and **10** (Figure 1) offer an exceptional opportunity to learn how the reactivity of α,β-unsaturated carbene complexes is modulated by interacting with carbonyl, imino, and amido groups, especially regarding the regioselectivity of the addition reactions to these polydentate electrophiles. Reported herein are the results obtained in the addition of hydrides to complexes **8**−**10**. These processes are an exquisite example of regioselectivity.

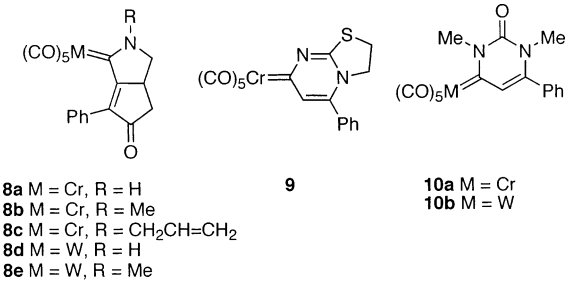


FIGURE 1.

Results and Discussion

Complexes **8** were prepared by our reported procedure using a Pauson−Khand reaction on the precursor enyne

(9) (a) Alcaide, B.; Casarrubios, L. Domínguez, G.; Retamosa, A.; Sierra, M. A. *Tetrahedron* **1996**, *52*, 13215. (b) Alcaide, B.; Casarrubios, L.; Domínguez, G.; Sierra, M. A.; Jiménez-Barbero, J. *Organometallics* **1994**, *13*, 2934. (c) Alcaide, B.; Casarrubios, L.; Domínguez, G.; Sierra, M. A. *Organometallics* **1996**, *15*, 4612. (d) Alcaide, B.; Domínguez, G.; Rodríguez-López, J.; Sierra, M. A. *Organometallics* **1992**, *11*, 1979. For a review on the reactions of group 6 Fischer carbene complexes with ylides and ylide-like derivatives, see: (e) Alcaide, B.; Casarrubios, L.; Domínguez, G.; Sierra, M. A. *Curr. Org. Chem.* **1998**, *2*, 551.

(10) Recent examples: (a) Wu, H. P.; Aumann, R.; Fröhlich, R.; Wibbeling, B. *Eur. J. Org. Chem.* **2000**, 1183. (b) Wu, H. P.; Aumann, R.; Fröhlich, R.; Wegelius, E.; Saavenketo, P. *Organometallics* **2000**, *19*, 2373. (c) Wu, H. P.; Aumann, R.; Fröhlich, R.; Saakenketo, P. *Chem. Eur. J.* **2001**, *7*, 700. (d) Wu, H. P.; Aumann, R.; Fröhlich, R.; Wibbeling, B.; Kataeva, O. *Chem. Eur. J.* **2001**, *7*, 5084. (e) Moretó, J. M.; Ricart, S.; Dötz, K. H.; Molins, E. *Organometallics* **2001**, *20*, 62. (f) Wu, H. P.; Aumann, R.; Fröhlich, R.; Wegelius, E. *Organometallics* **2001**, *20*, 2183. (g) Wu, H. P.; Aumann, R.; Fröhlich, R.; Wibbeling, B. *Chem. Eur. J.* **2002**, *8*, 910. (h) Wu, H. P.; Aumann, R.; Fröhlich, R.; Wegelius, E. *Eur. J. Org. Chem.* **2002**, 361.

(11) (a) Gómez-Gallego, M.; Mancheño, M. J.; Ramírez, P.; Piñar, C.; Sierra, M. A. *Tetrahedron* **2000**, *56*, 4893. (b) Mancheño, M. J.; Sierra, M. A.; Gómez-Gallego, M.; Ramírez, P. *Organometallics* **1999**, *18*, 3252.

(12) Barluenga, J.; Rubio, E.; López-Pelegrín, J. A.; Tomás, M. *Angew. Chem., Int. Ed.* **1999**, *38*, 1091.

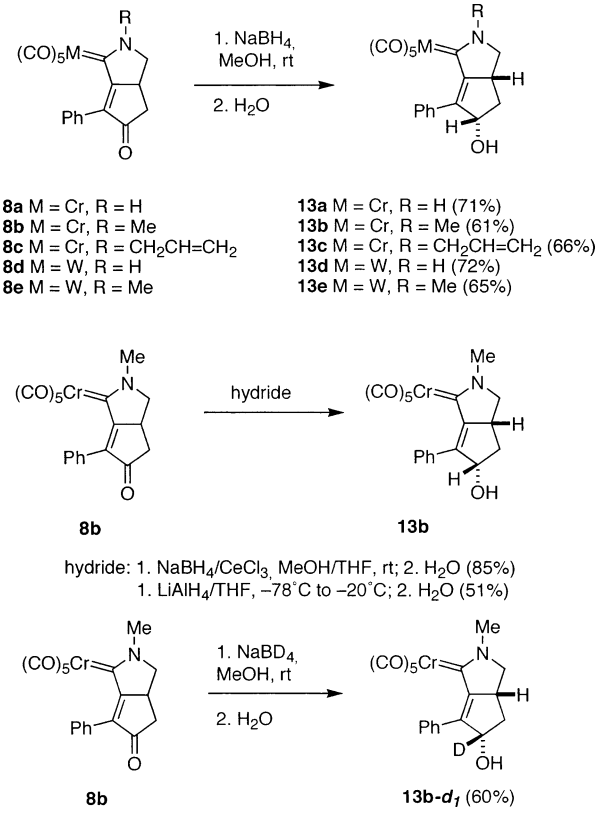
(13) (a) Barluenga, J.; Diéguez, A.; Rodríguez, F.; Flórez, J.; Fañanás, F. J. *J. Am. Chem. Soc.* **2002**, *124*, 9056. (b) Barluenga, J.; Montserrat, J. M.; Flórez, J.; García-Granda, S.; Martín, E. *Chem. Eur. J.* **1995**, *1*, 236.

(14) Mancheño, M. J.; Ramírez-López, P.; Gómez-Gallego, M.; Sierra, M. A. *Organometallics* **2002**, *21*, 989.

(15) Sierra, M. A.; Ramírez-López, P.; Gómez-Gallego, M.; Lejon, T.; Mancheño, M. J. *Angew. Chem., Int. Ed.* **2002**, *41*, 3442.

complexes **11**.[16] Mono- and bicyclic heterocyclic carbene complexes **9** and **10** were also prepared through the addition of either 2-aminothiazolidine (complex **9**) or *N*,*N*′-dimethylurea (complexes **10**) to alkynyl complex **12** following also our reported procedure (Figure 1).[17] Complexes **8a**−**c** were reacted in the presence of $NaBH_4$ in MeOH at room temperature. In this way, γ-hydroxy-α,β-unsaturated chromium(0) carbene complexes **13a**−**c** were obtained after aqueous quenching as single stereoisomers and as the exclusive reaction products. The substitution at the carbene nitrogen plays no role in the outcome of the reaction since both unsubstituted and *N*-alkyl-substituted carbenes reacted smoothly to produce the final alcohols. Furthermore, tungsten(0)bicyclic carbene complexes **8d**,**e** behave in entirely analogous way giving the corresponding γ-hydroxy-α,β-unsaturated tungsten-(0) carbene complexes **13d**,**e** (Scheme 3).

