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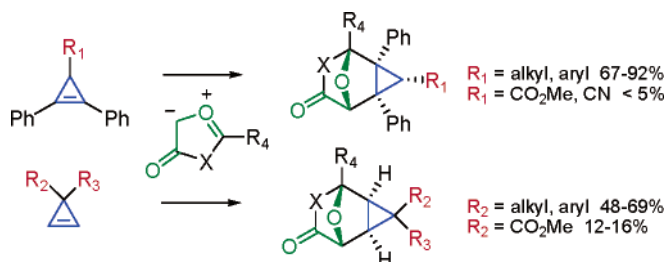
Cyclopropenes in the 1,3-Dipolar Cycloaddition with Carbonyl Ylides: Experimental and Theoretical Evidence for the Enhancement of σ -Withdrawal in 3-Substituted-Cyclopropenes

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The carbonyl ylide dipoles generated by the dirhodium tetra-acetate-catalyzed decomposition of diazocarbonyl precursors **1**, **5**, and **8** cycloadd to 3-substituted 1,2-diphenylcyclopropenes **3a–e** and 3,3-disubstituted cyclopropenes **13**, **14**, **19**, and **20** to give polycyclic compounds with 8-oxatricyclo[3.2.1.0^{2,4}]-octane and 9-oxatricyclo[3.3.1.0^{2,4}]nonane frameworks. Generally, reactions proceed stereoselectively to give adducts of exo stereochemistry with the approach of the carbonyl ylide dipoles from the less-hindered face of cyclopropenes. The electronic properties of the substituent at the C³ position of cyclopropenes play an important role in governing the reactivity of cyclopropenes: when the C³ position is substituted by electron-acceptors such as the methoxycarbonyl or cyano groups, the yields of adducts are decreased significantly or no adducts can be detected at all. Relative reactivities of cyclopropenes were quantified by competition experiments to give the best correlation with σ_F -Taft constants. Both measured photoelectron spectra and ground-state calculations of a series of 1,2-diphenylcyclopropenes indicate considerable lowering of cyclopropene π -HOMO energies by substitution with an acceptor group. Such changes in electronic structures of cyclopropenes may cause the inversion of frontier molecular orbital (FMO) interactions from HOMO_{cyclopropene}–LUMO_{ylide} to LUMO_{cyclopropene}–HOMO_{ylide} type. In terms of philicity, nucleophilic properties of acceptor-substituted cyclopropenes are diminished to such an extent that these species are no longer good nucleophiles in the reaction with carbonyl ylides, and neither are they good electrophiles, being unreactive. This was shown by the B3LYP calculations of addends.

Introduction

Tandem reactions are among the most powerful synthetic tools because they link the power of two or more transformations in one operation.¹ One of the examples of this reaction is the cyclization of the metallocarbenoid intermediate generated from the diazo precursor onto a neighboring carbonyl group to obtain

a carbonyl ylide and a subsequent 1,3-dipolar cycloaddition with the appropriate dipolarophile.² Highly substituted tetrahydrofuran structural units of such natural compounds as the ionophores, brevetoxins, and other marine products can be

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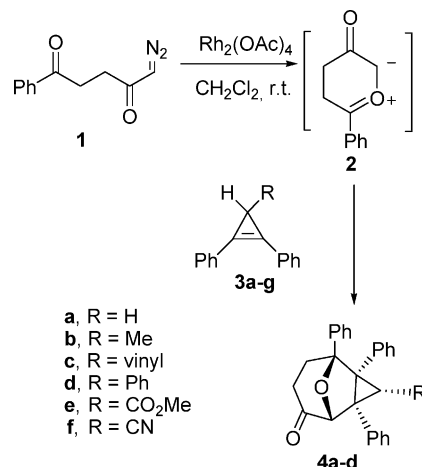
(1) (a) Tietze, L. F. *Chem. Rev.* **1996**, 96, 115. (b) Tietze, L. F.; Beifuss, U. *Angew. Chem., Int. Ed. Engl.* **1993**, 32, 131.

(2) For reviews, see: (a) Padwa, A.; Weingarten, M. D. *Chem. Rev.* **1996**, 96, 223. (b) Padwa, A. *Top. Curr. Chem.* **1997**, 189, 121. (c) Mehta, G.; Muthusamy, S. *Tetrahedron* **2002**, 58, 9477. (d) McMills, M. C.; Wright, D. In *Synthetic Application of 1,3-Dipolar Cycloaddition Chemistry Toward Heterocycles and Natural Products*; Padwa, A., Pearson, W. H., Eds.; Wiley: New York, 2002; Chapter 4. (e) Padwa, A. *J. Organomet. Chem.* **2005**, 690, 5533.

obtained by this route. Synthesis of illudins, phorbol ester derivatives, and different alkaloids have been carried out using the carbenoid cyclization–carbonyl ylide cycloaddition process.² Among recent applications of tandem carbonyl ylide formation and dipolar cycloaddition are enantioselective versions of the reaction reported by different research groups,³ as well as synthesis of natural compounds,⁴ aza- and oxapolyheterocycles.⁵ In most cases, 1,3-dipolar cycloaddition reactions of carbonyl ylides proceed with different exo/endo, regio-, and facial selectivity, depending on the properties of the substrates and the exact reaction conditions.²

Carbonyl ylides are highly reactive intermediates and known to cycloadd to a wide range of dipolarophiles, including simple alkenes, alkynes, carbonyl compounds, thioketones, and imines.^{2,6} The choice of dipolarophiles with strained C,C double bonds in a number of cycloadditions appeared especially interesting because the release of strain on the reactions with such substrates results in enhanced reactivity, and this makes these processes particularly attractive for synthetic applications.⁷ Though cyclopropenes,^{7a–f} methylenecyclopropanes,^{7a,g–i} and bicyclic propylidene^{7j} have been successfully used in [2+4] and [2+3] cycloadditions, there was until recently no published example of 1,3-dipolar cycloaddition of a carbonyl ylide to any of these alkenes. Earlier we have reported our results concerning the reactivity of carbonyl ylides generated from diazocarbonyl precursors toward methylenecyclopropane and bicyclic propylidene.⁸ The first example of carbonyl ylide cycloadditions to cyclopropenes reported in our preliminary publication clearly indicated the significance of electronic factors in determining

SCHEME 1. Cycloaddition Reactions of the Carbonyl Ylide **2** with 1,2-Diphenylcyclopropenes **3a–g**



the reactivity of cyclopropenes in the cycloaddition process.⁹ Thus, the generation of carbonyl ylide **2** by the Rh-catalyzed decomposition of diazocarbonyl precursor **1**, followed by cycloaddition to a number of 1,2-diphenylcyclopropenes **3a–d** (1.2 equiv) proceeded with the formation of the corresponding cycloadducts **4a–d** as single diastereomers in yields of up to 84%, but no reaction was observed with cyano- or methoxy-carbonyl-substituted analogues **3e,f** (see Scheme 1).

To broaden the scope of the reaction, the examination of cyclopropenes substituted at the C³ position as well as different types of carbonyl ylides have been carried out in the work reported herein. A number of 1,2-diphenylcyclopropenes mono-substituted at the C³ position and 3,3-disubstituted cyclopropenes were selected for investigation that would enable us to vary electronic properties of the substituent at the C³ position. Synthetically, cycloaddition reactions of a series of 3,3-disubstituted cyclopropenes with the retention of the cyclopropane ring are of special interest, because this way may lead to a number of compounds with the *gem*-dialkylcyclopropane moiety. This is a common molecular fragment in a variety of naturally occurring terpenoids and their analogues,¹⁰ including tumor-promoting phorbol ester derivatives,¹¹ chrysantemates, and other carane sesquiterpenoids.¹²

To gain insight into the factors influencing reactivity, we then focused on the evaluation of the electronic effects in cyclopropenes by considering the results of the theoretical calculations of their ground states and the photoelectron (PE) spectroscopic

(3) For recent examples, see: (a) Kitagaki, S.; Yasugahira, M.; Anada, M.; Nakajima, M.; Hashimoto, S. *Tetrahedron Lett.* **2000**, *41*, 5931. (b) Suga, H.; Kakehi, A.; Ito, S.; Inoue, K.; Ishida, H.; Ibata, T. *Org. Lett.* **2000**, *2*, 3145. (c) Hodgson, D. M.; Glen, R.; Redgrave, A. J. *Tetrahedron Lett.* **2002**, *43*, 3927. (d) Hodgson, D. M.; Stupp, P. A.; Pierard, F. Y. T. M.; Labande, A. H.; Johnstone, C. *Chem.–Eur. J.* **2001**, *7*, 4465. (e) Hodgson, D. M.; Glen, R.; Grant, G. H.; Redgrave, A. J. *J. Org. Chem.* **2003**, *68*, 581. (f) Inoue, K.; Suga, H.; Inoue, S.; Sato, H.; Kakehi, A. *Synthesis* **2003**, 1413. (g) Suga, H.; Inoue, K.; Inoue, S.; Kakehi, A.; Shiro, M. *J. Org. Chem.* **2005**, *70*, 47. (h) Hodgson, D. M.; Brückl, J.; Glenn, R.; Labande, A. H.; Selden, D. A.; Dosseter, A. G.; Redgrave, A. J. *Proc. Natl. Acad. Sci. U.S.A.* **2004**, *101*, 5450.

(4) (a) Graening, T.; Bette, V.; Neudörfl, J.; Lex, J.; Schmalz, H.-G. *Org. Lett.* **2005**, *7*, 4317. (b) Hodgson, D. M.; Avery, T. D.; Donohue, A. C. *Org. Lett.* **2002**, *4*, 1809. (c) Hodgson, D. M.; Le Strat, F.; Avery, T. D.; Donohue, A. C.; Brückl, J. *J. Org. Chem.* **2004**, *69*, 8796. (d) Hodgson, D. M.; Le Strat, F. *Chem. Commun.* **2004**, 822.

(5) (a) Padwa, A.; Lynch, S. M.; Mejía-Oneto, J. M.; Zhang, H. *J. Org. Chem.* **2005**, *70*, 2206. (b) Mejía-Oneto, J. M.; Padwa, A. *Org. Lett.* **2004**, *6*, 3241. (c) Oguri, H.; Shreiber, S. L. *Org. Lett.* **2005**, *7*, 47. (d) Muthusamy, M.; Gunanathan, C.; Suresh, H. *Tetrahedron* **2004**, *60*, 7885. (e) Padwa, A.; Boonsombat, J.; Rashatasakhon, P.; Willis, J. *Org. Lett.* **2005**, *7*, 3725. (f) Muthusamy, S.; Krishnamurthi, J.; Nethajib, M. *Chem. Commun.* **2005**, 3862.

