(6 mL). The mixture was filtered through silica gel, and the filtrate was concentrated in vacuo. The product was purified by bulb-to-bulb distillation under aspirator pressure to afford 2.1 g of alcohol **15** (80%) as a colorless liquid: $[\alpha]_D$ +12.77° (*c* 9.13, $CHCl_3$); ^1H NMR (90 MHz, $CDCl_3$) δ 3.55 (br s, 1 H), 3.35 (m, 2 H), 1.3 (m, 5 H), 0.8 (m, 6 H); IR ($CHCl_3$) 3620, 3450, 2900, 1460, 1030 cm^{-1}.

Preparation of Enoate 16. Me_2SO (3.3 mL, 46.2 mmol) was added dropwise to a solution of oxalyl chloride (1.84 mL, 21.7 mmol) in CH_2Cl_2 (120 mL) at −78 °C. After 5 min, alcohol **15** (1.85 g, 18.1 mmol) was added as a solution in CH_2Cl_2 (5 mL). After 30 min, the mixture was treated with Et_3N (12.7 mL, 90.5 mmol), and the solution was warmed to room temperature. (Carbethoxyethylidene)triphenylphosphorane (8 g, 22 mmol) was added, and the solution was heated to reflux and allowed to concentrate to ~80 mL. After 48 h at reflux, the mixture was concentrated, and the residue was filtered through silica gel (Et_2O eluant). The product was purified by bulb-to-bulb distillation (aspirator pressure) to afford 3.0 g (90%) of pure (*E*)-enoate **16**: $[\alpha]_D$ −27.04° (*c* 7.4, $CHCl_3$); IR ($CHCl_3$) 2900, 1700, 1650, 1450, 1265, 1100 cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 6.5 (br d, 1 H, *J* = 10 Hz), 4.2 (q, 2 H, *J* = 7 Hz), 2.5 (m, 1 H), 1.8 (br s, 3 H), 1.3 (m, 5 H), 0.9 (m, 5 H).

Preparation of Enal 17. DIBAL (57 mL of a 1 M solution in hexane, 57 mmol) was added to a solution of enoate **16** (3.0 g, 16.3 mmol) in CH_2Cl_2 (100 mL) at −78 °C. After 1 h the reaction was quenched by the addition of MeOH (1 mL) and saturated NH_4Cl solution (0.5 mL), and the mixture was warmed to room temperature. The mixture was diluted with ether (100 mL) and filtered through silica gel to afford 2.3 g of crude alcohol.

Me_2SO (2.9 mL, 40.5 mmol) was added dropwise to a solution of oxalyl chloride (1.65 mL, 19.4 mmol) in CH_2Cl_2 (100 mL) at −78 °C. After 5 min, the crude alcohol from above (2.3 g, 16.2 mmol) was added as a solution in CH_2Cl_2 (5 mL). After 30 min, the mixture was treated with Et_3N (11.4 mL, 81 mmol), and the solution was warmed to room temperature. The mixture was poured into brine (50 mL) and extracted with CH_2Cl_2 (3 × 100 mL). The organic layers were dried ($MgSO_4$) and concentrated in vacuo. The residue was purified by flash chromatography (5% ether/hexanes) to give 1.83 g of enal **17** (80%): $[\alpha]_D$ −22.18° (*c* 1.33, $CHCl_3$); ^1H NMR (90 MHz, $CDCl_3$) δ 9.4 (s, 1 H), 6.25 (d, 1 H, *J* = 9.0 Hz), 2.7 (m, 1 H), 1.75 (s, 3 H), 1.35 (m, 4 H), 1.08 (d, 3 H, *J* = 8 Hz), 0.9 (t, 3 H, *J* = 7 Hz); IR ($CHCl_3$) 1685, 1460, 1160 cm^{-1}.