SCHEME 3



The syn stereochemistry of the alcohols **13** was assigned on the basis of NOE measurements realized in compound **13b**. Thus, aliphatic hydrogens were first unambiguously assigned on the basis of their coupling constants and homonuclear decoupling experiments. Irradiation of H6 under NOE conditions resulted in an enhancement of 3.7% in the signal of carbinol hydrogen H5 and of 7.7% in the bridge hydrogen H7, confirming a syn arrangement of the three hydrogens. The NOE enhancements obtained after irradiation of H6, H7, H8, and H8′ were consistent with the proposed stereochemistry (Figure 2). The stereochemistry obtained is the

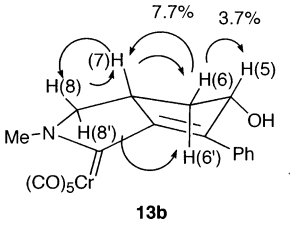


FIGURE 2. Main NOE enhancements for compound **13b**.

expected from the preferred attack of the hydride from the less hindered convex face of complexes **8**.

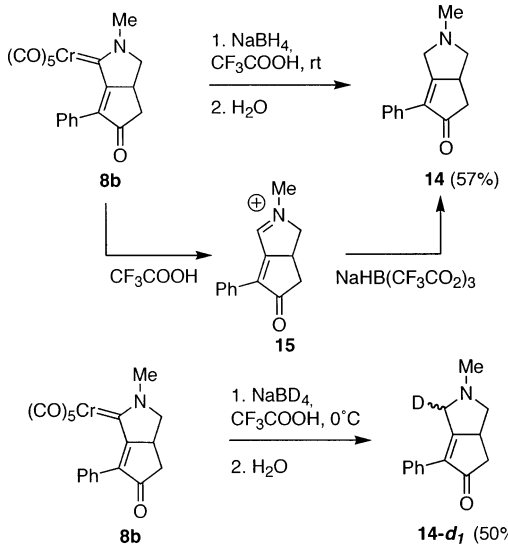
The results obtained with complexes **8** and collected in Scheme 3 are quite different from those reported previously by us for the analogous acyclic aminocarbene complexes.[11a] In those cases, products derived from the reduction of the carbene carbon having the double bond unaltered and double reduction products with both the carbene carbon and the double bond reduced were obtained. Neither of those products retained the metallic moiety. In clear contrast, bicyclic carbenes **8** were extraordinarily robust toward a second addition process. The use of $NaBH_4/CeCl_3$[18] or $LiAlH_4$ in THF instead of $NaBH_4$ in the reduction of complex **8b** resulted also in the formation of alcohol **13b**. Therefore, it seems that once the first hydride transfer has occurred, the resulting alkoxyde is inert toward the reducing agents. More striking was the absence of participation of the metal in the reduction process. In fact, acyclic aminocarbene complexes experienced the 1,3-rearrangement of the chromium center concomitant with the second hydride reduction. The reduction of complex **8b** with $NaBD_4$/MeOH produced the expected incorporation of deuterium at the former carbonyl group. In this way, the monodeuterated bicycle **13b-*d*$_1$** was formed. Furthermore, the reduction with $NaBH_4/CD_3OD$ followed by quenching with D_2O resulted in no label incorporation into the final product **13b** (Scheme 3).

The site of the reduction may be inverted by changing the reduction conditions. In fact, by using the method developed by Licandro[19] for aminochromium(0) carbene complexes on complex **8b**, the metal−carbene center was smoothly reduced to the corresponding methylene group, with concomitant loss of the metal moiety. Both the carbonyl group and the double bond remained intact. The reaction with $NaBD_4/CF_3COOH$ followed by quenching with water produced the monodeuterated bicycle **14-*d*$_1$**. The mechanism proposed for the reduction of group 6 carbenes using $NaBH_4/CF_3COOH$ involves the initial formation of iminium salt **15** by elimination of the metal moiety followed by reduction of the salt by the hydride. The selectivity of the substrate **8b** toward these reaction conditions is again remarkable (Scheme 4).

Clearly, the selectivity of the reactions above demonstrates that the ketone placed at the end of the conjugated system of complexes **8** is the most reactive moiety toward hydrides. No participation of the metal in these reactions was observed. It should be noted that neither 1,2- nor conjugated 1,4-additions were observed with $NaBH_4$, $NaBH_4/CeCl_3$, or $LiAlH_4$. We then decided to

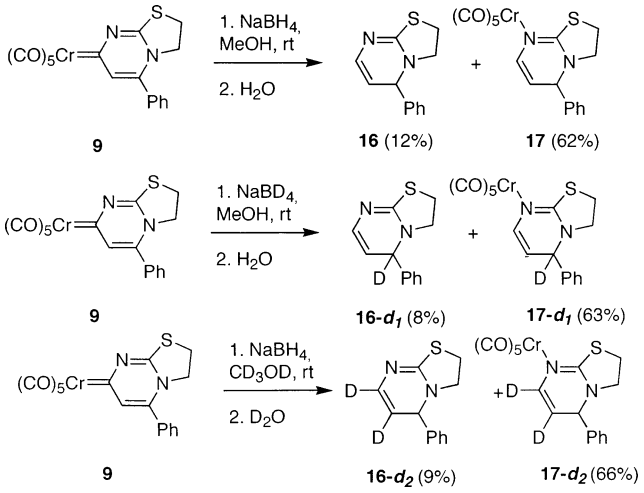
(16) Jordi, L.; Ricart, S.; Viñas, J. M.; Moretó, J. M. *Organometallics* **1997**, *16*, 2808.
(17) Polo, R.; Moretó, J. M.; Schick, U.; Ricart, S. *Organometallics* **1998**, *17*, 2135.
(18) Luche, J.-L. *J. Am. Chem. Soc.* **1978**, *100*, 2226.
(19) Baldoli, C.; Del Buttero, P.; Licandro, E.; Maiorana, S.; Papagni, A.; Zanotti-Gerosa, A. *Synlett* **1994**, 677.

SCHEME 4



change the electronic properties of the carbene carbon, while maintaining the bicyclic structure and the conjugation. In this regard, complex **9** was reacted with $NaBH_4$ yielding a 1:6 mixture of two compounds in excellent combined yield. The first one was assigned as 5-phenyl-2,3-dihydro-5*H*-thiazolo[3,2-*a*]pyrimidine **16** (Scheme 5).

