466 *Organometallics* **2011,** *30,* 466–476
DOI: 10.1021/om1007105

ORGANOMETALLICS
Article

DFT Study of Thermal 1,3-Dipolar Cycloaddition Reactions between Alkynyl Metal(0) Fischer Carbene Complexes and 3*H*-1,2-Dithiole-3-thione Derivatives

Diego M. Andrada,*[,†] Alejandro M. Granados,[†] Miquel Solà,[‡] and Israel Fernández*[,§]

[†]*Instituto de Investigaciones en Fisicoquímica de Córdoba, Departamento de Química Orgánica, Facultad de Ciencias Químicas, Universidad Nacional de Córdoba, Ciudad Universitaria 5016, Córdoba, Argentina,* [‡]*Institut de Química Computacional and Departament de Química, Universitat de Girona, Campus Montilivi 17071 Girona, Catalonia, Spain, and* [§]*Departamento de Química Orgánica, Facultad de Química, Universidad Complutense, 28040 Madrid, Spain*

Received July 20, 2010

The thermal 1,3-dipolar cycloaddition reaction between alkynyl metal(0) Fischer carbenes and 5-methyl-3*H*-1,2-dithiole-3-thione to yield 1,3-dithiafulvene has been studied computationally within the Density Functional Theory framework. The transformations involving Fischer carbene complexes and their isolobal analogues (organic esters and corresponding Lewis acid complexes) were compared in terms of regioselectivity, barrier and reaction energies, synchronicity, and aromaticity of the corresponding transition states. These reactions are found to be concerted and completely regioselective toward the formation of the *Z*-1,3-dithiafulvene isomer, which is kinetically favored. DFT calculations are in good agreement with the experimental outcome of the process, which can be explained by means of the corresponding frontier molecular orbitals of reactants and their electrostatic potentials.

Introduction

The chemistry of Fischer carbene complexes has been largely developed since the first synthesis of the [methoxy(methyl)carbene pentacarbonyl]tungsten(0) complex by Fischer and Maasböl in 1964.[1] Due to their special electronic features and multifunctional structure, most of the investigations performed so far have mainly focused on their applications in organic synthesis.[2] Nowadays, Fischer carbene complexes have shown themselves to be very efficient and versatile starting materials to carry out a wide variety of organic transformations under mild conditions.[3]

Group 6 metal(0) Fischer carbene complexes bearing an alkenyl or alkynyl group attached to the carbene carbon atom have been reported to be excellent dienophiles,[4] which are able to undergo different cycloadditions such as Diels–Alder reactions[4,5] or 1,3-dipolar cycloadditions.[6] Interestingly, the activating effect of the pentacarbonylchromium(0)

---

*Corresponding authors. E-mail: die@mail.fcq.unc.edu.ar; israel@quim.ucm.es.

(1) Fischer, E. O.; Maasböl, A. *Angew. Chem., Int. Ed.* **1964**, *3*, 580.

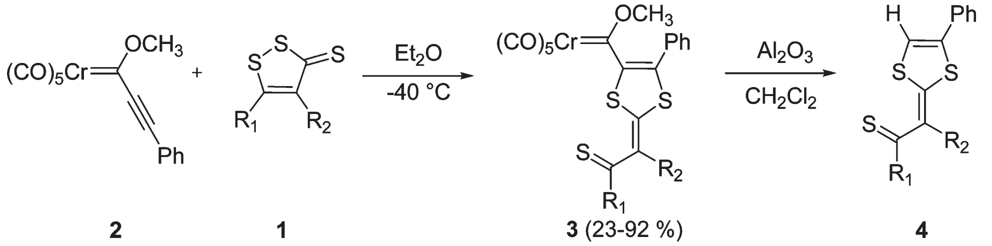
(2) (a) Dötz, K. H.; Fischer, H.; Hofmann, P.; Kreissl, R.; Schubert, U.; Weiss, K. *Transition Metal Carbene Complexes*; Verlag Chemie: Deerfield Beach, FL, 1983. (b) Dötz, K. H. *Angew. Chem., Int. Ed.* **1984**, *23*, 587. (c) Wulff, W. D. In *Comprehensive Organic Synthesis*; Pergamon: Oxford, 1991; 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*; Pergamon, Oxford, 1995; Vol. *12*, p 470. (h) Hegedus, L. S. In *Comprehensive Organometallic Chemistry II*; 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) Alcaide, B.; Casarrubios, L.; Domínguez, G.; Sierra, M. A. *Curr. Org. Chem.* **1998**, *2*, 551.

(3) (a) Sierra, M. A. *Chem. Rev.* **2000**, *100*, 3591. (b) Schirmer, H.; Duetsch, M.; Stein, F.; Labahn, T.; Knieriem, B.; De Meijere, A. *Angew. Chem., Int. Ed.* **1999**, *38*, 1285. (c) De Meijere, A.; Schirmer, H.; Duetsch, M. *Angew. Chem., Int. Ed.* **2000**, *39*, 3965. (d) Barluenga, J.; López, L. A.; Martínez, S.; Tomás, M. *Tetrahedron* **2000**, *56*, 4967. (e) Barluenga, J.; Flórez, J.; Fañanás, F. J. *J. Organomet. Chem.* **2001**, *624*, 5. (f) Barluenga, J.; Santamaría, J.; Tomás, M. *Chem. Rev.* **2004**, *104*, 2259. (g) Barluenga, J.; Fernández-Rodríguez, M. A.; Aguilar, E. *J. Organomet. Chem.* **2005**, *690*, 539. (h) Capriati, V.; Florio, S.; Luisi, R.; Perna, F. M.; Barluenga, J. *J. Org. Chem.* **2005**, *70*, 8255. (i) Wu, Y. T.; Noltemeyer, M.; De Meijere, A. *Eur. J. Org. Chem.* **2005**, 2802. (j) Gómez-Gallego, M.; Mancheño, M. J.; Sierra, M. A. *Acc. Chem. Res.* **2005**, *38*, 44. (k) Sierra, M. A.; Gómez-Gallego, M.; Martínez-Álvarez, R. *Chem.—Eur. J.* **2007**, *13*, 736. (l) Sierra, M. A.; Fernández, I.; Cossío, F. P. *Chem. Commun.* **2008**, 4671. (m) Dötz, K. H.; Stendel, J., Jr. *Chem. Rev.* **2009**, *109*, 3227.

(4) (a) Wulff, W. D.; Yang, D. C. *J. Am. Chem. Soc.* **1983**, *105*, 6726. (b) Wulff, W. D.; Yang, D. C. *J. Am. Chem. Soc.* **1984**, *106*, 7565. (c) Dötz, K. H.; Kuhn, W. *J. Organomet. Chem.* **1985**, *286*, C23.

(5) (a) Dötz, K. H.; Kuhn, W.; Müller, G.; Huber, B.; Alt, H. G. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 812. (b) Wulff, W. D.; Yang, D. C.; Murray, C. K. *J. Am. Chem. Soc.* **1988**, *110*, 2653. (c) Wulff, W. D.; Yang, D. C.; Murray, C. K. *Pure Appl. Chem.* **1988**, *60*, 137. (d) Wulff, W. D.; Bauta, W. E.; Kaesler, R. W.; Lankford, P. J.; Miller, R. A.; Murray, C. K.; Yang, D. C. *J. Am. Chem. Soc.* **1990**, *112*, 3642. (e) Dötz, K. H.; Noack, R.; Harms, K.; Maller, G. *Tetrahedron* **1990**, *46*, 1235. (f) Anderson, B. A.; Wulff, W. D.; Powers, T. S.; Tribbitt, S.; Rheingold, A. L. *J. Am. Chem. Soc.* **1992**, *114*, 10784. (g) Wulff, W. D.; Powers, T. S. *J. Org. Chem.* **1993**, *58*, 2381. (h) Adam, H.; Albrecht, T.; Sauer, J. *Tetrahedron Lett.* **1994**, *35*, 557. (i) Barluenga, J.; Aznar, F.; Barluenga, S. *J. Chem. Soc., Chem. Commun.* **1995**, 1973. (j) Barluenga, J.; Aznar, F.; Barluenga, S.; Martín, A.; García-Granda, S.; Martín, E. *Synlett* **1998**, 473. (k) Barluenga, J.; Aznar, F.; Barluenga, S.; Fernández, M.; Martín, A.; García-Granda, S.; Piñera-Nicolás, A. *Chem.—Eur. J.* **1998**, *4*, 2280. (l) Barluenga, J.; Fernández-Rodríguez, M. A.; Aguilar, E. *Org. Lett.* **2002**, *4*, 3659.

Scheme 1. Reaction between Alkynyl Fischer Carbene Complex and 3*H*-1,2-Dithiole-3-thione Derivatives



moiety makes the velocity of the reaction of [(methoxy)(vinyl)pentacarbonyl]chromium(0) carbene and isoprene comparable to the reaction rate of isoprene and methyl acrylate catalyzed by $AlCl_3$, and for this reason, the term "super ester" was coined for these complexes based on these and other analogous reactions.[2,3] Recently, we have reported a computational study aiming at understanding the role of the Fischer carbene moiety in 1,3-dipolar cycloadditions[7] and Diels–Alder reactions.[8] We demonstrated that either alkynyl or alkenyl group 6–Fischer carbene complexes act in these transformations as organometallic analogues of organic alkyl-propiolates with enhanced electrophilic character. In addition, these reactions occur through transition structures that are more asynchronous and less aromatic than their nonorganometallic isolobal analogues but quite similar to the transition structures for the reactions involving Lewis acid–ester complexes.

