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Copper-Catalyzed Addition of Ethyl Diazoacetate to Furans: An Alternative to Dirhodium(II) Tetraacetate

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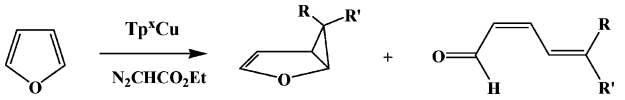
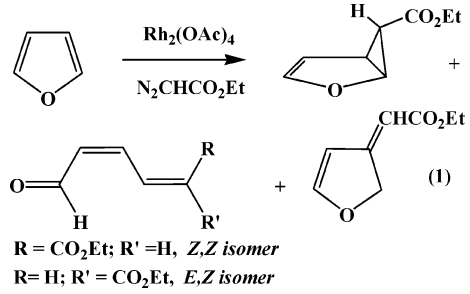


The complexes Tp^xCu (Tp^x = homoscorpionate ligand) catalyze the high yield addition of the carbene fragment :$CHCO_2Et$, from ethyl diazoacetate, to furans under mild conditions to give different cyclopropanes and dienes with ratios that depend on the Tp^x ligand employed, therefore inducing the control of the selectivity in this transformation.

The reaction of furan and diazo compounds has been known for decades since the first report of copper salts to catalyze this transformation,[1,2] in which this substrate was converted into a mixture of cyclopropanes and 1,6-dioxo-2,4-dienes, but with low yields. Although some improvements were later achieved with copper,[3] the discovery of $Rh_2(OAc)_4$ and related complexes as very good catalysts for carbene transfer processes from diazo compounds also applied to furans,[4,5] and copper was discarded. Thus, the use of rhodium acetate for the reaction of ethyl diazoacetate and furan, reported by Wenkert and co-workers, provided a 66% yield for the conversion into the mixture shown in eq 1, the cyclopropane and the *E*,*Z* diene being obtained as the major products. Since then, rhodium has been the catalyst of choice for these transformations. Only very recently, Reiser et al. have described[6] the use of bisoxazoline-copper catalysts for the asymmetric version of this reaction.



An interesting feature of this system is that, despite the different nature of the products obtained, the bulk could be converted into one final product, the *E*,*E* diene, upon treating the reaction mixture with elemental iodine.[1,4] On this characteristic resides precisely the interest of this transformation, since this type of diene finds very important applications in natural product synthesis. For example, ostopanic acid (Scheme 1) displays a certain inhibition activity toward P-368 leukemia linphocite. This natural product has been synthetically prepared[7] by Hong and co-workers following the methodology of the rhodium-catalyzed addition of ethyl 8-diazo-7-octanoate to 2-hexylfuran, in a reaction in which only the *E*,*E* isomer has been obtained.

In recent years, we have developed a copper-based system for the catalytic transfer of the :$CHCO_2Et$ from ethyl diazoacetate (EDA) to several saturated[8] and unsaturated[9] organic substrates. The catalysts consisted of a trispyrazolylborate ligand,[10] Tp^x, bound to copper, with the general formula Tp^xCu. These catalysts were very active toward the cyclopropanation of α-olefins with EDA, and a very important effect of the substituents in the pyrazolyl rings was observed in terms of the diastereoselectivity of the reaction.[9b,c] After these findings, we decided to continue our studies with other substrates that could

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(1) Doyle, M. P.; McKervey, M. A.; Ye, T. *Modern Catalytic Methods For Organic Synthesis with Diazo Compounds*; Wiley: New York, 1998.

(2) Novác, J.; Šorm, F. *Collect. Czech. Chem. Commun.* **1958**, *23*, 1126.

(3) (a) Nefedov, O. M.; Shostakovsky, V. M.; Samoilova, M. Ya.; Kravchenko, M. I. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1971**, *7*, 1590; **1972**, *10*, 2342. (b) Nwaji, M. N.; Onyiriuka, O. S. *Tetrahedron Lett.* **1974**, 2255. (c) Nefedov, O. M.; Shostakovsky, V. M.; Vasilvizky, E. *Angew. Chem., Int. Ed. Engl.* **1977**, *16*, 646. (d) Nefedov, O. M.; Shostakovsky, V. M.; Vasil'vitskii, A. E. *Izv. Akad. Nauk SSSR, Ser. Khim*. **1980**, *3*, 607. (e) Wenkert, E.; Bazukis, M. L. F.; Buckwalter, B. L.; Woodgate, P. D. *Synth. Commun*. **1981**, *11*, 533.