SCHEME 5



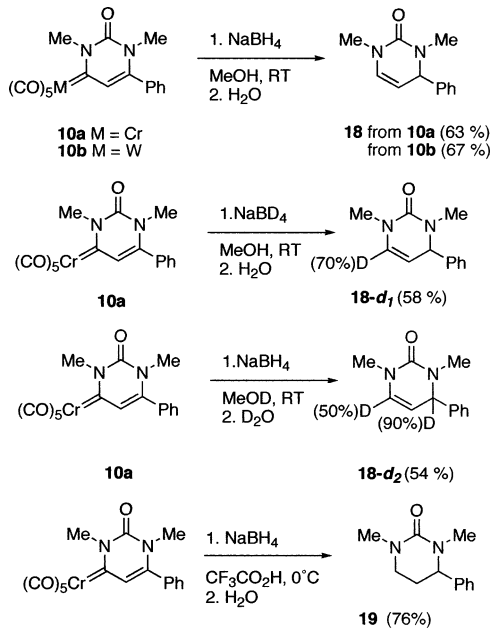
The second product obtained in this reaction was spectroscopically referable to **16** except for the presence of a $Cr(CO)_5$ moiety clearly shown in its ^{13}C NMR spectrum (δ = 220.8 ppm CO_{trans} and 214.2 ppm CO_{cis}) and was transformed into **16** by photooxidation. The structure of this compound was assigned as **17**, identical to **16** but with the $Cr(CO)_5$ moiety coordinated to the imine nitrogen. The reaction of **9** with $NaBD_4$ was attempted next. In this case, a 1:8 mixture of compounds **16-*d*$_1$** and **17-*d*$_1$** was obtained. The label was incorporated in both compounds at the conjugated position of the former α,β-unsaturated carbene complex. These results confirm that the addition of the hydride anion has occurred in this case in conjugated fashion, incorporating the label at the β-carbon when $NaBD_4$ was used. Interestingly, when the reaction of complex **9** and $NaBH_4$ was carried out in CD_3OD and quenched with D_2O the resulting reaction products, complexed **17-*d*$_2$** and uncomplexed **16-*d*$_2$**, were doubly labeled. The formation of double-labeled products **16-*d*$_2$** and **17-*d*$_2$**, when CD_3OD/D_2O was used indicates H/D interchange at the former α-carbon, which is now acidic due to its homo-enamine character. It should be pointed out that this is the first reported 1,4-addition process in the addition of metal hydrides to group 6 metal−carbene complexes.

We tested next monocyclic carbene complexes having electronic characteristics between complexes **8** and **9**. Reduction of complexes **10** with $NaBH_4$/MeOH under the usual conditions formed compounds **18** resulting from the apparent 1,4-addition of hydride. However, the reduction of complex **10a** with $NaBD_4$/MeOH followed by quenching with water formed complex **18-*d*$_1$** having the label placed at the former carbene carbon. It is mechanistically relevant to note that partial loss of label occurred in this case (70% instead of >95% expected deuterium incorporation). The labeling pattern demonstrates that no 1,4-addition has occurred. Furthermore, the reaction of complex **10a** with $NaBH_4/CD_3OD$ followed by quenching with D_2O produced the dideuterated tetrahydropyrimidinone **18-*d*$_2$**. Incorporation of the label at the former β-carbon demonstrates that migration of the metal center has occurred in this case.[20] It should be noted that the incorporation of the label at this position is complete (>95%). Furthermore, a second label has been incorporated in **18-*d*$_2$** at the former carbene carbon (variable incorporation depending on the reaction conditions; 50% of incorporation was the maximum observed) (Scheme 6). On the other hand, the reaction of complex **10a** and $NaBH_4/CF_3COOH$ formed exclusively perhydro-2-pyrimidinone **19** in 80% yield. In this case, a double-reduction process has clearly occurred (Scheme 6).

From the data above it is clear that cyclic group 6 metal−carbene complexes behave in two different ways in their reactions with simple reducing agents. Thus, bicycles **8** and **9** react without 1,3-migration of the metal center, and the reduction process stops after the transfer of the first hydride. The main difference between both complexes is the regioselectivity of the hydride addition: hydride addition onto the C=O group for complexes **8** and 1,4-addition for complex **9**. In contrast, in monocyclic carbene complexes **10** the 1,2-hydride addition is followed by 1,3-metal rearrangement. These results may be rationalized regarding the electron-donating ability of the groups joined to both the carbene and the β-carbon. Thus, a strong electron donor like the amino group bonded to

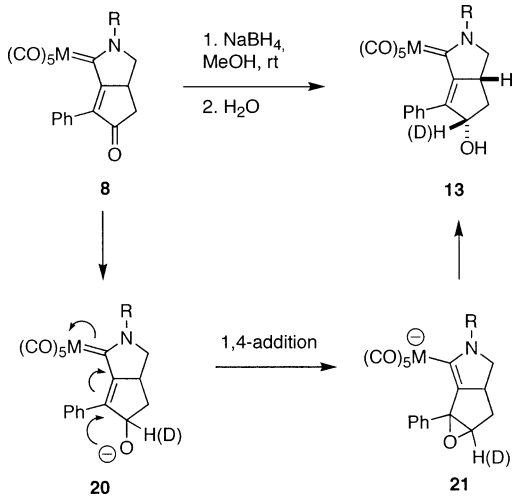
(20) Examples of 1,3-migrations of the $(CO)_5M$ moiety in the reactions of Fischer carbene complexes are scarce: (a) Barluenga, J.; Trabanco, A. A.; Flórez, J.; García-Granda, S.; Llorca, M.-A. *J. Am. Chem. Soc.* **1998**, *120*, 12129. (b) Fischer, H.; Schlageter, A.; Bidell, W.; Früh, A. *Organometallics* **1991**, *10*, 389. (c) Hegedus, L. S.; Lundmark, B. R. *J. Am. Chem. Soc.* **1989**, *111*, 9194. (d) Maxey, C. T.; Sleiman, H. F.; Massey, S. T.; McElwee-White, L. *J. Am. Chem. Soc.* **1992**, *114*, 5153. See also ref 11. In contrast, 1,2-migrations are more common: (e) Fischer, H.; Meisner, T.; Hofmann, J. *Chem Ber.* **1990**, *123*, 1799. (f) Iwasawa, N.; Maeyama, K.; Saitou, M. *J. Am. Chem. Soc.* **1997**, *119*, 1486. (g) Iwasawa, N.; Maeyama, K. *J. Org. Chem.* **1997**, *62*, 1918. (h) Iwasawa, N.; Ochiai, T.; Maeyama, K. *Organometallics* **1997**, *16*, 5137. (i) Iwasawa, N.; Ochiai, T.; Maeyama, K. *J. Org. Chem.* **1998**, *63*, 3164. (j) Barluenga, J.; Tomás, M.; Ballesteros, A.; Santamaria, J.; López-Ortiz, F.; Carbajo, R.; García-Granda, S.; Pertierra, P. *Chem. Eur. J.* **1996**, *2*, 88. (k) Barluenga, J.; Tomás, M.; Rubio, E.; López-Pelegrín, J. A.; García-Granda, S.; Pertierra, P. *J. Am. Chem. Soc.* **1996**, *118*, 695. (l) Barluenga, J.; Tomás, M.; Rubio, E.; López-Pelegrín, J. A.; García-Granda, S.; Pérez-Priede, M. *J. Am. Chem. Soc.* **1999**, *121*, 3065.

SCHEME 6



the carbene carbon (complexes **8**) disfavors the addition to the carbene carbon and results in the reduction of the carbonyl group. The γ-alkoxy-α,β-unsaturated carbene complexes **20** obtained from the first hydride addition are inert toward further reduction. It is not easy to understand the inertia of intermediates **20** toward a second hydride addition except by considering that they may be in ring-chain equilibrium with the 1,4-adduct epoxides **21**.[21] These compounds are not reactive toward hydrides and should lead to labeling patterns analogous to their open-chain isomers **20** upon treatment with D_2O (Scheme 7).

