a stream of nitrogen and the remaining solvent removed in vacuo. Chromatography (SiO_2, 1 × 6 cm, 10% tetrahydrofuran–ethyl acetate eluant) afforded 66.7 mg (74.2 mg theoretical, 90%) of **1** as a white foam. Recrystallization from ethyl acetate–hexane gave **1** as white needles: mp 188–189 °C; $[\alpha]^{25}_D$ −15.95° (*c* 1.56, methanol); ^{1}H NMR ($CDCl_3$) δ 6.01 (m, 1 H, NH), 5.50 (m, 2 H, CH=CH), 3.76 (m, 4 H, ethylene ketal CH_2's, overlapping m, 1 H, NCH), 3.60 (s, 3 H, CO_2CH_3), 3.05–1.25 (m, 9 H, aliphatic), 1.92 (s, 3 H, $NCOCH_3$); IR ($CHCl_3$) ν_{max} 3450, 3380, 3005, 2960, 1720, 1660, 1265, 1190 cm^{-1}; EIMS, *m/e* (relative intensity) 309 (M^+, 4), 250 (23), 191 (9), 99 (30), 87 (13), 86 (base), 77 (20), 56 (14).

Anal. Calcd for $C_{16}H_{23}NO_5$: C, 62.12; H, 7.49; N, 4.53. Found: C, 61.90; H, 7.50; N, 4.34.

(4*R*,9*R*,10*R*)-4-(*N*-Benzoyl-*N*-acetylamino)-9-(methoxycarbonyl)-*cis*-Δ^6-1-octalone Ethylene Ketal (22). Benzoyl chloride (12 μL, 14.5 mg, 0.103 mmol, 5.3 equiv) was added to a 25 °C solution of triethylamine (19 μL, 13.8 mg, 0.136 mmol, 7.0 equiv), 4-(dimethylamino)pyridine (0.05 equiv), and the acetylamide **1** (6.0 mg, 0.019 mmol) in dry methylene chloride (150 μL) and the resulting mixture was stirred at 25 °C for 15 h.[29] The reaction was quenched with saturated aqueous ammonium chloride (1 mL) and the resulting mixture was extracted with ethyl acetate (5 × 1 mL). The combined organic extracts were dried over sodium sulfate and concentrated in vacuo. Chromatography (SiO_2, 0.6 × 6 cm, 40% ethyl acetate–hexane eluant) gave 7.5 mg (7.9 mg theoretical, 96%) of the imide **22** as a solid: ^{1}H NMR ($CDCl_3$) δ 7.50 (m, 5 H, aromatic), 5.50 (m, 1 H, CH=CH), 3.84 (m, 4 H, ethylene ketal CH_2's; overlapping m, 1 H, NCH), 3.68 (s, 3 H, CO_2CH_3), 3.05–1.60 (m, 12 H, aliphatic); IR ($CHCl_3$) ν_{max} 3040, 1725, 1700 (shoulder), 1660, 1240 cm^{-1}; EIMS, *m/e* (relative intensity) 413 (M^+, 0.04), 371 (0.05), 273 (0.05), 272 (0.05), 250 (22), 105 (96), 99 (45), 86 (base), 77 (87), 43 (38).

(4*R*,9*R*,10*R*)-4-(Benzoylamino)-9-(methoxycarbonyl)-*cis*-Δ^6-1-octalone Ethylene Ketal (23) and 1. A solution of 2.0 M lithium methoxide in methanol (15 μL, 0.030 mmol, 1.7 equiv) was added to a 0 °C solution of the imide **22** (7.5 mg, 0.0018 mmol) in dry methanol (325 μL). The resulting mixture was stirred at 0–25 °C for 4 h and quenched with saturated aqueous ammonium chloride (1.5 mL).[30] The aqueous solution was extracted with ethyl acetate (6 × 1 mL), and the combined extracts were dried over sodium sulfate and concentrated in vacuo. Chromatography (SiO_2, 0.6 × 6 cm, 25 mL of 60% ethyl acetate–hexane, then 25 mL of 30% tetrahydrofuran–ethyl acetate eluant) afforded 3.3 mg (6.7 theoretical, 49%) of the benzoylamide **23** as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 7.68 (m, 2 H, aromatic), 7.43 (m, 3 H, aromatic), 5.88–5.45 (m, 3 H, CH=CH/NH), 4.10 (m, 1 H, NCH), 3.87 (m, 4 H, ethylene ketal), 3.70 (s, 3 H, CO_2CH_3), 3.10–1.50 (m, 9 H, aliphatic); IR ($CHCl_3$) ν_{max} 3450, 3010, 2960, 1720, 1655, 1510, 1265, 1200, 740, 660 cm^{-1}; EIMS, *m/e* (relative intensity) 371 (M^+, 5), 259 (5), 250 (12), 122 (63), 105 (base), 86 (27), 77 (55), 57 (12), 51 (17); HRMS, *m/e* 371.1734, $C_{21}H_{25}NO_5$ requires 371.1731.