Preparation of Tosylate 11. A solution of aldehyde **17** (381 mg, 2.72 mmol) in CH_2Cl_2 (20 mL) was treated with $TiCl_4$ (598 μL, 5.44 mmol) at −78 °C. After 15 min, silyl ketene acetal **18** (1.25 g, 4.08 mmol) was added dropwise. The solution turned dark red and was warmed to −50 °C for 4 h. The mixture was warmed to 0 °C and quenched with saturated $NaHCO_3$ (10 mL). The product was extracted with CH_2Cl_2 (3 × 30 mL), dried ($MgSO_4$), and concentrated in vacuo. The crude product was dissolved in THF (20 mL) and treated with LAH (7 mL of a 1 M solution in ether, 7 mmol) at 0 °C. After 1 h, the reaction was quenched by the sequential addition of H_2O (250 μL), 15% NaOH (250 μL), and H_2O (750 μL). The salts were filtered and the filtrate was concentrated. The residue was flash chromatographed (50% ethyl acetate/hexanes) to afford an 8:1 mixture of threo/erythro isomers with > 20:1 face selectivity in 50% overall yield. The mixture of diols (271 mg, 1.36 mmol) was selectively tosylated with TsCl (534 mg, 2.8 mmol) in pyridine (4 mL) and catalytic DMAP at 60 °C for 30 min to obtain (after flash chromatography) 365 mg (76%) of a mixture of primary tosylates **11**. The desired major isomer could be separated by careful column chromatography (15% ethyl acetate/hexanes) or by HPLC: $[\alpha]_D$ −14.7° (*c* 3.05, $CHCl_3$); ^1H NMR (250 MHz, $CDCl_3$) δ 7.8 (m, 2 H), 7.35 (m, 2 H), 5.22 (br d, 1 H, *J* = 9.5 Hz), 4.16 (m, 2 H), 3.76 (dd, 1 H, *J* = 9.5, 2.7 Hz), 2.48 (s, 3 H), 2.39 (m, 1 H), 1.95 (m, 1 H), 1.58 (s, 3 H), 1.2 (m, 3 H), 0.9 (m, 11 H); IR ($CHCl_3$) 3600, 1220, 970, 900, 700 cm^{-1}; MS (20 eV), *m/z* (relative intensity) 354 (9.1, M^+), 336 (5.1). Analysis C, H.

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Communications

Synthesis of Cycloalkenones via the Intramolecular Cyclopropanation of Furanyl Diazo Ketones

Summary: The reaction of α-diazo ketones derived from furanyl and benzofuranyl propionic acids with rhodium(II) acetate leads to cycloalkenones in high yield. Mechanistically, the reaction involves addition of the keto carbene to the furanyl π-bond followed by an electrocyclic ring opening reaction.

Sir: The general importance of cyclohexenones and cyclopentenones has led to the development of various methods for the synthesis of these compounds.[1,2] We report a new route to such systems that is based on the intramolecular cycloaddition reaction of an α-keto carbene.[3] Scheme I summarizes the approach. The key step is the thermal rearrangement of an oxabicyclo[3.1.0]hexene intermediate. Intramolecular cyclization of α-carbonyl carbenes and carbenoids has found widespread application for the preparation of a variety of theoretically and biologically interesting compounds.[4-12] Aside from Scott's elegant synthesis of azulene,[13] however, few other intra-