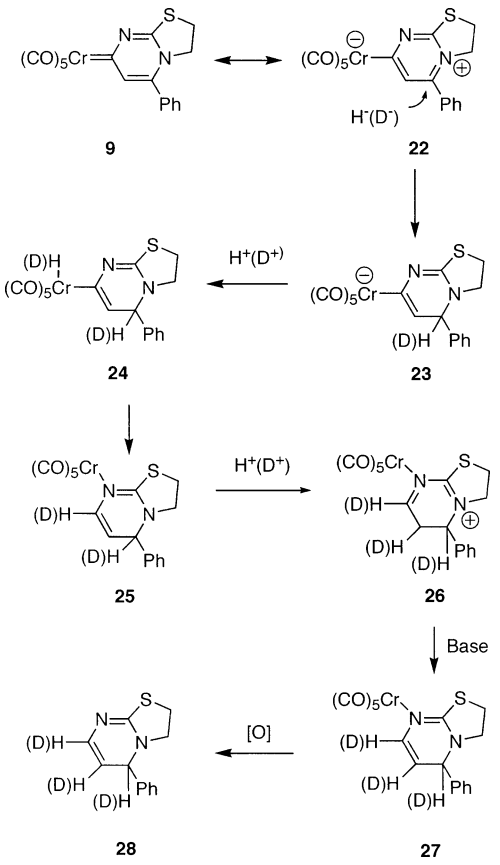
SCHEME 7



The alternate reduction using Licandro conditions ($NaBH_4/CF_3COOH$) occurs, as expected, at the carbene carbon, since the first reaction in this case is the elimination of the carbene moiety to form iminium salt **15** (Scheme 4). The labeling experiments described above are again fully consistent with these results.

Complex **9** is better described by their imino form, mesoionic 2,3-dihydro-5*H*-thiazolo[3,2-*a*]pyrimidine **22**,[22] and their reactivity is as expected from this form **22**, as we have demonstrated in open-chain enamino complexes.[23] The iminium character of the β-carbon renders this center more prone to attack by hydride than the carbene carbon. Again, the incorporation of the label to the β-position with $NaBD_4$ is fully consistent with this explanation. On the other hand, when the reaction was carried out in CD_3OD and quenched with D_2O the label was incorporated at the former carbene carbon (by deuteration of the metal center followed by reductive elimination) and at the α-position. The homoenamine nature of **25** makes the former α-position electrophilic and, therefore, suitable for subsequent label incorporation (Scheme 8).

SCHEME 8



Complexes **10** have, in turn, much more electrophilic carbene carbons since the electron-donor character of the amido nitrogen is considerably smaller than that of the amino or enamino substituents in complexes **8** and **9**, respectively. Thus, in this case, a clear 1,2-addition

(21) This type of intramolecular Michael addition of an alkoxyde group to a triple bond has been proposed to explain the formation of the product obtained during the reaction of the dilithium derivative of 2-methyl-3-butyn-2-ol to $Cr(CO)_6$ in the presence of acetyl chloride. See: Berke, H.; Härter, P.; Huttner, G.; v. Seyerl, J. *J. Organomet. Chem.* **1981**, *219*, 317.

(22) Elguero, J.; Marzin, C.; Katritzky, A. R.; Linda, P. In *The Tautomerism of Heterocycles, Advances in Heterocyclic Chemistry*; Katritzky, A. R., Boulton, A. J., Eds.; Academic Press: New York, 1976; Suppl. 1.

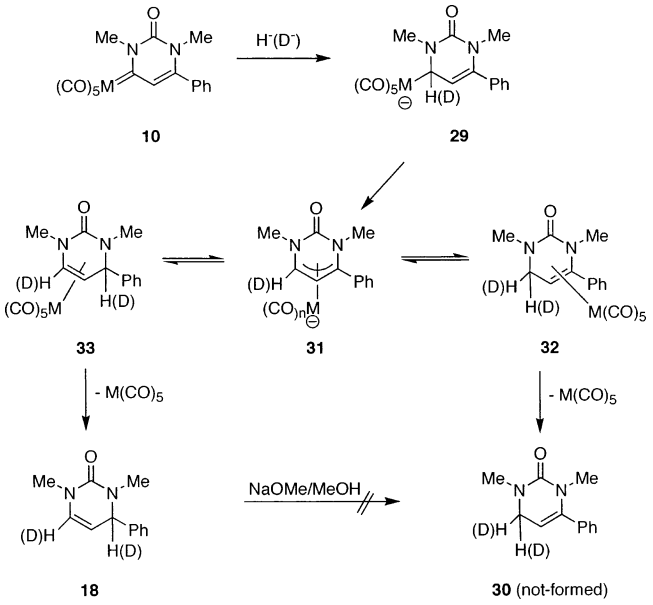
(23) Sierra, M. A.; del Amo, J. C.; Mancheño, M. J.; Gómez-Gallego, M.; Torres, M. R. *Chem. Commun.* **2002**, 1842.

process occurs as it is demonstrated by the exclusive incorporation of the deuterium label at the former carbene carbon when $NaBD_4$ was used. However, now the migration of the metal center in intermediates **29** promotes the formation of the products **18** having a rearranged double bond. This is confirmed by the presence of a label at the former β-position of the carbene complex when the reaction was carried out in CD_3OD and quenched with D_2O. The incorporation of deuterium in this position should occur after protonation of the metal-center and reductive elimination. However, the formation of compounds **18** is not so simple. It must be noted that this mechanism should yield exclusively a monodeuterated derivative, while when CD_3OD/ D_2O was used **18-*d*$_2$** was obtained. Further, the nonconjugated less stable product **18** ($\Delta H_f = +0.639$ kcal) was formed instead of the more stable conjugated derivative **30** ($\Delta H_f = -2.317$ kcal).[24]

These experimental results may be rationalized by the intermediacy of a π-allylchromium complex **31** formed after the initial hydride addition to the carbene carbon.[25] This π-allylchromium intermediate may be protonated at either extreme of the allyl ligand to yield either **32** or **33**. In the basic reaction medium, equilibrium between **32** and **33** may be established with complex **33** being the more stable form due to the absence of the strong steric interaction between the phenyl group and the $M(CO)_5$ moiety.[25,26] Thus, while the existence of the equilibrium between **32** and **33** may explain the deuterium incorporation in the extreme position of the allyl system, the decomposition of the complex should occur preferentially from **33** giving the less stable organic moiety. The absence of deuterium scrambling when monodeuterated **18-*d*$_1$** was submitted to treatment with NaMeO/MeOH discards the possibility of incorporation of labeling once the metal moiety has been removed (Scheme 9).[28]

In conclusion, the reduction of α,β-unsaturated cyclic group 6 metal−carbene complexes strongly depends on the electronic profile of the groups attached both to the carbene and the β-carbon, and it occurs with exquisite regioselectivity. Thus, for complexes **8** the reduction does not occur at the carbene carbon but at the γ-carbonyl group. The resulting carbinol **20** would evolve to a tricyclic epoxide structure **21** which precludes additional hydride transfers, in clear contrast with its acyclic congeners. Complex **9** experiences the exclusive 1,4-reduction because of the imino-character of the β-carbon (due to the participation of the aromatic resonance form **22**). In contrast, monocyclic carbene complexes **10** behave as their acyclic congeners and experience 1,2-hydride addition followed by 1,3-migration of the metal-center. In this case, the participation of η^3-$Cr(CO)_5$ species **31** allows to understand the labeling pattern found in the final products. Therefore, the reduction of cyclic α,β-unsaturated group 6 carbene complexes is mainly controlled by the electronic characteristics of the groups attached to the carbene and the β-carbon, and by the suitability of the metal center to experience a 1,3-migration (controlled by the strain of the transition states which precludes the migration in bicyclic carbene complexes). Further efforts to extend these results to control the reaction of group 6 cyclic carbene complexes and carbon anionic and radical nucleophiles are actively underway in our laboratories.