(6) For recent carbonyl ylide cycloadditions with imines, see: (a) Suga, H.; Ebiura, Y.; Fukushima, K.; Kakehi, A.; Baba, T. *J. Org. Chem.* **2005**, *70*, 10782. (b) Torrsell, S.; Kienle, M.; Somfai, P. *Angew. Chem., Int. Ed.* **2005**, *44*, 3096. (c) Padwa, A.; Precado, L.; Semones, M. A. *J. Org. Chem.* **1999**, *64*, 4079.

(7) For reviews, see: (a) *Methods of Organic Chemistry* (Houben-Weyl); de Meijere, A., Ed.; Thieme: Stuttgart, 1997; Vol. E17a–d. (b) Baird, M. S. *Chem. Rev.* **2003**, *103*, 1271. (c) Dolbier, W. R., Jr.; Battiste, M. A. *Chem. Rev.* **2003**, *103*, 1071. (d) Binger, P.; Büch, H. M. *Top. Curr. Chem.* **1987**, *135*, 77. (e) Deem, M. L. *Synthesis* **1972**, 675. (f) Deem, M. L. *Synthesis* **1982**, 701. (g) Goti, A.; Cordero, F. M.; Brandi, A. *Top. Curr. Chem.* **1996**, *178*, 1. (h) Brandi, A.; Goti, A. *Chem. Rev.* **1998**, *98*, 589. (i) Brandi, A.; Cicchi, S.; Cordero, F. M.; Goti, A. *Chem. Rev.* **2003**, *103*, 1213. (j) de Meijere, A.; Kozhushkov, S. I.; Khlebnikov, A. F. *Top. Curr. Chem.* **2000**, 207, 89.

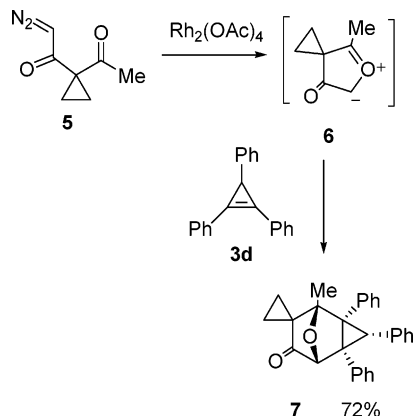
(8) Molchanov, A. P.; Diev, V. V.; Magull, J.; Vidović, D.; Kozhushkov, S. I.; de Meijere, A.; Kostikov, R. R. *Eur. J. Org. Chem.* **2005**, 593.

(9) Molchanov, A. P.; Diev, V. V.; Kopf, J.; Kostikov, R. R. *Zh. Org. Khim.* **2004**, *40*, 458; *Russ. J. Org. Chem. (Engl. Transl.)* **2004**, *40*, 431. For closely related oxidopyrylium-cyclopropenone acetal cycloaddition, see: Delgado, A.; Castedo, L.; Mascarenas, J. L. *Org. Lett.* **2002**, *4*, 3091.

(10) For recent reviews, see: (a) Wessjohann, L. A.; Brandt, W.; Thiemann, T. *Chem. Rev.* **2003**, *103*, 1625. (b) Saláün J. *Top. Curr. Chem.* **2000**, 207, 1.

(11) For reviews, see: (a) Marquez, V. E.; Blumberg, P. M. *Acc. Chem. Res.* **2003**, *36*, 434. (b) Kishi, Y.; Rando, R. R. *Acc. Chem. Res.* **1998**, *31*, 163. (c) Fraga, B. M. *Nat. Prod. Rep.* **1992**, *9*, 217. (d) *Naturally Occurring Phorbol Esters*; Evans, F. J., Ed.; CRC Press: Boca Raton, FL, 1986. For recent phorbol synthesis, see: (e) Wender, P. A.; Rice, K. D.; Schnute, M. E. *J. Am. Chem. Soc.* **1997**, *119*, 7897. (f) Lee, K.; Cha, J. K. *Org. Lett.* **1999**, *1*, 523. (g) Wender, P. A.; Jesudason, C. D.; Nakahira, H.; Tamura, N.; Tebbe, A. L.; Ueno, Y. *J. Am. Chem. Soc.* **1997**, *119*, 12976. (h) Lee, K.; Cha, J. K. *J. Am. Chem. Soc.* **2001**, *123*, 5590.

(12) (a) Henrick, C. A. In *Pyrethroids in Agrochemicals from Natural Products*; Godfrey, C. R. A., Ed.; Marcel Dekker: New York, 1995. (b) Aratani, T. *Pure Appl. Chem.* **1985**, *57*, 1839. (c) Arlt, D.; Jautelat, M.; Lantzsch, R. *Angew. Chem., Int. Ed. Engl.* **1981**, *20*, 703.

SCHEME 2. Cycloaddition Reaction of the Carbonyl Ylide 6 with 1,2,3-Triphenylcyclopropene 3d


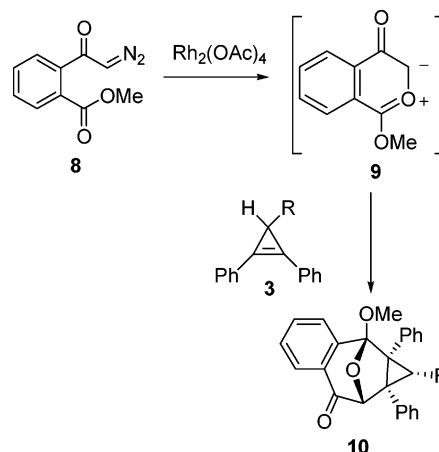
data. Finally, to determine energetics and the nature of transition states and intermediates, model quantum chemical calculations have been employed.

Results and Discussion

1,3-Dipolar Cycloaddition of Carbonyl Ylides with 1,2-Diphenylcyclopropenes. Since our initial communication of this work, we have also described the generation and cycloaddition of carbonyl ylide dipoles of other types to the double bond of various 1,2-diphenylcyclopropenes. First, we extended our investigations to the cycloaddition of the five-membered carbonyl ylide **6** generated through rhodium-catalyzed decomposition of diazocompound **5** (Scheme 2). Thus, stirring the reaction mixture containing diazocompound **5** and 1,2,3-triphenylcyclopropene **3d** (1.2 equiv) in dichloromethane at ambient temperature for 1 h in the presence of $\text{Rh}_2(\text{OAc})_4$ and subsequent chromatography afforded in 72% yield the exo cycloadduct **7** as a single isomer.

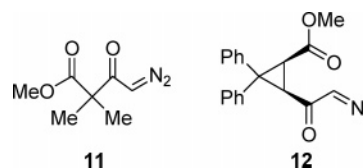
Both carbonyl ylides **2** and **6** are derived via cyclization of the metallo-carbenoid intermediate onto a ketone carbonyl group. Hence, both can be regarded as belonging to the dipole of the same type with respect to the nature of carbonyl group.² Carbonyl ylides formed via cyclization onto ester carbonyl groups are another important ylide species used in the synthesis of natural compounds.² However, we noticed that fewer examples of intramolecular cycloaddition of such carbonyl ylides with electron-rich dipolarophiles have been reported.^{2a,c,13} Stabilized ester-derived ylide **9** seems to be the only one that has been widely utilized for cycloaddition to various dipolarophiles, including electron-rich ones.^{2,13c} This carbonyl ylide **9**, generated by the decomposition of *o*-(methoxycarbonyl)- α -diazoacetophenone **8** under $\text{Rh}_2(\text{OAc})_4$ catalysis conditions in the presence of 1.2 equivalents of 1,2-diphenylcyclopropenes **3**, gave exo cycloadducts **10** in yields of up to 92% (Scheme 3, Table 1).

The studied cycloaddition reactions of 1,2-diphenylcyclopropenes proceed with complete diastereofacial selectivity with the approach of the dipolarophile from the less-hindered face, and, thus, the reaction is highly sensitive to the steric properties of the substituent at the C³ position. Like our previous results of

SCHEME 3. Cycloaddition Reaction of the Carbonyl Ylide 9 with 1,2-Diphenylcyclopropenes 3

TABLE 1. Compounds 4 and 10 Produced via Schemes 1 and 3

entry	cyclopropene	R	yield of 4 (%)	yield of 10 (%)
1	3a	H	4a (84%)	10a (92%)
2	3b	Me	4b (83%)	10b (76%)
3	3c	vinyl	4c (71%)	10c (70%)
4	3d	Ph	4d (68%)	10d (67%)
5	3e	CO ₂ Me	^a	10e (5%)
6	3f	CN	^a	^a

^a The cycloadducts were not detected, and the starting cyclopropenes were isolated quantitatively.

CHART 1. Structures of Diazocompounds 11 and 12


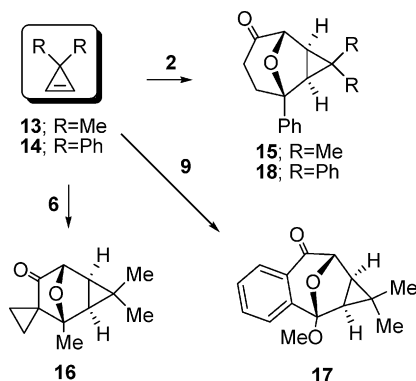
cycloadditions of carbonyl ylide **2**, the reactivity of cyclopropenes **3** is strongly affected by the electronic nature of the substituent at the cyclopropene C³ position, and cyclopropene **3e**, containing an electron-withdrawing methoxycarbonyl substituent, affords cycloadduct **10e** in only a 5% yield.¹⁴

In contrast to the cycloaddition reactions with the carbonyl ylides **2**, **6**, and **9**, no cycloadducts were isolated from the reactions between 1,2-diphenylcyclopropene **3a** and the ester-derived carbonyl ylides generated from diazoprecursors **11** and **12** (Chart 1). The fact is in accordance with the decreased reactivity of such ester-derived carbonyl ylides toward 1,3-dipolar cycloaddition with simple olefins.^{13a} This may be due to decreasing the electrophilicity of carbonyl ylides on substitution of the molecule of the dipole by a methoxy group served here as a π donor. Yet the possibility for ester-derived ylide **9** to cycloadd can be still rationalized when taking into account the stabilization effect of the condensed benzene ring within carbonyl ylide **9** offering the aromatic system of 3-oxidopyrilium.