(4) (a) Wenkert, E.; Guo, M.; Lavilla, R.; Porter, B.; Ramachandran, K.; Sheu, J.-H. *J. Org. Chem*. **1990**, *55*, 6203. (b) Wenkert, E.; Guo, M.; Pizzo, F.; Ramachandran, K. *Helv. Chim. Acta* **1987**, *70*, 1429. (c) Wenkert, E.; Decorzant, R.; Näft, F. *Helv. Chim. Acta* **1989**, *72*, 756. (d) Wenker, E.; Khatuya, H.; Klein, P. S. *Tetrahedron Lett.* **1999**, *40*, 5171.

(5) (a) Padwa, A.; Wisnieff, T. J.; Walsh, E. J. *J. Org. Chem.* **1986**, *51*, 5036. (b) Davies, H. M. L.; McAfee, M. J.; Oldenburg, C. E. M. *J. Org. Chem.* **1989**, *54*, 930.

(6) (a) Chhor, R. B.; Nosse, B.; Sörgel, S.; Böhm, C.; Seitz, M.; Reiser, O. *Chem.−Eur. J.* **2003**, *9*, 260. (b) Schinnerl, M.; Böhm, C.; Seitz, M.; Reiser, O. *Tetrahedron: Asymmetry* **2003**, *14*, 765. (c) Böhm, C.; Schinnerl, M.; Bubert, C.; Zabel, M.; Labahn, T.; Parisini, E.; Reiser, O. *Eur. J. Org. Chem.* **2000**, 2955.

(7) Sheu, J. H.; Yen, C. F.; Huang, H. C.; Hong, Y. L. V. *J. Org. Chem.* **1989**, *54*, 5126.

(8) (a) Caballero, A.; Díaz-Requejo, M. M.; Belderrain, T. R.; Nicasio, M. C.; Trofimenko S.; Pérez, P. J. *Organometallics* **2003**, *125*, 1446. (b) Caballero, A.; Díaz-Requejo, M. M.; Belderrain, T. R.; Nicasio, M. C.; Trofimenko, S.; Pérez, P. J. *J. Am. Chem. Soc*. **2003**, *125*, 1446−1447. (c) Díaz-Requejo, M. M.; Belderrain, T. R.; Nicasio, M. C.; Trofimenko, S.; Pérez, P. J. *J. Am. Chem. Soc.* **2002**, *124*, 896−897. (d) Morilla, M. E.; Díaz-Requejo, M. M.; Belderrain, T. R.; Nicasio, M. C.; Trofimenko, S.; Pérez, P. J. *Chem. Commun.* **2002**, 2998−2999. (e) Morilla, M. E.; Molina, M. J.; Díaz-Requejo, M. M.; Belderrain, T. R.; Nicasio, M. C.; Trofimenko, S.; Pérez, P. J. *Organometallics* **2003**, *22*, 2914−2918.

(9) (a) Morilla, M. E.; Díaz-Requejo, M. M.; Belderrain, T. R.; Nicasio, M. C.; Trofimenko, S.; Pérez, P. J. *Organometallics* **2004**, *23*, 293−295. (b) Díaz-Requejo, M. M.; Caballero, A.; Belderrain, T. R.; Nicasio, M. C.; Trofimenko, S.; Pérez, P. J. *J. Am. Chem. Soc.* **2002**, *124*, 978−983. (c) Díaz-Requejo, M. M.; Belderrain, T. R.; Trofimenko, S.; Pérez, P. J. *J. Am. Chem. Soc.* **2001**, *123*, 3167−3168. (d) Díaz-Requejo, M. M.; Mairena, M. A.; Belderrain, T. R.; Nicasio, M. C.; Trofimenko, S.; Pérez, P. J. *Chem. Commun.* **2001**, 1804−1805.

(10) Trofimenko, S. *Scorpionates: The Coordination Chemistry of Polypyrazolylborate Ligands*; Imperial College Press: London, 1999.

