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Tandem Cyclization−Cycloaddition Behavior of Rhodium Carbenoids with Carbonyl Compounds: Stereoselective Studies on the Construction of Novel Epoxy-Bridged Tetrahydropyranone Frameworks

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Investigations and stereoselective studies on the tandem reactions of carbonyl ylides generated from α-diazo ketones in the presence of carbonyl compounds are presented in this paper. Intramolecular cyclization of rhodium carbenoids generated the transient five- or six-membered-ring carbonyl ylide dipoles, which efficiently underwent 1,3-dipolar cycloaddition reactions with various dipolarophiles such as aromatic aldehydes **15**, α,*β*-unsaturated aldehydes **18/24**, α,*β*-unsaturated ketones **27/28/31**, and dienone **34**. The transient carbonyl ylides underwent cycloadditions with various aromatic aldehydes to furnish diverse epoxy-bridged tetrahydropyranone ring systems in a diastereoselective manner. The cycloaddition of carbonyl ylides with α,*β*-unsaturated aldehydes **18**/**24** or dienone **34** afforded C═O addition products in a chemoselective manner despite the presence of C═C bonds in the above dipolarophiles. Alternatively, the cycloaddition of carbonyl ylides with α,*β*-unsaturated ketones **27/28** provided both the C═O and C═C cycloaddition products. The cycloaddition of carbonyl ylides with carbonyl compounds occurred in good yields and was found to be highly regio- and stereoselective. Single-crystal X-ray analyses were performed to unambiguously establish the structure and stereochemistry of the novel epoxy-bridged tetrahydropyranone ring systems **35a/38**. Compound **35a** exhibited both intermolecular C−H···O and intramolecular C−H···π interaction motifs in the solid-state architecture. The regio-, chemo-, and stereoselectivity observed in these reactions have been investigated by semiempirical AM1 MO calculations. FMO analyses and transition state calculations have been performed for the cycloaddition of carbonyl ylides with α,*β*-unsaturated carbonyl compounds such as tetracyclone (**34**) and cyclopentenone (**27a**). Both FMO and transition state calculations correctly predicted the regio- and stereochemistry of the cycloadducts. The calculations further revealed that a severe steric interaction caused by the phenyl rings present in dipolarophile **34** with dipole **14a** increases the activation barrier of the transition state during the cycloaddition process.

Introduction

Tandem-cyclization processes are superior methods for the stereocontrolled construction of numerous carbon−carbon bonds and/or ring systems in a single mode of operation.[1] Cycloaddition reactions are among the most powerful tools for the efficient assembly of complex molecular structures.[2] In particular, the 1,3-dipolar cycloaddition reactions offer a versatile route for the construction of a variety of complex molecules.[3] The tandem cyclization−1,3-dipolar cycloaddition methodologies involving carbonyl ylides have been shown[4] as an important tool to construct many bonds with a high degree of regio- and stereocontrol. As a result, this technique continues to be a subject of considerable interest and intensive investigation in synthetic organic chemistry. Padwa and co-workers have well exploited this technique to synthesize a variety of complex molecules. Natural products such as illudins,[5−7] phorbol ester de-

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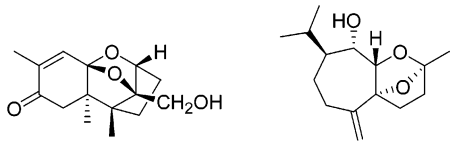
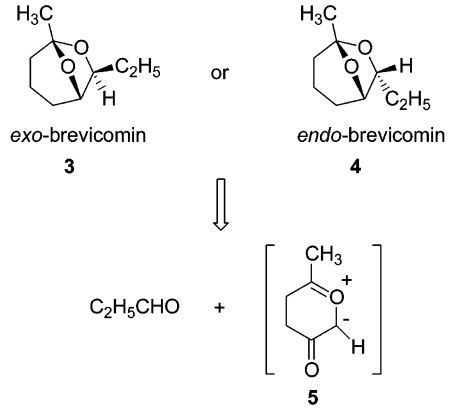
rivatives,[8,9] and various alkaloids[4a,b,10] have been synthesized using the tandem cyclization−cycloaddition method via an inter- or intramolecular manner. Intramolecular carbenoid−carbonyl group cyclizations have been represented as one of the most effective methods for generating carbonyl ylides from α-diazo ketones; their successive cycloaddition reactions with C=C bonds were well documented.[4] The stereoselective synthetic methods to oxacyclic compounds, mainly molecules comprising complex tetrahydrofuran and tetrahydropyran skeletons, have gained substantial interest.[4,11] The highly substituted epoxy-bridged polycyclic moieties are recognized as common structural units in naturally existing bioactive compounds, e.g. amberketal,[12] austalide B,[13] frontalin,[14] levoglucosenone,[15] and zaragozic acid A.[16] The epoxy-bridged tetrahydropyran skeleton is present in a wide range of natural products and exists as a part of polycyclic frameworks, e.g. loukacinols **1**,[17] xanthane epoxide **2**[18] (Scheme 1), sporol,[19] and isogosterones.[20]

SCHEME 1



Loukacinol B (1) **Xanthane epoxide (2)**

SCHEME 2



exo-brevicomin **3** *endo*-brevicomin **4**

5

The 1,3-dipolar cycloaddition chemistry involving various dipoles has been well documented[3] in the literature but not much studied in the presence of heterodipolarophiles. A survey of literature revealed that only a few reports are available on the reactions of carbonyl ylides with carbonyl groups as heterodipolarophiles. However, the chemistry and selectivity observed in these reactions have not been investigated well. It is worth mentioning that brevicomins[21] **3** and **4** (Scheme 2) and zaragozic acid A[16] have been inventively approached via the tandem cyclization−cycloaddition methodology in the presence of carbonyl compounds such as propionaldehyde and methyl glyoxalate, respectively. In the case of brevicomin, only the exo isomer is known to be a key component of the aggregation pheromone. Therefore, control of the stereoselectivity in cycloaddition of carbonyl ylides presents a challenge with the prospect of applications in the synthesis of natural products.

Reactions of carbonyl ylides derived from aliphatic α-diazo ketones with *o*-quinones,[22] benzaldehyde,[21,23] and isatins[24] in the presence of rhodium(II) carboxylates have been reported to afford the cycloaddition products with regioselectivity. Similarly, reactions of cyclic carbonyl ylides derived from alicyclic α-diazo carbonyl compounds with α,*β*-unsaturated ketones such as arylidenetetralones led to epoxy-bridged tetrahydropyranone ring systems in a regio- and chemoselective manner.[25] Reactions of five-

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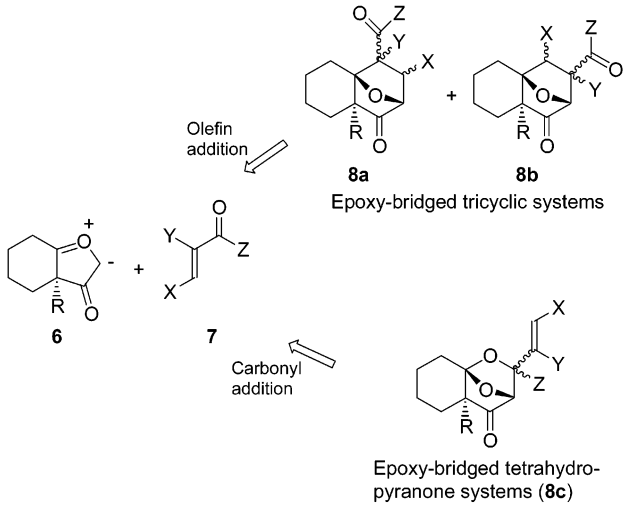
SCHEME 3



or six-membered-ring cyclic carbonyl ylides with *p*-benzoquinones[26a,27] and other carbonyl compounds[26b] have also been studied to afford 1:1 or 1:2 cycloadducts without any selectivity. In general, the reaction of carbonyl ylide **6** with an α,*β*-unsaturated ketone **7** may be represented as shown in Scheme 3 and the expected products are **8a**/**8b** and **8c** via C=C or C=O cycloadditions, respectively. The presence of two potential dipolarophilic functionalities (i.e. C=C or C=O) in **7** makes them interesting from the vantage point of 1,3-dipolar cycloadditions.

In continuation of our interest to explore the synthetic utility of α-diazo carbonyl compounds for the synthesis of highly substituted epoxy-bridged poly- or spirocyclic frameworks,[27−29] herein we report our results on the reactivity profile of carbonyl ylides with carbonyl compounds. The major objective of this work involves the stereoselective studies on the tandem cyclization−cycloaddition reactions of rhodium(II)−carbenoids with various carbonyl compounds, e.g. α,*β*-unsaturated aldehydes, aromatic/aliphatic aldehydes, and α,*β*-unsaturated ketones. The detailed results of these reactions including theoretical investigations are presented in this paper.

Results and Discussion

It was envisaged that the reaction of α-diazo ketones such as **12** with $Rh_2(OAc)_4$ could generate metallocarbenoid **13** based on our earlier work.[29a] The transient five- or six-membered-ring carbonyl ylides **14** could be formed when the lone pair of electrons on the ring carbonyl oxygen attack the highly electrophilic carbenoid center present in **13** (Scheme 4). For investigating the tandem intramolecular formation and intermolecular cycloaddition reactions of cyclic carbonyl ylides **14** with carbonyl groups as dipolarophiles, the required starting materials **12a**−**d** were prepared according to the literature work.[29a]

To explore the reaction of cyclic carbonyl ylides **14** with various carbonyl compounds, initially we planned to study the reaction of alicyclic diazo carbonyl compounds **12** with aromatic aldehydes. A catalytic amount of $Rh_2(OAc)_4$ was added to a dichloromethane solution containing diazo ketone **12a** and *p*-methyl benzaldehyde **15a** under an inert atmosphere. The reaction was monitored by TLC and concentrated under reduced pressure, and column chromatographic purification of the crude reaction mixture afforded the cycloadduct **16a** in 79% yield (Scheme 5). The cycloadduct **16a** was characterized as an epoxy-bridged tetrahydropyranone ring system based on its interrelated spectral data. The exo and endo stereochemistry of the cycloadduct **16a** can easily be distinguished by the coupling constant of H^a (H-8) and H^b (H-9) in the ^1H NMR spectrum as the dihedral angle between H^a and H^b in the exo cycloadduct **16a** is close to 90°, meaning that the coupling constant would be very small ($J \approx 0-2$ Hz). Therefore, the formation of exo cycloadduct **16a** was confirmed based on a characteristic singlet resonance signal for the bridgehead H^a proton in the ^1H NMR spectrum. This reaction revealed that the carbonyl ylide **14a** generated from diazo ketone **12a** cycloadds diastereoselectively with *p*-methyl benzaldehyde and this observation is in line with the literature.[23] Similarly, reaction of other diazo ketones **12a**−**c** with aromatic aldehydes gave the respective cycloadducts **16b**−**d** in good yield (Scheme 5, Table 2). The other expected regioisomeric products **17a**−**d** were not observed and this can be conveniently explained on the basis of the chemical shift value for the bridgehead H^c proton, which would be much more downfield than the observed value for H^a in regioisomers **16a**−**d**.

These results encouraged us for the further study of the 1,3-dipolar cycloaddition reactions of cyclic carbonyl ylides with α,*β*-unsaturated aldehydes in a tandem manner. To the best of our knowledge, there is no report[4] available on the reaction of carbonyl ylides with α,*β*-unsaturated aldehydes. Treatment of diazo ketone **12a** with *trans*-cinnamaldehyde (**18a**) in the presence of $Rh_2(OAc)_4$ provided the cycloadduct **19a** in 86% yield in a chemoselective manner. We have not observed any of the regioisomeric C=C addition products **20a**/**21a** (Scheme 6).

The FT-IR spectrum of compound **19a** exhibited a characteristic band at 1760 cm^{-1} indicating the presence of a carbonyl group. The ^1H NMR spectrum of product **19a** exhibited a characteristic singlet resonance at δ 4.46 for the bridgehead (H-8) proton, a doublet at δ 6.58 due to the presence of olefin proton H-13 with a coupling constant of $J = 15.8$ Hz, a doubled doublet at δ 6.07 with coupling constants of $J_1 = 15.8$ Hz and $J_2 = 7.1$ Hz for H-12, and a doublet at δ 4.37 for H-9 with a coupling constant of $J = 7.1$ Hz. ^{13}C NMR and dept-135 spectral analyses of product **19a** showed peaks for one CH_3 carbon, four CH_2 carbons, seven CH carbons, and four quaternary carbons, including a carbonyl group at δ

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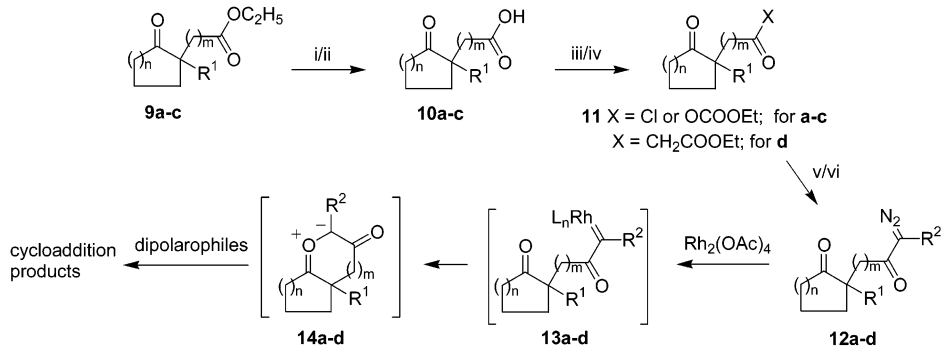
SCHEME 4[a]



[a] Reaction conditions: Reagents for substrates **a**−**c**: (i) 8% aq KOH, rt; (iii) oxalyl chloride, ether or $ClCO_2Et$, NEt_3, ether; (v) CH_2N_2, ether. Reagents for substrate **d**: (ii) 8% aq KOH, rt; (iv) (a) oxalyl chloride, ether; (b) *i*-PrMgBr, $EtO_2CCH_2CO_2H$, DCM/THF (1:5); (vi) MsN_3, NEt_3, DCM.