SCHEME 9



Experimental Section

General Methods. ^1H NMR and ^{13}C NMR spectra were obtained in $CDCl_3$ at 299.94 MHz for ^1H and 75.43 MHz for ^{13}C, 200.13 MHz for ^1H, and 50.03 MHz for ^{13}C or 300.13 MHz for ^1H and 75.48 MHz for ^{13}C. Chemical shifts are given in ppm relative to TMS (^1H, 0.0 ppm), or $CDCl_3$ (^{13}C, 77.0 ppm). Flame-dried glassware and standard Schlenck techniques were used for all the reactions. Silica gel (230−400 Mesh) was used as the stationary phase for purification of crude reaction mixtures by flash chromatography. Identification of products was made by TLC (Kiesegel 60F-254). UV light ($\lambda = 254$ nm), phosphomolibdic acid solution in 95% EtOH and iodine were also used to develop the plates. All commercially available compounds were used without further purification. Compounds **8**,[16] **9**,[17] and **10**[17] were prepared according to literature methods.

(24) PM3-calculations were effected using Chem 3D Pro 6.0 program.

(25) We have already proposed (ref 11a) the participation of these π-allyl species in the reduction of open-chain group 6 metal-carbene complexes. However, until now no direct experimental evidence about its participation in the reduction processes of group 6 metal-carbene complexes was obtained.

(26) (a) Schobert, R. *J. Organomet. Chem.* **2001**, *617*, 346. (b) Eigemann, S.-E.; Schobert, R. *J. Organomet. Chem.* **1999**, *585*, 115. (c) Review: Mitsudo, T. *Bull. Chem. Soc. Jpn.* **1998**, *71*, 1525. Although isolated and characterized Cr(I)−η^3-allyl complexes are scarce, their role as intermediates in diverse reactions of chromium(0) carbene complexes has been repeatedly proposed. See, among others: (d) Sakurai, H.; Tanabe, K.; Narasaka, K. *Chem. Lett.* **1999**, 309. (e) Hoffmann, M.; Reissig, H.-U. *Synlett* **1995**, 625. (f) Harvey, D. F.; Lund, K. P. *J. Am. Chem. Soc.* **1991**, *113*, 8916. (g) Buchert, M.; Reissig, H.-U. *Chem. Ber.* **1992**, *125*, 2723. (h) Sakurai, H.; Tanabe, K.; Narasaka, K. *Chem. Lett.* **2000**, 168. The participation of oxa-allyl intermediates in the rearrangement of carbon-centered pentacarbonylchromium enolates to oxygen-centered enolates has been shown using DFT calculations, see: (h) Arrieta, A.; Cossío, F. P.; Fernández, I.; Gómez-Gallego, M.; Lecea, B.; Mancheño, M. J.; Sierra, M. A. *J. Am. Chem. Soc.* **2000**, *122*, 11509.

(27) The rearrangement of bis-alkene tetracarbonyl complexes of tungsten to π-allyl hydrides is a prototypical reaction in the catalytic isomerization and methatesis of olefins. For a review, see: Szymanskabuzar, T. *Coord. Chem. Rev.* **1997**, *159*, 205.

(28) The presence of the isomers **30** as minor products in the crude reaction mixtures could be inferred from the ^1H NMR spectra of the crude reaction mixtures. However, we have been unable to obtain these compounds with a degree of purity enough to effect an unambiguous structural characterization.

General Procedure for the Hydride Reduction. A suspension of $NaBH_4$ in CH_3OH at room temperature was placed in a flame-dried airless flask containing a magnetic stirring bar, degassed by evacuation/back fill with argon (3×). Then, a solution of the carbene in CH_3OH was added by syringe at room temperature and the mixture was stirred at this temperature until the complete disappearance of the starting material (checked by TLC). After the addition of the water, the solvent was removed under reduced pressure and the crude was purified by flash column chromatography. For the deuterium experiments the same procedure was followed, using $NaBD_4$ in CH_3OH or $NaBH_4$ in CD_3OD as solvent (in these cases, the reaction was quenched by addition of D_2O instead of water).

Reaction of 8a with $NaBH_4$ in CH_3OH. The general procedure was followed using 400 mg (1.03 mmol) of **8a** and 58 mg (1.54 mmol) of $NaBH_4$. After 1 h of reaction, the crude was quenched with 0.1 mL of H_2O, concentrated under reduced pressure, and purified by chromatography on silica gel (hexane/AcOEt 2/1) to afford 287 mg (71%) of **13a** as a yellow oil: ^{1}H NMR δ 1.60 (m, 1H), 1.86 (d, J = 5.0 Hz, 1H), 2.63−2.80 (m, 1H), 3.25−3.38 (m, 2H), 3.79 (m, 1H), 5.43 (m, 1H), 7.35−7.35 (m, 5H), 8.81 (bs, 1H); ^{13}C NMR δ 260.6, 222.3, 217.1, 152.4, 152.2, 133.4, 129.5, 128.6, 128.3, 84.4, 58.2, 45.8, 39.8; IR (film) 3408, 2056, 1976, 1928 cm^{-1}. Anal. Calcd for $C_{18}H_{13}CrNO_6$: C, 55.25; H, 3.35. Found: C, 55.40; H, 3.53.

Reaction of 8b with $NaBH_4$ in CH_3OH. The general procedure was followed using 200 mg (0.50 mmol) of **8b** and 28 mg (0.75 mmol) of $NaBH_4$. After 30 min of reaction, the crude was quenched with 0.1 mL of H_2O, concentrated under reduced pressure, and purified by chromatography on silica gel (hexane/AcOEt 2/1) to afford 124 mg (61%) of **13b** as a yellow oil: ^{1}H NMR δ 1.56 (dt, J_1 = 12.5 Hz, J_2 = 8.8 Hz, 1H), 1.78 (d, J = 4.2 Hz, 1H), 2.71 (dt, J_1 = 12.5 Hz, J_2 = 6.8 Hz, 1H), 3.28−3.51 (m, 2H), 3.65−3.80 (m, 4H), 5.25 (m, 1H), 7.19−7.34 (m, 5H); ^{13}C NMR δ 255.3, 222.8, 217.3, 154.4, 148.5, 133.7, 129.7, 128.5, 84.4, 66.2, 45.9, 43.5, 39.0; IR (film) 3651, 3404, 2968, 2054, 1973, 1928 cm^{-1}. Anal. Calcd for $C_{19}H_{15}CrNO_6$: C, 56.30; H, 3.73; N, 3.46. Found: C, 56.50; H, 3.76; N, 3.55.