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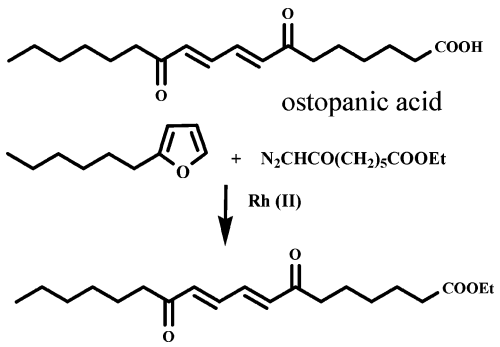
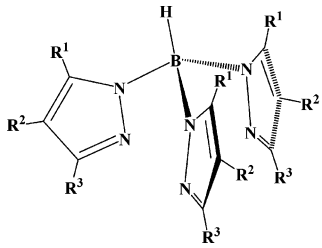
SCHEME 1. Synthesis of Ostopanic Acid by Carbene Insertion



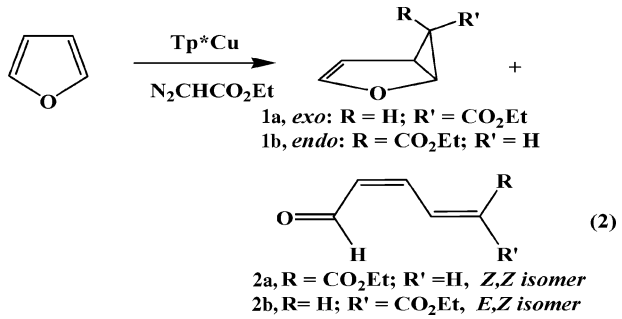
SCHEME 2. Trispyrazolylborate Ligand Employed in This Work



Tp^x	R^1	R^2	R^3
Tp^{Br3}	Br	Br	Br
Tp^{Ms}	H	H	2,4,6-$Me_3C_6H_2$
Tp^{Cy}	H	H	C_6H_{11}
Tp*	CH_3	H	CH_3

undergo a similar transformation, that is, the addition of EDA to a C−C double bond (e.g., furans), and to explore the effect that the different Tp^x ligands (Scheme 2) could exert in the selectivity of this complex transformation.

In the first test, we employed Tp*Cu as the catalyst in a reaction in which a solution of EDA was slowly added, for 3 h, into a solution of that complex and furan. Under these conditions, 52% of the initial EDA was converted into the mixture of products shown in eq 2, the remaining diazo ester yielding diethyl fumarate and maleate. Once we demonstrated the capabilities of this complex to induce the desired reaction, we carried out similar experiments with the other three complexes with different Tp^x ligands: Tp^{Cy}, Tp^{Ms}, and Tp^{Br3} (Scheme 2), with the results shown in Table 1. The overall yield from Tp* to Tp^{Br3} increased in such a way that both the Tp^{Ms}- and Tp^{Br3}-containing catalysts provided yields higher than the already reported $Rh_2(OAc)_4$. These degrees of conversion surpassed not only those of rhodium[4] but also any other reported, to date, for copper-based catalysts.[2,3,6] It is also observable from these data the existence of a certain effect of the catalyst in the selectivity of the reaction. The overall cyclopropane/diene ratio, nearly 1:1 in the rhodium case, varies with the Tp^x ligand employed.



(2)

TABLE 1. Tp^xCu-Catalyzed Reaction of EDA and Furan[a]

	Tp*Cu	$Tp^{Cy}Cu$	$Tp^{Ms}Cu$	$Tp^{Br3}Cu$	$Rh_2(OAc)_4$[b]
exo, **1a**	32	38	30	30	34
endo, **1b**	7	6	6	5	nd
Z,Z, **2a**	3	3	9	8	10
E,Z, **2b**	11	9	32	43	20
3	nd	nd	nd	nd	2
Yield	53	56	77	86	66

[a] EDA-based yields, determined by NMR using biphenyl as internal standard. Diethyl maleate and fumarate accounted for 100% of initial EDA. [b] Reference 4a.

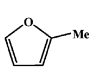
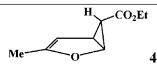
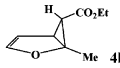
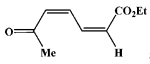
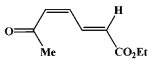
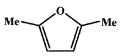
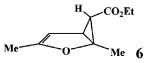
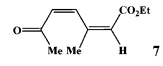
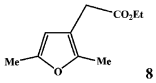
The 2.78:1 and 3.66:1 ratios observed for Tp* and Tp^{Cy} contrast with those found for Tp^{Ms}, 0.87:1, and Tp^{Br3}, 0.68:1. Since Tp* and Tp^{Br3} have been described as isosteric ligands[10] (i.e., with very similar steric hindrance), the differences in such ratios should be related to the different electronic effect that the Tp^x ligand exerts onto the copper center. The observed values of the ν(CO) absorption of the $Tp^xCu(CO)$ series are 2056 cm^{-1} for Tp* and 2105 cm^{-1} for Tp^{Br3}. Therefore, it could be proposed that the use of electron-withdrawing ligands would favor the formation of dienes, whereas more electron-donating ones would lead to cyclopropanes as the major products.