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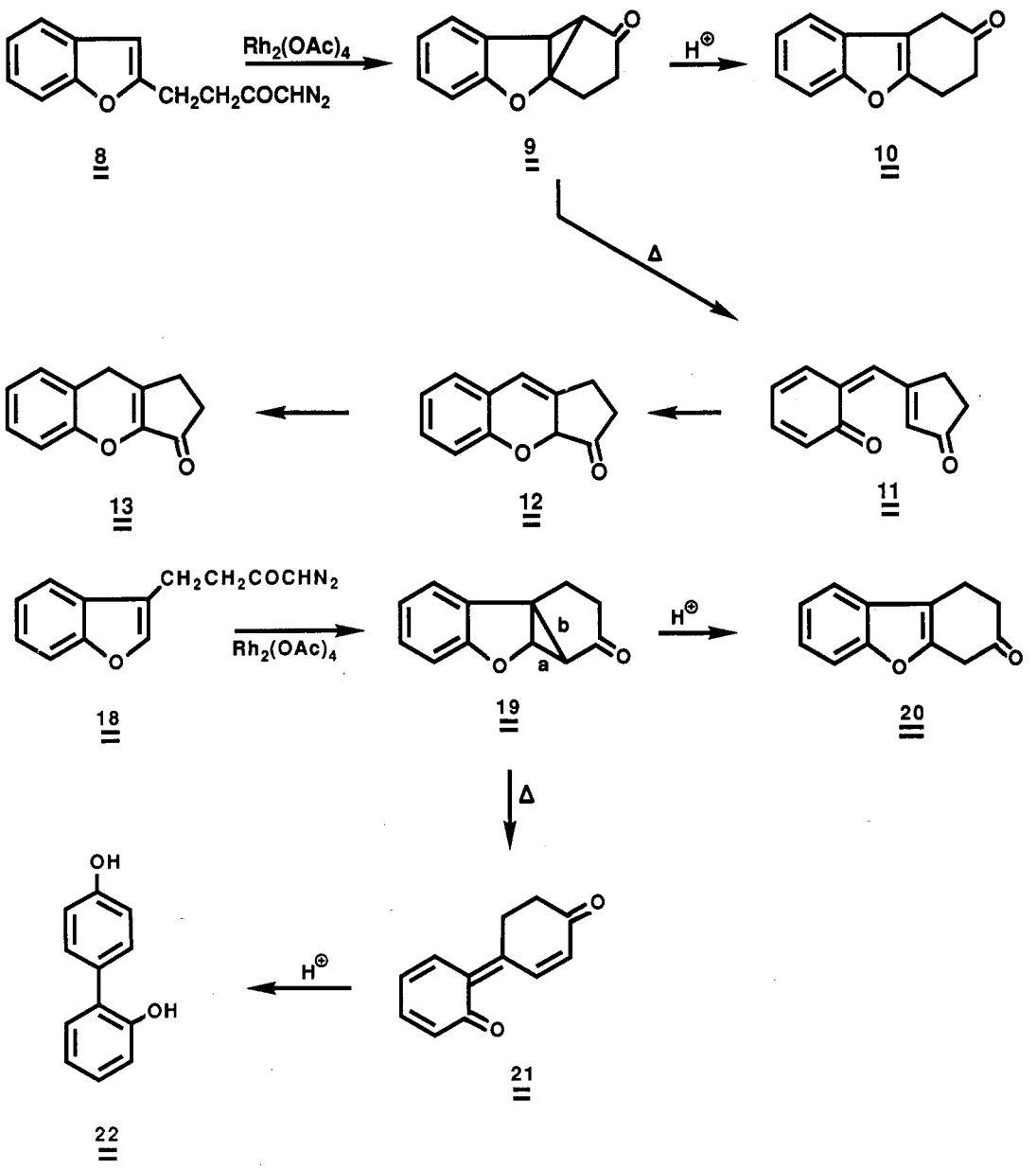
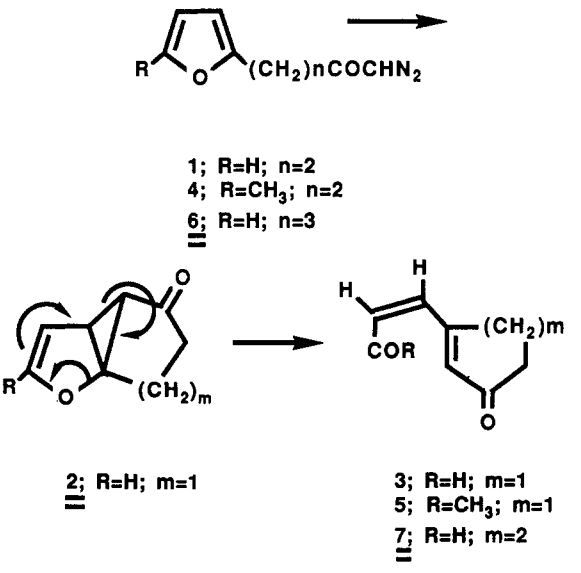


molecular keto carbene additions to aromatic rings have been reported.