In this regard, we have recently reported the first synthesis of pure regioisomer *E*-dithiafulvene thione via the 1,3-dipolar cycloaddition reaction between a series of 5-substituted-3*H*-1,2-dithiole-3-thione derivatives with alkynyl Fischer carbene complexes followed by a demetalation–decarboxylation step by treatment with neutral aluminum oxide (Scheme 1).[9] This transformation is important since it allows the easy access to reaction products that present interesting properties in the organic materials field[10] and because the cycloadditions that involve organic propiolates usually lead to mixtures of cycloadducts.[10a,f,g,j,11]A highly asynchronous cycloaddition reaction due to the thiono group of 3*H*-1,2-dithiole-3-thione was initially proposed for the first step of the transformation involving Fischer carbene complexes.[9] However, the reasons for the observed complete regioselectivity and the low temperatures required for the process to occur remain not fully understood.

Therefore, herein we report an extensive computational study on the origin of the regioselectivity of the 1,3-dipolar cycloaddition reaction between 3*H*-1,2-dithiole-3-thione derivatives and alkynyl Fischer carbene complexes (Scheme 2). The results will be compared with those obtained for the analogous process, which involves the respective isolobal organic esters and their corresponding Lewis acid-complexed counterparts. Finally, the synchronicity of the different transformations and the aromaticity of the corresponding saddle points will be discussed.

Computational Details

Theoretical calculations were performed with the GAUSSIAN 03 suite of programs.[12] All geometry optimizations were computed using the hybrid density functional B3LYP[13] and the standard 6-31+G(d) basis set[14] for hydrogen, carbon, oxygen, nitrogen, sulfur, fluorine, chlorine, and aluminum atoms. For the chromium, scandium, and tungsten atoms we used the Hay–Wadt small-core effective core potential (ECP) including

---

(6) (a) Chan, K. S.; Wulff, W. D. *J. Am. Chem. Soc.* **1986**, *108*, 5229. (b) Chan, K. S. *J. Chem. Soc., Perkin Trans. 1* **1991**, 2602. (c) Chan, K. S.; Yeung, M. L.; Chan, W. K.; Wang, R. J.; Mak, T. C. W. *J. Org. Chem.* **1995**, *60*, 1741. (d) Barluenga, J.; Fernández-Marí, F.; Viado, A. L.; Aguilar, E.; Olano, B. *J. Chem. Soc., Perkin Trans. 1* **1997**, 2267. (e) Yeung, M. L.; Li, W. K.; Liu, H. J.; Wang, Y.; Chan, K. S. *J. Org. Chem.* **1998**, *63*, 7670. (f) Barluenga, J.; Aznar, F.; Palomero, M. A. *Chem.—Eur. J.* **2001**, *7*, 5318. (g) Barluenga, J.; Fernández-Rodríguez, M. A.; Aguilar, E.; Fernández-Marí, F.; Salinas, A.; Olano, B. *Chem.—Eur. J.* **2001**, *7*, 3533. (h) Barluenga, J.; Fernández-Marí, F.; Aguilar, E.; Viado, A. L.; Olano, B. *Tetrahedron Lett.* **1998**, *39*, 4887. (i) Barluenga, J.; Fernández-Marí, F.; Viado, A. L.; Aguilar, E.; Olano, B.; García-Granda, S.; Moya-Rubiera, C. *Chem.—Eur. J.* **1999**, *5*, 883. (j) Barluenga, J.; Tomás, M.; Ballesteros, A.; Santamaría, J.; Brillet, C.; García-Granda, S.; Piñera-Nicolás, A.; Vázquez, J. T. *J. Am. Chem. Soc.* **1999**, *121*, 4516. (k) Barluenga, J.; Fernández-Marí, F.; González, R.; Aguilar, E.; Revelli, G. A.; Viado, A. L.; Fañanás, F. J.; Olano, B. *Eur. J. Org. Chem.* **2000**, 1773. (l) Merino, I.; Santosh Laxmi, Y. R.; Flórez, J.; Barluenga, J.; Ezquerra, J.; Pedregal, C. *J. Org. Chem.* **2002**, *67*, 648. (m) Barluenga, J.; López, S.; Flórez, J. *Angew. Chem., Int. Ed.* **2003**, *42*, 231. (n) Barluenga, J.; Vicente, R.; López, L. A.; Tomás, M. *J. Am. Chem. Soc.* **2006**, *128*, 7050.

(7) Fernández, I.; Sierra, M. A.; Cossío, F. P. *J. Org. Chem.* **2006**, *71*, 6178.

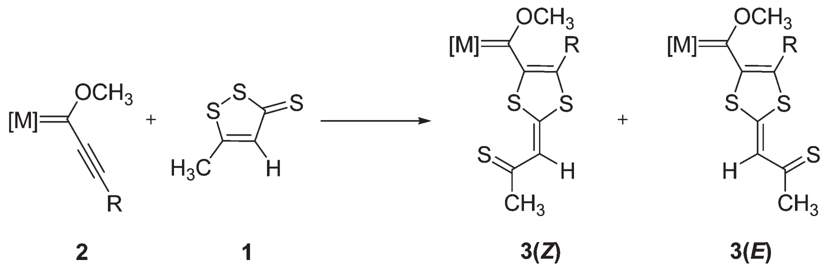
(8) (a) Fernández, I.; Sierra, M. A.; Cossío, F. P. *J. Org. Chem.* **2008**, *73*, 2083. (b) For a related study on 6π-electrocyclization processes, see: Fernández, I.; Cossío, F. P.; Sierra, M. A. *Organometallics* **2007**, *26*, 3010.

(9) Granados, A. M.; Fracaroli, A. M.; De Rossi, R. H.; Fuertes, P.; Torroba, T. *Chem. Commun.* **2008**, *8*, 483.

(10) (a) Frere, P.; Belyasmine, A.; Gorgues, A.; Duguay, G.; Boubekeur, K.; Batail, P. *Tetrahedron Lett.* **1993**, *34*, 4519. (b) Marcos, C. F.; Polo, C.; Rakitin, O. A.; Rees, C. W.; Torroba, T. *Chem. Commun.* **1997**, 879. (c) Barriga, S.; Fuertes, P.; Marcos, C. F.; Miguel, D.; Rakitin, O. A.; Rees, C. W.; Torroba, T. *J. Org. Chem.* **2001**, *66*, 5766. (d) Barriga, S.; Fuertes, P.; Marcos, C. F.; Rakitin, O. A.; Torroba, T. *J. Org. Chem.* **2002**, *67*, 6439. (e) Barriga, S.; Fuertes, P.; Marcos, C. F.; Torroba, T. *J. Org. Chem.* **2004**, *69*, 3672. (f) Barriga, S.; García, N.; Marcos, C. F.; Neo, A. G.; Torroba, T. *Arkivoc* **2002**, 212. (g) Barriga, S.; Marcos, C. F.; Riant, O.; Torroba, T. *Tetrahedron* **2002**, *58*, 9785. (h) García-Valverde, M.; Pascual, R.; Torroba, T. *Org. Lett.* **2003**, *5*, 929. (i) Gorgues, A.; Hudhomme, P.; Sallé, M. *Chem. Rev.* **2004**, *104*, 5151. (j) Ogurtsov, V. A.; Rakitin, O. A.; Rees, C. W.; Smolentsev, A. A.; Belyakov, P. A.; Golovanov, D. G.; Lyssenko, K. A. *Org. Lett.* **2005**, *7*, 791. (k) García-Valverde, M.; Torroba, T. *Eur. J. Org. Chem.* **2006**, 849. (l) Konstantinova, L. S.; Lysov, K. A.; Amelichev, S. A.; Obruchnikova, N. V.; Rakitin, O. A. *Tetrahedron* **2009**, *65*, 2178. (m) Frère, P.; Belyasmine, A.; Gouriou, Y.; Jubault, M.; Gorgues, A.; Duguay, G.; Wood, S.; Reynolds, C. D.; Bryce, M. R. *Bull. Soc. Chim. Fr.* **1995**, *132*, 975. (n) Andreu, R.; Aramburo, J.; Cerdán, M. A.; Garín, J.; Orduña, J.; Villacampa, B. *Tetrahedron Lett.* **2006**, *47*, 661. (o) Andreu, R.; Blesa, M. J.; Carrasquer, L.; Garín, J.; Orduña, J.; Alcalá, R.; Villacampa, B. *Phosphorus, Sulfur Silicon Relat. Elem.* **2005**, *180*, 1473. (p) Andreu, R.; Cerdán, M. A.; Garín, J.; Orduña, J. *Arkivoc* **2004**, 32. (q) Insuasty, B.; Atienza, C.; Seoane, C.; Martín, N.; Garín, J.; Orduña, J.; Alcalá, R.; Villacampa, B. *J. Org. Chem.* **2004**, *69*, 6986. (r) Saha, S.; Leung, K. C. F.; Nguyen, T. D.; Stoddart, J. F.; Zink, J. I. *Adv. Funct. Mater.* **2007**, *17*, 685. (s) Willner, I.; Basnar, B.; Willner, B. *Adv. Funct. Mater.* **2007**, *17*, 702. (t) Griffiths, K. E.; Stoddart, J. F. *Pure Appl. Chem.* **2008**, *80*, 485. (u) Gao, H. J.; Gao, L. *Prog. Surf. Sci.* **2010**, *85*, 28.

(11) (a) Katritzky, A. R.; Rees, C. W. In *Comprehensive Heterocyclic Chemistry*; 1984. (b) Rees, C. W.; Rakitin, O. A.; Marcos, C. F.; Torroba, T. *J. Org. Chem.* **1999**, *64*, 4376. (c) Timoshenko, V. M.; Bouillon, J. P.; Shermolovich, Y. G.; Portella, C. *Tetrahedron Lett.* **2002**, *43*, 5809. (d) Easton, D. B. J.; Leaver, D. *Chem. Commun.* **1965**, 585. (e) Easton, D. B. J.; Leaver, D.; Rawlings, T. J. *J. Chem. Soc., Perkin Trans. 1* **1972**, 41.