There are also two more differences with regard to the rhodium system: the endo isomer of the cyclopropane, **1b**, has now been observed in this copper system but not in the previously reported rhodium case;[4] on the other hand, the cyclic diene (see Table 1) formed in minor amounts with $Rh_2(OAc)_4$ has not been detected during our investigations. The observation of the endo isomer of the cyclopropane could be thought to be new in this transformation. Previous work by Doyle[11] and Wenkert[4,12] proposed that this isomer could be unstable and prone to undergo subsequent reactions in the reaction mixture. We have investigated the stability of this isomer in the following manner. Furan and EDA were reacted in the presence of Tp*Cu and $Tp^{Br3}Cu$ in two separate experiments. After workup, free-of-catalyst mixtures of products of the composition shown in Table 1 were obtained. These mixtures were redissolved in CH_2Cl_2, and amounts of the complexes Tp*Cu and $Tp^{Br3}Cu$ were added again: Tp*Cu was added to the mixture of products generated

(11) Doyle, M. P.; Chapman, B. J.; Hu, W.; Peterson, C. S.; McKervey, M. A.; Garcia, C. F. *Org. Lett.* **1999**, *1*, 1327−1329.

(12) Wenkert, E. Polyene Synthesis. In *New Trends in Natural Products Chemistry 1986*, Proceedings of the Second International Symposium and Pakistan-U.S. Binational Workshop on Natural Products Chemistry, Karachi, Pakistan, Jan 18−25, 1986; Atta-ur-Rahman, Le Quesne, P. W., Eds.; Studies in Organic Chemistry; Elsevier: Amsterdam, The Netherlands, 1986; Vol. 26, p 557.

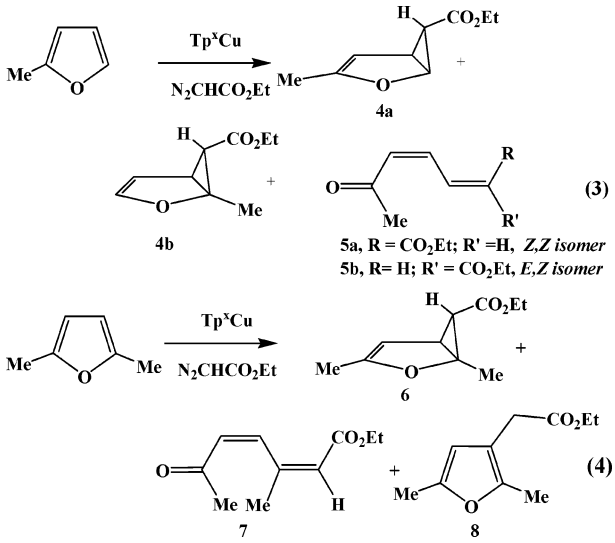
TABLE 2. Tp^{x}Cu-Catalyzed Reaction of EDA with Substituted Furan[a]

Substrates	Products	Tp*Cu	Tp^{Cy}Cu	Tp^{Ms}Cu	Tp^{Br3}Cu	Rh$_2$(OAc)$_4$[b]
	 **4a**	16	17	3	5	10
	 **4b**	4	4	2	9	2
	 **5a**, *Z,Z*	16	17	30	14	12
	 **5b**, *E,Z*	43	53	64	65	38
	Yield	79	91	99	93	62
	 **6**	26	29	30	64	30
	 **7**	6	4	37	12	44
	 **8**	5	4	9	12	2
	Yield	37	37	76	88.6[c]	76

[a] EDA-based yields, determined by NMR using biphenyl as internal standard. Diethyl maleate and fumarate accounted for 100% of initial EDA. [b] Reference 4a.