1,3-Dipolar Cycloadditions of Carbonyl Ylides with Sterically Hindered 3,3-Disubstituted Cyclopropenes. The most

(13) (a) Padwa, A.; Chinn, R. L.; Hornbuckle, S. F.; Zhang, Z. J. *J. Org. Chem.* **1991**, 56, 3271. (b) Curtis, E. A.; Worsencroft, K. J.; Padwa, A. *Tetrahedron Lett.* **1997**, 38, 3319. (c) Ibata, T.; Motoyama, T.; Hamaguchi, M. *Bull. Chem. Soc. Jpn.* **1976**, 49, 2298.

(14) As well, no cycloadducts were isolated from the attempted reactions of carbonyl ylides employed and closely related to 1,2-diphenylcyclopropenes 2,3-diphenyl-2-cyclopropene-1-one. This is obviously due to analogous decreasing of electron density at the C=O carbon atom in the molecule of diphenylcyclopropenone.

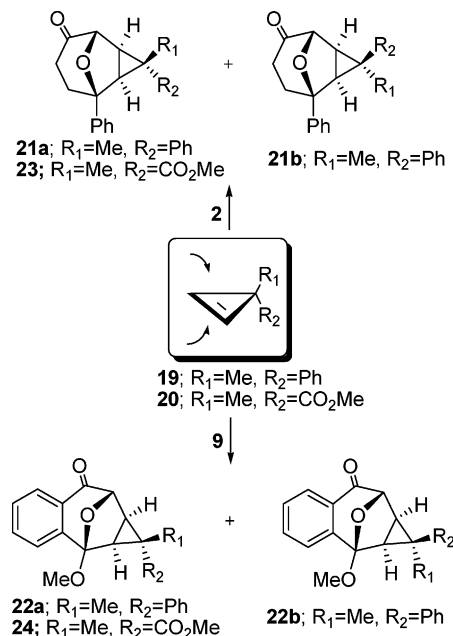
SCHEME 4. Cycloaddition Reactions of the Carbonyl Ylides with Symmetrically 3,3-Disubstituted Cyclopropenes **13** and **14****TABLE 2.** Compounds **15–18** and **21–24** Produced via Schemes 4 and 5

entry	cyclopropene	product/yield ^a (%)
1	13	15 /68 (80) ^b
2	13	16 /50 (81) ^b
3	13	17 /69 (85) ^b
4	14	18 /58
5	19	21a /46; 21b /17
6	19	22a /44; 22b /4
7	20	23 /12 (36) ^b
8	20	24 /16

^a Yields by using 3 equiv of cyclopropene. ^b Yields by using 5 equiv of cyclopropene.

attractive cyclopropenes for studies are 3,3-dialkyl substituted ones. The recent development of a convenient preparation of such cyclopropene derivatives starting from simple alkenes stimulates their further applications in organic synthesis.¹⁵ The double bond of 3,3-disubstituted cyclopropenes, however, is known to be shielded by substituents at the C³ position. As a consequence, such cyclopropenes possess diminished dienophilic reactivity in Diels–Alder reactions. For example, 3,3-dimethylcyclopropene does not cycloadd with cyclopentadiene on heating at 100 °C, whereas the parent unsubstituted cyclopropene forms the cycloadduct quantitatively in this Diels–Alder reaction even at room temperature.^{2e,16} 1,3-Dipolar cycloaddition reactions of sterically hindered cyclopropenes with different dipoles were shown to afford often the products of the rearrangements of initially formed adducts.^{7a,f} Starting with symmetrically substituted cyclopropenes **13** and **14**, any problems with diastereofacial selectivity can be excluded. Despite the above-mentioned limitation, the cycloaddition reactions of carbonyl ylides **2**, **6**, and **9** with 3–5 equivalents of 3,3-dimethylcyclopropene **13** resulted in the formation of the corresponding exo-adducts **15–17** as single isomers in good yields (50–85%; see Scheme 4 and Table 2). The analogous reaction of the ylide **2** with 3,3-diphenylcyclopropene **14** is slightly less effective, giving exo-cycloadduct **18** in 58% yield.¹⁷

In the reactions of the carbonyl ylides **2** and **9** with unsymmetrically substituted 3-methyl-3-phenylcyclopropene **19**,

SCHEME 5. Cycloaddition Reactions of the Carbonyl Ylides **2** and **9** with Unsymmetrically 3,3-Disubstituted Cyclopropenes **19** and **20**

the two isomeric cycloadducts **21a** and **21b** are formed in the ratio of 2.8:1 (total yield 63%) and **22a** and **22b** in the ratio of 12.6:1 (total yield 48%; see Scheme 5). Observed π -diastereofacial selectivity corresponds to the preferential approach of the molecule of carbonyl ylide from the less-hindered face of cyclopropene **19** (from the side containing the methyl group).¹⁸ Finally, the cycloaddition reaction between carbonyl ylides **2** and **9** and cyclopropene **20**, containing the electron-withdrawing methoxycarbonyl group, leads to the diastereoselective formation of the corresponding exo-adducts **23** and **24** as single isomers but in low yields of 12–36%.¹⁷ Again, this result demonstrates that electronic factors play a key role in determining the reactivity of cyclopropenes in the reactions with carbonyl ylides. The yields of the carbonyl ylide adducts with cyclopropene **20** are not so low compared to that of adducts with 1,2-diphenylcyclopropenes **3e,f**, probably because of partial compensation of the electron deficiency at the C³ position in cyclopropene **20** by the donor properties of the methyl group.

All cycloaddition reactions studied in this work proceed with complete exo/endo selectivity. When utilizing this cycloaddition reaction in the synthesis of various terpenoids, it is essential to note that the cycloadduct between the carbonyl ylide and 3,3-disubstituted cyclopropenes possess an exo stereochemistry. The same stereochemistry is found in most of the naturally occurring compounds with the *gem*-dialkylcyclopropyl moiety.^{10–12}

The structures of all new carbonyl ylide cycloadducts with 3,3-disubstituted cyclopropenes were assigned from their ¹H and ¹³C NMR spectra. The coupling constants of close to zero between protons at the bridgehead carbon atoms of the tetrahy-

(15) (a) Rubin, M.; Gevorgyan, V. *Synthesis* **2004**, 796 and references therein. (b) Al Dulayyami, J. R.; Baird, M. S.; Bolesov, I. G.; Nizovtsev, A. V.; Tverezovskiy, V. V. *J. Chem. Soc., Perkin Trans. 2* **2000**, 1603. (c) Bovin, N. V.; Surmina, L. S.; Yakushkina, N. I.; Bolesov, I. G. *Zh. Org. Khim.* **1977**, 13, 1888; *Russ. J. Org. Chem.* **1977**, 13, 1749.

(16) (a) Closs, G. L.; Closs, L. E.; Boll, W. A. *J. Am. Chem. Soc.* **1963**, 85, 3796. (b) Zaitseva, L. G.; Avezov, I. B.; Plemenkov, V. V.; Bolesov, I. G. *Zh. Org. Khim.* **1974**, 10, 2227; *Russ. J. Org. Chem.* **1974**, 10, 2242.

(17) In some cases, also products of the cycloaddition of the second molecule of carbonyl ylides to the C=O double bond of the primary formed adducts were isolated (see Supporting Information) in low yields (2–4%). For the analogous results, see refs 2.

(18) Analogous diastereofacial selectivity was found in the 1,3-dipolar cycloaddition of nitrile oxides with cyclopropene **19**: Bolesov, I. G.; Ignatchenko, A. V.; Bovin, N. V.; Prudchenko, I. A.; Surmina, L. S.; Plemenkov, V. V.; Petrovskiy, P. V.; Romanov, I. V.; Melnik, I. I. *Zh. Org. Khim.* **1990**, 26, 102; *Russ. J. Org. Chem.* **1990**, 26, 102.

dofuran ring and the neighboring bridgehead protons of the cyclopropane moiety in all cycloadducts indicate an exo stereochemistry of the products. Otherwise, a coupling constant of about 8 Hz should be expected.¹⁹ The relative configurations of cycloadducts **21a**, **21b**, and **23** (Scheme 5) were established on the basis of their NOESY ¹H NMR spectra (see Supporting Information). In its NOESY spectrum, only the cycloadduct **21b** exhibits interactions between protons of the methyl group and protons of the cyclopropane ring, which is consistent with their relative cis disposition. These results were used for analogous assignments of the cycloadducts **22a**, **22b**, and **24**.

Cycloaddition Competition Experiments. By means of competition experiments with diazoprecursors **1** and **8** each with **3**,²⁰ we could determine the relative rates of the cycloaddition reaction and correlate them with standard σ values. The relative rate data $\log(k_R/k_H)$ yielded an excellent linear correlation with the Taft σ_F constants²¹ (see Figures 1a,b) with significant correlation coefficients.²² These results indicate that the field/inductive effects of the substituents characterized by σ_F constants are the major factor in determining the reactivity pattern of cyclopropenes.²¹ The resulting Hammett ρ values equal to -3.72 in the plot of the reaction of the carbonyl ylide **2** and to -5.09 of the carbonyl ylide **9**. This suggests a substantial charge separation in the transition states for the reactions caused by electron withdrawal relative to simple alkenes. The observation that the cycloaddition process with the carbonyl ylide **9** is more sensitive to the nature of cyclopropenes, we ascribe to a more polar transition state.²³

The obtained data on the reactivity of both 1,2-diphenylcyclopropenes and 3,3-disubstituted cyclopropenes indicate that the electronic changes in the molecule of cyclopropene caused by the substitution of the C³ position with an electron-acceptor group govern the abilities of cyclopropenes to cycloadd with carbonyl ylide dipoles. Further theoretical investigations were performed for a detailed study of such σ withdrawal of electron density from cyclopropenes and for theoretical clarification of experimental observations. First of all, electronic structures of cyclopropenes were studied employing PE spectroscopy measurements and ground-state quantum chemical calculations of cyclopropenes.