SCHEME 5

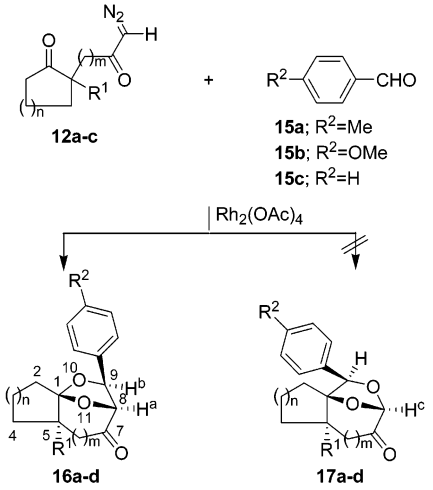


TABLE 1. Diazo Ketones 12a−d Produced via Scheme 4

substrate	*n*	*m*	R^1	R^2
a	2	0	CH_3	H
b	1	0	CH_3	H
c	2	1	H	H
d	2	0	CH_3	COOEt

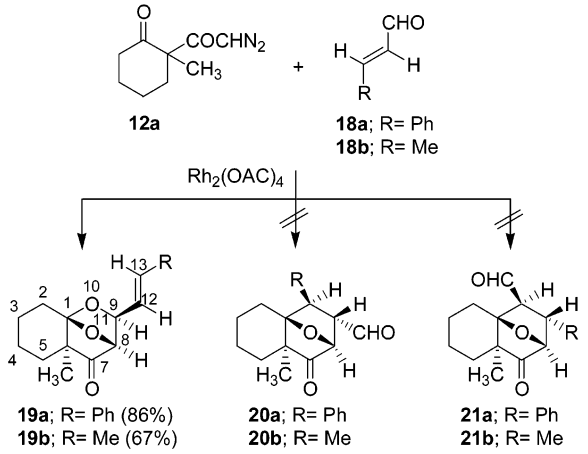
TABLE 2. Compounds 16a−d Produced via Scheme 5

product	*n*	*m*	R^1	R^2	reaction time, h	yield,[a] %
a	2	0	CH_3	Me	3.0	79
b	2	0	CH_3	OMe	3.5	73
c	1	0	CH_3	H	4.0	67
d	2	1	H	H	3.0	63[b]

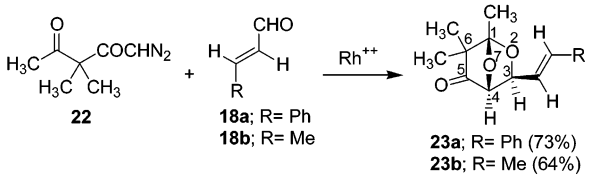
[a] Yields (unoptimized) refer to isolated and chromatographically pure compounds. [b] Isolated as a mixture of diastereomers in the ratio of 1:2.

213.3. These characteristic spectral data obviously confirmed the proposed structure of compound **19a** as the fused epoxy-bridged tetrahydropyranone ring system (Scheme 6). The stereochemical assignment of exo isomer **19a** was made based on the singlet resonance signal for H-8 proton in the ^1H NMR spectrum (as explained for the cycloadduct **16a**). Subsequently, the reaction of diazo ketone **12a** with *trans*-crotonaldehyde (**18b**) in the presence of $Rh_2(OAc)_4$ afforded the C═O cycloaddition product **19b** (Scheme 6).

SCHEME 6



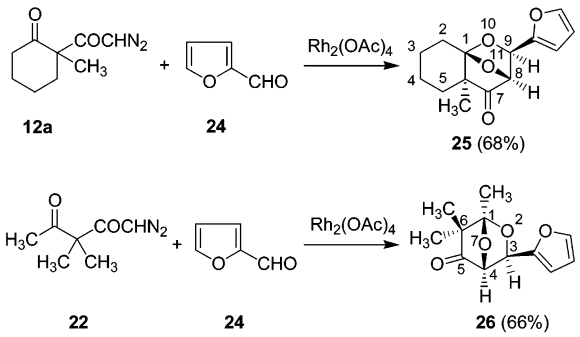
SCHEME 7



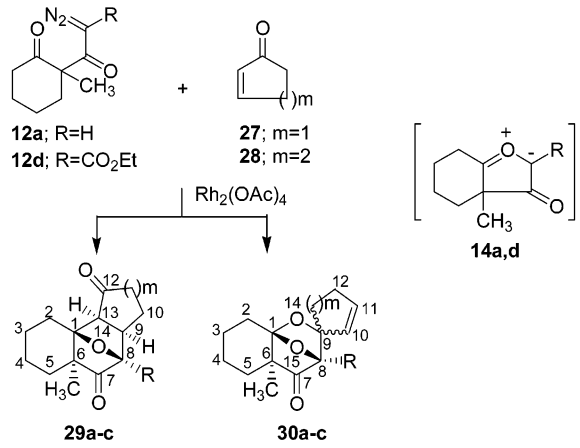
We generalized these results by further performing a similar experiment using aliphatic α-diazo ketone **22**. The reaction of diazo ketone **22** with *trans*-cinnamaldehyde (**18a**) or *trans*-crotonaldehyde (**18b**) in the presence of $Rh_2(OAc)_4$ catalyst was carried out. The column chromatographic purification of the resulting crude reaction mixtures gave the C═O cycloaddition products **23a** (73%) and **23b** (64%), respectively (Scheme 7), in a chemoselective manner.

Optimistic from the above results, we extended the carbonyl ylide reactions with heterocyclic aldehydes to obtain the highly substituted oxacyclic ring systems. For this purpose, reactions of diazo ketones **12a**/**22** with 2-furancarboxaldehyde (**24**) in the presence of $Rh_2(OAc)_4$ were carried out to obtain the respective products **25** (68%) and **26** (66%) in a chemoselective manner (Scheme 8). The structure of cycloaddition products **25**,**26** was evidently confirmed from their interrelated spectral data. We have confirmed the formation of exo-cycloadducts **25**/**26** based on the singlet resonance signal for the bridge-

SCHEME 8



SCHEME 9



head protons H-8 and H-4, respectively (as explained for the cycloadduct **16a**). It is interesting to note that in all the reactions, carbonyl ylides underwent cycloaddition only to the C=O group of α,*β*-unsaturated aldehydes to furnish various epoxy-bridged tetrahydropyranone ring systems with high regio- and stereoselectivity. Even though the furan ring is known to undergo cycloaddition with isomünchnone dipoles,[30] no other cycloadducts were observed in our experiments.

After obtaining various epoxy-bridged tetrahydropyranone ring systems using aldehydes, we were further interested to illustrate the scope and synthetic utility of the tandem cyclization−cycloaddition sequence using α,*β*-unsaturated cyclic ketones. Thus, we investigated the reaction of α-diazo carbonyl compounds with cycloalkenones **27/28**. Cycloalkenone derivatives were used as dipolarophiles in the synthesis of the pterosin family of sesquiterpenoids via the tandem cyclization−cycloaddition methodology.[5−7] α-Diazo ketone **12a** and 2-cyclohexen-1-one (**28**) were allowed to react in the presence of $Rh_2(OAc)_4$ catalyst to furnish the cycloadducts **29a** (64%) and **30a** (23%) (Scheme 9).

The FT-IR spectrum of compound **29a** exhibited strong bands at 1758 and 1700 cm^{-1}, indicating the existence of two carbonyl groups. The ^1H NMR spectrum of product **29a** exhibited a characteristic singlet resonance at *δ* 4.33 for the bridgehead (H-8) proton. ^{13}C NMR and dept-135 spectral analyses of product **29a** showed the signals for one CH_3 carbon, seven CH_2 carbons, three CH carbons,

(30) Padwa, A.; Hertzog, D. L.; Nadler, W. R. *J. Org. Chem.* **1994**, *59*, 7072−7084.

TABLE 3. Products 29a−c and 30a−c Produced via Scheme 9

				yield,[a] %	
product	*m*	R	reaction time, h	**29**	**30**[b]
a	2	H	3.5	64	23
b[c]	2	COOEt	8.0	12	67
c	1	H	2.5	44	6

[a] Yields (unoptimized) refer to isolated and chromatographically pure compounds **29** and **30**. [b] Isolated as a mixture of diastereomers in the ratio of 1:3. [c] Reaction was carried out in dry benzene at reflux.

and four quaternary carbons including two carbonyl groups at *δ* 217.2 and 212.2; these spectral data undoubtedly confirmed the proposed structure as an oxa-bridged tetracyclic system. Typically, the presence of a singlet resonance signal for the bridgehead proton (H-8) and the lack of coupling with the H-9 proton (which demands the dihedral angle near 90°) clearly indicated the exo stereochemistry for product **29a**.

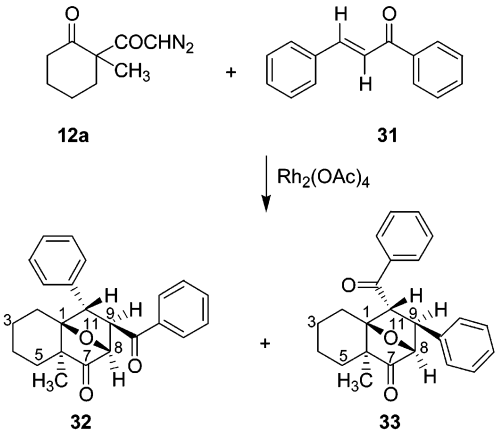
The FT-IR spectrum of compound **30a** exhibited bands at 1764 and 1650 cm^{-1}, indicating the presence of carbonyl and C=C groups, respectively. The ^1H NMR spectrum of product **30a** exhibited a characteristic singlet resonance at *δ* 4.24 for the bridgehead (H-8) proton. ^{13}C NMR and dept-135 spectral analyses of product **30a** showed peaks for one CH_3 carbon, seven CH_2 carbons, three CH carbons, and four quaternary carbons, including a carbonyl group at *δ* 214, which clearly confirmed the proposed structure as a spiro-dioxa ring system.

Further the Rh(II)-catalyzed reaction of diazo compound **12d** with cycloalkenone **28** was studied to furnish an exo isomer of an oxa-bridged tetracyclic system **29b** and a spiro epoxy-bridged tetrahydropyranone ring system **30b**. Similarly, the reaction of diazo compound **12a** with 2-cyclopenten-1-one (**27**) afforded the cycloadducts **29c** and **30c** (Scheme 9). The formation of cycloadducts **29** and **30** can be explained in that the carbonyl ylides **14** underwent C=C and C=O cycloadditions to cycloalkenones, respectively. This observation was in line with the recent reports[26,27] in which reactions of carbonyl ylides with electron-deficient *p*-quinones furnished both C=C and C=O addition products. Compounds **30a−c** were isolated as a mixture of diastereomers in the ratio of 1:3 (Table 3). It is known that the rhodium(II)-induced carbonyl ylide formation process is highly dependent on the electronic nature[31a] of the substituent attached to the diazo carbon atom. The yield of cycloaddition products **29b**/**30b** reversed when the electrophilicity of the intermediate rhodium carbenoid was increased (when R = COOEt). The methyl substituent in all diazo compounds was required because the apparently highly stabilized dipole **14** may transfer the proton at a faster rate than bimolecular 1,3-dipolar cycloaddition.[31b] Moreover, we have not isolated any competitive C−H insertion product during the course of these reactions.[32] It has been

(31) (a) Dean, D. C.; Krumpe, K. E.; Padwa, A. *J. Chem. Soc., Chem. Commun.* **1989**, 921−922. (b) Lottes, A.; Landgreb, J. A.; Larsen, K. *Tetrahedron Lett.* **1989**, *30*, 4089−4092.

(32) (a) Doyle, M. P.; Shanklin, M. S.; Oon, S. M.; Pho, H. Q.; van der Heide, F. R.; Veal, W. R. *J. Org. Chem.* **1988**, *53*, 3384−3386. (b) Doyle, M. P.; Tauton, J.; Pho, H. Q. *Tetrahedron Lett.* **1989**, *30*, 5397−5400.