Acetylamide **1** was isolated in 45% (2.5 mg, 5.6 mg theoretical) and was identical with original material prepared as described above.

Acknowledgment. This work was assisted financially by the Searle Scholars Program and the National Institutes of Health.

Regioselectivity of the Intermolecular Diels–Alder Reaction of Acyl Nitroso Compounds (*C*-Nitrosocarbonyl Compounds) and Nitrosoformates (*O*-Nitrosocarbonyl Compounds). Preparation of Functionalized *cis*-Δ^6-1-Octalones

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A study of the regioselectivity of the intermolecular Diels–Alder reaction of (nitrosocarbonyl)benzene and methyl nitrosoformate with representative electron-rich and electron-deficient 2-substituted 1,3-cyclohexadienes is described. The observed results are consistent with the prediction that nitrosocarbonyl compounds behave as dependable electron-deficient 2π components in a normal ($HOMO_{diene}$ controlled) Diels–Alder reaction with electron-rich 2-substituted dienes and additionally illustrate that they may serve as useful 2π components in regioselective Diels–Alder reactions with electron-deficient 2-substituted 1,3-cyclohexadienes. The latter results are consistent with either a normal ($HOMO_{diene}$ controlled) or inverse electron demand ($LUMO_{diene}$ controlled) Diels–Alder reaction. Utilization of the nitrosocarbonyl Diels–Alder adducts in a stereospecific preparation of functionalized, *cis*-Δ^6-1-octalones is detailed. In contrast to predictions based on secondary orbital control (allylic axial heteroatom orbital control), [4 + 2] cycloaddition of butadiene with the 5- and 6-substituted *N*-benzoyl 3-aza-2-oxobicyclo[2.2.2]oct-5-enes occurs on the face bearing the RCON–O bridge.

The orientation of the intermolecular Diels–Alder addition of aryl nitroso compounds with dienes has been investigated in detail and a rationalization of the observed regioselectivity has been presented based on the consideration of the relative stabilization of the two possible dipolar transition states.[2,3] The predicted and observed distal (ortho)[3] adduct in the cycloaddition of nitrosobenzene with isoprene is shown in eq 1. By contrast, a study of regioselectivity of the addition of nitrosobenzene with β-myrcene, a 2-alkyl-substituted 1,3-butadiene, re-

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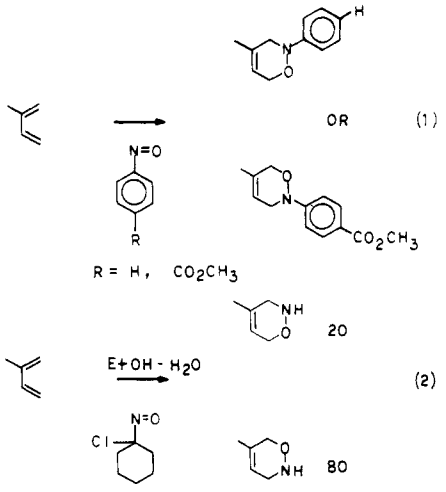
(2) For reviews including Diels–Alder reactions of electrophilic *C*-nitroso compounds see: Kirby, G. W. *Chem. Soc. Rev.* **1977**, *6*, 1. Weinreb, S. M.; Staib, R. R. *Tetrahedron* **1982**, *38*, 3087.