Reaction of 8b with $NaBD_4$ in CH_3OH. The general procedure was followed using 100 mg (0.25 mmol) of **8b** and 16 mg (0.38 mmol) of $NaBD_4$. After 30 min of reaction, the crude was quenched with 0.1 mL of H_2O, concentrated under reduced pressure, and purified by chromatography on silica gel (hexane/AcOEt 2/1) to afford 61 mg (60%) of **13b-*d*$_1$** as a yellow oil: ^{1}H NMR δ 1.55 (dd, J_1 = 12.3 Hz, J_2 = 8.5 Hz, 1H), 1.79 (s, 1H), 2.62 (dd, J_1 = 12.3 Hz, J_2 = 6.5 Hz, 1H), 3.22−3.48 (m, 2H), 3.61−3.79 (m, 4H), 7.18−7.38 (m, 5H); ^{13}C NMR δ 255.3, 222.8, 217.3, 154.5, 148.4, 133.7, 129.7, 128.5, 84.0 (J_{C-D} = 20 Hz), 66.2, 46.0, 43.4, 38.9; IR (film) 3402, 2972, 2054, 1975, 1927 cm^{-1}.

Reaction of 8c with $NaBH_4$ in CH_3OH. The general procedure was followed using 66 mg (0.15 mmol) of **8c** and 9 mg (0.23 mmol) of $NaBH_4$. After 30 min of reaction, the crude was quenched with 0.1 mL of H_2O, concentrated under reduced pressure, and purified by chromatography on silica gel (hexane/AcOEt 2/1) to afford 43 mg (66%) of **13c** as a yellow oil: ^{1}H NMR δ 1.46 (dt, J_1 = 12.5 Hz, J_2 = 8.3 Hz, 1H), 1.80 (bs, 1H), 2.64 (dt, J_1 = 12.5 Hz, J_2 = 6.2 Hz, 1H), 3.28−3.35 (m, 2H), 3.62−3.76 (m, 1H), 4.69 (m, 2H), 5.19−5.38 (m, 3H), 5.80−5.96 (m, 1H), 7.11−7.45 (m, 5H); ^{13}C NMR δ 257.3, 222.8, 217.3, 154.8, 148.7, 133.8, 131.2, 130.3, 128.7, 128.6, 121.2, 84.4, 63.3, 58.6, 46.1, 38.8; IR (film) 3420, 2968, 2926, 2856, 2054, 2013, 1975, 1928 cm^{-1}. Anal. Calcd for $C_{21}H_{17}CrNO_6$: C, 58.47; H, 3.97. Found: C, 58.55; H, 3.85.

Reaction of 8d with $NaBH_4$ in CH_3OH. The general procedure was followed using 250 mg (0.48 mmol) of **8d** and 27 mg (0.72 mmol) of $NaBH_4$. After 30 min of reaction, the crude was quenched with 0.1 mL of H_2O, concentrated under reduced pressure, and purified by chromatography on silica gel (hexane/AcOEt 2/1) to afford 180 mg (72%) of **13d** as a yellow oil: ^{1}H NMR δ 1.66 (m, 2H), 2.73 (dt, J_1 = 12.5 Hz, J_2 = 6.8 Hz, 1H), 3.22−3.41 (m, 2H), 3.76 (m, 1H), 5.42 (m, 1H), 7.19−7.35 (m, 5H), 8.70 (bs, 1H); ^{13}C NMR δ 237.1, 202.0, 197.8, 153.6, 152.3, 133.0, 129.6, 128.9, 128.5, 84.2, 58.4, 45.3, 39.9; IR (film) 3402, 2970, 2928, 2875, 2062, 1971, 1908 cm^{-1}. Anal. Calcd for $C_{18}H_{13}NO_6W$: C, 41.33; H, 2.50. Found: C, 41.42; H, 2.66.

Reaction of 8e with $NaBH_4$ in CH_3OH. The general procedure was followed using 200 mg (0.37 mmol) of **8e** and 21 mg (0.55 mmol) of $NaBH_4$. After 30 min of reaction, the crude was quenched with 0.1 mL of H_2O, concentrated under reduced pressure, and purified by chromatography on silica gel (hexane/AcOEt 2/1) to afford 130 mg (65%) of **13e** as a yellow oil: ^{1}H NMR δ 1.58 (dt, J_1 = 12.2 Hz, J_2 = 8.8 Hz, 1H), 1.73 (broad s, 1H), 2.68 (dt, J_1 = 12.2 Hz, J_2 = 6.2 Hz, 1H), 3.34−3.48 (m, 2H), 3.61 (s, 3H), 3.70 (dd, J_1 = 19.3 Hz, J_2 = 8.2 Hz, 1H), 5.28 (m, 1H), 7.21−7.35 (m, 5H); ^{13}C NMR δ 234.1, 202.3, 198.0, 155.4, 148.9, 133.5, 129.7, 128.5, 128.4, 84.1, 65.1, 46.0, 45.1, 39.1; IR (film) 3369, 2974, 2927, 2062, 1971, 1924 cm^{-1}. Anal. Calcd for $C_{19}H_{15}NO_6W$: C, 42.48; H, 2.81. Found: C, 42.42; H, 2.69.

Reaction of 8b with $NaBH_4$/$CeCl_3$ in CH_3OH/THF. A mixture of 200 mg (0.50 mmol) of **8b**, 25 mL of CH_3OH, 25 mL of THF, 38 mg (1.00 mmol) of $NaBH_4$, and 25 mg (0.10 mmol) of $CeCl_3$ was stirred for 30 min at room temperature until the complete disappearance of the starting material (checked by TLC). Then, the solvent was removed under reduced pressure and the residue extracted with Et_2O/water. The organic extracts were dried and evaporated, and purification by chromatography on silica gel (hexane/AcOEt 2/1) afforded 173 mg (85%) of **13b** as a yellow oil.

Reaction of 8b with $LiAlH_4$ in THF. A suspension of 12 mg (0.30 mmol) of $LiAlH_4$ (95%) in 3 mL of anhydrous THF at −78 °C was placed in a flame-dried airless flask containing a magnetic stirring bar, degassed by evacuation/back fill with argon (3×). Then, a solution of the 80 mg (0.20 mmol, 1.0 equiv) of **8b** in 2 mL of anhydrous THF was added by syringe at −78 °C, and the mixture was warmed to −20 °C for 30 min and allowed to stir at this temperature until the complete disappearance of the starting material (checked by TLC). After the addition of 0.1 mL of H_2O, the solvent was removed under reduced pressure and the residue extracted with Et_2O/water. The organic extracts were dried and evaporated, and purification by chromatography on silica gel (hexane/AcOEt 2/1) afforded 41 mg (51%) of **13b** as a yellow oil.