with Tp^{Br3}Cu, and Tp^{Br3}Cu was added to that generated using Tp*Cu as the catalyst. The mixtures were stirred for 24 h, with the aim of inducing any variation in the ratio of products due to the Lewis acidic nature of these copper complexes. However, after 24 h, NMR studies revealed no change in the initial ratio, therefore demonstrating that the final mixture of products is *exclusively* formed during the catalytic reaction. In contrast with these results, we use one of the above Tp*Cu-generated mixture of products to add Rh$_2$(OAc)$_4$. After being stirred for 24 h, the endo isomer disappeared, with the subsequent, proportional increase in the diene compounds. Thus, the lack of observation of the endo isomer at the end of the reaction in the rhodium-induced transformations reported to date could be related to its decomposition in the reaction mixture.

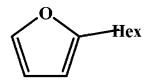
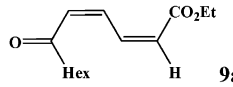
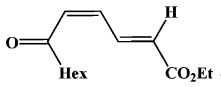
Reaction of Ethyl Diazoacetate with 2-Methylfuran and 2,5-Dimethylfuran. We have also employed these Tp^{x}Cu catalysts with other furans such as 2-methylfuran and 2,5-dimethylfuran (eqs 3 and 4). In both cases, mixtures of cyclopropanes and dienes were obtained, similar to the already reported behavior of the rhodium system.[4] Table 2 shows the results obtained with this set of substrates and the four catalysts. In the case of 2-methylfuran, the formation of the dienes is clearly favored over the cyclopropanation reaction. But on the other hand, the disubstituted dimethylfuran was preferentially converted into cyclopropanes, only in the case of the most hindered catalyst (Tp^{Ms}Cu) the dienes being the major products. The already commented electronic influence in the distribution of products in the case of furan seems to be insufficient to account for the trends now presented with these substituted furans. For the monosubstituted 2-methylfuran, the selectivity toward the mixture dienes is not greatly affected by the Tp^x ligand employed, with high conversions being observed with Tp^{Ms}Cu whereas the *Z,Z* and *E,Z* ratios clearly vary along the series of catalysts employed. In the case of the disubstituted furan, the steric pressure seems to be crucial, in contrast with the furan case. In good accord with this, the cyclopropane/dienes ratios for Tp* and Tp^{Br3} are now nearly identical (2.36:1 and 2.66:1, respectively).



At this point, some general trends can be extracted from the experiments shown in Tables 1 and 2. First, the catalytic activity of the Tp^{x}Cu complexes compares well with that of the catalyst commonly employed to date for these transformations, Rh$_2$(OAc)$_4$. The use of electron-withdrawing ligands increases the activity of the catalyst (in terms of overall yields) as well as, in the case of furan, favors the formation of the dienes. For 2-methylfuran, dienes are favored in all cases and also with high yields. Finally, the selectivity observed in the functionalization of 2,5-dimethylfuran appears to be affected by the steric pressure in a higher degree than the other substrates, although again the use of electron-withdrawing ligands allows the enhancement of the overall yields.

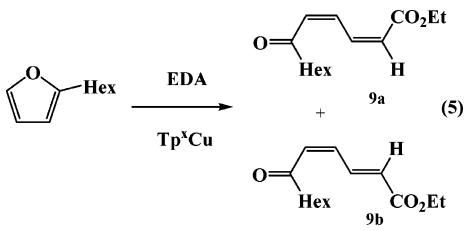
Toward a Practical Case: 2-Hexylfuran. As briefly mentioned above, one of the key steps in the synthesis of ostopanic acid consists of the reaction of 2-hexylfuran and a certain diazo compound, ethyl 8-diazo-7-octanoate, in the presence of Rh$_2$(OAc)$_4$ in a process reported by Hong and co-workers.[7] Previous work by Wenkert et al. with 2-octylfuran[4a] demonstrated that, in the reaction of EDA and 2-octylfuran, only dienes were obtained. To check the viability of our copper-based systems for this transformation, we have carried out a series of experiments with the set of four catalysts, 2-hexylfuran as the substrate and ethyl diazoacetate as the carbene source (eq 5, Table 3). We observed that, similar to those rhodium cases,[4a,7] no cyclopropanes were formed, only the dienes containing the ketone group (and not the aldehyde) being obtained. It is noteworthy that, for this substrate, little effect of the Tp^x ligand is observed, since the ratios of both dienes are quite similar. However, the degree of conversion observed with the perbromo Tp^{Br3}-Cu catalyst, nearly quantitative (using internal standard), contrasts with those reported with rhodium for the above related transformations: 58% for the reaction of ethyl 8-diazo-7-octanoate[7] with 2-hexylfuran and 60% for that of EDA with 2-octylfuran (isolated yields).[4a] The