Photoelectron Spectra and Electronic Structure of 1,2-Diphenylcyclopropenes. Molecular PE spectroscopy in combination with MO theory is known to be a useful method for the study of the electronic structure of molecules.^{24a} The PE spectra of a wide variety of π systems and formally saturated strained hydrocarbons have been investigated in several research groups.²⁴ For the interpretation of the PE spectra of the cyclopropane ring and its derivatives, the Walsh model and the related canonical SCF molecular orbitals, the two degenerate

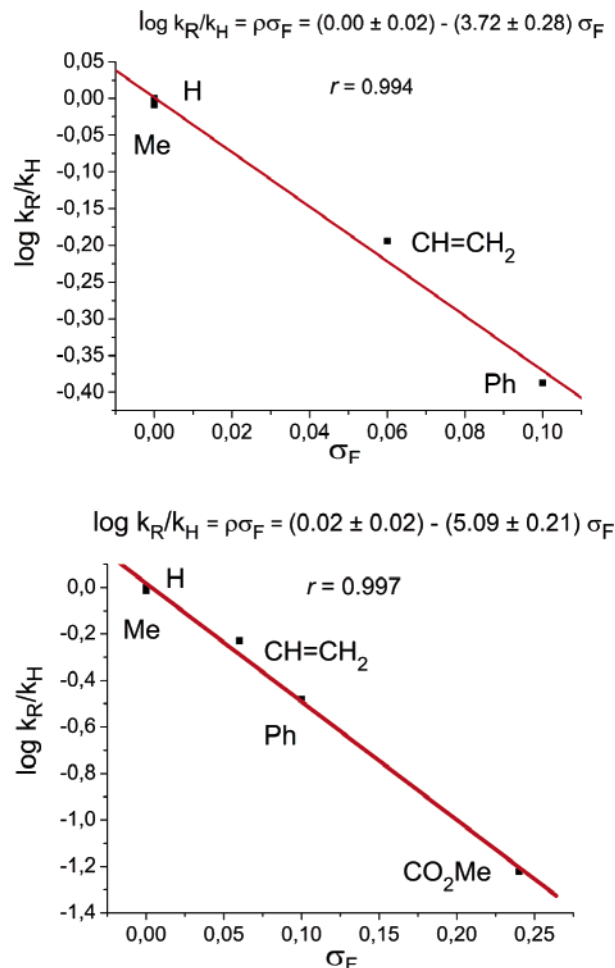


FIGURE 1. (a) Hammett plot for the 1,3-dipolar cycloaddition of carbonyl ylide **2** with 1,2-diphenylcyclopropenes **3a-d**. (b) Hammett plot for the 1,3-dipolar cycloaddition of carbonyl ylide **9** with 1,2-diphenylcyclopropenes **3a-e**.

σ_{C-C} orbitals ($2e'$) distinguished as ω_A and ω_S , are generally used.^{24a} In cyclopropene, these orbitals are no longer degenerate by symmetry, and in addition, there is a high-lying $\pi_{C=C}$ orbital of the C,C double bond.²⁴ The three transitions in the low-energy region in the PE spectrum of cyclopropene are assigned to the ejection of electrons from the $\pi_{C=C}$ (9.86 eV), ω_A (10.89 eV) and ω_S (12.7 eV) orbitals, the latter being stabilized by almost 2 eV relative to those in cyclopropane. Though the database of the PE spectra for cyclopropane derivatives is large enough to account for unusual structural as well as chemical properties of acceptor-substituted cyclopropanes, the related data for cyclopropenes are limited to series of 3-substituted and 3-methylcyclopropenes.^{24a} As have been observed, the electron-acceptor nitrile group is the most efficient in increasing ionization energy (IE) values so that IE₁ (10.71 eV, $\pi_{C=C}$) of 3-cyano-3-methylcyclopropene is 1.29 eV larger than IE₁ (9.42 eV, $\pi_{C=C}$) of 3,3-dimethylcyclopropene.^{24a} Similarly, the calculated HOMO

(19) Padwa, A.; Fryxell, G. E.; Zhi, L. *J. Am. Chem. Soc.* **1990**, *112*, 3100.

(20) Essentially, the anti approach of carbonyl ylides from the less-hindered face of 3-monosubstituted cyclopropenes seems to be determined by electronic factors rather than by steric factors. Hence, both the reactivities of substrates and the calculated energetics can be used as a measure of the electronic effects of the substituent.

(21) (a) Hansch, C.; Leo, A.; Taft, R. W. *Chem. Rev.* **1991**, *91*, 165. (b) Taft, R. W.; Topsom, R. D. *Prog. Phys. Org. Chem.* **1987**, *16*, 1.

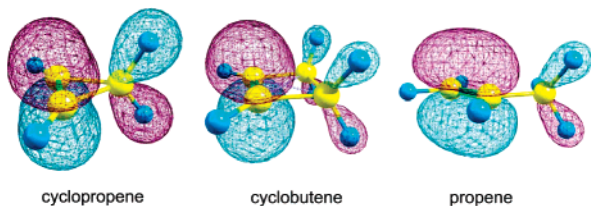
(22) Connors, K. A. *Chemical Kinetics*; VCH: New York, 1990; p 315.

(23) The analogous competition experiment was carried out with 1,2-diphenylcyclopropene, *N*-(*p*-methylphenyl)maleimide, and carbonyl ylide **2**. The found relative rate value ($k_{\text{imide}}/k_{\text{cyclopropene}} = 7.0$) indicates that 1,2-diphenylcyclopropene **3a**, shown here to be the donor-type dipolarophile, nevertheless, are significantly less reactive than an acceptor type dipolarophile like *N*-arylmaleimides.

(24) For reviews, see: (a) Rademacher, P. *Chem. Rev.* **2003**, *103*, 933 and references therein. (b) Gleiter, R.; Spanget-Larsen, J. *Adv. Strain Org. Chem.* **1992**, *2*, 143. (c) Heilbronner, E. The Photoelectron Spectra of Saturated Hydrocarbons. In *The Chemistry of Alkanes and Cycloalkanes*; Patai, S., Rappaport, Z., Eds.; Wiley: Chichester, 1992; p 455. (d) Balard, R. E. Photoelectron Spectroscopy. In *The Chemistry of the Cyclopropyl Group*; Rappaport, Z., Ed.; Wiley: Chichester, 1987; Vol. 1, Chapter 5, p 213. (e) Gleiter, R. *Top. Curr. Chem.* **1979**, *86*, 197.

TABLE 3. Calculated Energies of π HOMOs for Cyclopropene, Cyclobutene, Propene, ϵ_H , Energies of π HOMOs for Their Cyano-Substituted at α -Position Analogues, ϵ_{CN} , and Corresponding $\Delta\epsilon_{H-CN}$ Values (HF/6-31G*)^a

alkene	ϵ_H (eV)	ϵ_{CN} (eV)	$\Delta\epsilon_{H-CN}$ (eV)
cyclopropene	-9.68	-11.17	1.49
cyclobutene	-9.49	-10.45	0.96
propene	-9.72	-10.66	0.94

^a Calculations performed for the molecules of the same conformation.**FIGURE 2.** Graphic representation of the HOMOs of cyclopropene, cyclobutene, and propene, as calculated by HF/6-31G*.

energies for a number of 3-monosubstituted cyclopropenes (HF/6-311++G**) are well correlated with the electronegativities of the substituents. In this case, the effect of increasing the HOMO energy is the most pronounced for fluoro-substituted cyclopropene.²⁵ An evaluation of this effect in other alkenes has been carried out here. Thus, π -HOMO energies ϵ_H of the corresponding parent alkenes and π -HOMO energies of their cyano-substituted at the α -position to the double bond analogues ϵ_{CN} have been calculated at HF/6-31G* level within the series of cyclopropene, cyclobutene, and propene. Obtained energy differences between π HOMOs of the corresponding alkene and its cyano-monosubstituted derivative $\Delta\epsilon_{H-CN}$ can characterize electronic effects of the acceptor cyano-group. According to data obtained (Table 3), this effect is about 0.5 eV more pronounced for cyclopropene than for such simple alkenes as propene and cyclobutene.²⁶ This can be explained by the appreciable hyperconjugative interactions between $\pi_{C=C}$ and π_{CH_2} orbital fragments in the three-membered ring of cyclopropene to form two new orbitals. The HOMOs in all cases correspond to an antibonding combination of $\pi_{C=C}$ and π_{CH_2} (for propene – π_{CH_3}) with much less-important contribution of the latter orbital component to the HOMOs of cyclobutene and propene (Figure 2).

Substitution of the double bond of cyclopropene with two phenyl groups to form diphenylcyclopropene **3a** causes significant changes both in electronic structure and in PE spectra, which is due to the possibility of conjugative interaction between the double bond of cyclopropene and the π -orbital fragments of aromatic rings. In this work, the effect of substituent variation in 3-monosubstituted 1,2-diphenylcyclopropenes **3a–f** on their electronic structure has been systematically studied applying PE spectroscopy.²⁷

(25) Xidos, J. D.; Gosse, T. L.; Burke, E. D.; Poirier, R. A.; Burnell, D. *J. Am. Chem. Soc.* **2001**, 123, 5482.

(26) The possibility of σ -electron withdrawal from the cyclopropenyl ring of 3-cyanocyclopropene was proposed earlier: (a) Greenberg, A.; Liebman, J. F.; Dolbier, W. R., Jr.; Medinger, K. S.; Skancke, A. *Tetrahedron* **1983**, 39, 1533. (b) Lien, M. H.; Hopkinson, A. C. *J. Mol. Struct. (THEOCHEM)* **1987**, 149, 139. (c) Staley, S. W.; Norden, T. D.; Su, C. F.; Rall, M.; Harmony, M. D. *J. Am. Chem. Soc.* **1987**, 109, 2880. For the possibility of interactions between nonconjugated π systems, see: (d) Gleiter, R.; Schäfer, W. *Acc. Chem. Res.* **1990**, 23, 369 and references therein.