Reaction of 9 with $NaBH_4$ in CH_3OH. The general procedure was followed using 300 mg (0.74 mmol, 1.0 equiv) of **9** and 84 mg (2.22 mmol, 3.0 equiv) of $NaBH_4$. After 2 h of reaction, the crude was quenched with 0.1 mL of H_2O and concentrated under reduced pressure. The ^{1}H NMR spectrum of the reaction crude showed a 6:1 mixture of 5-phenyl-2,3-dihydro-5*H*-thiazolo[3,2-*a*]pyrimidines **17** and **16**. The products were separated by chromatography on silica gel (hexane to AcOEt). Compound **17** (187 mg, 62%) was obtained as a yellow solid: ^{1}H NMR δ 2.99−3.06 (m, 2H), 3.34−3.50 (m, 2H), 4.80 (m, 1H), 4.96 (m, 1H), 6.12 (d, J = 7.1 Hz, 1H), 7.26−7.34 (m, 5H); ^{13}C NMR δ 220.8, 214.2, 169.1, 140.4, 137.7, 129.3, 129.1, 127.2, 106.6, 59.8, 53.6, 26.4; IR (KBr) 2064, 1979, 1931, 1890 1654, 1541 cm^{-1}. Anal. Calcd for $C_{17}H_{12}CrN_2O_5S$: C, 50.00; H, 2.96. Found: C, 50.14; H, 2.78. Compound **16** (19 mg, 12%) was obtained as a yellow oil: ^{1}H NMR δ 2.92−3.12 (m, 2H), 3.18−3.41 (m, 2H), 4.79 (dd, J_1 = 7.1 Hz, J_2 = 3.2 Hz, 1H), 5.08 (d, J = 3.2 Hz, 1H), 6.33 (d, J = 7.1 Hz, 1H), 7.29−7.33 (m, 5H); ^{13}C NMR δ 163.3, 141.8, 132.9, 128.8, 128.3, 127.1, 105.8, 60.9, 51.5, 25.2; IR (film) 1625, 1547 cm^{-1}. Anal. Calcd for $C_{12}H_{12}N_2S$: C, 66.63; H, 5.59. Found: C, 66.80; H, 5.78.

Reaction of 9 with $NaBD_4$ in CH_3OH. The general procedure was followed using 250 mg (0.61 mmol) of **9** and 77 mg (1.83 mmol) of $NaBD_4$. After 2 h of reaction, the crude was quenched with 0.1 mL of H_2O and concentrated under reduced pressure. The ^{1}H NMR spectrum of the reaction crude showed an 8:1 mixture of 5-deutero-5-phenyl-2,3-dihydrothiazolo[3,2-

a]pyrimidines **17-*d*$_1$** and **16-*d*$_1$**. The products were separated by chromatography on silica gel (hexane to AcOEt). Compound **17-*d*$_1$** (160 mg, 63%) was obtained as a yellow solid: ^{1}H NMR δ 3.01−3.05 (m, 2H), 3.37−3.45 (m, 2H), 4.79 (d, J = 7.3 Hz, 1H), 6.12 (d, J = 7.3 Hz, 1H), 7.25−7.33 (m, 5H); ^{13}C NMR δ 220.7, 214.2, 169.0, 140.3, 137.7, 129.2, 129.0, 127.2, 106.5, 59.4 (J_{C-D} = 20 Hz), 53.5, 26.4; IR (KBr) 2066, 1931, 1890, 1653 cm^{-1}. Compound **16-*d*$_1$** (10 mg, 8%) was obtained as a yellow oil: ^{1}H NMR δ 2.95−3.15 (m, 2H), 3.26−3.41 (m, 2H), 4.81 (m, 1H), 6.36 (m, 1H), 7.19−7.31 (m, 5H); ^{13}C NMR δ 163.6, 141.6, 132.5, 129.0, 128.6, 127.3, 106.0, 60.6 (J_{C-D} = 20 Hz), 51.7, 25.6; IR (film) 1628, 1541 cm^{-1}.

Reaction of 9 with NaBH$_4$ in CD$_3$OD. The general procedure was followed using 300 mg (0.74 mmol) of **9** and 84 mg (2.22 mmol) of $NaBH_4$. After 2 h of reaction, the crude was quenched with 0.1 mL of D_2O and concentrated under reduced pressure. The ^{1}H NMR spectrum of the reaction crude showed a 7:1 mixture of 6,7-dideutero-5-phenyl-*5H*-2,3-dihydrothiazolo[3,2-*a*]pyrimidines **17-*d*$_2$** and **16-*d*$_2$**. The products were separated by chromatography on silica gel (hexane to AcOEt). Compound **17-*d*$_2$** (201 mg, 66%) was obtained as a yellow solid: ^{1}H NMR δ 2.98−3.08 (m, 2H), 3.28−3.50 (m, 2H), 4.79 (m, 0.7H), 4.95 (m, 1H), 6.12 (d, J = 7.5 Hz, 0.6H), 7.19−7.37 (m, 5H); ^{13}C NMR δ 221.8, 214.3, 169.2, 140.4, 137.7 (m), 129.3, 129.1, 127.3, 106.6 (m), 59.9, 53.6, 26.4; IR (KBr) 2066, 1931, 1626, 1543 cm^{-1}. Compound **16-*d*$_2$** (16 mg, 9%) was obtained as a yellow oil: ^{1}H NMR δ 3.00−3.12 (m, 2H), 3.24−3.33 (m, 2H), 4.80 (m, 0.8H), 5.08 (m, 1H), 6.33 (m, 0.6H), 7.30−7.42 (m, 5H); ^{13}C NMR δ 163.5, 142.2, 132.3 (m), 128.9, 128.5, 127.3, 105.9 (m), 61.1, 51.6, 25.3; IR (film) 1653, 1545 cm^{-1}.

Reaction of 10a with NaBH$_4$ in CH$_3$OH. The general procedure was followed using 250 mg (0.64 mmol) of **10a** and 48 mg (1.28 mmol) of $NaBH_4$. After 2.5 h of reaction, the crude was quenched with 0.1 mL of H_2O, concentrated under reduced pressure, and purified by chromatography on silica gel (hexane/AcOEt 2/1) to afford 81 mg (63%) of **18** as a yellow oil: ^{1}H NMR δ 2.70 (s, 3H), 3.03 (s, 3H), 4.69 (dd, J_1 = 7.9 Hz, J_2 = 4.2 Hz, 1H), 4.85 (d, J = 4.2 Hz, 1H), 5.89 (dd, J_1 = 7.9 Hz, J_2 = 0.8 Hz, 1H), 7.16−7.33 (m, 5H); ^{13}C NMR δ 153.8, 142.0, 128.8, 128.4, 127.9, 126.4, 101.8, 64.0, 35.1, 33.6; IR (film) 1686, 1639, 1491, 1450, 1421 cm^{-1}. Anal. Calcd for $C_{12}H_{14}N_2O$: C, 71.26; H, 6.98. Found: C, 71.40; H, 6.82.