SCHEME 10



reported[5−7,33] that the reaction of 1-acetyl-1-(diazoacetyl)-cyclopropane with cycloalkenone in the presence of rhodium(II) carboxylate catalyst gave exclusively C=C but not C=O cycloaddition product during the synthesis of the pterosin family of sesquiterpenoids.

Cosequently, we performed the reaction of diazo ketone **12a** with acyclic α,*β*-unsaturated ketone to understand the reactivity of a carbonyl ylide. To this end, the reaction of diazo ketone **12a** and benzylideneacetophenone (**31**, *trans*-chalcone) in the presence of $Rh_2(OAc)_4$ was carried out. Concentration followed by purification afforded products **32** and **33** as an inseparable mixture. On the basis of ^1H, ^{13}C NMR, and dept-135 spectral data, epoxy-bridged compounds **32**,**33** were characterized as regioisomers in the ratio of 1:2 (Scheme 10). Surprisingly, this reaction revealed that the intermediate carbonyl ylide **14a** underwent cycloaddition only to the C=C but not the C=O group of *trans*-chalcone.

Furthermore, we became involved in widening the synthetic utility of diazo ketone to obtain distinctive spiro epoxy-bridged tetrahydropyranone molecules and interested in probing the stereoselective aspects of the tandem cyclization-cycloaddition sequence. To this end, we decided to use tetracyclone (**34**) as a dipolarophile that has been widely used in Diels−Alder reactions as a 4π[34−36] or 2π[37] component to synthesize many complex molecules. The reaction of diazo ketone **12b** and dienone **34** in the presence of $Rh_2(OAc)_4$ catalyst was carried out. Purification of the crude reaction mixture on silica gel column chromatography provided the cycloadduct **35a** in 60% yield (Scheme 11). This reaction divulged that the carbonyl ylide underwent cycloaddition to the C=O group of dienone **34**, resulting in an interesting novel spiro epoxy-bridged tetrahydropyranone ring system in a chemoselective manner.

The FT-IR spectrum of compound **35a** exhibited a characteristic strong band at 1762 cm^{-1}, indicating the presence of a carbonyl group. The ^1H NMR spectrum of the cycloadduct **35a** exhibited a characteristic singlet resonance at δ 0.13, 4.72 for a methyl group and bridgehead (H-7) protons (Scheme 11, $n = 1$; $m = 0$), respectively. It is interesting to note that methyl group protons were shielded from the expected (or reported for

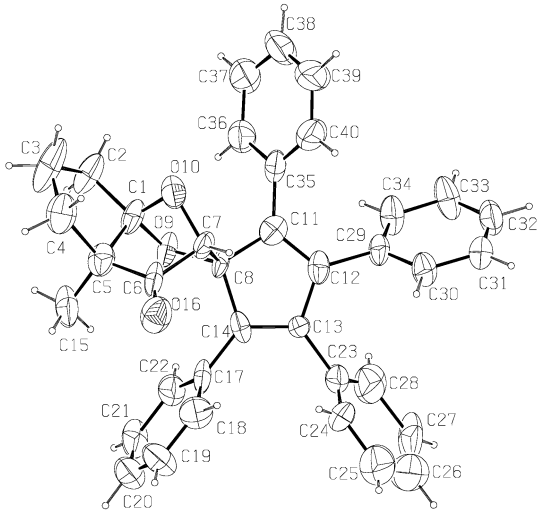
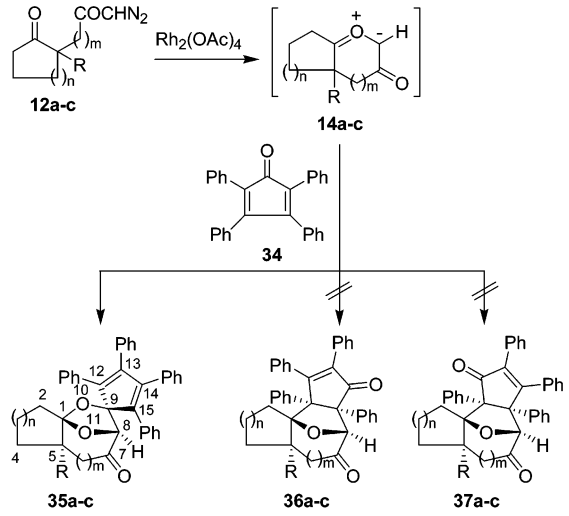


FIGURE 1. ORTEP view of compound **35a**.

SCHEME 11



other similar compounds) value of around 1 ppm. ^{13}C NMR and dept-135 spectral analyses of the cycloadduct **35a** showed peaks for one CH_3 carbon, three CH_2 carbons, eleven CH carbons, and twelve quaternary carbons, including one carbonyl group at 208.6 ppm. The mode of cycloaddition of carbonyl ylide to tetracyclone and the regio- and stereochemistry of the interesting cycloadduct **35a** (Figure 1) were unambiguously established by the single-crystal X-ray analysis. The single-crystal X-ray structure revealed that the presence of the methyl group at the ring juncture is endo with respect to the oxido-bridge and the observed angle of oxa-bridge (C1−O10−C7) is 97.1° in compound **35a**. All these spectral data clearly revealed that the carbonyl ylide underwent cycloaddition to the carbonyl group despite the presence of the C=C bond in **34**.

To generalize, the rhodium(II)-catalyzed behavior of other diazo carbonyl compounds **12a** and **12c** in the presence of **34** was studied to furnish the respective spirodioxa ring systems **35b** and **35c** (Scheme 11, Table 4). Similar to compound **35a**, methyl group protons of **35b** were also shifted upfield (0.25 ppm). The reaction of diazo ketone **12c** in the presence of rhodium(II) acetate pro-

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TABLE 4. Products 35a−c Obtained via Scheme 11

products	*n*	*m*	R	reaction time, h	yield,[a] %
a	1	0	CH_3	3.0	60
b	2	0	CH_3	2.5	65
c	2	1	H	2.0	59[b]

[a] Yields (unoptimized) refer to isolated and chromatographically pure compounds. [b] Isolated as a mixture of diastereomers in the ratio of 1:3.

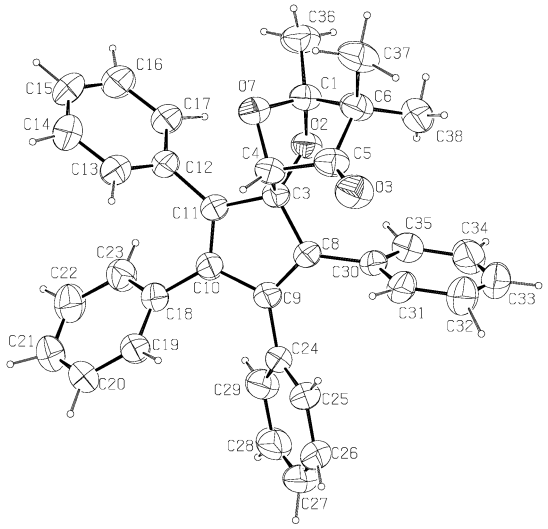
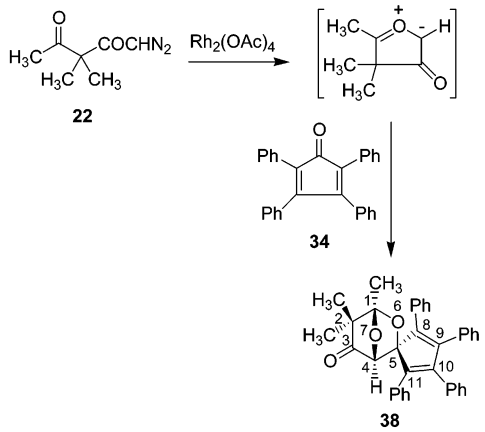


FIGURE 2. ORTEP view of compound **38**.

SCHEME 12



vided the cycloadducts as separable diastereomers **35c$_1$**/**35c$_2$** in the ratio of 1:3. We did not observe any C=C addition products **36/37** in the presence of dienone **34** as a dipolarophile (Scheme 11).

Finally, we performed an analogous experiment using aliphatic diazo carbonyl compound **22** with tetracyclone (**34**) in the presence of rhodium(II) acetate. This reaction also afforded the cycloadduct **38** in 53% yield (Scheme 12) as a result of the cycloaddition of carbonyl ylide to the C=O group of **34**. The structure and regio- and stereochemistry of product **38** were established based on its interrelated spectral data, including single-crystal X-ray analysis (Figure 2). The observed angle of the oxa-bridge (C1−O7−C4) is 96.5° in compound **38**. It may be noted that in the ^{1}H NMR spectrum of compound **38**, one of the singlet resonance signals of methyl group protons was shifted upfield due to its close proximity with the phenyl group in the conformation as it was observed for compounds **35a**,**b**. The single-crystal analysis of product **35a** revealed that the presence of the methyl group at the ring juncture is endo with respect to the oxido-bridge and the same is tentatively assigned for all other cycloadducts based on their similarity in spectral data.

Single-Crystal and Solid-State Structure Analyses. The cell parameters and intensity were measured on an Enraf-Nonius CAD-4 diffractometer using graphite monochromatized Mo Kα radiation (0.7107) in the θ range 2−22.5° and 2−25° for compounds **35a** and **38**, respectively, at room temperature. Twenty-five reflections with $\theta = 8-11°$ were used to obtain the accurate cell dimensions. Three standard reflections were monitored every 1 h, which showed no significant crystal decay for the entire period of data collection for both compounds. The crystal orientation, cell refinement, and intensity measurements were carried out using the program CAD-4PC.[38a] The raw intensity data were corrected for Lorentz Polarization effects. The Lorentz Polarization correction and data reduction were carried out using the NRCVAX program.[38b] The structure was solved using direct method. The full-matrix least-squares refinement of all non-hydrogen atoms with isotropic temperature factor was carried out using SHELXL-97.[38c]

After the complete convergence of the isotropic refinement for molecule **35a**, six peaks appeared in the difference Fourier map with electron density ranging from 3 to 1.4 Å^{-3} that were accounted for by the highly disordered solvent molecule. These peaks were incorporated as carbon atoms of the disordered solvent moiety with the occupancy factor assigned according to their peak heights. The isotropic refinement of the disordered solvent molecule incorporating these peaks improved the *R*-value and GOF, but we could not model the solvent molecule because of its high dynamic disorderliness. Since the number of reflections-to-parameter ratio was low, the phenyl rings in the molecule were put in four different blocks and the rest of the atoms in the fifth block, using the SHELXL-97 program for anisotropic refinement. Refinement with anisotropic thermal parameters except for the disordered solvent moiety (which was refined only isotropically) was done in a blocked fashion and yielded the *R* value of 11.76% ($wR_2 = 22.882\%$) for compound **35a** in the final cycles of least-squares refinement. All the H-atoms were included stereochemically in the calculated positions and treated as riding atoms. After the complete anisotropic refinement of all the non-hydrogen atoms for the cycloadduct **38**, eight peaks with electron density ranging from 3.3 to 1.5 Å^{-3} appeared in the difference Fourier map, which were accounted for by carbon atoms of the disordered solvent molecule and refined isotropically with temperature factor depending

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(36) Allen, C. H. F. *Chem. Rev.* **1962**, *62*, 653−664.
(37) Nair, V.; Nair, A. G.; Radhakrishnan, K. V.; Nandakumar, M. V.; Rath N. P. *Synlett* **1997**, 767−768.
(38) (a) *Enraf-Nonius CAD-4 Software*, Version 5.0; Enraf-Nonius: Delft, The Netherlands, 1989. (b) Gabe, E. J.; Le Page, Y.; Lee, F. L.; White, P. S. *J. Appl. Crystallogr.* **1989**, *22*, 384−387. (c) Sheldrick, M. *SHELX*97, Program for the solution of crystal structures; University of Gottingen: Gottingen, Germany, 1997.