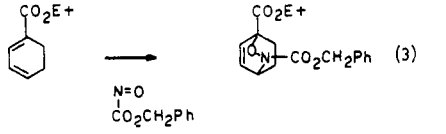
(3) (a) Kresze, G.; Firl, J. *Fortschr. Chem. Forsch.* **1969**, *11*, 245. (b) Wichterle, D.; Kolinsky, M. *Chem. Listy* **1953**, *47*, 1787. Kresze, G.; Kosbahn, W. *Tetrahedron* **1971**, *27*, 1931. Kresze, G.; Saitner, H.; Firl, J.; Kosbahn, W. *Ibid.* **1971**, *27*, 1941. Taylor, E. C.; McDaniel, K.; Skotnicki, J. S. *J. Org. Chem.* **1984**, *49*, 2500. "Proximal" and "distal" refer to the relative orientation (distance) of the dienophile center of highest priority (nitroso oxygen) with the diene center of highest priority (substituted center of cyclohexadiene). We thank a referee for suggesting this terminology.

0022-3263/85/1950-1911$01.50/0

vealed a marked dependence on reaction temperature and solvent.[4a] Similarily, the observed, though not predicted, product of the addition of α-chloro nitrosocyclohexone with isoprene, eq 2, possesses the reversed orientation of addition.[5] In the absence of a better rationalization this reversal in regioselectivity has been attributed to steric factors despite the fact that such effects must be relatively removed from the reaction centers. Addition of a para electron-withdrawing group to nitrosobenzene, *p*-(methoxycarbonyl)nitrosobenzene, reverses the regioselectivity of [4 + 2] addition with isoprene, eq 1, and affords exclusively the proximal (para)[3] Diels–Alder adduct.[4b] This latter work suggests that electron-deficient nitrosocarbonyl compounds would behave as dependable electron-deficient 2π components in a normal ($HOMO_{diene}$ controlled) Diels–Alder reaction with electron-rich dienes and guidelines governing the regioselective predictions of such reactions may be applicable.[6]



The reaction of nitrosocarbonyl compounds with electron-deficient dienes bearing an electron-withdrawing substituent at the 1-position have been extensively studied and have found significant synthetic applicability. The addition affords exclusively the proximal (meta)[3] adducts as illustrated in eq 3.[7] In the absence of a better rationalization, the formation of the proximal adducts in such instances has been attributed to steric factors.[3,7]



Herein, we describe full details[8] of a study of the orientation of the intermolecular[2,8] Diels–Alder reaction of nitrosocarbonyl compounds, (nitrosocarbonyl)benzene and methyl nitrosoformate, with weakly electron-rich and electron-deficient 2-substituted 1,3-cyclohexadienes,[2,8] systems relatively free of important steric considerations. The observed results are consistent with the prediction that nitrosocarbonyl compounds behave as well-defined electron-deficient 2π components in a normal ($HOMO_{diene}$ controlled)[9] Diels–Alder reaction with electron-rich 2-substituted dienes *and* additionally illustrate that they may serve as useful 2π components in regioselective Diels–Alder reactions with electron-deficient 2-substituted 1,3-cyclohexadienes. The latter results are consistent with either a normal ($HOMO_{diene}$ controlled) or inverse electron demand ($LUMO_{diene}$ controlled)[9] Diels–Alder reaction.

Table I. Diels–Alder Reaction of Nitrosocarbonyl Compounds with 2-Substituted 1,3-Cyclohexadienes

substrate	conditions[a]	product(s), % yield[b]
1	A, CH_2Cl_2, 25 °C, 1 h	**2/3**, 45/16
	A, CH_2Cl_2, 0 °C, 1 h	31/24
	A, DMF, 25 °C, 3 h	23/5
	A, DMF, 0 °C, 3 h	30/13
	B, CH_2Cl_2, 40 °C, 5 h	11/4
	B, C_6H_6, 60 °C, 5 h	43/12
1	C, CH_2Cl_2, 25 °C, 1 h	**4/5**, 72 (50/16)[c]
6	A, CH_2Cl_2, 25 °C, 1 h	**7/8**, 47/16
	A, DMF, 25 °C, 3 h	47/16
6	C, DMF, 25 °C, 3 h	**9/10**, 30/11