Reaction of 10a with NaBD$_4$ in CH$_3$OH. The general procedure was followed using 250 mg (0.64 mmol) of **10a** and 54 mg (1.28 mmol) of $NaBD_4$. After 2 h of reaction, the crude was quenched with 0.1 mL of H_2O, concentrated under reduced pressure, and purified by chromatography on silica gel (hexane/AcOEt 2/1) to afford 75 mg (58%) of **18-*d*$_1$** as a yellow oil: ^{1}H NMR δ 2.70 (s, 3H), 3.02 (s, 3H), 4.68 (m, 1H), 4.89 (d, J = 4.2 Hz, 1H), 5.89 (dd, J_1 = 7.9 Hz, J_2 = 1.1 Hz, 0.3H), 7.15−7.33 (m, 5H); ^{13}C NMR δ 153.9, 142.1, 128.9, 128.3 (m), (128.0), 126.5**,** 101.7, 64.0, 35.1, 33.6; IR (film) 1709, 1637, 1491, 1448, 1416 cm^{-1}.

Reaction of 10a with NaBH$_4$ in CD$_3$OD. The general procedure was followed using 250 mg (0.64 mmol) of **10a** and 48 mg (1.28 mmol) of $NaBH_4$. After 2.5 h of reaction, the crude was quenched with 0.1 mL of D_2O, concentrated under reduced pressure, and purified by chromatography on silica gel (hexane/AcOEt 2/1) to afford 71 mg (54%) of **18-*d*$_2$** as a yellow oil: ^{1}H NMR δ 2.71 (s, 3H), 3.04 (s, 3H), 4.68 (m, 1H), 4.86 (d, J = 4.2 Hz, 0.1 H), 5.90 (d, J = 7.9 Hz, 0.5H), 7.17−7.29 (m, 5H); ^{13}C NMR δ 153.9, 142.2, 128.9, 128.4 (m), 128.0, 126.5, 101.7, 64.1 (m), 35.2, 33.7; IR (film) 1709, 1641, 1448, 1418 cm^{-1}.

Reaction of 10b with NaBH$_4$ in CH$_3$OH. The general procedure was followed using 250 mg (0.48 mmol) of **10b** and 36 mg (0.96 mmol) of $NaBH_4$. After 3 h of reaction, the crude was quenched with 0.1 mL of H_2O, concentrated under reduced pressure, and purified by chromatography on silica gel (hexane/AcOEt 2/1) to afford 65 mg (67%) of **18** as a yellow oil.

General Procedure for the Hydride Reduction with NaBH$_4$ in CF$_3$COOH. A mixture of the corresponding complex, $NaBH_4$, and CF_3COOH at 0 °C was placed in a flame-dried airless flask containing a magnetic stirring bar, degassed by evacuation/back fill with argon (3×). The reaction was stirred at 0 °C until the complete disappearance of the starting material (checked by TLC). Then, a 0.2 M solution of NaOH was carefully added and the resulting mixture extracted with Et_2O/water. The organic extracts were dried, the solvent was removed under reduced pressure, and the crude was purified by flash column chromatography. For the deuterium experiments the same procedure was followed, using $NaBD_4$ in CF_3-COOH.

Reaction of 8b with NaBH$_4$ in CF$_3$COOH. The general procedure was followed using 250 mg (0.62 mmol) of **8b**, 2 mL of CF_3COOH, and 47 mg (1.24 mmol) of $NaBH_4$. The reaction was stirred for 10 min at 0 °C, and its progress was monitored by TLC. After the disappearance of the starting compound, a 0.2 M solution of NaOH was carefully added and the resulting solution extracted with Et_2O/water. The organic extracts were dried and evaporated, and purification by chromatography (hexane/AcOEt 2/1) afforded 75 mg (57%) of bicycle **14**: ^{1}H NMR δ 1.94 (dd, J_1 = 10.5 Hz, J_2 = 7.8 Hz, 1H), 2.31 (dd, J_1 = 17.7 Hz, J_2 = 3.6 Hz, 1H), 2.50 (s, 3H), 2.78 (dd, J_1 = 17.7 Hz, J_2 = 6.3 Hz, 1H), 3.17 (d, J = 18.0 Hz, 1H), 3.29−3.40 (m, 2H), 4.35 (d, J = 18.0 Hz, 1H), 7.26−7.60 (m, 5H); ^{13}C NMR δ 207.3, 179.9, 134.2, 131.1, 128.5, 128.2, 128.0, 59.0, 55.3, 43.1, 41.1, 40.1; IR (film) 1701 cm^{-1}. Anal. Calcd for $C_{14}H_{15}NO$: C, 78.84; H, 7.09. Found: C, 79.01; H, 7.16.

Reaction of 8b with NaBD$_4$ in CF$_3$COOH. The general procedure was followed using 100 mg (0.25 mmol) of **8b**, 1 mL of CF_3COOH, and 21 mg (0.50 mmol) of $NaBD_4$. The reaction was stirred for 10 min at 0 °C, and its progress was monitored by TLC. After the disappearance of the starting compound, a 0.2 M solution of NaOH was carefully added and the resulting solution extracted with Et_2O/water. The organic extracts were dried and evaporated, and purification by chromatography (hexane/AcOEt 2/1) afforded 27 mg (50%) of the corresponding monodeuterated bicyclic compound **14-*d*$_1$**: ^{1}H NMR δ 1.96 (dd, J_1 = 10.4 Hz, J_2 = 7.9 Hz, 1H), 2.27 (dd, J_1 = 17.7 Hz, J_2 = 3.6 Hz, 1H), 2.50 (s, 3H), 2.76 (dd, J_1 = 17.7 Hz, J_2 = 6.1 Hz, 1H), 3.11−3.35 (m, 2.5H), 4.39 (d, J = 17.2 Hz, 0.5H), 7.19−7.52 (m, 5H); ^{13}C NMR δ 206.4, 176.9, 134.9, 130.3**,** 128.5, 128.2, 128.0, 59.8, 55.9 (m), 43.6, 41.9, 41.0; IR (film) 1701 cm^{-1}.

Reaction of 10 with NaBH$_4$ in CF$_3$COOH. The general procedure was followed using 250 mg (0.64 mmol) of **10**, 2 mL of CF_3COOH, and 97 mg (2.56 mmol) of $NaBH_4$.The reaction was stirred for 2.5 h at 0 °C, and its progress was monitored by TLC. After the disappearance of the starting compound, a 0.2 M solution of NaOH was carefully added and the resulting solution extracted with Et_2O/water. The organic extracts were dried and evaporated, and purification by chromatography (hexane/AcOEt 2/1) afforded 100 mg (76%) of 1,3-dimethylperhydropyrimidin-3-one **19**: ^{1}H NMR δ 1.83 (m, 1H), 2.29 (m, 1H), 2.83−3.01 (m, 8H), 4.41 (m, 1H), 7.07−7.29 (m, 5H); ^{13}C NMR δ 157.0, 140.7, 128.7, 127.5, 126.0, 61.0, 43.7, 36.0, 35.0, 29.1; IR (film) 1776, 1740, 1695, 1608, 1541 cm^{-1}. Anal. Calcd for $C_{12}H_{16}N_2O$: C, 70.56; H, 7.90. Found: C, 70.73; H, 7.76.

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