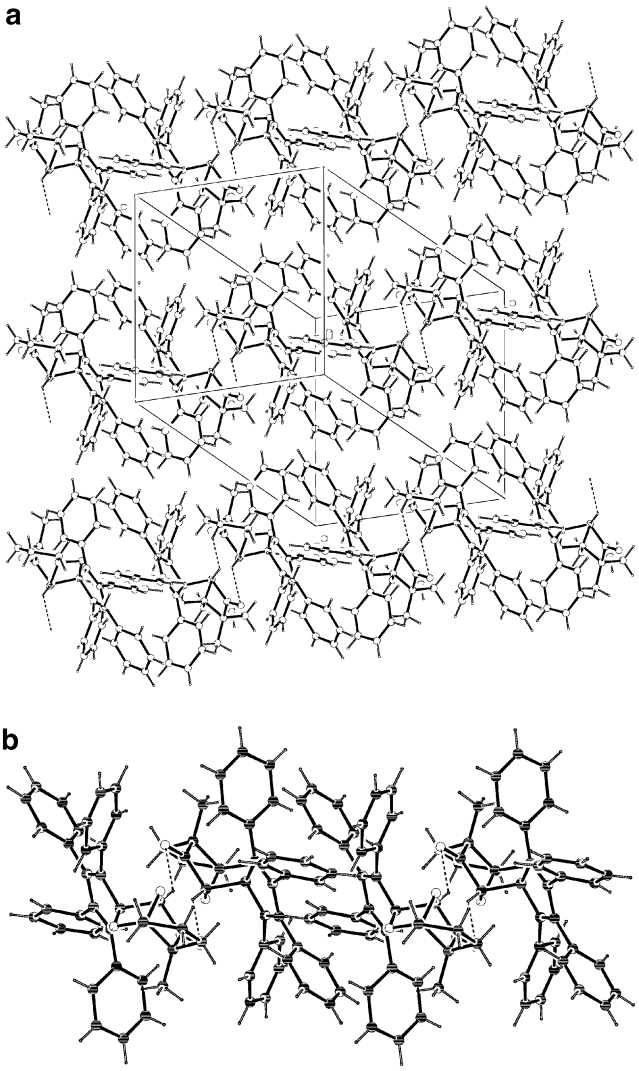

FIGURE 3. (a) Network of C−H···O interactions in the *ab*-plane of **35a.** (b) A close view showing the dimeric C−H···O interactions and $\pi\cdots\pi$ stacking in molecule **35a.**

upon their peak height. We could not model the disordered solvent molecule because of its highly dynamic disorderliness (as in the case of **35a**). The H-atoms were either fixed or obtained from the difference Fourier map and the final cycles of refinement yielded an *R* -value of 8.52% (wR_2 = 11.29%) for compound **38**.

Next, we analyzed the solid-state architecture arrangements of the interesting molecule **35a**. The crystal packing pattern (Figure 3a) of compound **35a** divulged a large number of close intermolecular links between the molecules, which are associated as dimers via an intermolecular C−H···O hydrogen bonding interaction[39] between the carbonyl oxygen and the hydrogen from the C7 carbon atom (H-bonding parameters are C7−H7···O16, C7−H7 = 1.00 Å, H7···O16 = 2.53 Å, C7···O16 = 3.35 Å, ∠C7−H7···O16 = 140°, symmetry code = 1 − *x*, −*y*, 1 − *z*). The dimers (Figure 3b) are extended to form a linear chain through stacking interaction between the phenyl rings (C23 to C27). The centroid···centroid and the nearest C−C distances between the offset stacked phenyl rings are 3.990 and 3.334 Å, respectively. In addition to an intermolecular H-bonding, the methyl group hydrogen is involved in C−H···π interaction with the phenyl ring (C15−H15C···C1g; H15C···C1g = 2.80 Å, C15···C1g = 3.62 Å and ∠C15−H15C···C1g = 144°, where C1g is the centroid of the phenyl ring (C17 to C22). The C−H···π interaction is evident from an unusual upfield shift of the methyl group hydrogens to 0.13 ppm from the expected value of around 1 ppm in the ^{1}H NMR spectrum of compound **35a**.

Frontier Molecular Orbital (FMO) Analysis. The above experimental results show that diazo ketones **12/22** were converted into the epoxy-bridged tetrahydropyranone systems via the rapid cyclization of the transient rhodium carbenoids **13a**−**d** onto the neighboring ring carbonyl group resulting in carbonyl ylides **14a**−**d**, which further underwent 1,3-dipolar cycloaddition with carbonyl groups. In all the above reactions, the cycloaddition of carbonyl ylides to dipolarophiles was highly regio-, chemo-, and stereoselective. The carbonyl group of tetracyclone (**34**) underwent 1,3-dipolar cycloaddition with carbonyl ylides and no C═C cycloadduct has been detected. To understand the factors that influence these stereoselective cycloadditions, we decided to perform a detailed computational study. Application of theoretical aspects of FMO analysis to cycloaddition chemistry has been used to envisage the relative rate and regiochemical outcome of many cycloaddition reactions.[40−42] In perturbation theory, a few occupied and virtual molecular orbitals of appropriate symmetry surrounding the frontier MO gap of reactants have been considered. The calculated energy differences and orbital coefficients are used to model the transition state. Such a qualitative approach is ideally suited to predict and understand the stereochemical products of cycloaddition reactions.

Initially, we performed frontier molecular orbital analysis (FMO) for the reaction of diazo ketone **12a** and dienone **34**. The exclusive formation of [3+2] cycloadducts from carbonyl ylide **14a** and dienone **34** can be examined in terms of the energies and orbital coefficients of the frontier orbitals of reacting centers. The calculated energy levels and orbital coefficients of HOMO and LUMO for **34** and **14a** are shown in Figure 4.

From the correlation diagram, it is evident that the energy gap between HOMO of **14a** and LUMO of **34** is favored over HOMO of **34** and LUMO of **14a** (Figure 4). Examining the orbital coefficients calculated at the AM1 level of theory showed that these are largely comparable at both C═C and C═O centers of dipolarophile **34**. Hence, the 1,3-cycloaddition between dipolarophile **34** and dipole **14a** should lead to the formation of both C═C and C═O addition products. Contrary to this, only C═O addition

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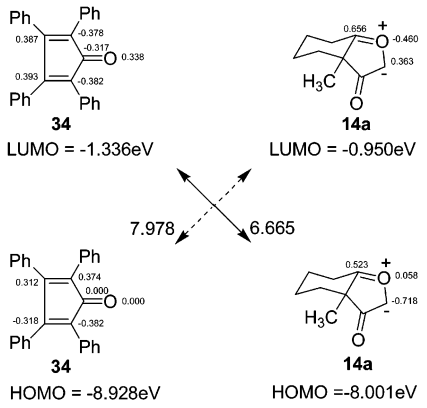

FIGURE 4.

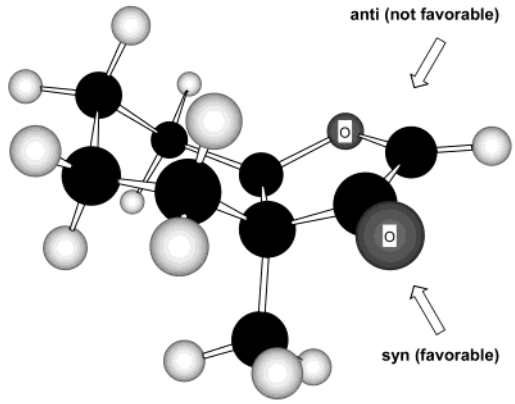

FIGURE 5. Energy-minimized cyclic carbonyl ylide **14a**.

products have been observed. Therefore, it appears that the chemo- and regioselectivity observed in the above reactions are not associated with the electronic factors of the FMO model of the dipolar transition state. At this stage, we decided to perform transition state calculations for the formation of different cycloadducts between dipolarophile **34** and dipole **14a**. The transition state energies calculated for cycloadducts and their relative energy differences will indicate the formation of most stable cycloadducts. Considering the relatively large size of the dipolarophile and the dipole, the AM1 semiempirical model has been employed to locate the transition state for this 1,3-dipolar cycloaddition reaction.

The AM1 calculated cyclohexane fused five-membered-ring cyclic carbonyl ylide dipole **14a** is shown in Figure 5. The calculated results showed that the reactive center ($C{=}O^{+}{-}C^{-}$) of dipole **14a** is completely planar and the fused cyclohexane ring adopts a chairlike conformation. A dipolarophile approach can be either syn or anti to the methyl group of dipole **14a** (Figure 5). The presence of a fused cyclohexane ring and a methyl group in dipole **14a** makes it facially dissymmetric for the approach of a dipolarophile. In this study, we have considered both syn and anti approaches of dipolarophile **34** toward dipole **14a**. It is important to note that the C=C unit of dipolarophile **34** can approach the dipole **14a** in two different orientations, having the carbonyl group of dipolarophile **34** close (*in*) or away (*out*) from the cyclohexane ring of dipole **14a** (Figure 6).

Six transition states have been calculated for the 1,3-dipolar cycloaddition between dipolarophile **34** and dipole

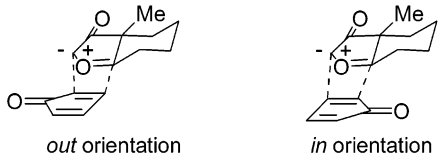

FIGURE 6.

14a based on the AM1 level of theory. The calculated transition state energies predicted that the "syn C=O attack" (Figure 7) is preferred compared to other modes of cycloaddition. This calculated result is in accord with the experimentally observed products (Schemes 11 and 12 and Figure 7). Transition state energies calculated for the 1,3-dipolar cycloaddition between the C=C unit of dipolarophile **34** and dipole **14a** are much higher (~12.0 kcal/mol) compared to the corresponding transition states of the C=O unit addition of dipolarophile (**34**). Such energy differences should exclusively lead to the formation of the C=O cycloadduct and this is evident from our experimental observation.

An analysis of AM1 transition state geometries suggested that the computed transition states for C=O addition of dipolarophile **34** to dipole **14a** were concerted and slightly asynchronous in nature (Figure 7). The transition state structures obtained for the C=C cycloaddition of dipolarophile **34** with dipole **14a** were highly unsymmetrical in nature. One of the newly forming bonds was much smaller (2.0 Å) than the other bond (3.50 Å). Such a high asynchronicity observed in the transition states might be due to severe steric interactions between phenyl rings present in the C=C unit of dipolarophile **34** and dipole **14a**. Considering the nature of the 1,3-dipolar transition states, it is worth mentioning that the mechanism of 1,3-dipolar cycloaddition has been a topic of lively debate.[43−45] The results of different molecular orbital calculations for the cycloaddition reactions have provided support for both the concerted and two-step diradical mechanisms.[44,46] Padwa and co-workers have demonstrated that a ground-state biradical carbonyl ylide begins the bond-making process at the cycloaddition transition state.[47]

Representatively, we extended our theoretical studies to the reaction of diazo ketone **12a** with unsubstituted cyclopentenone (**27**). Other groups have reported the formation of only one cycloadduct between a dipolarophile such as **27** and a dipole derived from an aliphatic diazo carbonyl compound in the presence of rhodium(II) acetate dimer. Presently, we have observed a detectable amount of another cycloadduct (C=O cycloaddition product **30**) in the 1,3-dipolar cycloaddition reactions of carbonyl

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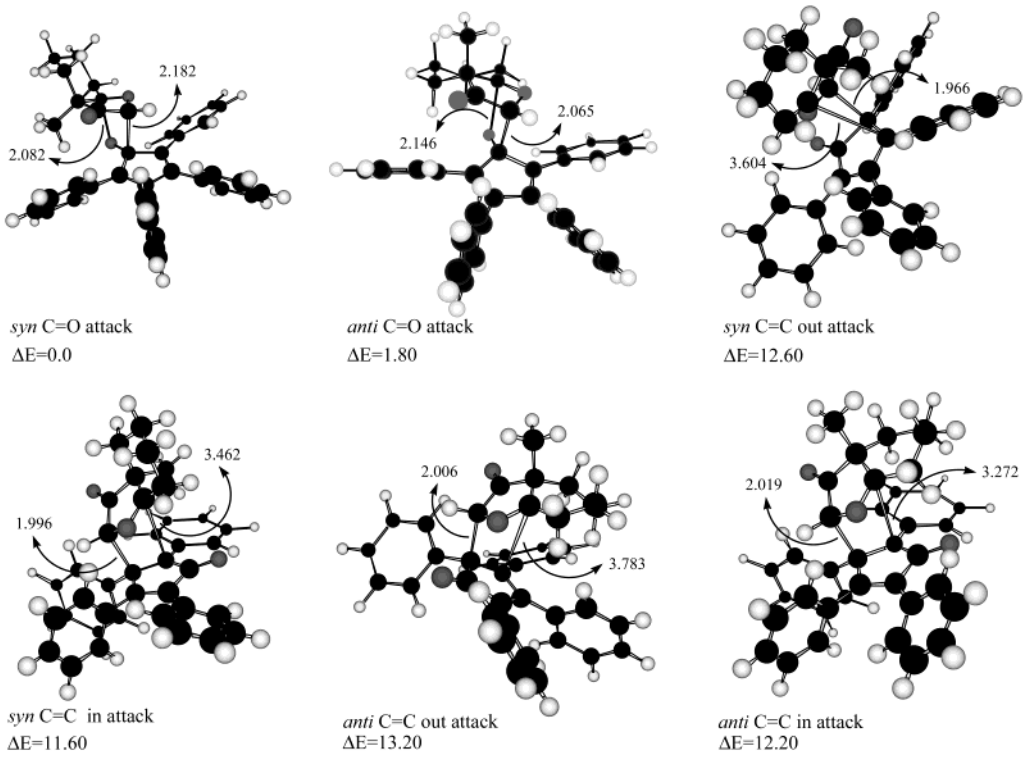

FIGURE 7. The AM1-calculated TS structures for dipolarophile **34** and dipole **14a** and their relative energies (in kcal/mol).