[a] A: Benzohydroxamic acid[16a] (2.2 equiv) was added dropwise to a solution of diene and $(n\text{-Bu})_4NIO_4$[16b] (2.31 equiv). B: A solution of diene and the (nitrosocarbonyl)benzene 9,10-dimethylanthracene adduct[3,8] (1.1 equiv) was warmed at the described temperature. C: Methyl *N*-hydroxycarbamate[16c] (2.2 equiv) was added dropwise to a solution of the diene and $(n\text{-Bu})_4NIO_4$[16b] (2.31 equiv). [b] All products exhibited the expected ^1H NMR, IR, and MS characteristics consistent with the assigned structure and gave satisfactory CHN analysis or HRMS information. All yields (ratios) are based on purified, separated material isolated by chromatography (SiO_2). [c] The inseparable, purified adducts **4/5** (72% combined yield) were deprotected, 1.2 equiv $(n\text{-Bu})_4NF$, THF, 25 °C, 30 min, and the isomeric alcohols were separated (50% and 16% yield, respectively) and fully characterized.

Regioselectivity of the Diels–Alder Reaction of Nitrosocarbonyl Compounds with 2-Substituted 1,3-Cyclohexadienes. Table I and eq 4 and 5 detail the results of a study of the regioselectivity of the [4 + 2] cycloaddition of nitrosocarbonyl compounds with representative 2-substituted 1,3-cyclohexadienes. Thermal cycloaddition of (nitrosocarbonyl)benzene and methyl nitrosoformate with the weakly electron-rich 2-[[(*tert*-butyldimethylsilyl)oxy]methyl]-1,3-cyclohexadiene (**1**) afforded predominately the proximal (para) adducts **2** and **4**, eq 4. The structure of **2**, the major regioisomer of the addition of (nitrosocarbonyl)benzene with 2-[[(*tert*-butyldimethylsilyl)oxy]methyl-1,3-cyclohexadiene (**1**), was confirmed by X-ray analysis of **11**.[10] The identification of **4**, the major adduct of the reaction of methyl nitrosoformate with **1**, was drawn by analogy with the results obtained with (nitrosocarbonyl)benzene. The reaction solvent, reaction temperature, and source of the nitrosocarbonyl compound, while influencing the overall yield of the reaction, have little effect on the observed ratio of

(4) (a) Sasaki, T.; Eguchi, S.; Ishii, T.; Yamada, H. *J. Org. Chem.* **1970**, *35*, 4273. (b) Givens, R. S.; Choo, D. J.; Merchant, S. N.; Stitt, R. P.; Matuszewski, B. *Tetrahedron Lett.* **1982**, *23*, 1327 and reference 3a.

(5) Labaziewicz, H.; Riddell, F. G. *J. Chem. Soc., Perkin Trans. 1* **1979**, 2926. Riddell, F. G. *Tetrahedron* **1975**, *31*, 523. Leonard, N. J.; Playtis, A. J.; Skoog, F.; Schmitz, R. Y. *J. Am. Chem. Soc.* **1971**, *93*, 3056. Leonard, N. J.; Playtis, A. J. *J. Chem. Soc., Chem. Commun.* **1972**, 133.

(6) The regioselectivity of [4 + 2] cycloaddition reactions of nitrosocarboxyl compounds with 2-substituted-1,3-dienes may be comparable to that of α,β-unsaturated carbonyl compounds.

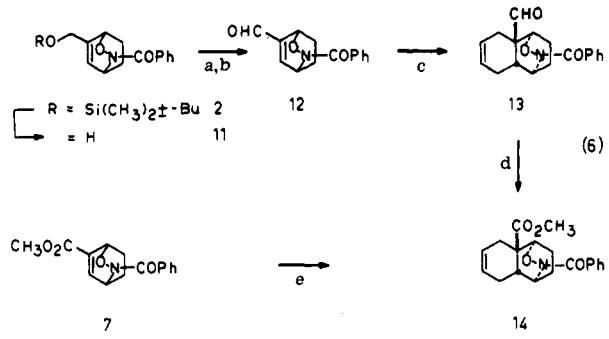
(7) Baldwin, J. E.; Bailey, P. D.; Gallacher, G.; Singleton, K. A.; Wallace, P. M. *J. Chem. Soc., Chem. Commun.* **1983**, 1049. For related studies, see: Belleau, B.; Au-Young, Y.-K. *J. Am. Chem. Soc.* **1963**, *85*, 64 and reference 3a.