TABLE 3. Tp^{x}Cu-Catalyzed Reaction of EDA and 2-*n*-Hexylfuran[a]

	Tp*Cu	Tp^{Cy}Cu	Tp^{Ms}Cu	Tp^{Br3}Cu
 **9a**, *Z,Z*	20	17	17	31
 **9b**, *E,Z*	55	57	57	68
Yield	75	74	74	99

[a] EDA-based yields, determined by NMR using biphenyl as internal standard. Diethyl maleate and fumarate accounted for 100% of initial EDA.

addition of elemental iodine induced the well-known transformation of the mixture of dienes in eq 5 into the *E,E* isomer, **9c** (see Experimental Section).



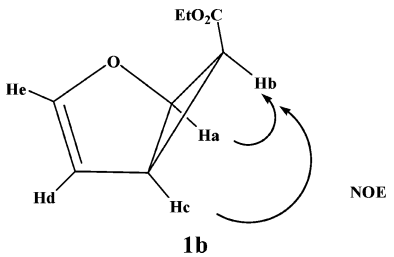
(5)

Summary Remarks. The results presented in this contribution suppose the discovery of the complexes Tp^x-Cu as an alternative to the use of $Rh_2(OAc)_4$ as the catalyst for the addition of :$CHCO_2Et$ units, from ethyl diazoacetate, to furans. The overall yields in products were comparable or higher than those reported for rhodium, with the additional advantage of the existence of a certain effect that the Tp^x ligand exerts in the selectivity of this reaction.

Experimental Section

General. ^{1}H NMR spectra were run at 400 MHz (^{13}C NMR at 100 MHz) using $CDCl_3$ as the solvent. Solvents were dried and degassed before use. Furans and ethyl diazoacetate were purchased from a commercial supplier and employed without any further purification. The copper complexes[8,9] and 2-hexylfuran[4a] were prepared following literature procedures.

General Catalytic Reaction of Furans and EDA. A solution of EDA (1 mmol) in CH_2Cl_2 (10 mL) was added with a syringe pump, over 3 h, to a solution of Tp^{x}Cu (0.05 mmol) in CH_2Cl_2 (10 mL) and the corresponding furan (5 mL). After the addition, volatiles were removed under vacuum and the reaction crude was analyzed by ^{1}H NMR spectroscopy. Most of the products have been identified by comparison with data previously reported.[4a] The addition of 30 mg of biphenyl as internal reference provided both mass balance, referred to initial EDA, and the ratio of products formed in each transformation.

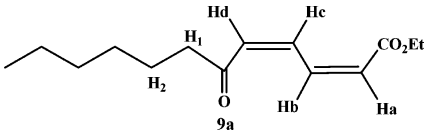


1b

NMR Data for Ethyl Endo-2-oxabiciclo[3.1.0]hex-3-ene-6-carboxylate, 1b. The reaction of furan with EDA gave small but detectable amounts of a species that has been characterized from NMR studies of the crude reaction.

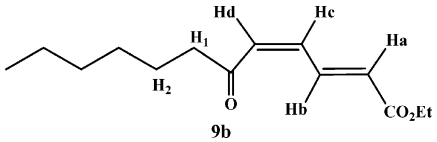
The drawing displays the NOEs observed between H_a and H_c with H_b, a feature not displayed by the *exo* isomer. ^{1}H NMR (400 MHz, $CDCl_3$), δ (ppm): 1.25 (*t*, 3H, J = 7 Hz), 1.5 (*ddd*, H_c, ^3Jac = 5.4 Hz, ^3Jbc = 9.0 Hz, ^4Jce = 0.8 Hz), 2.8 (*ddd*, H_b, ^3Jab = 5.2 Hz, ^4Jbd = 2.6 Hz, ^3Jbc = 9 Hz), 4.06 (*q*, 2H, J = 7 Hz, OCH_2), 4.75 (*t*, H_a ^3Jab = 5.2 Hz, ^3Jac = 5.2 Hz), 5.19 (*t*, H_d, ^3Jde = 2.7 Hz, ^4Jdb = 2.6 Hz), 6.42 (*d*, H_e,^3Jde = 2.7 Hz). ^{13}C NMR (100.5 MHz, $CDCl_3$): δ 14.2 (C_c), 14.4 (Me), 29.8 (C_b), 70.0 (OCH_2), 79.2 (C_a), 100.2 (C_d), 145.5 (C_e), 173.4 (C=O). GC/MS for **1b**: 154 (M^+), 126, 109, 81.