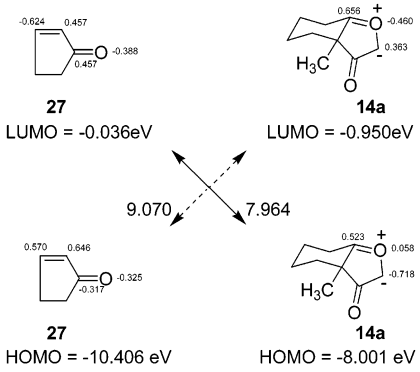

FIGURE 8.

ylides. ^{1}H, ^{13}C, and dept-135 NMR studies confirmed that the formation of C═C cycloaddition products **29a**,**c** was predominant. To examine the regioselectivity observed in these 1,3-dipolar cycloaddition reactions, FMO and transition state analyses have been performed at the AM1 level.

The orbital correlation diagram (Figure 8) predicted the formation of predominant C═C cycloaddition for 1,3-dipolar cycloaddition between dipolarophile **27** and dipole **14a**. The calculated energy levels suggested that the energy gap between HOMO of **14a** and LUMO of **27** is considerably lower than that of HOMO of **27** and LUMO of **14a** and hence the former interaction is energetically favored for cycloaddition. It was also evident from the size of the orbital coefficients calculated at the AM1 level that the C═C unit of dipolarophile **27** has a larger coefficient and will have better interaction than the corresponding C═O coefficient with dipole **14a** (Figure 8). From such analyses, it can be concluded that the HOMO of **14a** and LUMO of **27** controls the chemo- and regioselection in these reactions. However, the approach of the dipolarophile **27** toward the π-face of dipole **14a** (syn vs anti) remains to be answered. Therefore, we considered possible modes of approach (syn vs anti) of dipolarophile **27** toward the dipole **14a** π-face and calculated the transition states for such modes of cycloaddition. The two possible orientations of the C═C unit of dipolarophile **27** cycloaddition have also been taken into account (Figure 6). AM1 calculated transition states and their relative energies are summarized in Figure 9. The overall calculated results predicted that the "syn in C═C attack" (Figure 9) is energetically favored compared to other transition states. Generally, transition states appear to be concerted and slightly asynchronous in nature. Overall, FMO and transition state calculations have predicted correctly the chemo- and regioselectivity as observed in our experiments.

Finally, it is interesting to note that no anti cycloadducts have been observed in the 1,3-dipolar cycloaddition reactions studied herein. Examination of the AM1 calculated ground-state structure of dipole **14a** revealed that the anti face is sterically more hindered compared to the corresponding syn face (Figure 5). The 1,3-diaxial hydrogens of the cyclohexane ring sterically hinder one of the reactive centers (C═O$^+$−C$^-$) in the anti face and hence the dipolarophile prefers to approach from the syn face of dipole **14a**.

The above studies show that the mechanism by which α-diazo carbonyl compounds were converted into highly substituted epoxy-bridged tetrahydropyranone ring systems involved rapid cyclization of the rhodium carbenoid onto the neighboring ring carbonyl group to afford the corresponding five- or six-membered-ring cyclic carbonyl ylides as intermediates, followed by subsequent [3+2] cycloaddition with various carbonyl groups such as

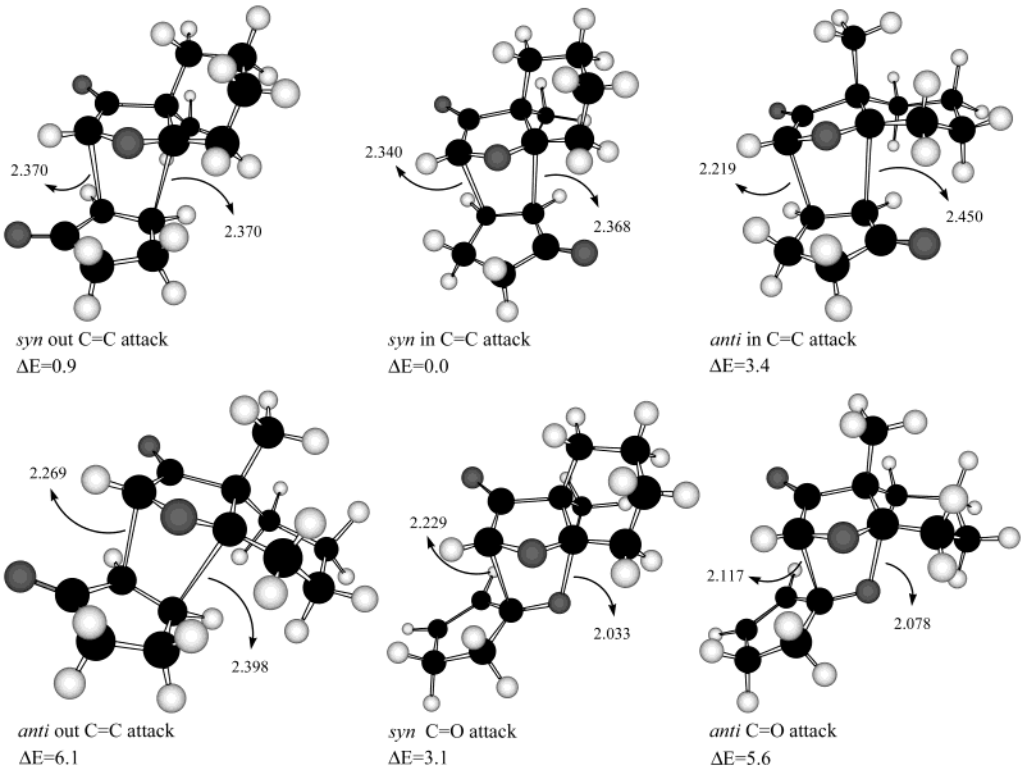

FIGURE 9. The AM1-calculated TS structures for dipolarophile **27** and dipole **14a** and their relative energies (in kcal/mol).

heterodipolarophiles. It is evident that all the above reactions furnished functionalized oxapoly- and spirocyclic frameworks with a high degree of regio-, chemo-, and stereocontrol. Theoretical calculations for tandem cyclization−cycloaddition reactions afforded supporting evidence in addition to spectral data to assign the regio- and stereochemistry of the products. It is important to note that starting from relatively simple precursors and dipolarophiles, these tandem cyclization−cycloaddition reactions resulted in the formation of new C−C and C−O bonds in a stereoselective manner.

Conclusion

In summary, we have established the scope of the stereoselective 1,3-dipolar cycloaddition of carbonyl ylides with carbonyl compounds, e.g. aromatic aldehydes, *trans*-cinnamaldehyde, *trans*-crotonaldehyde, 2-furancarboxaldehyde, chalcone, cycloalkenones, and 2,3,4,5-tetraphenylcyclopenta-2,4-dienone. The construction of poly- and spirocyclic frameworks incorporating the epoxy-bridged tetrahydropyranone moiety has been well demonstrated in the case of cyclic or alicyclic α,*β*-unsaturated ketones and aldehydes. Although three or more possible cycloadducts could be expected to form in each cycloaddition reaction, only C═O addition products were obtained in the case of α,*β*-unsaturated aldehydes **18**/**24** and 2,3,4,5-tetraphenylcyclopenta-2,4-dienone (**34**). These cycloaddition reactions were found to be highly chemo-, regio-, and stereoselective, giving the exo cycloadducts in good yields. FMO analyses and transition state calculations have been performed for the better understanding of the reaction of carbonyl ylides with carbonyl compounds. Currently, we are investigating the application of this methodology in the synthesis of complex epoxy-bridged natural products.

Experimental Section

General. The melting points are uncorrected. The FT-IR spectra were recorded using KBr or neat method unless otherwise stated. ^{1}H NMR and ^{13}C NMR spectra were (200 and 50.3 MHz, respectively) referenced to TMS. Carbon types were determined from DEPT ^{13}C NMR experiments. Mass analyses were performed with an ionizing voltage of 70 eV or FD$^+$ method in absolute dichloromethane. Single-crystal X-ray crystallographic analyses were carried out in an Enraf Nonius CAD-4 diffractometer with Mo Kα radiation. All AM1 semiempirical calculations have been performed using MOPAC version 6.0.[48] Complete vibrational analyses have been performed at the same level of theory to characterize the transition states and ground-state geometries. All reactions were carried out under an argon atmosphere and solutions dried with anhydrous magnesium sulfate. Analytical thin-layer chromatography (TLC) was performed on silica/alumina plates and components were visualized by observation under iodine or by sulfuric acid charring. Column chromatography was performed on neutral alumina/silica gel (100−200 mesh). Care was taken to avoid light during the course of reaction in the synthesis of diazo compounds and their further conversion. Solvents were purified by distillation under dry argon. Diethyl ether/THF was distilled from sodium benzophenone ketyl immediately before use. Benzene was dried over sodium. DCM was dried using P_2O_5.

General Procedure for the Synthesis of Diazo Ketones.[29a] **(a) For Substrates 12a,b.** Cycloalkanone ester **9** (12 mmol) was carefully hydrolyzed using 8% aqueous potassium hydroxide solution (20 mL) with stirring at room temperature. The reaction was monitored by TLC and con-

(48) Dewar, M. J. S.; Zoebish, E. G.; Healy, E. F.; Stewart, J. J. P *J. Am. Chem. Soc.* **1985**, *107*, 3902−3909.

tinued until the disappearance of the starting material. The reaction mixture was extracted with ether (3 × 10 mL), acidified the aqueous layer (pH 5), and extracted with ether (3 × 15 mL). The organic phase was concentrated under reduced pressure at room temperature to obtain the corresponding keto acids **10**. Freshly distilled oxalyl chloride (20 mmol) was added dropwise to a stirring solution of the appropriate acid (10 mmol, **10a**,**b**) in dry ether (25 mL) at 25 °C, and the stirring was continued for 2 h. The solution was evaporated under reduced pressure; the crude residual acid chloride was dissolved in freshly prepared dry ether (100 mL) and used for the next step without further purification. The crude acid chloride solution was added dropwise over a 0.5-h period to a stirring solution of freshly prepared diazomethane (13 mmol) and freshly distilled triethylamine (10 mmol) in dry ether (50 mL) at 0 °C, and the stirring was continued for 2 h. The mixture was filtered and concentrated. Chromatography of the residue through a short silica gel column (prewashed by ethyl acetate) led to the corresponding diazo ketone **12a**,**b** with 10% ethyl acetate−hexane elution. The diazo ketone **22**[26] was synthesized in a similar manner.

(b) For Substrate 12c. To a solution containing 10 mmol of keto acid **10c** (1 equiv) in freshly prepared dry ether (100 mL) was added freshly distilled ethyl chloroformate (1.2 equiv) followed by the slow addition of dry triethylamine (1.5 equiv). The resulting mixture was stirred at room temperature for 45 min and the solid that formed was filtered under an inert atmosphere. The filtrate was added to freshly prepared ethereal diazomethane solution (20 mmol) and then the mixture was stirred for 12 h at 0 °C after which it was allowed to warm to 10 °C for a period of 2 h under an argon atmosphere. The solvent was removed under reduced pressure and the residue purified as described above to obtain **12c**.

(c) For Substrate 12d. To a solution of freshly distilled monoethyl malonate (35 mmol) in dry DCM (8 mL) was added dropwise a solution of isopropylmagnesium bromide (70 mmol) in THF (50 mL) until propane was evolved. The temperature rises to 40−50 °C. The green solution was then cooled in an ice/salt bath and crude appropriate acid chloride obtained from the corresponding acid **10a** (14 mmol) in DCM (2 mL) was added dropwise with efficient stirring. The stirring was continued for 1 h, the cooling bath was removed, and the resultant mixture was poured into cold 10% hydrochloric acid (20 mL). After cessation of the carbon dioxide evolution, the clear solution was extracted with EtOAc (3 × 20 mL) and washed with saturated sodium bicarbonate (30 mL) and brine solution. The organic phase was dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The residue was subjected to column chromatography on silica gel to afford the corresponding active methylene compound **11d**.

To a solution containing active methylene compound **11d** (1 equiv) and freshly distilled methanesulfonyl azide (1.2 equiv) in dry dichloromethane (5 mL) was added freshly distilled triethylamine (2 equiv) under an argon atmosphere at room temperature. The reaction was continued until TLC analysis indicated complete disappearance of starting material. The solvent was removed under reduced pressure at room temperature and the residue subjected to short neutral alumina column chromatography to afford pure diazo ketone **12d** with 15% ethyl acetate−hexane elution.

General Procedure for the Rhodium(II)-Catalyzed Cycloaddition Reaction of α-Diazo Ketones with Carbonyl Compounds. Method A: To an oven-dried flask containing a dichloromethane solution of the appropriate α-diazo carbonyl compound (1.0 mmol) and appropriate dipolarophile (2.0 mmol) was added 1 mol % of rhodium(II) acetate dimer catalyst under an argon atmosphere at room temperature. The reaction mixture was stirred and monitored by TLC until the disappearance of the starting diazo ketones. The solvent was removed under reduced pressure and the crude residue was purified using a silica gel/neutral alumina column (EtOAc−hexane mixture as eluent) to afford the respective cycloadducts.