(8) (a) Boger, D. L.; Patel, M. *J. Org. Chem.* **1984**, *49*, 4098. (b) For recent intramolecular acyl nitroso Diels–Alder reactions, see: Keck, G. E.; Nickell, D. G. *J. Am. Chem. Soc.* **1980**, *102*, 3632. Keck, G. E.; Fleming, S. A. *Tetrahedron Lett.* **1978**, 4763. Keck, G. E. *Tetrahedron Lett.* **1978**, 4767.

(9) Houk, K. N. *J. Am. Chem. Soc.* **1973**, *95*, 4092. Burnier, J. S.; Jorgensen, W. L. *J. Org. Chem.* **1983**, *48*, 3923.

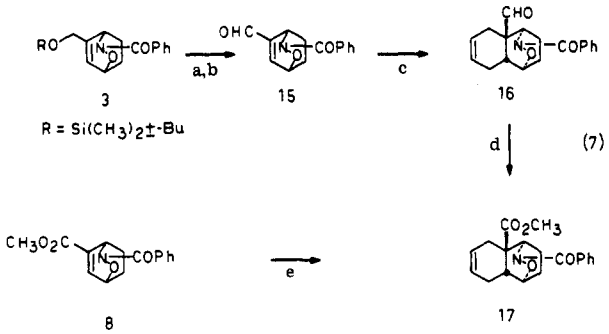
(10) (a) X-ray structure analysis was carried out on the free alcohol **11** generated from **2** and was performed by Crystalytics Company, Lincoln, NE. Full details of the X-ray structure determination are provided in the supplementary material of ref 8a. (b) X-ray structure analysis was performed by Professor F. Takusagawa, Department of Chemistry, University of Kansas and full details are provided as supplementary material.

Scheme I[a]



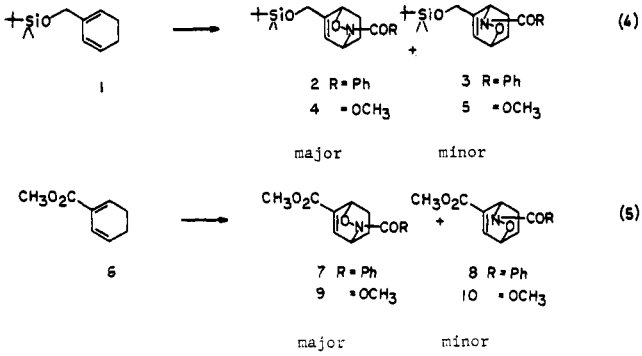
[a] (a) $(n\text{-Bu})_4NF$, THF, 25 °C, 15 min, 74%. (b) MnO_2, CH_2Cl_2, 25 °C, 1 h, 77%. (c) 1,3-Butadiene, mesitylene, 140 °C, 48 h, 81%. (d) PDC, DMF, 25 °C, 9 h; CH_2N_2, ether, 0 °C, 52%. (e) 1,3-Butadiene, mesitylene, 140 °C, 48 h, 70%.

Scheme II[a]



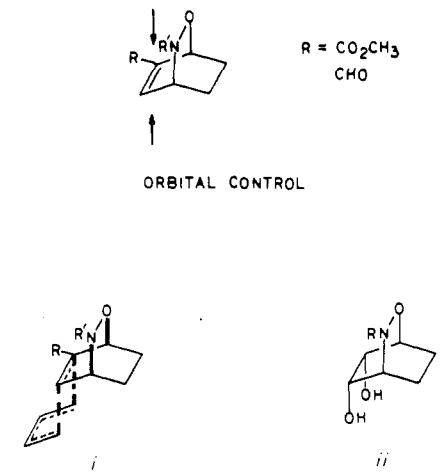
[a] (a) $(n\text{-Bu})_4NF$, THF, 25 °C, 15 min. (b) MnO_2, CH_2Cl_2, 25 °C, 1 h. (c) 1,3-Butadiene, mesitylene, 140 °C, 48 h. (d) PDC, DMF, 25 °C, 9 h; CH_2N_2, ether, 0 °C. 12% unoptimized overall yield from 3. (e) 1,3-Butadiene, mesitylene, 140 °C, 48 h, 64%.

regioadducts, indicating little polar character in the transition state of the cycloaddition.