Ethyl-6-oxo-2(*Z*),4(*Z*)-dodecadienoate, 9a: ^{1}H NMR (400 MHz, $CDCl_3$), δ (ppm): 0.88 (*t*, 3H, ^3J = 7 Hz), 1.2−1.4 (*m*, 6H), 1.31 (*t*, 3H, ^3J = 7 Hz), 1.62 (*quint*, 2H, ^3J = 7 Hz, H_2), 2.50 (*t*, 2H, ^3J = 7 Hz, H_1), 4.23 (*q*, 2H, ^3J = 7 Hz), 6.30 (*m*, 2H, H_a and H_d), 7.70 (*m*, 2H, H_b and H_c). ^{13}C NMR (100.5 MHz, $CDCl_3$): δ 14.3, 14.4, 22.7, 28.2, 29.0, 31.7, 44.5, 60.4, 129.0, 130.5, 138.3, 139.0, 165.7, 201.7. GC/MS for **9a**: 238 (M − 1), 209, 165, 152, 139, 125, 97, 81, 69, 43.



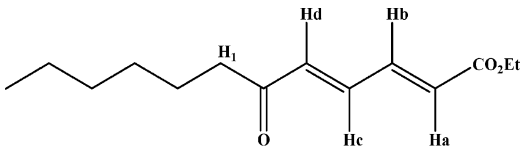
9a

Ethyl-6-oxo-2(*E*),4(*Z*)-dodecadienoate, 9b: ^{1}H NMR (400 MHz, $CDCl_3$), δ (ppm): 0.88 (*t*, 3H, ^3J = 7 Hz), 1.2−1.4 (*m*, 6H), 1.31 (*t*, 3H, ^3J = 7 Hz), 1.65 (*quint*, 2H, ^3J = 7 Hz, H_2), 2.53 (*t*, 2H, ^3J = 7 Hz, H_1), 4.23 (*q*, 2H, ^3J = 7 Hz), 6.10 (*d*, H_a, ^3Jab = 15 Hz), 6.30 (*d*, H_d, ^3Jcd = 11 Hz), 6.45 (*t*, H_c, ^3Jbc = 11 Hz and ^3Jcd = 11 Hz), 8.30 (*dd*, H_b, ^3Jab = 15 Hz and ^3Jbc = 11 Hz). ^{13}C NMR (100.5 MHz, $CDCl_3$): δ 14.1, 14.2, 22.6, 28.1, 28.9, 31.8, 44.5, 60.8, 129.8, 130.8, 138.0, 139.3, 166.2, 201.0. GC/MS for **9b**: 238 (M − 1), 209, 165, 152, 139, 125, 97, 81, 69, 43.



9b

Ethyl-6-oxo-2(*E*),4(*E*)-dodecadienoate, 9c: ^{1}H NMR (400 MHz, $CDCl_3$), δ (ppm): 0.90 (*t*, 3H, ^3J = 7 Hz), 1.2−1.6 (*m*, 8H), 1.30 (*t*, 3H, ^3J = 7 Hz), 2.55 (*t*, 2H, ^3J = 7 Hz, H_1), 4.24 (*q*, 2H, ^3J = 7 Hz), 6.22 (*d*, H_a, ^3Jab = 15 Hz), 6.45 (*d*, H_d, ^3Jcd = 15 Hz), 7.17 (*dd*, H_b, ^3Jbc = 11 Hz and ^3Jab = 15 Hz), 7.30 (*dd*, H_c, ^3Jbc = 11 Hz and ^3Jcd = 15 Hz). ^{13}C NMR (100.5 MHz, $CDCl_3$): δ 14.2, 14.5, 22.8, 28.1, 29.1, 31.9, 44.6, 60.8, 129.9, 135.4, 138.1, 140.8, 166.1, 200.7. GC/MS for **9c**: 238 (M − 1), 209, 165, 152, 139, 125, 97, 81, 69, 43.



9c

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