Method B: The procedure was followed as in method A using dry benzene as solvent and the reaction mixture was allowed to reflux under an argon atmosphere. The refluxing was continued until the disappearance of the starting diazo ketone and purified through a neutral alumina column as described above.

Reaction of α-Diazo Ketone 12a with 15a, Preparation of 6-Methyl-9-*p*-tolyl-10,11-dioxatricyclo[6.2.1.0^{1,6}]undecan-7-one (16a). A mixture of 4-methylbenzaldehyde (120 mg, 1.0 mmol) and diazo ketone **12a** (90 mg, 0.5 mmol) was allowed to react with rhodium(II) acetate dimer (2.2 mg) in dry DCM (10 mL) for 3 h at room temperature under an argon atmosphere according to the general method A to afford the cycloadduct **16a** (108 mg) in 79% yield as a colorless solid: mp 113−115 °C ($CHCl_3$/hexane); IR (KBr) 2947, 2863, 1763, 1460, 1444, 1034, 973 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.24 (2H, d, J = 7.6 Hz, arom-*H*), 7.29 (2H, d, J = 7.6 Hz, arom-*H*), 4.78 (1H, s, OC*H*), 4.47 (1H, s, OC*H*), 2.33 (3H, s, CH_3), 2.30−1.35 (8H, m), 1.20 (3H, s, CH_3); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 213.7 (*C*═O), 138.8 (*quat*-C), 136.5 (*quat*-C), 129.6 (═*C*H), 126.7 (═*C*H), 110.3 (*quat*-C), 86.8 (O*C*H), 77.5 (O*C*H), 52.4 (*quat*-C), 31.4 (*C*H$_2$), 27.2 (*C*H$_2$), 23.6 (*C*H$_2$), 21.5 (*C*H$_3$), 20.6 (*C*H$_2$), 16.2 (*C*H$_3$); MS (FD$^+$) *m*/*z* 272 (M$^+$). Anal. Calcd for $C_{17}H_{20}O_3$: C, 74.97; H, 7.40. Found: C, 74.97; H, 7.41.

Reaction of α-Diazo Ketone 12a with 15b, Preparation of 9-(4-Methoxyphenyl)-6-methyl-10,11-dioxatricyclo-[6.2.1.0^{1,6}]undecan-7-one (16b). A mixture of 4-methoxybenzaldehyde (136 mg, 1.0 mmol) and diazo ketone **12a** (90 mg, 0.5 mmol) was allowed to react with rhodium(II) acetate dimer (2.2 mg) in dry DCM (10 mL) for 3.5 h at room temperature under an argon atmosphere according to the general method A to afford the cycloadduct **16b** (105 mg) in 73% yield as a colorless oil: IR (neat, NaCl) 2946, 1762, 1461, 1443, 973 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.30 (2H, d, J = 7.6 Hz, arom-*H*), 6.84 (2H, d, J = 7.6 Hz, arom-*H*), 4.76 (1H, s, OC*H*), 4.45 (1H, s, OC*H*), 3.78 (3H, s, CH_3), 2.24−2.10 (1H, m), 1.99−1.85 (2H, m), 1.76−1.25 (5H, m), 1.19 (3H, s, CH_3); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 213.3 (*C*═O), 159.7 (*quat*-C), 138.9 (*quat*-C), 127.6 (═*C*H), 113.9 (═*C*H), 113.0 (*quat*-C), 86.3 (O*C*H), 77.7 (O*C*H), 55.2 (O*C*H$_3$), 51.9 (*quat*-C), 30.9 (*C*H$_2$), 26.7 (*C*H$_2$), 23.2 (*C*H$_2$), 20.1 (*C*H$_2$), 15.7 (*C*H$_3$); MS (EI, 70 eV) *m*/*z* 288 (M$^+$). Anal. Calcd for $C_{17}H_{20}O_4$: C, 70.81; H, 6.99. Found: C, 70.97; H, 6.87.

Reaction of α-Diazo Ketone 12b with 15c, Preparation of 5-Methyl-8-phenyl-9,10-dioxatricyclo[5.2.1.0^{1,5}]decan-6-one (16c). A mixture of benzaldehyde (108 mg, 1.0 mmol) and diazo ketone **12b** (85 mg, 0.5 mmol) was allowed to react with rhodium(II) acetate dimer (2.2 mg) in dry DCM (10 mL) for 4 h at room temperature under an argon atmosphere according to the general method A to afford the cycloadduct **16c** (82 mg) in 67% yield as a colorless oil: IR (neat, NaCl) 2965, 2927, 1763, 1452, 1036, 985 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.39−7.33 (5H, m, arom-*H*), 4.90 (1H, s, OC*H*), 4.43 (1H, s, OC*H*), 2.32−2.25 (2H, m), 2.06−1.92 (2H, m), 1.63−1.56 (2H, m), 1.21 (3H, s, CH_3); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 211.7 (C═O), 139.2 (*quat*-C), 129.2 (═*C*H), 127.0 (═*C*H), 123.7 (*quat*-C), 87.1 (O*C*H), 79.0 (O*C*H), 58.1 (*quat*-C), 32.4 (*C*H$_2$), 26.4 (*C*H$_2$), 21.4 (*C*H$_2$), 18.6 (*C*H$_3$); MS (EI, 70 eV) *m*/*z* 244 (M$^+$). Anal. Calcd for $C_{15}H_{16}O_3$: C, 73.75; H, 6.60. Found: C, 74.00; H, 6.61.

Reaction of α-Diazo Ketone 12c with 15c, Preparation of 10-Phenyl-11,12-dioxatricyclo[7.2.1.0^{1,6}]dodecan-8-one (16d). A mixture of benzaldehyde (106 mg, 1.0 mmol) and diazo ketone **12c** (90 mg, 0.5 mmol) was allowed to react with rhodium(II) acetate dimer (2.2 mg) in dry DCM (10 mL) for 3 h at room temperature under an argon atmosphere according to the general method A to afford the cycloadduct **16d** (81 mg) as a colorless oil in 63% yield as a mixture of diastereomers in the ratio of 1:2: IR (neat, NaCl) 3065, 3032, 2936, 2859, 1733, 1448, 1272, 1014 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ

7.29−7.17 (5H, m, arom-*H*), 4.99 (1H, s, OC*H*), 4.25 (1H, s, OC*H*), 2.86 (1H, dd, J_1 =17.3, J_2 = 8.2 Hz), 2.45−1.66 (10H, m); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 203.9 (*C*=O), 140.8 (*quat*-C), 128.9 (=*C*H), 128.6 (=*C*H), 126.3 (=*C*H), 110.1 (*quat*-C), 87.2 (O*C*H), 80.2 (O*C*H), 45.4 (*C*H), 40.2 (CH_2), 34.3 (CH_2), 31.3 (CH_2), 25.2 (CH_2), 24.1 (CH_2); MS (FD^+) *m/z* 258 (M^+). Anal. Calcd for $C_{16}H_{18}O_3$: C, 74.40; H, 7.02. Found: C, 74.43; H, 7.08.

Reaction of α-Diazo Ketone 12a with 18a, Preparation of 6-Methyl-9-styryl-10,11-dioxatricyclo[6.2.1.0^{1,6}]undecan-7-one (19a). A mixture of 3-phenylpropenal (270 mg, 2.0 mmol) and diazo ketone **12a** (180 mg, 1.0 mmol) was allowed to react with rhodium(II) acetate dimer (4.4 mg) in dry DCM (10 mL) for 3 h at room temperature under an argon atmosphere according to the general method A to afford the cycloadduct **19a** (245 mg) in 86% yield as a colorless solid: mp 77−79 °C ($CHCl_3$/hexane); IR (KBr) 2952, 1760, 1450, 1371, 1274, 981, 939 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.34−7.19 (5H, m, arom-*H*), 6.58 (1H, d, J = 15.8 Hz, =C*H*), 6.07 (1H, dd, J_1 = 15.8 Hz, J_2 = 7.1 Hz, =C*H*), 4.46 (1H, s, OC*H*), 4.37 (1H, d, J = 7.1 Hz, OC*H*), 2.20−1.19 (8H, m), 1.13 (3H, s, CH_3); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 213.3 (*C*=O), 136.5 (*quat*-C), 133.7 (=*C*H), 129.0 (=*C*H), 128.5 (=*C*H), 127.2 (=*C*H), 126.4 (=*C*H), 113.4 (*quat*-C), 85.1 (O*C*H), 77.3 (O*C*H), 52.8 (*quat*-C), 31.3 (CH_2), 27.4 (CH_2), 23.6 (CH_2), 20.6 (CH_2), 16.0 (CH_3); MS (FD^+) *m/z* 284 (M^+). Anal. Calcd for $C_{18}H_{20}O_3$: C, 76.03; H, 7.09. Found: C, 76.06; H, 7.06.

Reaction of α-Diazo Ketone 12a with 18b, Preparation of 6-Methyl-9-propenyl-10,11-dioxatricyclo[6.2.1.0^{1,6}]undecan-7-one (19b). A mixture of but-2-enal (70 mg, 1.0 mmol) and diazo ketone **12a** (90 mg, 0.5 mmol) was allowed to react with rhodium(II) acetate dimer (2.2 mg) in dry DCM (5 mL) for 3 h at room temperature under an argon atmosphere according to the general method A to afford the cycloadduct **19b** (74 mg) in 67% yield as a colorless oil: IR (neat, NaCl) 2942, 2866, 1766, 1450, 1038, 987 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 5.90−5.65 (1H, m, =C*H*), 5.43 (1H, dd, J_1 = 15.2 Hz, J_2 = 6.4 Hz, =C*H*), 4.38 (1H, s, OC*H*), 4.19 (1H, d, J = 7.4 Hz, OC*H*), 2.10−1.35 (8H, m), 1.71 (3H, d, J = 6.2 Hz, CH_3), 1.11 (3H, s, CH_3); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 213.8 (*C*=O), 130.7 (=*C*H), 128.3 (=*C*H), 113.0 (*quat*-C), 85.0 (O*C*H), 77.1 (O*C*H), 52.6 (*quat*-C), 31.2 (CH_2), 27.3 (CH_2), 23.5 (CH_2), 20.5 (CH_2), 18.0 (CH_3), 15.9 (CH_3); MS (FD^+) *m/z* 222 (M^+). Anal. Calcd for $C_{13}H_{18}O_3$: C, 70.24; H, 8.16. Found: C, 70.26; H, 8.13.

Reaction of α-Diazo Ketone 22 with 18a, Preparation of 1,6,6-Trimethyl-3-styryl-2,7-dioxabicyclo[2.2.1]heptan-5-one (23a). A mixture of 3-phenylpropenal (270 mg, 2.0 mmol) and diazo ketone **22** (155 mg, 1.0 mmol) was allowed to react with rhodium(II) acetate dimer (4.4 mg) in dry DCM (10 mL) for 3.5 h at room temperature under an argon atmosphere according to the general method A to afford the cycloadduct **23a** (189 mg) in 73% yield as a colorless solid: mp 111−113 °C ($CHCl_3$/hexane); IR (KBr) 2983, 1766, 1500, 1454, 1382, 1267, 1134 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.37−7.21 (5H, m, arom-*H*), 6.58 (1H, d, J = 15.8 Hz, =C*H*), 6.09 (1H, dd, J_1 = 15.8 Hz, J_2 = 7.1 Hz, =C*H*), 4.42 (1H, s, OC*H*), 4.36 (1H, d, J = 7.1 Hz, OC*H*), 1.59 (3H, s, CH_3), 1.09 (3H, s, CH_3), 1.06 (3H, s, CH_3); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 213.8 (*C*=O), 136.5 (*quat*-C), 133.8 (=*C*H), 129.1 (=*C*H), 128.6 (=*C*H), 127.2 (=*C*H), 126.4 (=*C*H), 113.8 (*quat*-C), 84.8 (O*C*H), 77.4 (O*C*H), 53.4 (*quat*-C), 21.0 (CH_3), 19.2 (CH_3), 15.3 (CH_3); MS (FD^+) *m/z* 258 (M^+). Anal. Calcd for $C_{16}H_{18}O_3$: C, 74.40; H, 7.02. Found: C, 74.31; H, 7.04.

Reaction of α-Diazo Ketone 22 with 18b, Preparation of 1,6,6-Trimethyl-3-propenyl-2,7-dioxabicyclo[2.2.1]heptan-5-one (23b). A mixture of but-2-enal (70 mg, 1.0 mmol) and diazo ketone **22** (75 mg, 0.5 mmol) was allowed to react with rhodium(II) acetate dimer (2.2 mg) in dry DCM (5 mL) for 3.5 h at room temperature under an argon atmosphere according to the general method A to afford the cycloadduct **23b** (63 mg) in 64% yield as a colorless solid: mp 73−75 °C ($CHCl_3$/hexane); IR (KBr) 2990, 2973, 2941, 1765, 1468, 1306, 1097 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 5.90−5.60 (1H, m, =C*H*), 5.44 (1H, dd, J_1 = 15.2 Hz, J_2 = 7.4 Hz, =C*H*), 4.33 (1H, s, OC*H*), 4.16 (1H, d, J = 7.4 Hz, OC*H*), 1.72 (3H, d, J = 6.4 Hz, CH_3), 1.56 (3H, s, CH_3), 1.06 (6H, s, CH_3); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 214.0 (*C*=O), 130.5 (=*C*H), 128.4 (=*C*H), 114.0 (*quat*-C), 84.7 (O*C*H), 77.1 (O*C*H), 53.1 (*quat*-C), 20.8 (CH_3), 19.1 (CH_3), 18.0 (CH_3), 15.2 (CH_3); MS (FD^+) *m/z* 196 (M^+). Anal. Calcd for $C_{11}H_{16}O_3$: C, 67.32; H, 8.22. Found: C, 67.32; H, 8.26.