Assignments of the six lowest IEs in the low-energy region can be achieved with high confidence from the PE spectra of cyclopropenes **3a–g** (Figure 3) by means of Koopmans' theorem.²⁸ The interpretation of five transitions in the PE spectrum of the parent 1,2-diphenylcyclopropene **3a** was discussed earlier.²⁹ The sequence of the highest occupied molecular orbitals of **3a** can be derived from an interaction diagram for the two π MOs of two phenyl groups and the π HOMO of unsubstituted cyclopropene (Figure 4).³⁰ From this simple consideration, interactions of the appropriate benzene π_A or π_S molecular orbitals and the cyclopropene π HOMO give corresponding antibonding π_1 , nonbonding π_4 , and bonding π_5 linear combinations.³¹ On the other hand, π_2 and π_3 are combinations of nearly unperturbed π_A and π_S , the sixth band in the PE spectrum being the corresponding Walsh orbital ω_A of the three-membered ring. Though the sequence of π_5 and ω_A was not deduced in previous publications,²⁹ the fifth band in the PE spectrum of 1,2-diphenylcyclopropene **3a** should be assigned to transition from π_5 , which is proposed both by analyzing values of SCF-orbital energies (see Supporting Information) and by comparing IEs in PE spectra of different 1,2-diphenylcyclopropenes **3**.

A correlation of the six lowest IEs for 1,2-diphenylcyclopropenes **3a–f** (Figure 5), arranged in the sequence of the electronegativity of the substituent in going from **3b** (R = Me) to **3f** (R = CN), demonstrates that the most sensitive of the substituent variations are IE values related to the ejection of electrons from π_1 and π_5 orbitals, the magnitude of the effect being the most substantial for the acceptor-substituted cyclopropenes **3e,f**. Thus, the IE₁ value for cyano-cyclopropene **3f** (R = CN) is 0.8 eV higher than the relevant IE₁ of the parent 1,2-diphenylcyclopropene **3a**. This is close to the effect that has the substitution of both hydrogen atoms at the methylene carbon of 1,2-diphenylcyclopropene **3a** by an oxygen atom leading to 2,3-diphenylcyclopropenone (IE₁ = 8.30 eV).^{29a} Because HF/6-31G* calculations place the ω_A orbital above π_5 , the fifth band in the PE spectrum of cyclopropene **3f** with the IE₅ = 11.1 eV is assigned to the ionization from ω_A followed by the sixth band with IE₆ = 11.45 related to the π_5 orbital. These results show an even greater sensitivity of π_5 orbital energy toward substitution by an acceptor cyano group than that of π_1 orbital.

There are two additional bands in the PE spectrum of cyclopropene **3c** and one band in the spectrum of **3d** that arise from the removal of electrons from the π orbitals of substituents at the C³ position. Principally, conformational effects should be taken into account in considering PE spectra of alkenyl- and aryl-substituted cyclopropenes.^{24a} According to a previous conformational study, 1,2,3-triphenylcyclopropene **3d** (R = Ph) adopts a conformation with a bisected orientation of the 3-phenyl group in the crystalline state, that is, the phenyl group is

(27) Spectra of the following cyclopropenes were measured previously in different conditions: **3a** (R = H), ref 29a; **3e** (R = CO₂Me), Baidin, V. N.; Domnin, I. N.; Prokhorenko, O. A.; Elbel, S.; de Meijere, A. *J. Electron Spectrosc. Relat. Phenom.* **1984**, 34, 103.

(28) Koopmans, T. *Physica* **1934**, 1, 104.

(29) (a) Müller, C.; Schweig, A.; Vermeer, H. *J. Am. Chem. Soc.* **1978**, 100, 8056. (b) Hohlneicher, G.; Müller, M.; Demmer, M.; Lex, J.; Penn, J. H.; Gan, L.-X.; Loesel, P. *J. Am. Chem. Soc.* **1988**, 110, 4483. (c) Eckert-Maksic, M.; Maksimović, L.; Zrinski, I.; Kuznetsova, T. S.; Zefirov, N. S. *Croat. Chem. Acta* **1996**, 69, 1521.

(30) Calculated MO energy at HF/6-31G* level of theory and measured IP values of the lowest six transitions differs generally by less than 0.5 eV.

(31) In addition to the coefficients in the benzene rings, orbital π_4 exhibits an admixture of the unoccupied antibonding π orbital: see ref 29c.

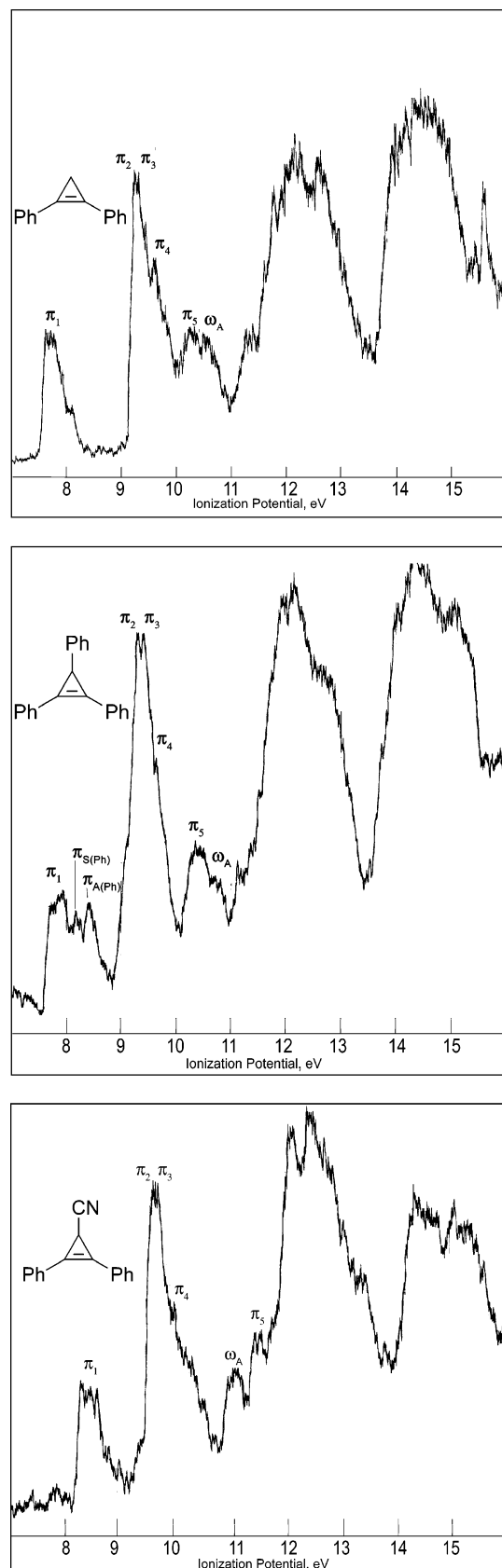


FIGURE 3. Representative PE spectra of cyclopropenes **3a** (R = H), **3d** (R = Ph), and **3f** (R = CN).

perpendicular to the plane of the three-membered ring.³² The most reasonable conformation for cyclopropene **3c** (R = vinyl)

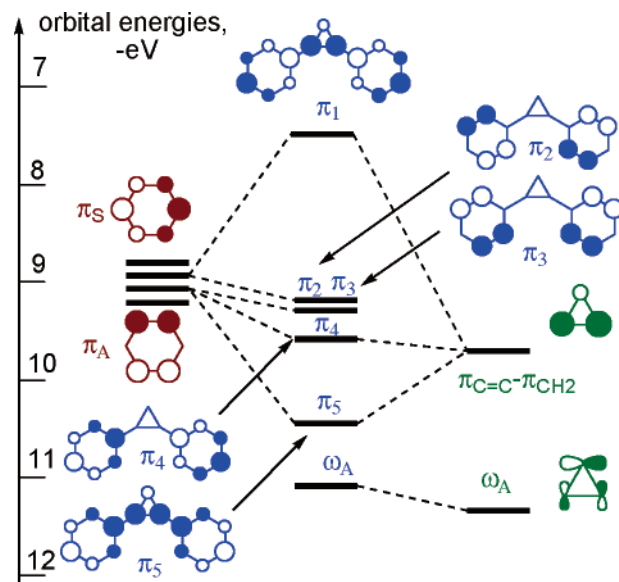


FIGURE 4. Qualitative interaction diagram between the two highest π MOs of the two phenyl groups and the π HOMO of a three-membered ring to give 1,2-diphenylcyclopropene **3a**.

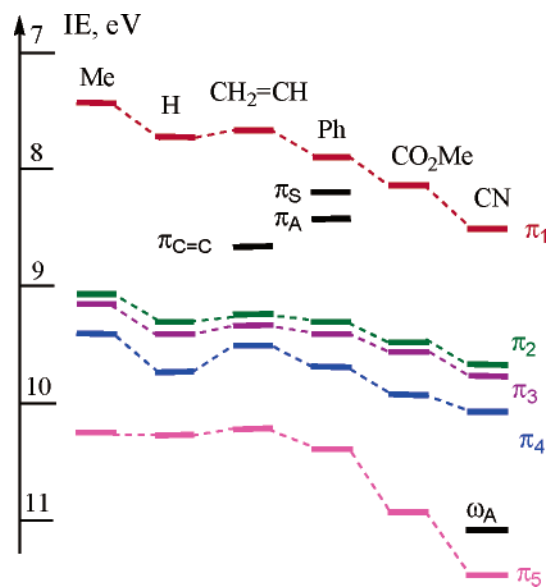


FIGURE 5. Correlation of the six lowest IEs in a series of 1,2-diphenylcyclopropenes **3a–f**.

is an antiperiplanar one, as supported by calculations at the B3LYP/6-31G* level (see Supporting Information).³³ For compound **3c**, ionization from the vinylic $\pi_{C=C}$ orbital occurred at 8.7 eV, which is significantly lower by 0.5 and 0.8 eV than IEs related to electron ejection from the $\pi_{C=C}$ of vinylcyclopropane ($IE_1 = 9.15$ eV)³⁴ and 3-methyl-1-butene ($IE_1 = 9.53$).³⁵ Similarly, two bands related to ionizations from the π_S and π_A

(32) Domnin, I. N.; Kopf, J.; Keyaniyan, S.; de Meijere, A. *Tetrahedron* **1985**, *41*, 5377.

(33) For compound **3c** there are no additional bands in the PE spectrum that are compatible with the existence of another conformer. For the previous conformational analysis of 3-isopropenyl-1,2-diphenylcyclopropene, see ref 29c.

(34) Bruckmann, P.; Klessinger, M. *Chem. Ber.* **1974**, *107*, 1108.

(35) Masclet, P.; Grosjean, D.; Mouvier, G.; Dubois, J. *J. Electron Spectrosc. Relat. Phenom.* **1973**, *2*, 225.