Parallel studies with an electron-deficient 2-substituted 1,3-cyclohexadiene, methyl 1,3-cyclohexadiene 2-carboxylate (**6**), eq 5 and Table I, provided related findings. The proximal (para) adducts **7** and **9** were formed predominately and the ratio of products, **7**:**8** and **9**:**10**, showed no marked dependence on the reaction conditions. The observed regioselectivity is consistent with either a normal ($HOMO_{diene}$ controlled) or inverse electron demand ($LUMO_{diene}$ controlled)[9] Diels–Alder reaction *and* appears to contradict the predictions that can be drawn intuitively from similar studies with methyl 1,3-cyclohexadiene-1-carboxylate.[7] The structures of the major adducts **2** and **7** were confirmed by independent conversion to **14** and chemical correlation as detailed in eq 6. An identical correlation of the minor adducts **3** and **8** confirmed the remaining structure **8** and provided **17**, eq 7. The assignment of the adducts **9**/**10** were made by analogy to **7**/**8**.

Chart I



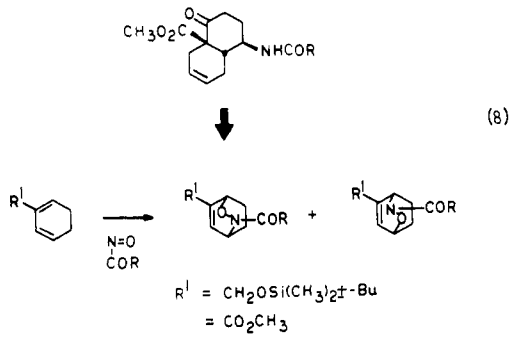
Preparation of Functionalized *cis*-Δ^6-1-Octalones. A Probe of Diels–Alder Stereocontrol (π-Facial Selectivity) by Allylic Heteroatom Substituents Utilizing a Rigid Cyclic Dienophile. Recent, considerable interest in potential stereocontrol effected by allylic substituents based on the observations that, in the absence of complexation or chelation control, the attack at an unsaturated system (C=C or C=O double bond) prefers an antiperiplanar approach to a large or heteroatom allylic substituent[11] provided the basis for the expectation that [4 + 2] cycloaddition of butadiene with the nitrosocarbonyl adducts should approach from the face opposite the RCON–O bridge. This π-facial selectivity, referred to as secondary orbital control,[12] has provided the basis for the rationalization of the observed stereocontrol in a Diels–Alder reaction of a nonrigid acyclic dienophile,[12] Chart I. Similarly, conventional considerations would seem to predict that approach of butadiene should occur on the face opposite to the RCON–O bridge.[13] For instance, treatment of *N*-(*p*-chlorophenyl)-3-aza-2-oxabicyclo-[2.2.2]oct-5-ene with potassium permanganate affords predominantly the diol ii which arises from attack of $KMnO_4$ from the face opposite the RN–O bridge, Chart

(11) The empirical generalizations of Cram, which allow qualitative predictions in the direction of nucleophilic attack at a carbonyl center [Cram, D. J.; Abd Elhafez, F. A. *J. Am. Chem. Soc.* **1952**, *74*, 5828. Cram, D. J.; Greene, F. D. *Ibid.* **1953**, *75*, 6005] have been shown to arise from a strong preference for nucleophilic attack to occur antiperiplanar to the vicinal bond to the largest group [Cherest, M.; Felkin, H.; Prudent, N. *Tetrahedron Lett.* **1968**, *2199*. Cherest, M.; Felkin, H. *Ibid.* **1968**, 2205. Anh, N. T.; Eisenstein, O. *Nouv. J. Chim.* **1977**, *1*, 61] and have been generalized to encompass π-facial stereoselectivity in additions (nucleophilic, electrophilic, radical, and cycloaddition) to π bonds: Caramella, P.; Rondan, N. G.; Paddon-Row, M. N.; Houk, K. N. *J. Am. Chem. Soc.* **1981**, *103*, 2438. This has been stated as "attack at an unsaturated site occurs such as to minimize antibonding secondary orbital interactions between the critical frontier molecular orbital of the reagent and those of the vicinal bonds". See also: Paddon-Row, M. N.; Rondan, N. G.; Houk, K. N. *J. Am. Chem. Soc.* **1982**, *104*, 7162. Rondan, N. G.; Paddon-Row, M. N.; Caramella, P.; Mareda, J.; Mueller, P. H.; Houk, K. N. *Ibid.* **1982**, *104*, 4974.