Scheme 2



2a, M = Cr(CO)$_5$, R = Me
2b, M = Cr(CO)$_5$, R = Ph
2c, M = W(CO)$_5$, R = Me
2d, M = W(CO)$_5$, R = Ph
2e, M = O, R = Me
2f, M = O-AlCl$_3$, R = Me

a double-ζ valence basis set (LanL2DZ keyword).[15] Spin−orbit corrections have not been included in the calculations.

The stationary points were located with the Berny algorithm[16] using redundant internal coordinates. Analytical Hessians were computed to determine the nature of stationary points (one and zero imaginary frequencies for transition states and minima, respectively)[17] and to calculate unscaled zero-point energies (ZPEs) as well as thermal corrections and entropy effects using the standard statistical-mechanics relationships for an ideal gas.[18] Transition structures (TSs) show only one negative eigenvalue in their diagonalized force constant matrices, and their associated eigenvectors were confirmed to correspond to the motion along the reaction coordinate under consideration using the intrinsic reaction coordinate (IRC) method.[19] Unless otherwise stated, Gibbs energies have been computed at 298 K.

Nonspecific solvent effects were described by using the self-consistent reaction field (SCRF) approach in Tomasi's formalism.[20] Single-point PCM[B3LYP/LanL2DZ&6-31+G(d)] calculations were performed to estimate the change in the Gibbs energy profile of the reaction in the presence of different solvents.

The synchronicity (S_y) of the reaction,[21] proposed by Moyano et al.,[22] is commonly used to represent the global nature of bond-breaking/forming processes in the reaction, and it was calculated as[23]

$$S_y = 1 - \frac{\sum_{i=1}^{n} \frac{|\delta B_i - \delta B_{\mathrm{AV}}|}{\delta B_{\mathrm{AV}}}}{2n-2} \tag{1}$$

where n refers to the number of bonds directly involved in the reaction (in this case, $n = 5$) and δB_i stands for the relative variation of a given bond index B_i at the transition state (TS), according to the following formula:

$$\delta B_i = \frac{B_i^{\mathrm{TS}} - B_i^{\mathrm{R}}}{B_i^{\mathrm{P}} - B_i^{\mathrm{R}}} \tag{2}$$

where B_i is the bond order and the superscripts TS, R, and P stand for transition state, reactant, and product, respectively, for an elementary step of a given reaction. The average value of δB_i, denoted as δB_{AV}, is therefore

$$\delta B_{\mathrm{AV}} = n^{-1} \sum_{i=1}^{n} \delta B_i \tag{3}$$

The reported Wiberg bond indices[24] were computed using the natural bond orbital (NBO) method.[25]

The aromatic character of the transition states has been confirmed by the computation of the nuclear independent chemical shift (NICS)[26] values. These calculations have been carried out using the gauge invariant atomic orbital (GIAO) method,[27] at the B3LYP/6-31+G(d)&LanL2DZ level.

---

(12) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Montgomery, J. A., Jr.; Vreven, T.; Kudin, K. N.; Burant, J. C.; Millam, J. M.; Iyengar, S. S.; Tomasi, J.; Barone, V.; Mennucci, B.; Cossi, M.; Scalmani, G.; Rega, N.; Petersson, G. A.; Nakatsuji, H.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Klene, M.; Li, X.; Knox, J. E.; Hratchian, H. P.; Cross, J. B.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Ayala, P. Y.; Morokuma, K.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Zakrzewski, V. G.; Dapprich, S.; Daniels, A. D.; Strain, M. C.; Farkas, O.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Ortiz, J. V.; Cui, Q.; Baboul, A. G.; Clifford, S.; Cioslowski, J.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Gonzalez, C.; Pople, J. A. *Gaussian 03*, Revision C.02 ed.; Gaussian, Inc.: Wallingford, CT, 2004.

(13) (a) Becke, A. D. *J. Phys. Chem.* **1993**, *98*, 5648. (b) Lee, C.; Yang, W.; Parr, R. G. *Phys. Rev. B* **1998**, *37*, 785. (c) Stephens, P. J.; Devlin, F. J.; Chabalowski, C. F.; Frisch, M. J. *J. Phys. Chem.* **1994**, *98*, 11623.

(14) Hehre, W. J.; Radom, L.; Scheleyer, P. v. R.; Pople, J. A. In *Ab Initio Molecular Orbital Theory*; Wiley: New York, 1986; p 76, and references therein.

(15) Hay, P. J.; Wadt, W. R. *J. Chem. Phys.* **1985**, *82*, 299.

(16) Peng, C. Y.; Ayala, P. Y.; Schlegel, H. B.; Frisch, M. J. *J. Comput. Chem.* **1996**, *17*, 49.

(17) McIver, J. W.; Komornicki, A. K. *J. Am. Chem. Soc.* **1972**, *94*, 2625.

(18) Atkins, P. W.; De Paula, J. *Physical Chemistry*, 8th ed.; Oxford University Press: New York, 2006.

(19) González, C.; Schlegel, H. B. *J. Phys. Chem.* **1990**, *94*, 5523.

(20) (a) Miertus, S.; Scrocco, E.; Tomasi *J. Chem. Phys.* **1981**, *55*, 117. (b) Barone, V.; Cossi, M.; Tomasi, J. *J. Comput. Chem.* **1998**, *19*, 404.

(21) (a) Dewar, M. J. S. *J. Am. Chem. Soc.* **1984**, *106*, 209. (b) Borden, W. T.; Loncharich, R. J.; Houk, K. N. *Annu. Rev. Phys. Chem.* **1988**, *39*, 213. (c) Leroy, G.; Sana, M. *Tetrahedron* **1975**, *31*, 2091.

(22) Moyano, A.; Pericás, M. A.; Valentí, A. *J. Org. Chem.* **1989**, *54*, 573.

(23) (a) Lecea, B.; Arrieta, A.; López, X.; Ugalde, J. M.; Cossío, F. P. *J. Am. Chem. Soc.* **1995**, *117*, 12314. (b) Lecea, B.; Arrieta, A.; Roa, G.; Ugalde, J. M.; Cossío, F. P. *J. Am. Chem. Soc.* **1994**, *116*, 12314.

(24) Wiberg, K. B. *Tetrahedron* **1968**, *24*, 1083.

(25) (a) Foster, J. P.; Weinhold, F. *J. Am. Chem. Soc.* **1980**, *102*, 7211. (b) Reed, A. E.; Weinhold, F. J. *J. Chem. Phys.* **1985**, *83*, 1736. (c) Reed, A. E.; Weinstock, R. B.; Weinhold, F. *J. Chem. Phys.* **1985**, *83*, 735. (d) Reed, A. E.; Curtiss, L. A.; Weinhold, F. *Chem. Rev.* **1988**, *88*, 899.

(26) Chen, Z.; Wannere, C. S.; Corminboeuf, C.; Puchta, R.; Schleyer, P. v. R. *Chem. Rev.* **2005**, *105*, 3842.

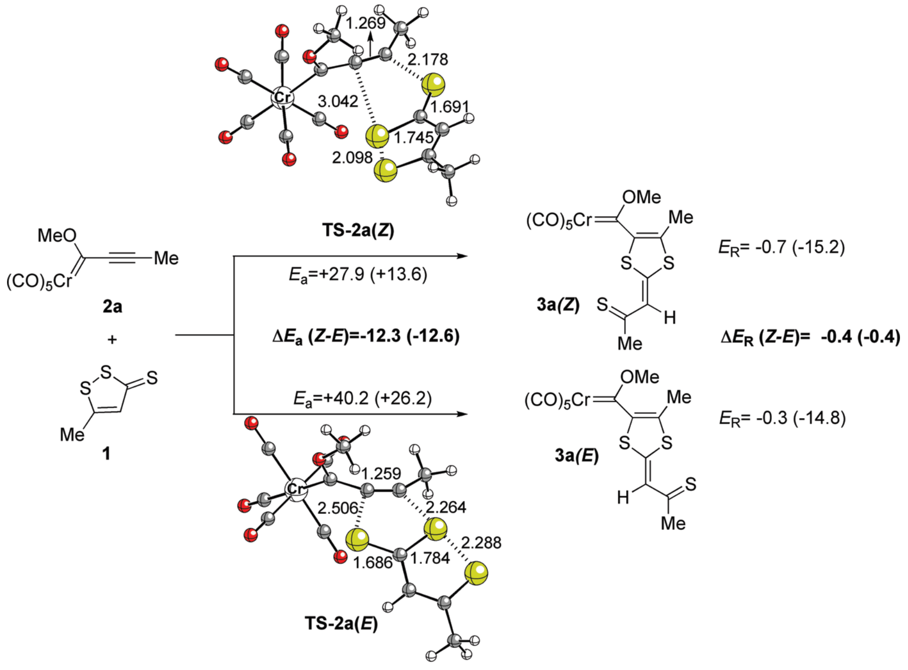


Figure 1. Calculated pathways associated with the formation of the two possible regioisomers in the [3+2] cycloaddition reaction between Fischer carbene (**2a**) and 5-methyl-3*H*-1,2-dithiole-3-thione (**1**). The numbers close to the arrows (in kcal/mol) are the relative Gibbs energies and electronic energy + ZPVE (in parentheses). Bond lengths are given in Å. All values have been computed at the B3LYP/LANL2DZ&6-31+G(d) level.