TABLE 4. Global Properties and Global Electrophilicities for Cyclopropenes **3a–f** and **27a–f** and Carbonyl Ylides **9**, **25**, and **26**

	HOMO	LUMO	$\Delta_{(\text{Ly}-\text{Hc})}^a$	$\Delta_{(\text{Lc}-\text{Hy})}^b$	μ (a.u.)	η (a.u.)	ω (eV)	$\Delta\omega^c$
3a	−0.1999	−0.0528	0.1235	0.1318	−0.1264	0.1471	1.48	0.00
3b	−0.1991	−0.0524	0.1227	0.1322	−0.1258	0.1467	1.47	−0.01
3c	−0.2045	−0.0555	0.1281	0.1291	−0.1300	0.1490	1.54	0.06
3d	−0.2050	−0.0555	0.1286	0.1291	−0.1303	0.1495	1.55	0.07
3e	−0.2094	−0.0577	0.1330	0.1269	−0.1336	0.1517	1.60	0.12
3f	−0.2222	−0.0691	0.1458	0.1115	−0.1457	0.1531	1.89	0.41
27a	−0.2478	0.0172	0.1714	0.2018	−0.1153	0.2650	0.68	0.00
27b	−0.2461	0.0169	0.1697	0.2015	−0.1146	0.2630	0.68	0.00
27c	−0.2568	0.0107	0.1804	0.1953	−0.1231	0.2675	0.77	0.09
27d	−0.2968	−0.0224	0.2204	0.1622	−0.1596	0.2744	1.26	0.58
27e	−0.2905	−0.0019	0.2141	0.1827	−0.1462	0.2886	1.01	0.33
27f	−0.2806	−0.0063	0.2042	0.1783	−0.1435	0.2743	1.02	0.34
9	−0.1789	−0.0741			−0.1265	0.1047	2.08	
25	−0.1846	−0.0764			−0.1305	0.1082	2.14	
26	−0.1679	−0.0593			−0.1136	0.1086	1.62	

$$^a \Delta_{(\text{Ly}-\text{Hc})} = E_{(\text{LUMO}_{\text{ylide}})} - E_{(\text{HOMO}_{\text{cyclopropene}})}, \quad ^b \Delta_{(\text{Lc}-\text{Hy})} = E_{(\text{LUMO}_{\text{cyclopropene}})} - E_{(\text{HOMO}_{\text{ylide}})}, \quad ^c \Delta\omega = \omega_{(3x \text{ or } 27x)} - \omega_{(3a \text{ or } 27a)}.$$

of the phenyl group at the C³ position of cyclopropene **3d** arise at 8.2 and 8.4 eV, correspondingly, and, therefore, differ from relevant orbitals of cyclopropylbenzene (IE₁ = 8.7 eV, π_A ; IE₂ = 9.3 eV, π_S)³⁴ by about 0.3 and 1.1 eV. Evidently, low-energy shifts of vinyl and phenyl π orbitals are due to the even stronger electron-donating properties of the 2-cyclopropenyl group than that of the cyclopropyl group.³⁶ In general, investigations of the ground-state electronic structure of 1,2-diphenylcyclopropenes **3** by PE spectroscopy and ab initio MO calculations further support the importance of through-bond interactions between the π fragments of the 3-substituted cyclopropenes via a π -type orbital of the H–C³–R unit. This leads to the increased sensitivity of the cyclopropene $\pi_{\text{C}=\text{C}}$ orbital energy toward variation of substituents as compared to that in simple alkenes. An electron-acceptor substituent causes the most striking changes in electronic structure of cyclopropenes by withdrawing electrons from the electron-rich C=C double bond of cyclopropenes.

Theoretical Calculations. Frontier molecular orbital (FMO) analysis of addends based on perturbation theory has been widely used to explain and predict regiochemical outcomes and relative reactivity patterns in different cycloaddition reactions.³⁷ Most 1,3-dipolar cycloaddition reactions can be classified into three types of cycloadditions on the basis of the relative energies of the FMOs of the dipole and dipolarophile.³⁸ Carbonyl ylides are known to be dipoles of type II because they possess one of the smallest HOMO–LUMO gaps of the common 1,3-dipoles.^{2a} This means that carbonyl ylides can be regarded as both donors and acceptors of electrons depending on the nature of the dipolarophile. From this point of view, the cycloaddition reactions of carbonyl ylides with the cyclopropenes studied in this work should be controlled by the interactions of high-energy HOMOs of cyclopropenes and low-energy LUMOs of carbonyl

ylides,³⁹ as was shown above by kinetic data. Furthermore, an analysis of the FMO energies of cyclopropenes **3a–f**, **27a–f**, and model carbonyl ylide **25** also predicts inverse-electron-demand HOMO_{cyclopropene}–LUMO_{ylide} interactions for 1,3-dipolar cycloaddition processes. Thus, for common cyclopropenes **3a–d** and **27a–c**, energy differences $\Delta_{(\text{Ly}-\text{Hc})}$ between the energy of the LUMO_{ylide} and the energy of the HOMO_{cyclopropene} are less than the difference $\Delta_{(\text{Lc}-\text{Hy})}$ between the energy of the LUMO_{cyclopropene} and the energy of the HOMO_{ylide}, as calculated at the B3LYP/631G* level (Table 4). Interestingly, substitution of the cyclopropene molecule with an electron-withdrawing group causes an inversion of the FMO interactions for cyclopropenes **3e,f** and **27d–f** to the normal electron demand type. However, this simple qualitative consideration fails to predict the order of reactivity of cyclopropenes **3a–e**, which might be taken as the difference between the corresponding dominant $\Delta_{(\text{L}-\text{H})}$ values for different cyclopropenes.

Recent studies of different cycloaddition reactions based on conceptual density functional theory⁴⁰ proved to be another powerful tool in explaining the substituent effects within addends.⁴¹ Especially attractive is the use of the global electrophilicity index ω proposed by Parr.⁴² Thus, a simple systematization of the 1,3-dipolar cycloaddition reactions based on the electrophilicity index ω have been proposed recently.^{41f} The obtained absolute scale of electrophilicity was used to rationalize the chemical reactivity, and the effect of chemical substitution on the electrophilicity of the molecules have been evaluated for a series of common dipoles and dipolarophiles. In this work, the electrophilicity/nucleophilicity of carbonyl ylides **9**, **25**, **26**, 3-substituted cyclopropenes **27a–f**, and

(39) Cycloaddition of cyclopropenes with dienes are also inverse-electron-demand Diels–Alder reactions, as was shown both experimentally and predicted theoretically. See ref 25 and the following: Battiste, M. A. *Tetrahedron Lett.* **1964**, 5, 3795.

(40) (a) Parr, R. G.; Yang, W. *Density Functional Theory of Atoms and Molecules*; Oxford University Press: New York, 1989. (b) Geerlings, P.; De Proft, F.; Langenaeker, W. *Chem. Rev.* **2003**, 103, 1793.

(41) [4+2] Cycloadditions: (a) Domingo, L. R.; Aurell, M. J.; Pérez, P.; Contreras, R. *Tetrahedron* **2002**, 58, 4417. (b) Domingo, L. R.; Arno, M.; Contreras, R.; Pérez, P. *J. Phys. Chem. A* **2002**, 106, 952. (c) Domingo, L. R.; Aurell, M. J. *J. Org. Chem.* **2002**, 67, 959. (d) Domingo, L. R.; Andres, J. *J. Org. Chem.* **2003**, 68, 8662. (e) Domingo, L. R. *Eur. J. Org. Chem.* **2004**, 4788. [3+2] Cycloadditions: (f) Pérez, P.; Domingo, L. R.; Aurell, M. J.; Contreras, R. *Tetrahedron* **2003**, 59, 3117. (g) Sáez, J. A.; Arno, M.; Domingo, L. R. *Tetrahedron* **2003**, 59, 9167. (h) Domingo, L. R.; Picher, M. T. *Tetrahedron* **2004**, 60, 5053.

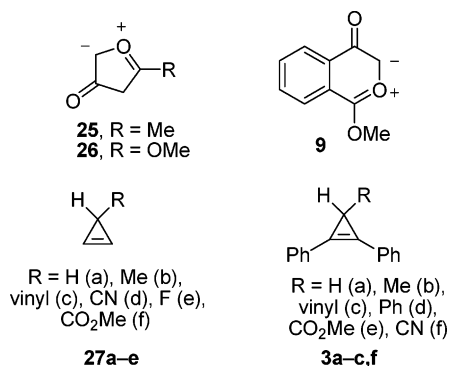
(42) Parr, R. G.; Von Szentpály, L. V.; Liu, S. *J. Am. Chem. Soc.* **1999**, 121, 1922.

(36) 2,3-Diphenyl and 2,3-dipropyl-2-cyclopropenyl groups were found to possess the strong donor properties with calculated σ_p Hammett constants of −0.52 and −0.43, respectively: (a) Komendantov, M. I.; Fomina, T. B.; Kuzina, N. A.; Domnin, I. N. *Zh. Org. Khim.* **1974**, 10, 215; *Russ. J. Org. Chem.* **1974**, 10, 219. (b) Breslow, R.; Lockhart, J.; Small, A. *J. Am. Chem. Soc.* **1962**, 84, 2793.

(37) (a) Fukui, K. *Acc. Chem. Res.* **1971**, 4, 57. (b) Houk, K. N. *Acc. Chem. Res.* **1975**, 8, 361. (c) Fleming, I. *Frontier Orbitals and Organic Chemical Reactions*; Wiley: New York, 1976.

(38) (a) Sustmann, R. *Tetrahedron Lett.* **1971**, 12, 2717. (b) Sustmann, R.; Trill, H. *Angew. Chem., Int. Ed. Engl.* **1972**, 11, 838.