(12) Franck, R. W.; John, T. V.; Olejniczak, K. *J. Am. Chem. Soc.* **1982**, *104*, 1106. For related examples, see: Franck, R. W.; John, T. V. *J. Org. Chem.* **1983**, *48*, 3269. Primeau, J. L; Anderson, R. C.; Fraser-Reid, B. *J. Am. Chem. Soc.* **1983**, *105*, 5874. Jurczak, J.; Tkacz, M. *Synthesis* **1979**, 42. For a pertinent example utilizing a rigid dienophile which similarly demonstrates π-facial approach of a diene syn to a heteroatom bridge, see: Grieco, P. A.; Zelle, R. E.; Lis, R.; Finn, J. *J. Am. Chem. Soc.* **1983**, *105*, 1403. However, exo attack antiperiplanar to the C_1–C_6 and C_3–C_7 vicinal bonds may be preferred, geometrically, over antiperiplanar C_1–O/C_3–O approach in the 2-oxobicyclo[2.2.1]hept-4-ene system. For example, see ref 11.

(13) Kresze, G.; Heidegger, P.; Asbergs, A. *Liebigs Ann. Chem.* **1970**, *738*, 113. See also: Streith, J.; Augelmann, G.; Fritz, H.; Strub, H. *Tetrahedron Lett.* **1982**, *23*, 1909.

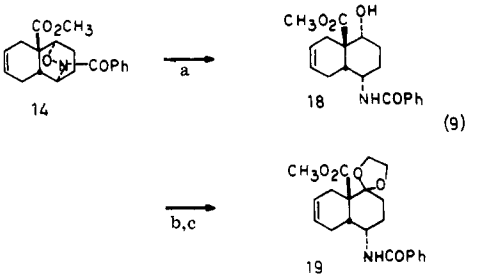
I. In the preceeding article we described a synthesis of an optically active, functionalized *cis*-Δ^6-1-octalone suitable for further elaboration to the morphine-related analgesics.[14] As an alternative to the approach detailed therein, in a chemical correlation of the nitrosocarbonyl Diels–Alder adducts, and in an exploration of the Diels–Alder π-facial selectivity due to the presence of an allylic heteroatom substituent we have investigated the potential utility of the nitrosocarbonyl Diels–Alder adducts as precursors to functionalized *cis*-Δ^6-1-octalones, eq 8.



In contrast to simple nitrosocarbonyl Diels–Alder adducts,[15] the 5- and 6-methoxycarbonyl or -formyl *N*-benzoyl-3-aza-2-oxobicyclo[2.2.2]oct-5-enes proved thermally stable to Diels–Alder conditions. Reaction of butadiene with **7**, **8**, **12**, and **15** provided the [4 + 2] cycloaddition adducts **14**, **17**, **13**, and **16**, respectively, as a single stereoisomer in each instance. Conversions of **13** to **14** and **16** to **17** confirmed the structure assignments by chemical correlation. The assignment of stereochemistry, which was anticipated to be opposite that shown for the adducts **13**, **14** and **16**, **17**, was initially proven by the comparison of **19**, prepared from **14**, eq 9, with an authentic sample of (4*R*,9*R*,10*R*)-4-(benzoylamino)-9-(methoxycarbonyl)-*cis*-Δ^6-1-octalone ethylene ketal[14] of secure relative configuration on the *cis*-Δ^6-1-octalone ring system. The noncorrelation of these two samples suggested that the observed stereochemistry of the Diels–Alder adducts **13**, **14** and **16**, **17** is in fact that shown in eq 6–7. X-ray structural analysis of **13**,[10] which unambiguously allows the structural and stereochemical assignments of **13**, **14**, **16–19**, eq 6, 7, and 9, confirmed the assignments. Thus the face selectivity of the Diels–Alder reaction of 3-aza-2-oxobicyclo[2.2.2]-oct-5-enes does not appear to be under secondary orbital control as it is currently advanced. The origin of the face selectivity of the Diels–Alder reaction of rigid systems is under continued investigation.