Results and Discussion

The regiochemistry of the [3+2] cycloaddition reaction was addressed first. Due to the asymmetry of the dipole 5-methyl-3*H*-1,2-dithiole-3-thione (**1**) and the dipolarophiles considered (**2**, see Scheme 2), several reaction pathways can be envisaged for the 1,3-dipolar cycloaddition reaction between these species, which mainly lead to the *Z*- and/or *E*-cycloadducts **3**. But before starting the discussion of the computational results, let us briefly mention the experimental findings related to the observed regiochemistry when Fischer carbene complexes, organic esters, or Lewis acid-catalyzed organic esters act as dipolarophiles. In the case of Fischer carbene complexes, we have recently reported that the reaction between 5-cyclopentylthio-3*H*-1,2-dithiole-3-thione and [methoxy(phenylethynyl)carbene pentacarbonyl]-chromium(0) (**2b**) is complete in 30 min in dry ether at −40 °C under nitrogen atmosphere. A correct characterization of the crude reaction confirmed the *Z*-isomer as the only observed cycloadduct.[9]

On the other hand, the reaction between acetylene dietilacetal carbaldehyde and 4-phenyl-1,2-dithiole-3-thione in CH_2Cl_2 at 20 °C after 1 h results in almost quantitative production of the *E*- and *Z*-isomers in approximately equal amounts.[10a] The use of the less nucleophilic thione derivative 4,5-dichloro-1,2-dithiole-3-thione as starting material has been reported to react similarly but much more slowly with monosubstituted alkynes. Methyl propiolate required refluxing in toluene for 3 h, while phenylacetylene required refluxing in toluene for 32 h. Both give inseparable mixtures of two isomers (ratio 1(*Z*):3(*E*) and ratio 2(*Z*):3(*E*), respectively).[10j]

The use of scandium triflate [$Sc(OTf)_3$] as a Lewis acid catalyst produces an enhancement of the reaction rate in this cycloaddition reaction. For instance, the cycloaddition of 1-ferrocenylprop-2-yn-1-one and bisdithiolothiazine ketothione in the presence of $Sc(OTf)_3$, in CH_2Cl_2 at room temperature for 10 min, yields a mixture of isomers in a ratio of 2(*Z*):1(*E*).[10g] In addition, the reaction of ethynyl *p*-tolyl sulfone with dithiolothiazine in the same conditions yields a new dithiolane derivative as the *Z* + *E* mixture of isomers.[10f]

On the basis of the aforementioned experimental evidence, the regiochemistry of the reaction was studied first in the reaction between Fischer carbene **2a** and thione **1**. DFT calculations (B3LYP/LANL2DZ&6-31+G*) were performed beginning with the *syn*-form of alkynyl metal−carbenes (an orientation where the heteroatom substituent is not directed toward the pentacarbonyl metal moiety), which is the most stable conformer in the gas phase as well as in solid state.[28] The results are shown in Figure 1. As seen from the energy difference between both cycloadducts, which can be considered as negligible ($\Delta E_R(Z-E) = -0.4$ kcal/mol), it is clear that the experimental observed regioselectivity is not due to thermodynamic control. Our calculations suggest that this regioselectivity takes place under kinetic control, in view of the considerably higher activation Gibbs energy required for the formation of the *E*-cycloadduct as compared to the *Z*-products ($\Delta E_a(Z-E) = -12.3$ kcal/mol). No significant differences in the computed Gibbs energies at the temperature

---

(27) Wolinski, K.; Hinton, J. F.; Pulay, P. *J. Am. Chem. Soc.* **1990**, *112*, 8251.

(28) (a) Fernández, I.; Mancheño, M. J.; Gómez-Gallego, M.; Sierra, M. A.; Lejon, T.; Hansen, L. K. *Organometallics* **2004**, *23*, 1851. (b) Andrada, D. M.; Zoloff Michoff, M. E.; Fernández, I.; Granados, A. M.; Sierra, M. A. *Organometallics* **2007**, *26*, 5854. (c) Fernández, I.; Cossío, F. P.; Arrieta, A.; Lecea, B.; Mancheño, M. J.; Sierra, M. A. *Organometallics* **2004**, *23*, 1065. (d) Jiménez-Halla, J. O. C.; Solà, M. *Chem.—Eur. J.* **2009**, *15*, 12503.

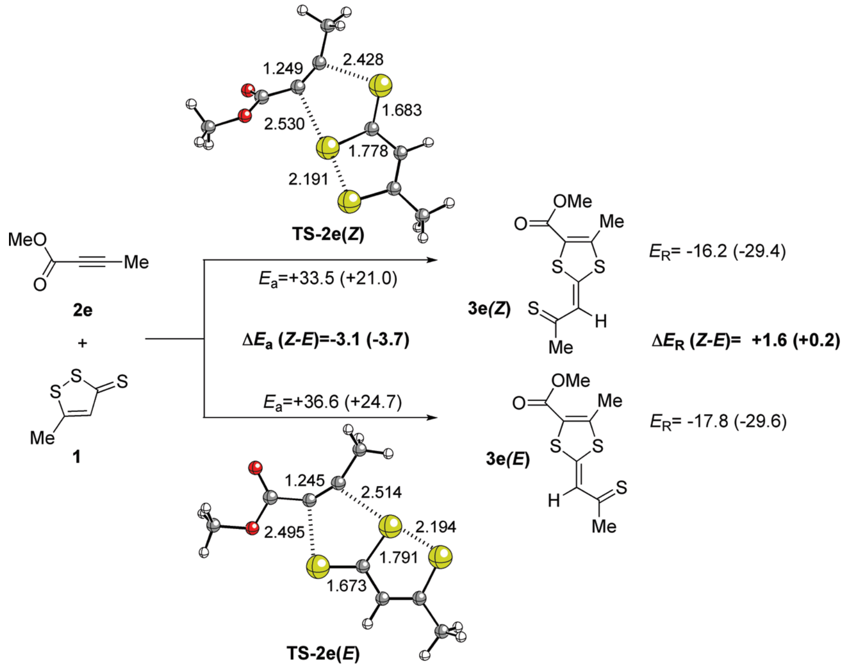


Figure 2. Calculated pathways associated with the formation of the two possible regioisomers in the [3+2] cycloaddition reaction between ester (**2e**) and 5-methyl-3*H*-1,2-dithiole-3-thione (**1**). The numbers close to the arrows (in kcal/mol) are the relative Gibbs energies and electronic energy + ZPVE (in parentheses). Bond lengths are given in Å. All values have been computed at the B3LYP/LANL2DZ&6-31+G(d) level.

used in the experiment (−40 °C) were observed (ΔE_R($Z-E$) = −0.3 kcal/mol and ΔE_a($Z-E$) = −12.8 kcal/mol).

From these results and in good agreement with the experimental findings, we can conclude that the reaction is completely regioselective, leading to the exclusive formation of cycloadduct **3a**(***Z***). It is important to remark that the formed *Z*-isomer slowly isomerizes at room temperature to the *E*-isomer. An activation energy of 12.7 kcal/mol has been determined for the corresponding metal-free 4-phenyl-1,3-dithiafulvene (thiobutyl 2-(4-phenyl-1,3-dithiole-2-ylidene)-thionoacetate).[29] However, this value is subject to error because, under experimental conditions, rate measurements present thermodynamic contributions due to self-aggregation/association processes.[29] Thus, we have computed a Gibbs activation energy of 28.3 kcal/mol for the **3a**(***Z***) → **3a**(***E***) isomerization process, which suggests that in experimental synthesis conditions this process is slow (see a representation of the isomerization process in Figure S1).

Quite significant differences are observed when we consider the analogous organic methyl but-2-ynoate (**2e**) as dipolarophile in its cycloaddition reaction with thione **1** (Figure 2). Similarly, the *Z*- and *E*-cycloadducts are practically degenerate (ΔE_R($Z-E$) = 1.6 kcal/mol). However, the difference in the activation barriers of both reaction pathways is strongly reduced (ΔE_a($Z-E$) = −3.1 kcal/mol) compared to the cycloaddition reaction involving the alkynyl Fischer carbene complex **2a** (see above). Even though the pathway leading to the *Z*-isomer is slightly favored, the computed small difference in the activation barriers in this model reaction is in agreement with the experimentally observed mixture of cycloadducts using organic propiolates as diporalophiles compared to the complete regioselectivity observed with Fischer carbene complexes. Furthermore, for the kinetically favored process (through **TS-2e**(***Z***)) the activation barrier is 5.6 (7.4) kcal/mol higher for ester **2e** than for the complex **2a**. This is again in line with the well-known enhanced reaction rates observed for carbene complexes in comparison with their isolobal organic ester analogues[2,3,7] and justifies the lower reaction temperatures required for this organometallic cycloaddition.

To compare the effect of the pentacarbonyl−metal moiety with that of the Lewis acid catalyst, the reaction between the methyl but-2-ynoate-$AlCl_3$ complex (**2f**) and thione **1** was also calculated (Figure 3a). The results are shown in Figure 3. In this case, reaction energies predict an exergonic conversion, with the *Z*-cycloadduct being 1.4 kcal/mol more stable than the *E*-isomer. Analogously, the regioselectivity of the transformation takes place mainly under kinetic control, which strongly favors the formation of the *Z*-cycloadduct (ΔE_a($Z-E$) = −12.0 kcal/mol). Our results predict therefore a complete regioselectivity in this process that is not in agreement with the mixture of cycloadducts observed in the 1,3-dipolar reaction in the presence of $Sc(OTf)_3$.[10f,g] For this reason, we also computed the same transformation from the methyl but-2-ynoate-$Sc(OTf)_3$ complex (**2f′**). However, the computed values indicate that the process is completely regioselective toward the formation of the *Z*-cycloadduct (ΔE_a($Z-E$) = −12.0 kcal/mol) as well (Figure 3b). A possible explanation for the disagreement with the experimental findings might be the use of complex **2f′** as model instead of the larger experimental reactants 1-ferrocenyl-prop-2-yn-1-one[10g] and ethynyl *p*-tolyl sulfone.[10f] Anyway and similar to other related cycloadditions,[7,8] the activation barriers for the preferred reaction pathway follows the order organic ester > Fischer carbene > Lewis acid complex, which clearly shows the reaction rate enhancement provoked by the presence of the Lewis acid or the pentacarbonylmetal(0) moiety.