CHART 2. Structure of 3-Substituted 1,2-Diphenylcyclopropenes **3a–f**, 3-Monosubstituted Cyclopropenes **27a–f**, and Carbonyl Ylides **9**, **25**, and **26** Employed for Theoretical Calculations



diphenylcyclopropenes **3a–f** (Chart 2) were analyzed using global electrophilicity index ω , defined by the expression, $\omega = \mu^2/(2\eta)$, where the electronic chemical potential $\mu \approx (\epsilon_{\text{HOMO}} + \epsilon_{\text{LUMO}})/2$ and chemical hardness $\eta \approx \epsilon_{\text{LUMO}} - \epsilon_{\text{HOMO}}$ (Table 4). According to the proposed electrophilicity scale, model carbonyl ylide **25**, having a ω value of 2.14 eV, should be classified as a strong electrophile, whereas common 3-substituted cyclopropenes **27a–f** and diphenylcyclopropenes **3a–d**, with a ω value in a range of 0.68–1.55 eV, possess lower electrophilic properties and, therefore, proposed to serve as nucleophiles along the cycloaddition process. For both series, substitution with an electron-acceptor group significantly increases the electrophilicity of cyclopropenes so that cyano-substituted cyclopropenes **3f** and **27d** are more electrophilic by $\Delta\omega = 0.41$ and 0.58 eV, correspondingly. Generally, the difference in the global electrophilicity index $\Delta\omega$ of 3-substituted (R = X) and parent unsubstituted (R = H) diphenylcyclopropenes **3a–f** are in quantitative agreement with the experimental order of reactivity of these cyclopropenes. On the other hand, the electrophilicity index ω can also account for the differing abilities for carbonyl ylides to cycloadd. Thus, model five-membered carbonyl ylide **25**, which can be regarded to result in the cyclization of the metallo-carbenoid intermediate onto an acetyl group, is a better electrophile than model ester-derived carbonyl ylide **26** and, therefore, should be more suitable for cycloaddition with nucleophilic cyclopropenes. Because carbonyl ylide **26** has a ω value close to that of common cyclopropenes, it is less preferable for the cycloaddition reaction. In contrast, another ester-derived ylide **9**, shown above in this work, which gives cycloadducts with cyclopropenes with yields of up to 92%, has an electrophilicity index ω of 2.08 eV and, hence, resembles model carbonyl ylide **25** rather than ester-derived ylide **26**.

To obtain more detailed information on the factors that govern the reactivity of cyclopropenes in the cycloaddition with carbonyl ylides, we have performed a computational investigation to model the entire reaction path with the employment of the hybrid density functional theory calculations with B3LYP functional. Initially, the interactions of model carbonyl ylide **25** with a series of 3-monosubstituted cyclopropenes **27a–e** were studied at the B3LYP/6-311++G** level of theory.⁴³ Calculations showed the preferential exo orientation of the parent cyclopropene **27a** and carbonyl ylide **25** in the transition states by about 2 kcal/mol, which is in accord with our experimental observations. The reaction course and the energy profile of the reaction of carbonyl ylide **25** with unsubstituted cyclopropene

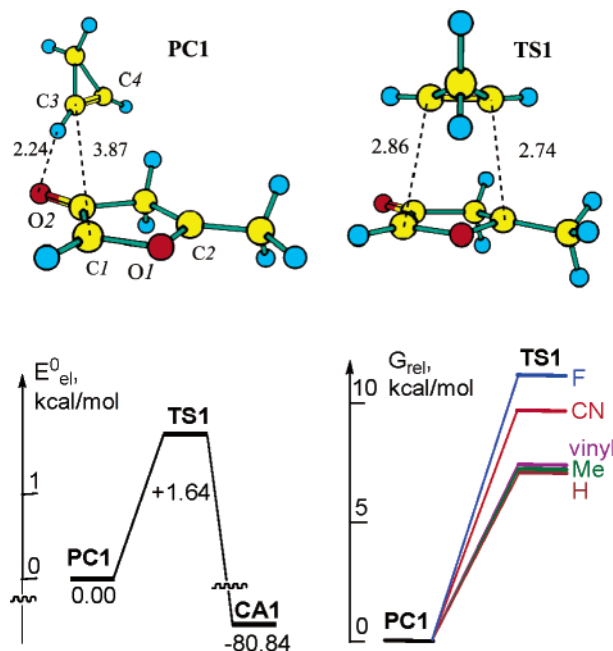


FIGURE 6. Optimized stationary points, their relative electronic energies in the reaction of cyclopropene **27a** (R = H) with carbonyl ylide **25**, and activation-free energies for reactions of cyclopropenes **27a–e** obtained from B3LYP/6-311++G** calculations.

27a (R = H) are shown in Figure 6. For the rest of cyclopropenes **27b–e** (R = Me, vinyl, CN, F), analogous points have been found (see Supporting Information).⁴⁴ In all cases, the interaction between the cyclopropene and the carbonyl ylide proceeds from nonplanar pre-coordination complex **PC1** to form the final cycloadduct **CA1** via transition states **TS1**.⁴⁵ The exocyclic oxygen atom O2 in the molecule of the initial carbonyl ylide **25** is the most negatively charged (−0.378, Lowdin), thus, the carbonyl ylide **25** possesses the partial character of the enolate anion. This can be the explanation for the relative stabilization of complex **PC1** compared to all other spatial orientations of the addends due to charge transfer from the oxygen lone pair onto the antibonding σ^* C–H orbital of cyclopropene, as shown by NBO analysis. As a result, the interatomic distance between the hydrogen atom of cyclopropene and the O2 atom of carbonyl ylide in **PC1** is shortened to 2.24 Å. Transition state **TS1** for unsubstituted cyclopropene **27a** (R = H) occurs at the distances of the new forming bonds of 2.74 and 2.86 Å and, thus, corresponds to a slightly nonsynchronous concerted mechanism of the dipolar cycloaddition. Such early transition states are not unusual for such highly reactive

(43) Mechanistic investigations were carried out on an assumption that a free carbonyl ylide was involved. Though there are a number of arguments to consider metal-stabilized carbonyl ylides (see ref 2), it is not clear whether such species are restricted to a rather limited cases or not (see refs 3d,h). Furthermore, our recent results of metal-free 1,3-dipolar cycloaddition between cyclopropenes and nitrones, dipoles, which are very similar to carbonyl ylides in their FMO characteristics, indicated just the same reactivity pattern, with 1,2-diphenylcyclopropenes that are acceptor substituted at the C³ position being inert: Diev, V. V.; Kostikov, R. R.; Molchanov, A. P. Unpublished results. For considering singlet–triplet energy differences in model carbonyl ylides, see Supporting Information.

(44) Also, a rather weak π complex has been found on the reaction course with cyclopropenes **27**. However, this complex is insignificant and its formation at 298 K was calculated to be endothermic.

(45) Similarly, dichlorocarbene–cyclopropene was recently found to follow an asymmetric, nonleast-motion approach: Merrer, D. C.; Rablen, P. R. *J. Org. Chem.* **2005**, *70*, 1630.

molecules as carbonyl ylide **25** and cyclopropenes **27**. In the case of 3-cyano or 3-fluoro-substituted cyclopropenes **27d,e**, transition states occur at closer distances, which is consistent with the decreased reactivity of these cyclopropenes **27d,e** ($R = \text{CN}, \text{F}$) compared to that of the parent cyclopropene **27a** ($R = \text{H}$).⁴⁶

Calculations of harmonic frequencies were carried out to identify minima (zero imaginary frequencies) and transition state structures (one imaginary frequency) and to obtain zero point vibrational energies and thermal contributions.⁴⁷ In general, reactions are characterized by rather low activation free energies, which are significantly increased by substitution of the C³ position of cyclopropenes with the electron-acceptor cyano- or fluoro- groups by about 2.5 and 3.8 kcal/mol.

Similar theoretical analyses of the cycloaddition of carbonyl ylide **25** with 1,2-diphenylcyclopropenes **3a–c,f** were performed to relate computational results with experimental kinetic data on the reactivity of cyclopropenes **3**. The energy profile for the reaction of the model carbonyl ylide **25** with 1,2-diphenylcyclopropene **3a** ($R = \text{H}$) is shown in Figure 7. As in the previous case, the reactions with cyclopropenes **3a–c,f** proceed from the pre-coordinational van der Waals complex **PC2** to form cycloadducts **CA2** via transition states **TS2**. As shown by NBO analysis, complex **PC2** is stabilized by a charge transfer from the lone pairs of the oxygen atom of the carbonyl ylide exocyclic C=O bond to σ^* C–H orbitals of the phenyl rings (see Supporting Information). It is characterized by the shortening of interatomic distances between the corresponding exocyclic oxygen center of the carbonyl ylide and the nearest hydrogen atoms of the two phenyl groups of 1,2-diphenylcyclopropene **3a** to 2.43 and 2.47 Å (Figure 7). An early transition state **TS2** for 1,2-diphenylcyclopropene **3a** occurs at the distances of the new forming bonds of 2.58 and 2.78 Å, as shown in Figure 7. The sequence of reactivities of cyclopropenes **3a–c,f** in the cycloaddition reaction are in quantitative agreement with the data of the above competition experiments, and the activation free energies for the cycloaddition of the carbonyl ylide **25** are increased for the cyano-substituted cyclopropene **3f** ($R = \text{CN}$) by 2.25 kcal/mol.

An orbital correlation diagram of several FMOs of the carbonyl ylide **25** and cyclopropene along the cycloaddition reactions of 1,2-diphenylcyclopropene **3a** ($R = \text{H}$) and cyano-substituted analogue **3f** ($R = \text{CN}$) is shown in Figure 8. The two highest occupied orbitals of the carbonyl ylide **25** can be described as the orbital localized mainly on the C–O–C moiety

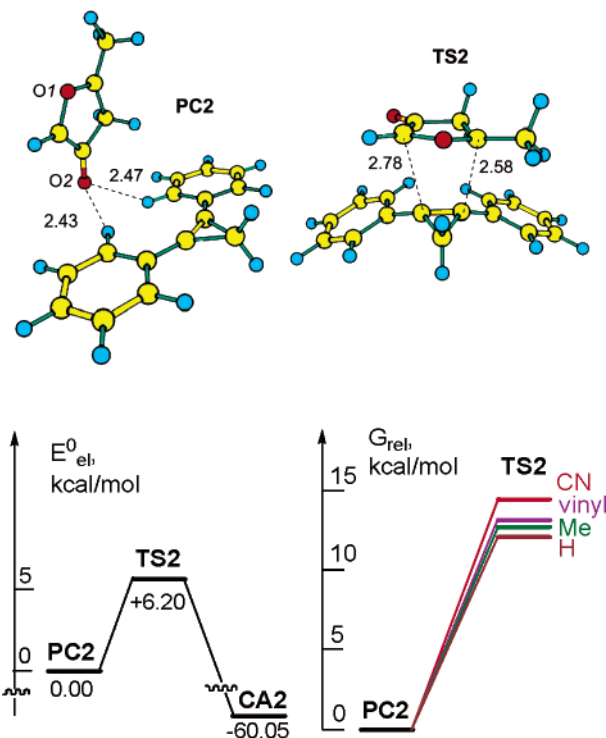


FIGURE 7. Optimized stationary points, their relative electronic energies in the reaction of 1,2-diphenylcyclopropene **3a** with carbonyl ylide **25**, and activation-free energies for reactions of cyclopropenes **3a–c,f** obtained from B3LYP/6-311++G** calculations.