In seeking to develop a general synthetic entry into the 3-vinylcycloalkenone series for eventual Diels–Alder chemistry, we have investigated the reaction of α-diazo ketones derived from furanyl- and benzofuranylpropionic acids.[14,15] α-Diazo ketones **4** and **6** afforded cycloalkenones **5** and **7** in excellent yield when exposed to rhodium(II) acetate in benzene at 25 °C. Mechanistically, this reaction involves addition of the keto carbene across the furanyl π-bond to give an oxabicyclo[3.1.0]hex-2-ene intermediate (**2**) that undergoes a subsequent cycloreversion reaction.[16]

Scheme I



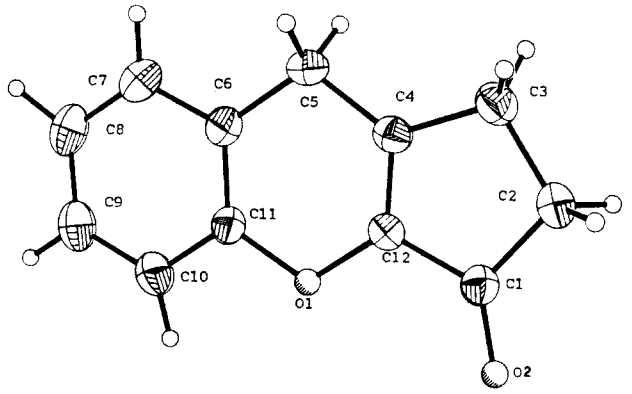
Support for the postulated mechanism was obtained by treating the closely related benzo diazo ketone **8** with

(13) Scott, L. T. *J. Chem. Soc., Chem. Commun.* **1973**, 882. Scott, L. T.; Minton, M. A.; Kirms, M. A. *J. Am. Chem. Soc.* **1980**, *102*, 6311.

(14) α-Diazo ketone **1**, the parent member of the series of compounds studied, had previously been reported to afford *trans*-cyclopentenone **3b** in 60% yield when exposed to copper sulfate in refluxing cyclohexane.[15] In actuality, the product actually formed was the cis isomer **3a**: mp 65–66 °C; NMR ($CDCl_3$, 90 MHz) δ 2.57 (t, 2 H, J = 5.0 Hz), 2.95 (t, 2 H, J = 5.0 Hz), 6.21 (dd, 1 H, J = 13.0 and 8.0 Hz), 6.33 (s, 1 H), 7.21 (d, 1 H, J = 13.0 Hz), and 10.19 (d, 1 H, J = 8.0 Hz). This material was converted into the trans isomer **3b** by treatment with iodine in benzene. **3b**: mp 112–113 °C; NMR ($CDCl_3$, 90 MHz) δ 2.54 (t, 2 H, J = 5.0 Hz), 2.88 (t, 2 H, J = 5.0 Hz), 6.46 (s, 1 H), 6.53 (dd, 1 H, J = 17.0 and 7.0 Hz), 7.61 (d, 1 H, J = 17.0 Hz), and 9.77 (d, 1 H, J = 7.0 Hz).

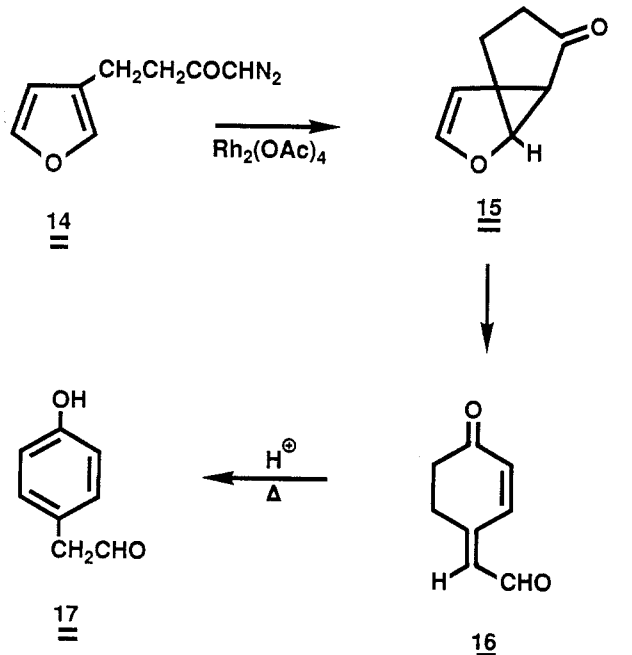
(15) Nwaji, M. N.; Onyiriuka, O. O. *Tetrahedron Lett.* **1974**, 2255.