---

(29) Fracaroli, A. M.; Granados, A. M.; de Rossi, R. H. *J. Org. Chem.* **2009**, *74*, 2114.

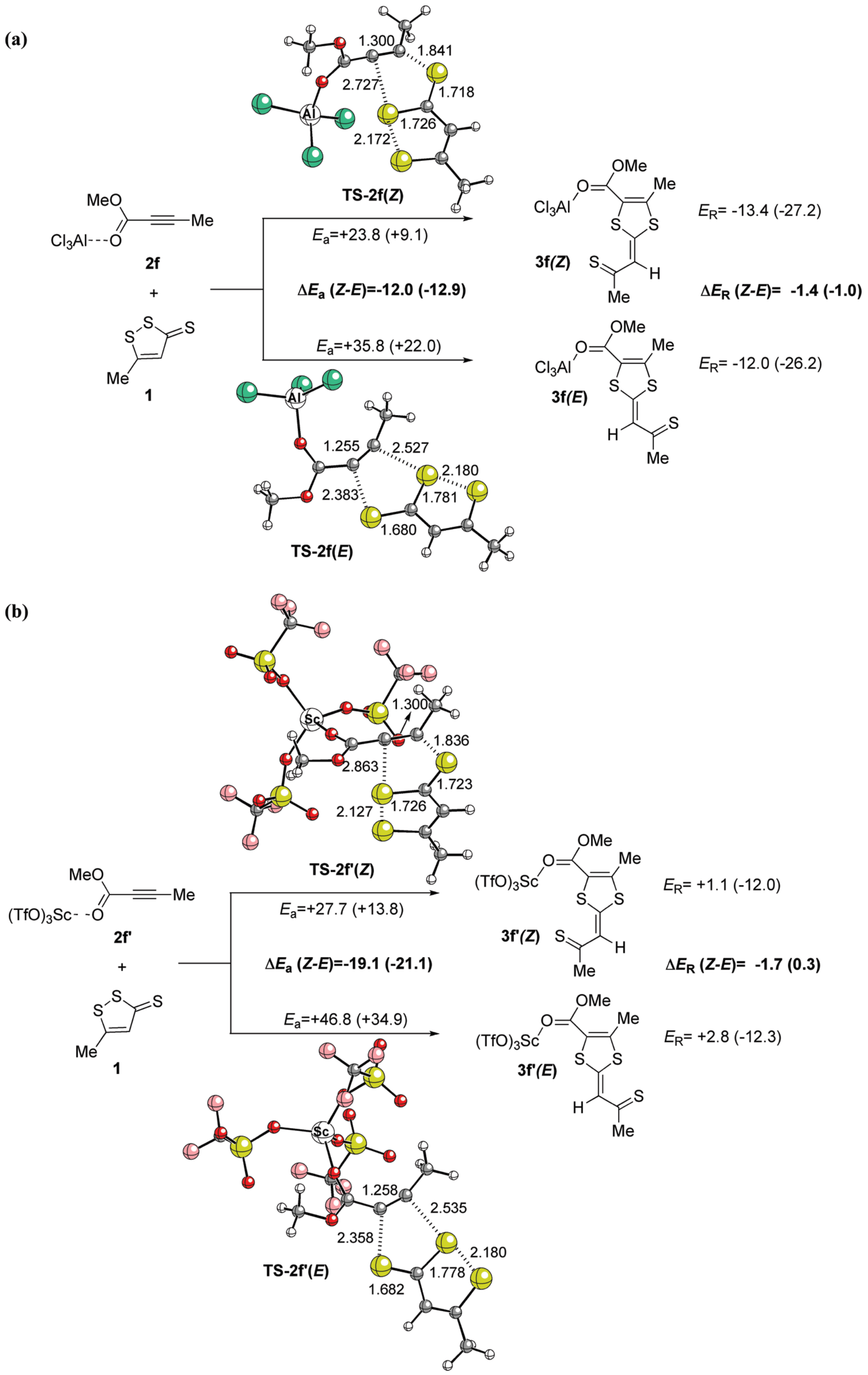


Figure 3. Calculated pathways associated with the formation of the two possible regioisomers in the [3+2] cycloaddition reaction between $AlCl_3$-ester (**2f**, top) and $Sc(OTf)_3$-ester (**2f′**, bottom) with 5-methyl-3*H*-1,2-dithiole-3-thione (**1**). The numbers close to the arrows (in kcal/mol) are the relative Gibbs energies and electronic energy + ZPVE (in parentheses). Bond lengths are given in Å. All values have been computed at the B3LYP/LANL2DZ&6-31+G(d) level.

A simple way to predict the regiochemistry of the considered 1,3-dipolar cycloaddition reaction is by means of the inspection of the calculated electrostatic potential surface of the reactants and the computation of the NBO charges of the atoms involved in the cycloaddition reaction (Figure 4). For the 1,3-dipole **1**, the sulfur atom denoted as S_1 bears a negative charge of −0.028 au, while a positive charge of +0.267 au is computed on the S_2 atom, which is in good agreement with the dipolar character of this species (see Figure 4). On the other hand, all the considered dipolarophiles possess a positive charge on the C_β atom, while the C_α bears a negative charge. This charge analysis easily explains

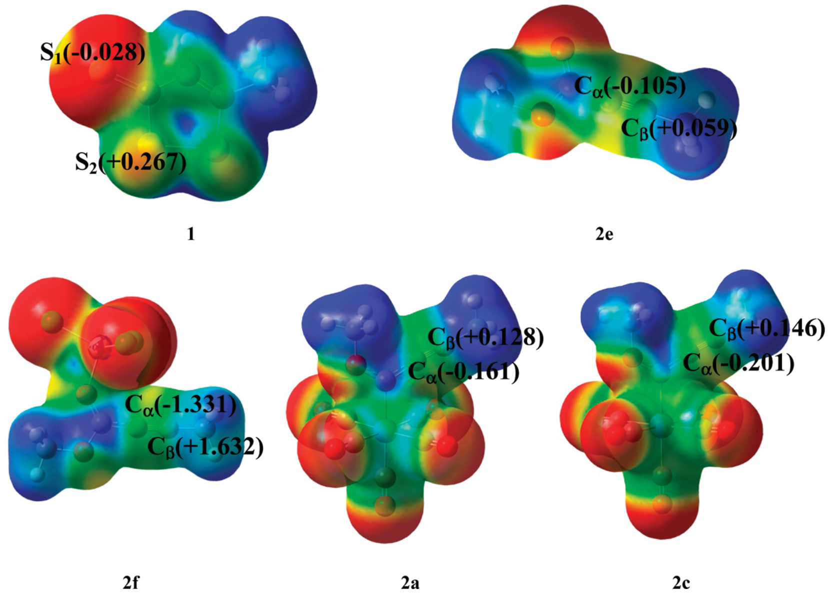


Figure 4. NBO charges and electrostatic potential surface for selected compounds. Electron density (0.004 isocontour) was computed at the B3LYP/LANL2DZ&6-31+G(d) level of theory. Negative values are in red, and positive values are in blue.

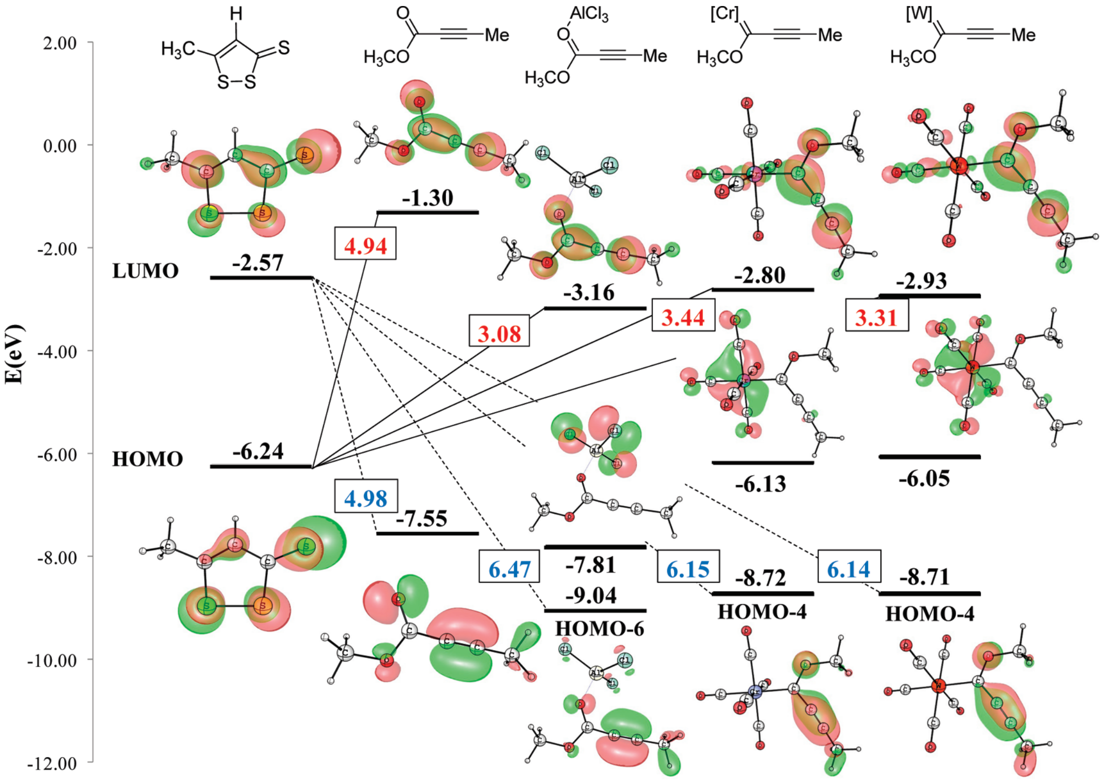


Figure 5. Frontier orbital energies of 5-methyl-3*H*-1,2-dithiole-3-thione **1** and dipolarophiles **2a**, **2c**, **2e**, and **2f**. All values (in eV) were computed at the B3LYP/LANL2DZ&6-31+G(d) level.

the preference for the nucleophilic attack of the S_1 of thione **1** to the C_β atom of the dipolarophile, which necessarily leads to the formation of the *Z*-cycloadduct. The differences in the experimentally observed reaction rates and regioselectivities can be interpreted in terms of the absolute values of the positive charge on the C_β atom, which follows the order organic ester (+0.059) < chromium(0)−Fischer carbene (+0.128) < tungsten(0)−Fischer carbene (+0.146) ≪ Lewis acid complex (+1.632). These data clearly reflect the increase of the electron-withdrawing capacity of the pentacarbonyl−metal fragment or the $AlCl_3$ complex compared to the isolobal ester analogue.