(π_{COC} -orbital) and the lone pair of oxygen atom n_{O} . The highest occupied orbital of cyclopropene is its π_1 orbital described above. The lowest unoccupied orbitals are the antibonding orbital of cyclopropene π^*_1 , with contributions from p_z components of C–C double bond and aromatic rings, and the π^*_{COC} orbital of carbonyl ylide **25**. According to the diagram, the energies of the two HOMOs (π_{COC} and n_{O}) of the carbonyl ylide **25** remain almost unchanged in energy, and the energy of the cyclopropene π HOMO is lowered by 0.15 eV in the transition state **TS** for the reaction of 1,2-diphenylcyclopropene **3a** compared to that of the relevant orbital energies of separated reactants denoted as (**25** + **3a**) in Figure 8. At the same time, for the reaction of cyano-cyclopropene **3f**, both π_{COC} and n_{O} orbitals of the carbonyl ylide **25** are significantly lowered by 0.40 and 0.44 eV, correspondingly, whereas the energy of the cyclopropene π HOMO is nearly the same. This means that 1,2-diphenylcyclopropene **3a** possesses donor properties in the model reaction studied. This contrasts the reaction with 3-cyano-substituted cyclopropene **3f**, where the carbonyl ylide is obviously the donor of electrons. Furthermore, other 1,2-diphenylcyclopropenes examined **3b,c** ($R = \text{Me}, \text{vinyl}$) exhibit almost the same picture of orbital energy changes as 1,2-diphenylcyclopropene **3a** ($R = \text{H}$) does. Hence, electronic properties of the acceptor-substituted cyano-cyclopropene **3f** ($R = \text{CN}$) are unique in all series of 1,2-diphenylcyclopropenes. First, this different behavior of cyclopropenes can be explained by the significant difference in electrophilicity/nucleophilicity evaluated above with the aim of global electrophilicity index ω . We also tried to interpret these results in terms of FMO theory. Thus, a cycloaddition reaction between ylide **25** and 1,2-diphenylcyclopropene **3a** can be regarded to proceed under dominant $\text{HOMO}_{\text{cyclopropene}}-\text{LUMO}_{\text{ylide}}$ interactions. Simple inversion of FMO interactions to the $\text{HOMO}_{\text{cyclopropene}}-\text{LU}$

(46) For the interaction of 3-monosubstituted cyclopropenes **27** with butadiene analogous transition states were found at closer distances between two reacting centers at B3LYP/6-31++G**/HF6-31++G* level (for **27a**, about 2.26 Å). See ref 25.

(47) 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.; Bakken, V.; 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 B.04; Gaussian, Inc.: Pittsburgh, PA, 2003.

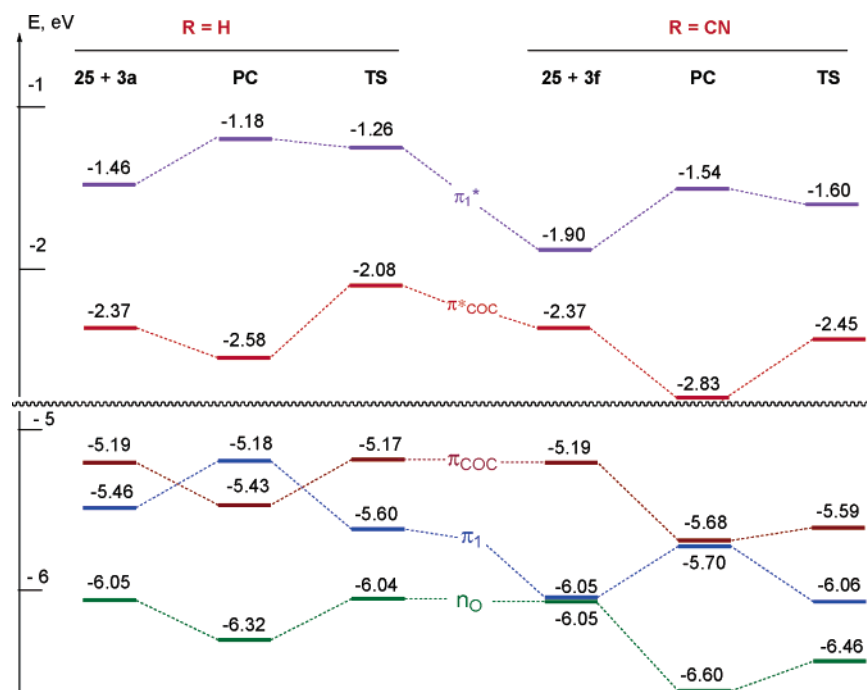


FIGURE 8. Correlation of energies of the FMOs of carbonyl ylide **25** and cyclopropenes **3a** and **3f** along cycloaddition reactions, as calculated at B3LYP/631G level.

MO_{ylide} type could be proposed along the reaction of cyclopropene **3f**. However, the picture of FMO interactions in the latter case is more complex: energies of four out of five FMOs presented are consistent with electron flow from carbonyl ylide to cyclopropene. The exception is the energy of the cyclopropene π^*_1 orbital: in both cases it becomes higher in energy, indicating that for a reasonable interpretation of the cycloaddition process from FMO theory positions, other orbitals should be also taken into account, not only the first HOMOs and LUMOs.

Similarly, the stabilization of the pre-coordination complex **PC** through charge transfer from the carbonyl ylide moiety to the molecules of cyclopropenes is the most pronounced for cyano-substituted cyclopropene **3f**. This can be illustrated by the significant lowering of energy levels of the π_{COC} and n_O orbitals by 0.49 and 0.55 eV, correspondingly, compared to that of noninteracting separated reactants (**25** + **3f**), as shown in Figure 8.

Conclusions

In summary, we have demonstrated the scope of the 1,3-dipolar cycloaddition of carbonyl ylides generated from diazo-carbonyl precursors with strained C,C double bonds of such cyclopropenes as 1,2-diphenylcyclopropenes substituted at the C³ position and sterically hindered 3,3-disubstituted cyclopropenes. The highly stereoselective formation of polycyclic frameworks containing a condensed cyclopropane fragment proceed in most cases with good to excellent yields. Cycloadducts of 3,3-disubstituted cyclopropenes containing a *gem*-alkylcyclopropyl group are believed to be valuable synthetic blocks in the synthesis of various natural sesquiterpenoids and their analogues. Among the factors that strongly effected the cycloaddition reactions is that the electronic properties of the substituent at the C³ of the three-membered ring should be mentioned first of all. Thus, in contrast to common cyclopropenes examined, the reactivity of the acceptor-substituted

cyclopropenes **3e,f** (less pronounced for **20**) diminished to such an extent that very low yields of the corresponding cycloadducts could be obtained or the cycloadducts could not be detected at all. Empirical data of competition experiments of a series of 1,2-diphenylcyclopropenes support this finding. Furthermore, both PE spectroscopy data of 1,2-diphenylcyclopropenes and PE spectroscopy data of ground state quantum chemical calculations of various 3-substituted cyclopropenes clearly indicate the significant lowering of the cyclopropene π -HOMO energy by substitution of the C³ position with an electron-acceptor group. According to simple FMO theory consideration, the effect of the suitable acceptor, for example, a cyano group, can be strong enough to cause the inversion of the FMO interactions from HOMO_{cyclopropene}–LUMO_{ylide} type for the reactions of common cyclopropenes substituted at the C³ position to LUMO_{cyclopropene}–HOMO_{ylide} controlled type for acceptor-substituted cyclopropenes. In terms of philicity, such strong electrophiles as carbonyl ylides are highly reactive with common cyclopropenes, which act as good nucleophiles. The electrophilicity of the acceptor substituted at the C³ position cyclopropenes are increased to such an extent that these cyclopropenes are no longer good nucleophiles in the reaction with carbonyl ylides, but neither are they good electrophiles. As a result, these species are unreactive.

Experimental Section

General Procedure for the Cycloaddition Reactions of Carbonyl Ylides with Cyclopropenes. To a stirred solution of the corresponding diazocompound (1 equiv) and the appropriate cyclopropene (1.2–5 equiv) in CH₂Cl₂ under an argon atmosphere was added a catalytic amount of Rh₂(OAc)₄ (0.3–0.7 mol %) in one portion. Evolution of nitrogen was observed for about 5 min. The reaction mixture was stirred at ambient temperature for an additional 1 h, the solvent was removed under reduced pressure, and the products were isolated by chromatography of the residue on silica gel, eluting with a hexane/ethyl acetate mixture, unless

otherwise stated. According to general procedure, the following cycloadducts were obtained: **7**, **10**, **15–18**, and **21–24**.

Computational Methods. All calculations were performed using the Gaussian03 program package.⁴⁷ Geometries for all the stationary structures have been optimized at the B3LYP level by using the standard 6-311++G** (reaction: **25** + **27**) and 6-31+G** (reaction: **3** + **25**) basis sets. All minima and transition states were characterized by their vibrational frequencies, and all the reported thermodynamic data are given at 298.15 K from unscaled vibrational frequencies in the harmonic approximation. Saddle points were confirmed also by the intrinsic reaction coordinate calculation.

Photoelectron Spectroscopic Investigations. The PE spectra were recorded at the following temperatures: **3a**, 70 °C; **3b**, 45 °C; **3c**, 60 °C; **3d**, 90 °C; **3e**, 80 °C; **3f**, 90 °C. The spectra were calibrated with Ar and Xe. A resolution of 20 meV was obtained for the ²P_{3/2} line of Ar. The recorded ionization energies are listed in Table S4 of the Supporting Information.

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Supporting Information Available: Details of experimental procedures, kinetic competition experiments, spectroscopic data of the reaction products **7**, **10**, **15–18**, and **21–24**, PE spectroscopy data of **3b,c,e**, computational data of carbonyl ylides, and model cycloaddition processes. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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