Reaction of α-Diazo Ketone 12a with 24, Preparation of 9-Furan-2-yl-6-methyl-10,11-dioxatricyclo[6.2.1.0^{1,6}]-undecan-7-one (25). A mixture of 2-furancarboxaldehyde (100 mg, 1.0 mmol) and diazo ketone **12a** (90 mg, 0.5 mmol) was allowed to react with rhodium(II) acetate dimer (2.2 mg) in dry DCM (5 mL) for 3 h at room temperature under an argon atmosphere according to the general method A to afford the cycloadduct **25** (84 mg) in 68% yield as a colorless oil: IR (neat, NaCl) 2940, 2866, 1767, 1503, 1450, 1378, 1229, 1039 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.38 (1H, t, J = 1.3 Hz, =C*H*), 6.33 (2H, d, J = 1.3 Hz, =C*H*), 4.83 (1H, s, OC*H*), 4.69 (1H, s, OC*H*), 2.10−1.35 (8H, m), 1.17 (3H, s, CH_3); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 212.8 (*C*=O), 151.7 (*quat*-C), 143.2 (=*C*H), 113.6 (*quat*-C), 110.9 (=*C*H), 108.8 (=*C*H), 84.3 (O*C*H), 71.7 (O*C*H), 52.5 (*quat*-C), 31.3 (CH_2), 27.1 (CH_2), 23.5 (CH_2), 20.4 (CH_2), 16.0 (CH_3); MS (FD^+) *m/z* 248 (M^+). Anal. Calcd for $C_{14}H_{16}O_4$: C, 67.73; H, 6.50. Found: C, 67.71; H, 6.51.

Reaction of α-Diazo Ketone 22 with 24, Preparation of 3-Furan-2-yl-1,6,6-trimethyl-2,7-dioxabicyclo[2.2.1]-heptan-5-one (26). A mixture of 2-furancarboxaldehyde (100 mg, 1.0 mmol) and diazo ketone **22** (75 mg, 0.5 mmol) was allowed to react with rhodium(II) acetate dimer (2.2 mg) in dry DCM (5 mL) for 3 h at room temperature under an argon atmosphere according to the general method A to afford the cycloadduct **26** (73 mg) in 66% yield as a colorless oil: IR (neat, NaCl) 2976, 2940, 2875, 1770, 1503, 1467, 1445, 1395, 1103 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.35 (1H, t, J = 1.3 Hz, =C*H*), 6.30 (2H, d, J = 1.3 Hz, =C*H*), 4.78 (1H, s, OC*H*), 4.60 (1H, s, OC*H*), 1.59 (3H, s, CH_3), 1.09 (3H, s, CH_3), 1.06 (3H, s, CH_3); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 213.2 (*C*=O), 151.9 (*quat*-C), 143.1 (=*C*H), 114.6 (*quat*-C), 110.9 (=*C*H), 108.7 (=*C*H), 84.1 (O*C*H), 71.8 (O*C*H), 53.1 (*quat*-C), 21.0 (CH_3), 19.2 (CH_3), 15.1 (CH_3); MS (FD^+) *m/z* 222 (M^+). Anal. Calcd for $C_{12}H_{14}O_4$: C, 64.85; H, 6.35. Found: C, 64.84; H, 6.32.

Reaction of α-Diazo Ketone 12a with 2-Cyclohexen-1-one, Preparation of Cycloadducts 29a and 30a. A mixture of 2-cyclohexen-1-one (215 mg, 2.0 mmol) and diazo ketone **12a** (200 mg, 1.1 mmol) was allowed to react with rhodium(II) acetate dimer (4.9 mg) in dry DCM (10 mL) for 3.5 h at room temperature under an argon atmosphere according to the general method A to afford the cycloadducts **29a** and **30a** in 64% (175 mg) and 23% (63 mg) yield, respectively. **29a**: Colorless thick oil; IR (neat, NaCl) 2931, 2863, 1758, 1700, 1455, 1270, 1120, 1036, 995 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 4.33 (1H, s, OC*H*), 2.71 (1H, d, J = 8.7 Hz), 2.52−2.11 (5H, m), 1.94−1.25 (10H, m), 1.10 (3H, s, CH_3); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 217.2 (*C*=O), 212.2 (*C*=O), 92.0 (*quat*-C), 87.1 (O*C*H), 54.6 (*C*H), 51.6 (*quat*-C), 42.1 (*C*H), 41.1 (CH_2), 31.2 (CH_2), 27.8 (CH_2), 27.5 (CH_2), 22.9 (CH_2), 21.0 (CH_2), 20.6 (CH_2), 13.0 (CH_3); MS (FD^+) *m/z* 248 (M^+). Anal. Calcd for $C_{15}H_{20}O_3$: C, 72.55; H, 8.12. Found: C, 72.63; H, 8.16. **30a**: Mixture of diastereomers in the ratio of 1:0.3, colorless thick oil; IR (neat, NaCl) 2935, 2866, 1764, 1650, 1451, 1376, 1283, 1099, 1042, 948 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 5.95−5.90 (1H, m), 5.69 (1H, d, J = 10.4 Hz), 4.24 (1H, s, OC*H*), 2.14−1.17 (14H, m), 1.13 (3H, s, CH_3); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 214.0 (*C*=O), 132.0 (=*C*H), 129.4 (=*C*H), 112.9 (*quat*-C, C-1), 87.9 (O*C*H), 79.8 (*quat*-C, C-9), 53.9 (*quat*-C), 32.6 (CH_2), 30.8 (CH_2), 28.1 (CH_2), 25.3 (CH_2), 23.8 (CH_2), 20.8 (CH_2), 20.1 (CH_2), 15.5 (CH_3); MS (FD^+) *m/z* 248 (M^+). Anal. Calcd for $C_{15}H_{20}O_3$: C, 72.55; H, 8.12. Found: C, 72.56; H, 8.09.

Reaction of α-Diazo Ketone 12d with 2-Cyclohexen-1-one, Preparation of Cycloadducts 29b and 30b. A mixture of 2-cyclohexen-1-one (155 mg, 2.0 mmol) and diazo ketone **12d** (200 mg, 0.8 mmol) was allowed to react with rhodium(II) acetate dimer (3.5 mg) in dry benzene (10 mL) for 8 h at reflux under an argon atmosphere according to the general method B to afford the cycloadducts **29b** and **30b** in 12% (31 mg) and 67% (170 mg) yield, respectively. **29b**: Colorless thick oil; IR (neat, NaCl) 2937, 2862, 1769, 1739, 1715, 1457, 1376, 984 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 4.34 (2H, q, J = 7.1 Hz, OCH_2), 2.75−1.97 (8H, m), 1.94−1.47 (8H, m), 1.36 (3H, t, J = 7.1 Hz, CH_2CH_3), 1.16 (3H, s, CH_3); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 218.5 (*C*=O), 211.0 (*C*=O), 161.7 (*C*OO), 106.9 (*quat*-C), 90.0 (*quat*-C), 62.5 (O*C*H_2), 54.8 (*C*H), 51.9 (*quat*-C), 44.8 (*C*H), 41.2 (*C*H_2), 31.3 (*C*H_2), 27.0 (*C*H_2), 25.1 (*C*H_2), 22.5 (*C*H_2), 20.8 (*C*H_2), 20.3 (*C*H_2), 16.9 (*C*H_3), 14.9 (*C*H_3); MS (EI, 70 eV) *m*/*z* 320 (M^+). Anal. Calcd for $C_{18}H_{24}O_5$: C, 67.48; H, 7.55. Found: C, 67.51; H, 7.49. **30b**: Mixture of diastereomers in the ratio of 1:0.3 as a colorless thick oil; IR (neat, NaCl) 2939, 2869, 1775, 1746, 1650, 1518, 1456, 1381, 1132, 1085 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 6.06−5.98 (1H, m), 5.60 (1H, d, J = 10.4 Hz), 4.30 (2H, q, J = 7.1 Hz, OCH_2), 2.17−1.97 (4H, m), 1.96−1.33 (10H, m), 1.29 (3H, t, J = 7.1 Hz, CH_2CH_3), 1.19 (3H, s, CH_3); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 207.4 (*C*=O), 163.6 (*C*OO), 134.4 (=CH), 125.9 (=CH), 110.7 (*quat*-C, C-1), 93.2 (*quat*-C, C-8), 80.4 (*quat*-C, C-9), 62.4 (O*C*H_2), 54.1 (*quat*-C), 32.1 (*C*H_2), 30.8 (*C*H_2), 27.7 (*C*H_2), 25.2 (*C*H_2), 23.3 (*C*H_2), 20.5 (*C*H_2), 19.6 (*C*H_2), 15.6 (*C*H_3), 14.7 (*C*H_3); MS (FD^+) *m*/*z* 320 (M^+). Anal. Calcd for $C_{18}H_{24}O_5$: C, 67.48; H, 7.55. Found: C, 67.54; H, 7.54.

Reaction of α-Diazo Ketone 12a with 2-Cyclopenten-1-one, Preparation of Cycloadducts 29c and 30c. A mixture of 2-cyclopenten-1-one (85 mg, 1.0 mmol) and diazo ketone **12a** (90 mg, 0.5 mmol) was allowed to react with rhodium(II) acetate dimer (2.2 mg) in dry DCM (10 mL) for 2.5 h at room temperature under an argon atmosphere according to the general method A to afford the cycloadducts **29c** and **30c** in 44% (51 mg) and 6% (6 mg) yield, respectively. **29c**: Colorless solid; mp 88−90 °C (DCM/hexane); IR (KBr) 2932, 2861, 1755, 1729, 1466, 1378, 1179, 988 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 4.43 (1H, s, OC*H*), 2.69−2.53 (2H, m), 2.32−2.03 (4H, m), 1.84−1.29 (8H, m), 1.08 (3H, s, CH_3); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 217.7 (*C*=O), 213.8 (*C*=O), 91.0 (*quat*-C), 87.9 (*C*H), 54.3 (*C*H), 49.9 (*quat*-C), 41.6 (*C*H), 39.5 (*C*H_2), 30.4 (*C*H_2), 25.8 (*C*H_2), 25.3 (*C*H_2), 22.2 (*C*H_2), 20.1 (*C*H_2), 16.4 (*C*H_3); MS (EI, 70 eV) *m*/*z* 234 (M^+). Anal. Calcd for $C_{14}H_{18}O_3$: C, 71.77; H, 7.74. Found: C, 71.72; H, 7.69. **30c**: Mixture of diastereomers in the ratio of 1:0.4 as a colorless thick oil; IR (neat, NaCl) 2938, 2864, 1758, 1698, 1455, 1350, 1261, 1124, 1045, 984 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 6.03−5.99 (1H, m), 5.72 (1H, d, J = 10.4 Hz), 4.27 (1H, s, OC*H*), 2.50−1.29 (12H, m), 1.23 (3H, s, CH_3); MS (FD^+) *m*/*z* 234 (M^+). Anal. Calcd for $C_{14}H_{18}O_3$: C, 71.77; H, 7.74. Found: C, 71.79; H, 7.79.

Reaction of α-Diazo Ketone 12a with 1,3-Diphenylpropenone (31), Preparation of Cycloadducts 32/33.[49] A mixture of 1,3-diphenylpropenone (208 mg, 1.0 mmol) and diazo ketone **12a** (90 mg, 0.5 mmol) was allowed to react with rhodium(II) acetate dimer (2.2 mg) in dry DCM (10 mL) for 3.5 h at room temperature under an argon atmosphere according to the general method A to afford the cycloadducts 9-benzoyl-6-methyl-10-phenyl-11-oxatricyclo[6.2.1.$0^{1,6}$]undecan-7-one (**32**)/10-benzoyl-6-methyl-9-phenyl-11-oxatricyclo[6.2.1.$0^{1,6}$]-undecan-7-one (**33**) in 57% (103 mg) yield as a mixture of regioisomers in the ratio of 1:2.1 as a colorless thick oil: IR (neat, NaCl) 2937, 2801, 1758, 1675, 1594, 1449, 1369, 1273 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.99 (2H, d, J = 7.4 Hz, arom-*H*), 7.61−7.10 (8H, m, arom-*H*), 4.84 (1H, d, J = 6.3 Hz), 4.54 (1H, t, J = 6.4 Hz), 4.30 (1H, d, J = 6.6 Hz), 1.79−1.38 (8H, m), 1.35 (3H, s, CH_3); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 214.4 (*C*=O), 199.2 (*C*=O), 141.5 (*quat*-C), 138.0 (*quat*-C), 133.6 (=*C*H), 129.2 (=*C*H), 129.0 (=*C*H), 128.6 (=*C*H), 128.3 (=*C*H), 127.8 (=*C*H), 127.1 (=*C*H), 91.8 (*quat*-C), 84.1 (O*C*H), 51.9 (*C*H), 51.3 (*quat*-C), 50.7 (*C*H), 31.4 (*C*H_2), 26.9 (*C*H_2), 21.9 (*C*H_2), 20.1 (*C*H_2), 15.3 (*C*H_3); MS (EI, 70 eV) *m*/*z* 360 (M^+). Anal. Calcd for $C_{24}H_{24}O_3$: C, 79.97; H, 6.71. Found: C, 79.91; H, 6.66.