Similar conclusions can be drawn by the inspection of the frontier molecular orbitals (FMO) of the reactants. According to the FMO theory, the interaction between orbitals is favored when they are closer in energy. Figure 5 summarizes

Table 1. Global Properties (electronic chemical potential μ, chemical hardness η, and chemical softness S values are in au; electrophilicity power ω values are in eV), Local Softness (s^+ for nucleophilic and s^- for electrophilic attack) of 1 and 2a−f, and Values of the $\Delta(Z)$ and $\Delta(E)$ Quantities (in au) Defined in eqs 4 and 5[a]

	μ^b	η^c	S^d	ω^e	s^-_{S1} or $s^+_{C\alpha}$ [f]	s^-_{S2} or $s^+_{C\beta}$ [f]	$\Delta(Z)$	$\Delta(E)$
1	−0.162	0.135	3.704	2.642	1.563	0.701		
2e	−0.163	0.230	2.178	1.565	0.073	0.616	1.29	2.23
2f	−0.202	0.171	2.926	3.234	−0.094	0.822	1.18	2.76
2a	−0.164	0.123	4.075	2.985	−0.021	0.795	1.11	2.52
2c	−0.165	0.114	4.369	3.236	0.007	0.849	0.99	2.45
2b	−0.170	0.110	4.532	3.546	0.024	0.662	1.27	2.37
2d	−0.168	0.103	4.842	3.729	0.012	0.702	1.22	2.41

[a] All values have been calculated at the B3LYP/LANL2DZ&6-31+G(d) level. [b] μ values have been computed as $(\varepsilon_{\text{HOMO}} + \varepsilon_{\text{LUMO}})/2$. [c] $\eta = \varepsilon_{\text{LUMO}} - \varepsilon_{\text{HOMO}}$. [d] $S = 1/(2\eta)$. [e] $\omega = \mu^2/2\eta$. [f] $s^+ = Sf^+$ with $f^+ = [q(N+1) - q(N)]$ and $s^- = Sf^-$ with $f^- = [q(N) - q(N-1)]$, where q is the NBO population (see in the text and refs 30 and 33).

the energies of the frontier orbitals of the carbene complexes **2a** and **2c**, their organic ester analogue **2e**, the $AlCl_3$ complex **2f**, and the 1,3-dipole **1**. As expected, in all cases the preferred interaction involves the HOMO of the dipole and the LUMO of the diporalophile, which can be considered as the π^* molecular orbital of the delocalized X=C−C≡C moiety. Interestingly, the coefficient of the HOMO in dipole **1** in the S_1 atom is higher than in S_2, which is a clear indication of the higher nucleophilicity of the former sulfur atom. This result points to an *electronic control* of the regioselectivity of the transformation. Strikingly, the HOMO(dipole)−LUMO(dipolarophile) gap is reduced in the order M = O ≫ $Cr(CO)_5$ > $W(CO)_5$ > $AlCl_3$, which matches the above-mentioned withdrawing abilities of the [M] moiety (Scheme 2) and justifies the computed activation barriers for the considered [3+2] cycloaddtions.

To provide further support for the above findings, we have also analyzed the cycloaddition reaction computing the static global properties (electronic chemical potential, μ, chemical hardness, η, global electrophilicity, ω, and global softness, S) and significant local indices (local softness s^+ and s^-)[30] for **1** and **2a−f** (Table 1).

The electronic chemical potential of the thione **1** is higher than the electronic chemical potential of all dipolarophiles considered. These values indicate that along the reaction the net charge transfer will take place from **1** toward reactant **2a−f**, thereby suggesting that the latter compounds will, in general, act as electron acceptors in agreement with the FMO results. Moreover, the electrophilicity power of thione **1** is 2.642 eV, a value that is in the range of strong electrophiles within the ω scale.[31] This value is higher than that expected on the basis of computed energy barriers. For instance, the reaction between **2a** and *N*-methylnitrone has an energy barrier 2 kcal/mol lower than **TS-2a(*Z*)**,[7] while the electrophilicity power of the nitrone is 0.81 eV.[31] The strong electrophilic character of **1** could be ascribed to the dithiole ring.[32]

On the other hand, the difference in the reactivity could also be explained in terms of the electrophilicity of dipolarophiles **2a−f**. Higher ω values make the dipolarophile more electrophilic and therefore more reactive.[31] However, ω values do not correlate with NBO charges and HOMO(**1**)−LUMO(**2a−f**) gaps, probably due to the fact that electrophilicity powers have been computed using the HOMO energies instead of the HOMO−4 and HOMO−6 energies (see Figure 5). Indeed, when the energies of the latter molecular orbitals are considered, the corresponding "corrected" electrophilicity power ω' increases in the order **2e** (1.565 eV) < **2a** (2.797 eV) < **2c** (2.932 eV) < **2f** (3.163 eV) ≈ **2b** (3.201 eV) ≈ **2d** (3.281 eV); that is, it becomes more intense with the higher electron-withdrawing character of the dipolarophile, which nicely matches the orders found with the above-mentioned NBO charges and FMO analyses.

Besides the global indices, Table 1 also gathers the local reactivity indices derived directly from the electron density. The local softness s (for each involved atom with superscript being either −, for an electrophilic attack, or +, for a nucleophilic one) has been calculated as a product Sf, where f is the condensed form of Fukui functions calculated as reported elsewhere,[30c,33] utilizing the NBO populations. In order to explain the observed regioselectivity in cycloaddition reactions with two bond-forming interactions by means of the local hard and soft acids and bases (HSAB) principle, we have calculated the Δ quantity obtained by a local softness matching square sum criterion, as Chandra and Nguyen suggested for a normal electron demand cycloaddition process.[34]

$$\Delta(Z) = (s^-_{S1} - s^+_{C\beta})^2 + (s^-_{S2} - s^+_{C\alpha})^2 \qquad (4)$$

$$\Delta(E) = (s^-_{S1} - s^+_{C\alpha})^2 + (s^-_{S2} - s^+_{C\beta})^2 \qquad (5)$$

where $\Delta(E)$ and $\Delta(Z)$ refer to both *E*- and *Z*-isomer pathways, respectively. According to these equations, the reaction associated with a lower Δ value will be the preferred one.

In all cases, the *Z*-cycloadduct is preferred over the *E*-cycloadduct, as indicated by the computed lower $\Delta(Z)$ values. The regiochemical preference for the *Z*-isomer follows the order M = O < $Cr(CO)_5$ < $W(CO)_5$ < $AlCl_3$ since the differences between $\Delta(E)$ and $\Delta(Z)$ increase, in agreement with the computed energy barriers. This clearly explains the observed regioselectivity of these cycloaddition reactions.

---

(30) (a) Parr, R. G.; Pearson, R. G. *J. Am. Chem. Soc.* **1983**, *105*, 7512. (b) Parr, R. G.; Szentpály, L. V.; Liu, S. *J. Am. Chem. Soc.* **1999**, *121*, 1922. (c) Yang, W.; Parr, R. G. *Proc. Natl. Acad. Sci. U. S. A.* **1985**, *82*, 6723.

(31) Pérez, P.; Domingo, L. R.; Aurell, M. J.; Contreras, R. *Tetrahedron* **2003**, *59*, 3117.

(32) (a) Abasq, M. L.; Burgot, J. L.; Darchen, A.; Dervout, S. E. *J. Electroanal. Chem.* **2002**, *537*, 145. (b) Abasq, M. L.; Burgot, J. L.; Darchen, A.; Saidi, M. *Electrochim. Acta* **2005**, *50*, 2219. (c) Abasq, M. L.; Saidi, M.; Burgot, J. L.; Darchen, A. *J. Organomet. Chem.* **2009**, *694*, 36.

(33) (a) Yang, W.; Mortier, W. J. *J. Am. Chem. Soc.* **1986**, *108*, 5708. (b) Gâzquez, J. L.; Méndez, F. *J. Phys. Chem.* **1994**, *98*, 4591.

(34) (a) Chandra, A. K.; Nguyen, M. T. *J. Comput. Chem.* **1998**, *19*, 195. (b) Chandra, A. K.; Nguyen, M. T. *J. Phys. Chem. A* **1998**, *102*, 6181. (c) Chandra, A. K.; Uchimaru, T.; Nguyen, M. T. *J. Chem. Soc., Perkin Trans. 2* **1999**, 2117. (d) Damoun, S.; Van De Woude, G.; Méndez, F.; Geerlings, P. *J. Phys. Chem. A* **1997**, *101*, 886. (e) Le, T. N.; Nguyen, L. T.; Chandra, A. K.; De Proft, F.; Geerlings, P.; Nguyen, M. T. *J. Chem. Soc., Perkin Trans. 2* **1999**, 1249. (f) Sengupta, D.; Chandra, A. K.; Nguyen, M. T. *J. Org. Chem.* **1997**, *62*, 6404.