rhodium(II) acetate at 25 °C. Under these conditions, cyclopropyl ketone **9** could be isolated in 85% yield as a crystalline solid, mp 99–100 °C. Treatment of **9** with a trace of acid produced dihydrobenzofuranone **10** in excellent yield. On heating a sample of **9** at 180 °C for 7 h, a novel rearrangement occurred, producing benzopyranone **13** in 82% yield. The structure of **13** was assigned on the basis of its characteristic spectral data. Unequivocal proof of this assignment derives from a single-crystal X-ray structure analysis. The unexpected conversion of **9** to **13**



can be rationalized in terms of a ring cleavage reaction to give the *o*-quinoidal intermediate **11**, which undergoes a subsequent electrocyclic ring closure followed by an acid-induced 1,3-hydrogen shift.

Since we were interested in the synthetic utility of this reaction, we undertook a study of the cycloaddition with several 3-furanyl substituted diazo ketones. Addition of rhodium(II) acetate to a solution of **14** in benzene produced



an efflux of nitrogen gas and provided *cis*-(4-oxo-2-cyclohexen-1-ylidene)acetaldehyde (**16**) in 88% yield: NMR ($CDCl_3$, 360 MHz) δ 2.65 (t, 2 H, J = 5.0 Hz), 2.90 (t, 2 H, J = 5.0 Hz), 6.14 (d, 1 H, J = 7.0 Hz), 6.29 (d, 1 H, J = 10.0 Hz), 8.01 (d, 1 H, J = 10.0 Hz), and 10.14 (d, 1 H, J = 7.0 Hz). Chemical support for this structure was obtained by its acid-catalyzed rearrangement to *p*-hydroxyphenylacetaldehyde (**17**). Formation of **16** can be rationalized by assuming intramolecular keto carbene addition to the furan π-bond to give **15**, which is rapidly converted to **16** via a 4 + 2 cycloreversion reaction.[17]

In order to examine the above transformation in a more general context, we undertook an investigation of 3-benzofuranyl diazo ketone **18**. Of particular interest was the possibility of isolating the suspected internal cycloadduct and studying its chemistry. Decomposition of **19** and intramolecular cycloaddition of the resulting carbenoid was efficiently accomplished by using the conventional rhodium(II) acetate protocol. This led to the formation of the internal cycloadduct **19** in 91% yield, mp 90–91 °C. Treatment of **19** with a catalytic amount of acid afforded dihydrobenzofuranone **20** in high yield. Ring opening of an unsymmetrical, conjugated cyclopropyl ketone has been shown to be a highly stereospecific process in rigid systems.[18] It is generally found that rupture occurs at the cyclopropane bond which has maximum overlap with the π-orbital of the carbonyl group. Examination of molecular models indicates that, on this basis, the cyclopropane linkage favored for an acid-induced scission is the exterior one (i.e., bond a). Cleavage of the interior bond (bond b) would violate the stereoelectronic principle formulated by Norin and Dauben,[18] since this linkage is aligned almost orthogonally to the carbonyl group. Thus, the isolation of **20** is quite surprising since its formation requires ring opening of the interior bond. One possible explanation is that **20** is actually formed by cleavage of the exterior bond to give a transient spiro cation which then undergoes a subsequent Wagner–Meerwein rearrangement. Reversible 1,2-group migrations that interconvert spiro and fused ring systems are known and provide reasonable analogy for this suggestion.[19] Unfortunately, a clear distinction between these two options is not possible without labelling studies. Cyclopropyl ketone **19** was also found to undergo a clean thermal rearrangement to diphenol **22**. The formation of **22** probably proceeds via the intermediacy of **21** which then undergoes a series of hydrogen shifts to give the fully aromatized system.

In conclusion, the internal cycloaddition reaction of furanyl diazo ketones provides a useful route to a series of substituted cycloalkenones. We are interested in expanding this approach to different heterocycles with varying ring sizes and will discuss further details of this reaction in subsequent papers.

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Supplementary Material Available: ^1H NMR and X-ray data for important compounds (1 page). Ordering information is given on any current masthead page.

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