Reaction of α-Diazo Ketone 12b with 2,3,4,5-Tetraphenylcyclopenta-2,4-dienone, Preparation of Cycloadduct 35a.[50] A mixture of 2,3,4,5-tetraphenylcyclopenta-2,4-dienone (575 mg, 1.5 mmol) and diazo ketone **12b** (165 mg, 1.0 mmol) was allowed to react with rhodium(II) acetate dimer (4.4 mg) in dry DCM (10 mL) for 3 h at room temperature under an argon atmosphere according to the general method A to afford the cycloadduct **35a** (313 mg) in 60% yield as a colorless solid: mp 157−159 °C (DCM/hexane); IR (KBr) 2962, 2931, 1762, 1600, 1491, 1444, 1139, 909, 734 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.25−7.00 (10H, m, arom-*H*), 6.98−6.75 (10H, m, arom-*H*), 4.72 (1H, s, OC*H*), 2.15−1.55 (4H, m), 1.37−0.90 (2H, m), 0.13 (3H, s, CH_3); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 208.6 (*C*=O), 146.8 (*quat*-C), 145.0 (*quat*-C), 142.0 (*quat*-C), 140.4 (*quat*-C), 136.6 (*quat*-C), 134.5 (*quat*-C), 134.1 (*quat*-C), 133.7 (*quat*-C), 132.6 (=*C*H), 130.3 (=*C*H), 129.8 (=*C*H), 129.5 (=*C*H), 127.5 (=*C*H), 127.4 (=*C*H), 127.1 (=*C*H), 127.0 (=*C*H), 126.8 (=*C*H), 126.7 (=*C*H), 123.5 (*quat*-C), 96.0 (*quat*-C), 86.9 (O*C*H), 59.2 (*quat*-C), 33.8 (*C*H_2), 25.3 (*C*H_2), 19.6 (*C*H_2), 13.2 (*C*H_3); MS (FD^+) *m*/*z* 522 (M^+). Anal. Calcd for $C_{37}H_{30}O_3$: C, 85.03; H, 5.79. Found: C, 85.19; H, 5.89.

Reaction of α-Diazo Ketone 12a with 2,3,4,5-Tetraphenylcyclopenta-2,4-dienone, Preparation of Cycloadduct 35b.[50] A mixture of 2,3,4,5-tetraphenylcyclopenta-2,4-dienone (575 mg, 1.5 mmol) and diazo ketone **12a** (180 mg, 1.0 mmol) was allowed to react with rhodium(II) acetate dimer (4.4 mg) in dry DCM (10 mL) for 2.5 h at room temperature under an argon atmosphere according to the general method A to afford the cycloadduct **35b** (348 mg) in 65% yield as a colorless solid: mp 151−153 °C (DCM/hexane); IR (KBr) 3058, 2942, 1764, 1600, 1492, 1443, 1375, 1036 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.25−7.13 (10H, m, arom-*H*), 6.99−6.75 (10H, m, arom-*H*), 4.81 (1H, s, OC*H*), 1.99−1.26 (8H, m), 0.25 (3H, s, CH_3); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 210.2 (*C*=O), 146.5 (*quat*-C), 146.0 (*quat*-C), 142.1 (*quat*-C), 140.6 (*quat*-C), 136.8 (*quat*-C), 134.5 (*quat*-C), 134.3 (*quat*-C), 133.8 (*quat*-C), 132.8 (=*C*H), 130.4 (=*C*H), 129.7 (=*C*H), 129.5 (=*C*H), 127.5 (=*C*H), 127.3 (=*C*H), 127.1 (=*C*H), 126.9 (=*C*H), 126.8 (=*C*H), 126.6 (=*C*H), 114.9 (*quat*-C), 94.5 (*quat*-C), 87.1 (O*C*H), 53.6 (*quat*-C), 32.8 (*C*H_2), 26.1 (*C*H_2), 22.8 (*C*H_2), 19.7 (*C*H_2), 12.2 (*C*H_3); MS (FD^+) *m*/*z* 536 (M^+). Anal. Calcd for $C_{38}H_{32}O_3$: C, 85.05; H, 6.01. Found: C, 85.01; H, 6.04.

Reaction of α-Diazo Ketone 12c with 2,3,4,5-Tetraphenylcyclopenta-2,4-dienone, Preparation of Cycloadducts $35c_1/c_2$.[50] A mixture of 2,3,4,5-tetraphenylcyclopenta-2,4-dienone (575 mg, 1.5 mmol) and diazo ketone **12c** (180 mg, 1.0 mmol) was allowed to react with rhodium(II) acetate dimer (4.4 mg) in dry DCM (10 mL) for 2 h at room temperature under an argon atmosphere according to the general method A to afford the cycloadducts $\mathbf{35c_1}$ and $\mathbf{35c_2}$ (316 mg) in 59% over all yield in the ratio of 1:0.35. $\mathbf{35c_1}$: Colorless solid; mp 155−157 °C (DCM/hexane); IR (KBr) 2931, 2854, 1723, 1598, 1489, 1440 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.25−7.00 (10H, m, arom-*H*), 6.98−6.94 (6H, m, arom-*H*), 6.79−6.75 (4H, m, arom-*H*), 4.97 (1H, s, OC*H*), 1.95−1.45 (5H, m), 1.41−0.80 (6H, m); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 202.4 (*C*=O), 148.3 (*quat*-C), 145.4 (*quat*-C), 142.2 (*quat*-C), 138.2 (*quat*-C), 135.8 (*quat*-C), 134.4 (*quat*-C), 134.0 (*quat*-C), 131.4 (=*C*H), 130.9 (=*C*H), 129.7 (=*C*H), 127.6 (=*C*H), 127.4 (=*C*H), 127.3 (=*C*H), 127.2 (=*C*H), 127.1 (=*C*H), 126.8 (=*C*H), 126.7 (=*C*H), 111.8 (*quat*-

(49) Spectral data (Proton and Carbon NMR) given for the predominant isomer in the mixture.

(50) A mixture of benzene−hexane was used as eluent. Initially, the crude residue was allowed to adsorb in the silica gel column for a longer time to obtain the pure products.

C), 94.6 (*quat*-C), 85.9 (O*C*H), 41.5 (*C*H_2), 40.7 (*C*H_2), 33.9 (*C*H_2), 33.8 (*C*H_2), 29.7 (*C*H_2), 27.8 (*C*H_2), 23.2 (*C*H_2); MS (FD$^+$) *m*/*z* 536 (M$^+$). Anal. Calcd for $C_{38}H_{32}O_3$: C, 85.05; H, 6.01. Found: C, 85.00; H, 5.99. **35c$_2$**: Colorless solid; mp 159−161 °C (DCM/hexane); IR (KBr) 3057, 2932, 2859, 1725, 1599, 1491, 1444 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.25−7.20 (10H, m, arom-*H*), 6.99−6.94 (6H, m, arom-*H*), 6.79−6.75 (4H, m, arom-*H*), 4.91 (1H, s, OC*H*), 2.00−1.05 (8H, m), 0.87−0.62 (3H, m); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 202.4 (*C*═O), 148.5 (*quat*-C), 145.5 (*quat*-C), 142.0 (*quat*-C), 138.4 (*quat*-C), 136.1 (*quat*-C), 134.4 (*quat*-C), 134.3 (*quat*-C), 134.0 (*quat*-C), 131.8 (═*C*H), 130.9 (═*C*H), 129.7 (═*C*H), 127.6 (═*C*H), 127.5 (═*C*H), 127.3 (═*C*H), 127.2 (═*C*H), 127.1 (═*C*H), 126.8 (═*C*H), 126.7 (═*C*H), 111.0 (*quat*-C), 95.5 (*quat*-C), 85.4 (O*C*H), 43.5 (*C*H_2), 39.9 (*C*H_2), 33.6 (*C*H_2), 33.8 (*C*H_2), 29.7 (*C*H_2), 25.0 (*C*H_2), 23.5 (*C*H_2); MS (FD$^+$) *m*/*z* 536 (M$^+$). Anal. Calcd for $C_{38}H_{32}O_3$: C, 85.05; H, 6.01. Found: C, 84.96; H, 6.02.

Reaction of α-Diazo Ketone 22 with 2,3,4,5-Tetraphenylcyclopenta-2,4-dienone, Preparation of Cycloadduct 38.[50] A mixture of 2,3,4,5-tetraphenylcyclopenta-2,4-dienone (575 mg, 1.5 mmol) and diazo ketone **22** (155 mg, 1.0 mmol) was allowed to react with rhodium(II) acetate dimer (4.4 mg) in dry DCM (10 mL) for 2.5 h at room temperature under an argon atmosphere according to the general method A to afford the cycloadduct **38** (271 mg) in 53% yield as a colorless solid: mp 159−162 °C (DCM/hexane); IR (KBr) 3028, 1765, 1489, 1441, 1299, 1266, 1129 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.26−7.10 (10H, m, arom-*H*), 6.98−6.80 (10H, m, arom-*H*), 4.77 (1H, s, OC*H*), 1.39 (3H, s, CH_3), 0.85 (3H, s, CH_3), 0.27 (3H, s, CH_3); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 210.8 (*C*═O), 147.0 (*quat*-C), 146.7 (*quat*-C), 142.7 (*quat*-C), 141.2 (*quat*-C), 137.5 (*quat*-C), 134.9 (*quat*-C), 134.8 (*quat*-C), 134.3 (*quat*-C), 133.2 (═*C*H), 131.0 (═*C*H), 130.2 (═*C*H), 130.1 (═*C*H), 128.0 (═*C*H), 127.8 (═*C*H), 127.6 (═*C*H), 127.5 (═*C*H), 127.3 (═*C*H), 127.2 (═*C*H), 116.3 (*quat*-C), 95.9 (*quat*-C), 87.5 (O*C*H), 54.9 (*quat*-C), 23.5 (*C*H_3), 16.0 (*C*H_3), 14.8 (*C*H_3); MS (FD$^+$) *m*/*z* 510 (M$^+$). Anal. Calcd for $C_{36}H_{30}O_3$: C, 84.68; H, 5.92. Found: C, 84.76; H, 5.91.

X-ray Crystal Structure Analyses. Crystal data for compound **35a**: $C_{37}H_{33}O_3$, M = 522.64, 0.20 × 0.14 × 0.06 mm^3, triclinic, $P\bar{1}$, a = 11.37(2) Å, b = 11.623(7) Å, c = 13.455(13) Å, α = 110.83(9)°, β = 114.86(10)°, γ = 93.10(13)°, V = 1464(3) Å^3, T = 293(2) K, R_1 = 0.1176, wR_2 = 0.22882 on observed data, z = 2, D_{calcd} = 1.227 g cm^{-3}, F(000) = 572, absorption coefficient = 0.079 mm^{-1}, λ = 0.7107 Å, 3822 reflections were collected on a CAD-4 diffractometer, 1438 observed reflections ($I \geq 2\sigma(I)$). The largest difference peak and hole = 0.870 and −0.450e Å^{-3}, respectively.

Crystal data for compound **38**: $C_{36}H_{30}O_3$, M = 510.63, 0.20 × 0.16 × 0.10 mm^3, triclinic, $P\bar{1}$, a = 11.515(3) Å, b = 11.841(4) Å, c = 13.366(3) Å, α = 113.61(2)°, β = 112.17(2)°, γ = 93.78(2)°, V = 1495(7) Å^3, T = 293(2) K, R_1 = 0.0852, wR_2 = 0.2795 on observed data, z = 2, D_{calcd} = 1.041 g cm^{-3}, F(000) = 492, absorption coefficient = 0.066 mm^{-1}, λ = −0.7107 Å, 5247 reflections were collected on a CAD-4 diffractometer, 3582 observed reflections ($I \geq 2\sigma(I)$). The largest difference peak and hole = 1.013 and −0.204e Å^{-3}, respectively. The structures were solved by direct methods and refined by full-matrix least squares on F^2 using SHELXL-97.

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Supporting Information Available: Tables of X-ray crystallographic data and CIF files of spiro epoxy-bridged tetrahydropyranone derivatives **35a** and **38**. This material is available free of charge via the Internet at http://pubs.acs.org.

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