In order to validate our model, we replaced the pentacarbonyl-chromium(0) fragment in complex **2a** by $W(CO)_5$ to check the effect of the metal in the cycloaddition reaction with thione **1**. Our model predicts that the activation barrier should be slightly lower for tungsten complex **2c** than for its chromium counterpart in view of the slightly higher positive charge of the C_β atom of the alkynyl fragment (Δq = 0.018 au), the slightly lower HOMO−LUMO gap ($\Delta\Delta E$ = 0.08 eV, see above), and higher electrophilicity power ω. The computed data agree with this prediction, as the activation barrier for the pathway leading to the *Z*-isomer is 0.7 kcal/mol lower for complex **2c** compared to chromium(0) complex **2a** (Table 2). However, the replacement of the terminal methyl group by a phenyl substituent (entries 5 and 6, Table 2) leads to practically degenerate saddle points, and therefore, the effect of the metal in these cycloaddition reactions can be considered negligible. This is not surprising if we take into account the higher stabilization of the positive charge exerted by the phenyl group by conjugation in complexes **2b**,**d** compared to the weaker hyperconjugation by the methyl group in complexes **2a**,**c**. In fact, the computed NBO charges of the C_β atom are 0.100 and 0.099 au for complexes **2b** and **2d**, respectively (for complexes **2a**,**c** charges of the C_β atom are 0.128 and 0.146; see Figure 4). Therefore and according to our model, quite similar barrier energies should be expected for complexes **2b** and **2d**. As a consequence of this charge stabilization process, phenyl-substituted alkynyl carbenes should exhibit higher activation barriers than methyl-substituted analogues. This is again confirmed in view of the computed data, which are gathered in Table 2.

Table 2. Relative Gibbs Energies (ΔG) and Electronic Energies ($\Delta E + \Delta ZPVE$ included, in kcal/mol) Associated with the Formation of the *Z*-Isomer Product[a]

		kinetic		thermodynamic	
entry		ΔG_a	ΔE_a	ΔG_R	ΔE_R
1	**2e**, M = O, R = Me	+33.5	+20.9	−16.2	−29.4
2	**2f**, M = O-$AlCl_3$, R = Me	+23.9	+9.1	−13.4	−27.2
3	**2a**, M = $(CO)_5Cr$, R = Me	+27.9	+13.6	−0.7	−15.2
4	**2c**, M = $(CO)_5W$, R = Me	+27.2	+13.4	−1.4	−15.9
5	**2b**, M = $(CO)_5Cr$, R = Ph	+29.4	+16.0	+2.5	−12.1
6	**2d**, M = $(CO)_5W$, R = Ph	+29.3	+16.1	+1.6	−12.4

[a] All values have been calculated at the B3LYP/LANL2DZ&6-31+G(d) level. ΔG_a values computed as $\Delta G_a = G(\mathbf{TS\text{-}2(}\boldsymbol{Z}\mathbf{)}) - G(\mathbf{2}) - G(\mathbf{1})$. ΔG_R values computed as $\Delta G_R = G(\mathbf{3(}\boldsymbol{Z}\mathbf{)}) - G(\mathbf{2}) - G(\mathbf{1})$.

Particularly for the chromium(0) complex **2b**, we also calculated the two different pathways because this complex was the experimentally used reagent.[9] Again, the data in Figure 6 show that the formation of the *Z*-cycloadduct is completely regioselective ($\Delta E_a(Z-E)$ = −10.6 kcal/mol) and kinetically controlled. This transformation was also chosen to check the effect of the solvent in the cycloaddition. Table 3 gathers the relative Gibbs energies of the TSs and corresponding cycloadducts in different solvents using the polarized continuum model (PCM). Similar to other dipolar cycloaddition reactions involving Fischer carbene complexes,[7] the activation barriers of the process are larger in solution than in the gas phase. This was expected because the large zwitterionic character of the 1,3-dipoles diminishes along the reaction coordinate, thereby resulting in lower

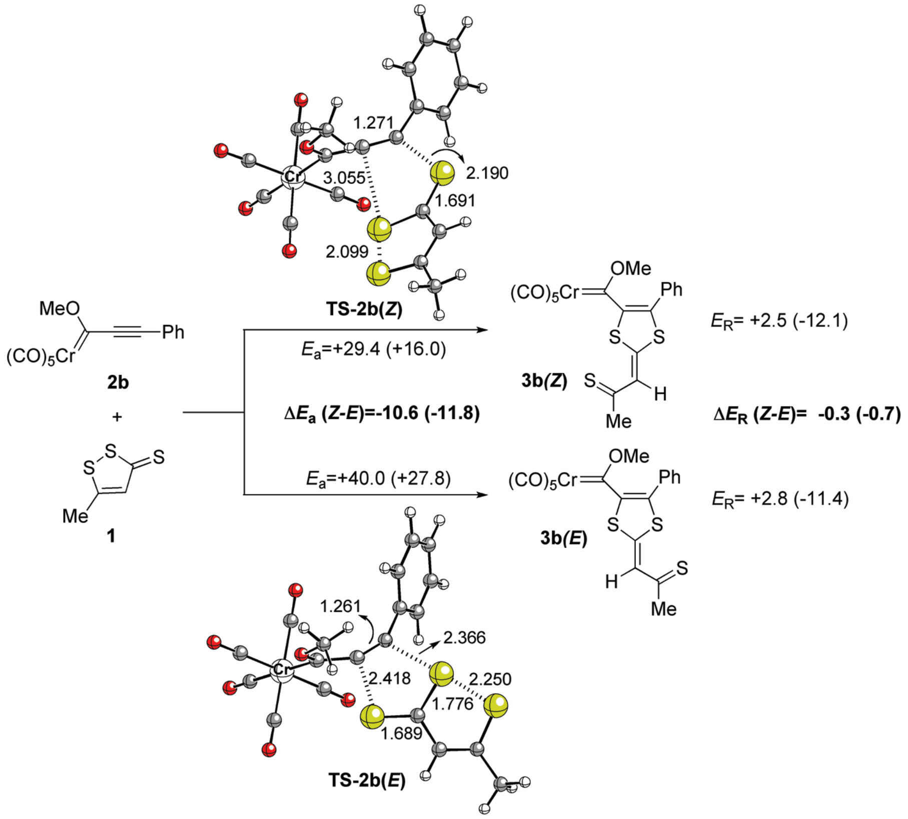


Figure 6. Calculated pathways associated with the formation of the two possible regioisomers in the [3+2] cycloaddition reaction between complex **2b** and 5-methyl-3*H*-1,2-dithiole-3-thione (**1**). The numbers close to the arrows (in kcal/mol) are the relative Gibbs energies and electronic energy + ZPVE (in parentheses). Bond lengths are given in Å. All values have been computed at the B3LYP/LANL2DZ&6-31+G(d) level.

Table 3. Reaction and Energy Barrier Gibbs Energies (kcal/mol) Associated with the Formation of *Z*- and *E*-Isomer for 2b[a]

	kinetic			thermodynamic		
solvent	$\Delta G_a(Z)$	$\Delta G_a(E)$	$\Delta\Delta G_a(Z-E)$	$\Delta G_R(Z)$	$\Delta G_R(E)$	$\Delta\Delta G_R(Z-E)$
gas (ε = 1.00)	+29.4	+40.0	−10.6	+2.5	+2.8	−0.3
ether (ε = 4.335)	+29.7	+43.1	−13.4	+5.0	+5.1	−0.1
THF (ε = 7.58)	+29.8	+43.8	−14.0	+5.5	+5.6	−0.1
acetone (ε = 20.7)	+30.0	+44.5	−14.5	+5.9	+6.0	−0.1

[a] All values have been calculated at the B3LYP/LANL2DZ&6-31+G(d) level. ΔG_a values computed as $\Delta G_a(Z) = G(\mathbf{TS\text{-}2b(}Z\mathbf{)}) - G(\mathbf{2b}) - G(\mathbf{1})$. ΔG_R values computed as $\Delta G_R(Z) = G(\mathbf{3b}\text{-}Z) - G(\mathbf{2b}) - G(\mathbf{1})$. $\Delta\Delta G_a(Z-E)$ values computed as $\Delta\Delta G_a(Z-E) = \Delta G_a(Z) - \Delta G_a(E)$.

solvation energies for the transition structures with respect to the starting reactants.[35] Interestingly, the increase of the barrier for the pathway leading to the *E*-cycloadduct is larger than for the pathway forming the *Z*-isomer. As a consequence, our calculations predict that the regioselectivity toward the *Z*-cycloadduct can be increased with the polarity of the reaction solvent (i.e., $\Delta G_a(Z-E) = -10.6$ kcal/mol in gas phase and $\Delta G_a(Z-E) = -14.5$ kcal/mol in acetone). Moreover, the solvent has a minor effect in the computed reaction energies, increasing the endothermicity of the process by 2−3 kcal/mol.[36]

We want to point out that the so-called *strain* (i.e., the energy needed to promote the reactants from their equilibrium geometries to the geometries they adopt in the transition states) has been reported to be the major contributor in controlling the activation barriers of other metal-free pericyclic reactions like [3+2] or [4+2] cycloadditions.[37,38] A similar finding has been reported by us in different double group transfer reactions,[39] where the *strain* controls the process despite the highly aromatic character of the corresponding saddle points. Therefore, we can speculate that this factor also plays an important role in controlling the barrier energies of the [3+2] cycloaddition reactions considered in this report. A strain-analysis study of these and related metal-assisted cycloaddition reactions is currently underway.

Synchronicity and Aromaticity. As discussed above, the considered 1,3-dipolar cycloaddition reactions occur via concerted TSs independently of the nature of the dipolarophile. However, striking differences are observed in view of the geometries of these saddle points and the computed synchronicity of the transformations.

Table 4. Synchronicities (S_y) and NICS Values (in ppm) for the Reactions between Fischer Carbene Complexes 2a−d and Organic Esters 2e and 2f with 5-Methyl-3*H*-1,2-dithiole-3-thione 1 (see Scheme 2)[a]

entry	reaction	NICS(**TS-2(*Z*)**)	S_y
1	**2e** + **1** → **3e(*Z*)**	−4.8	0.74
2	**2f** + **1** → **3f(*Z*)**	−5.3	0.48
3	**2a** + **1** → **3a(*Z*)**	−5.5	0.50
4	**2c** + **1** → **3c(*Z*)**	−5.2	0.50
5	**2b** + **1** → **3b(*Z*)**	−4.8	0.51
6	**2d** + **1** → **3d(*Z*)**	−5.1	0.54

[a] Values have been computed at the B3LYP/LANL2DZ&6-31+G(d) level of theory.

Figure 2 shows that the transition state **TS-2e(*Z*)**, which is associated with the transformation of propiolate **2e** into cycloadduct **3e(*Z*)**, exhibits quite similar C−S bond lengths. This results in the high value of the synchronicity computed for this cycloaddition ($S_y = 0.74$, entry 1 in Table 4). However, this value is significantly lower than that computed for a similar cycloaddition reaction involving nitrones as dipoles ($S_y = 0.95$),[7] which may be attributed to the effect of the endocyclic sulfur atom of the tione **1**, which polarizes the reactive S_2−C carbon bond. As a result, the computed NBO-Wiberg bond orders for C_β−S_1 and C_α−S_2 are quite different (0.36 and 0.19 au, respectively) despite the quite similar bond lengths (see Figure 2). This effect is therefore translated to a lower value of the synchronicity of the process.

Interestingly, the transition states **TS-2a-d** and **TS-2f**, which involve the Fischer carbene and the Lewis acid complexes, respectively, present a quite asynchronous character in view of the quite different C_β−S_1 and C_α−S_2 bond lengths (see Figures 1,3,6). The corresponding Wiberg bond orders (ca. 0.56 au for C_β−S_1 and ca. 0.05 au for C_α−S_1) also confirm that while the C_β−S_1 bond is almost fully developed, the C_α−S_2 bond is only emerging. Therefore, it is not surprising that quite low values of the synchronicity have been computed (entries 2−6, Table 4). In fact, these low values are actually in the limit between concerted and stepwise mechanisms. For that reason, we tried to find a stepwise mechanism for these transformations, but all attempts to locate the corresponding intermediates and transition states for a stepwise process on the potential energy surface met with no success. It can be therefore concluded that, despite the quite low values computed for the synchronicity of the latter cycloadditions, the 1,3-dipolar reactions involving Fischer carbene complexes or $AlCl_3$-complexed organic esters occur via concerted TSs, which are clearly more asynchronous than their isolobal organic esters analogues.

It has been proposed that either the standard [3+2] cycloaddition between dipoles and organic propiolates or that involving alkynyl Fischer carbenes occurs via in-plane

---

(35) A similar effect has been observed experimentally in [3+2] cycloaddition between nitrones and allenes: (a) Huisgen, R.; Schug, R. *J. Am. Chem. Soc.* **1976**, *98*, 7819. (b) Huisgen, R. *Pure Appl. Chem.* **1980**, *52*, 2283. (c) Huisgen, R.; Hauck, H.; Seidl, H.; Burger, M. *Chem. Ber.* **1969**, *102*, 1117. (d) Kadaba, P. K. *Synthesis* **1973**, 71.

(36) It is probable that the Gibbs energy barriers in solution given in this table are somewhat overestimated for two reasons. First, because the entropic contributions in solution are overestimated when calculated using the ideal gas-phase expressions (see: (a) Strajbl, M.; Sham, Y. Y.; Villà, J.; Chu, Z.-T.; Warshel, A. *J. Phys. Chem. B* **2000**, *104*, 4578. (b) Hermans, J.; Wang, L. *J. Am. Chem. Soc.* **1997**, *119*, 2707. (c) Liang, Y.; Liu, S.; Xia, Y.; Li, Y.; Yu, Z.-X. *Chem.—Eur. J.* **2008**, *14*, 4361) and, second, because of the lack of dispersion effects included in the B3LYP functional that, in general, reduce the energy barriers (this may also affect the barriers in the gas phase; see: . (d) Siegbahn, P. E. M.; Blomberg, M. R. A.; Chen, S.-L. *J. Chem. Theory Comput.* **2010**, *6*, 2040. (e) Rakow, J. R.; Tüllmann, S.; Holthausen, M. C. *J. Phys. Chem. A* **2009**, *113*, 12035). It is likely that both effects have a similar influence on the energy of all computed TSs and, therefore, the methodology used remains valid for comparison purposes.

(37) Ess, D. H.; Houk, K. N. *J. Am. Chem. Soc.* **2008**, *130*, 10187.

(38) (a) Hayden, A. E.; Houk, K. N. *J. Am. Chem. Soc.* **2009**, *131*, 4084. (b) Osuna, S.; Houk, K. N. *Chem.—Eur. J.* **2009**, *15*, 13219.

(39) Fernández, I.; Bickelhaupt, F. M.; Cossio, F. P. *Chem.—Eur. J.* **2009**, *15*, 13022.

aromatic TSs.[7,40] Thus, we finally investigate the aromaticity of the cycloaddition reactions involving the thione **1**. To this end, we computed the nucleus-independent chemical shifts (NICSs) at the (3, +1) ring critical point of the electron density as defined by Bader in the respective transition states.[41] Given the strongly unsymmetrical character of our cyclic saddle points, we needed to define the inner points of these systems unambiguously. Particularly, the (3, +1) ring critical point is an unambiguous choice for the calculation of the NICSs since only at this point is the electron density a minimum with respect to motion on the ring's plane and maximum with respect to motion perpendicular to the plane defined by the ring. All transition structures exhibit low but negative NICSs values (ca. −5 ppm, see Table 4), which may be attributed to a diamagnetic shielding due to the aromatic character of these TSs. A possible explanation for the negative NICS values observed for the transition structures is that the six electrons involved in the cycloaddition lie approximately in the molecular plane and give rise to an appreciable ring current. In turn, this ring current promotes a diamagnetic shielding at the ring critical point. On the other hand, these values are clearly lower than those computed for the cycloaddition of alkynyl Fischer carbenes and nitrones (ca. −11 ppm),[7] which is very likely due to the shielding effect of the sulfur atoms. Interestingly, the effect of the metal fragment in the aromaticity of the transition states, which in some complexes can be substantial,[42] can be considered negligible in view of the computed quite similar NICS values for the considered processes (Table 4).

Conclusions

From the computational study reported in this paper, the following conclusions can be drawn: (i) the thermal cycloaddition reaction between alkynyl metal(0) Fischer carbenes and 3*H*-1,2-dithiole-3-thione takes place via concerted and slightly in-plane aromatic transition structures that are more asynchronous than their nonorganometallic isolobal analogues. (ii) In nice agreement with the experimental findings, these reactions are also found to be completely regioselective in favor of the *Z*-cycloadduct due to kinetic control. (iii) These results are consistent with the role of the Fischer carbene moiety as an electron-withdrawing group that enhances the electrophilic character of the alkyne group acting as a Michael acceptor as a dipolarophile. (iv) The regioselectivity and activation barriers of the transformations can be qualitatively predicted by a simple model that combines the computation of the NBO charges, the frontier molecular orbitals analysis, and local softness within the local HSAB principle.

Acknowledgment. This research was partly supported by the Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET), Ministerio de Ciencia y Tecnología (Provincia de Córdoba), and the Universidad Nacional de Córdoba, Argentina. D.M.A. is a grateful recipient of a fellowship from CONICET. Financial support by the Spanish MCINN (grants CTQ2007-67730-C02-01, CTQ2008-03077/BQU, and Consolider-Ingenio 2010 (CSD2007-0006)) and the CAM (P2009/PPQ1634-AVANCAT) is acknowledged. M.S. is grateful to the DIUE of the Generalitat de Catalunya for financial help through project No. 2009SGR637 and through the ICREA Academia 2009 prize for excellence in research. In addition, the authors thank Dr. Martin Zoloff Michoff for the very useful discussions. I.F. is a Ramón y Cajal fellow.

Supporting Information Available: Cartesian coordinates (in Å) and total B3LYP/LANL2DZ&6-31+G(d) energies (in au, noncorrected zero-point vibrational energies included) of all the stationary points discussed in the text are available free of charge via the Internet at http://pubs.acs.org.

---

(40) (a) Morao, I.; Lecea, B.; Cossío, F. P. *J. Org. Chem.* **1997**, *62*, 7033. (b) Cossío, F. P.; Morao, I.; Jiao, H.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1999**, *121*, 6737. For related in-plane aromatic transition states, see also: (c) Fernández, I.; Sierra, M. A.; Cossío, F. P. *J. Org. Chem.* **2007**, *72*, 1488. (d) Fernández, I.; Cossío, F. P.; de Cózar, A.; Lledós, A.; Mascareñas, J. L. *Chem.—Eur. J.* **2010**, *16*, 12147.

(41) Bader, R. F. W. *Atoms in Molecules: A Quantum Theory*; Clarendon: Oxford, 1990.

(42) (a) Feixas, F.; Jiménez-Halla, J. O. C.; Matito, E.; Poater, J.; Solà, M. *Pol. J. Chem.* **2007**, *81*, 783. (b) Feixas, F.; Matito, E.; Poater, J.; Solà, M. *J. Comput. Chem.* **2008**, *29*, 1543.