Experimental Section[17]

Methyl 1,3-Cyclohexadiene-2-carboxylate (6).[18] Anhydrous ammonia (500 mL) was condensed into a stirred solution of benzoic acid (10 g, 81.96 mmol) in 65 mL of dry ethanol at −78 °C. Sodium (5.64 g, 245 mmol) was added in small portions at −78 °C. After the blue color had disappeared, ammonium chloride



(a) Na(Hg), CH_3OH, 25 °C, 1.5 h, 68%; (b) PCC, CH_2Cl_2, 25 °C, 0.5 h, 71%; (c) ethylene glycol, *p*-TsOH cat., C_6H_6, H_2O, 80 °C, 6 h, 83%

(13.11 g, 245 mmol) was added cautiously and the mixture allowed to stir at −78 °C for 1 h before being allowed to warm to 25 °C with the evaporation of ammonia. The remaining solution was poured onto ice water and acidified to pH 4 with 10% HCl. Ether extraction and concentration in vacuo afforded crude 1,4-cyclohexadiene-3-carboxylic acid.[18a]

A solution of crude 1,4-cyclohexadiene-3-carboxylic acid in 335 mL of 10% KOH containing hydroquinone (902 mg, 8.20 mmol) was warmed at reflux for 2 h. The cooled reaction mixture was acidified to pH 4 with 10% HCl and extracted with ether. The combined extracts were dried ($MgSO_4$) and concentrated in vacuo. Chromatography (SiO_2 plug, ether eluant) removed hydroquinone and gave 1,3-cyclohexadiene-2-carboxylic acid as a pale yellow oil.[18b]

Oxalyl chloride (14.4 mL, 164 mmol) was added dropwise to a stirred solution of crude 1,3-cyclohexadiene 2-carboxylic acid in 400 mL of dry THF containing two drops of dry DMF at 0 °C. The reaction mixture was allowed to stir at 25 °C for 18 h before being concentrated in vacuo. The crude acid chloride in 50 mL of dry tetrahydrofuran was added dropwise to a stirred solution of methanol (16 mL) and pyridine (33 mL) at 0 °C. The reaction mixture was allowed to stir at 25 °C for 1 h, poured onto 10% HCl, and extracted with ether. The combined ether extracts were dried ($MgSO_4$) and concentrated in vacuo. Chromatography (SiO_2, 30% ether–hexane eluant) gave 8.29 g (11.31 g theoretical, 72.5%) of methyl 1,3-cyclohexadiene-2-carboxylate (6).[18]

2-[[(*tert*-Butyldimethylsilyl)oxy]methyl]-1,3-cyclohexadiene (1). Diisobutylaluminum hydride (318 mL of 1.0 M in hexane, 318 mmol, 2.0 equiv) was added dropwise to a stirred solution of **6** (22 g, 159 mmol) in 800 mL of dry toluene at 0 °C. The reaction mixture was allowed to stir for 1 h at 25 °C before the addition of saturated NH_4Cl and ether extraction. The combined organic extracts were dried ($MgSO_4$) and concentrated in vacuo. Chromatography (SiO_2, 50% ether–hexane eluant) gave 18.6 g (quantitative) of crude 2-(hydroxymethyl)-1,3-cyclohexadiene.

The alcohol (13.0 g, 118 mmol) in 30 mL of dry dimethylformamide was added to a solution of imidazole (16.07 g, 236 mmol) and *tert*-butyldimethylsilyl chloride (21.24 g, 141.6 mmol) in 30 mL of dry dimethylformamide.[19] The reaction mixture was allowed to stir at 25 °C for 1 h, poured onto water, and extracted with ether. The combined ether extracts were dried ($MgSO_4$) and concentrated in vacuo. Chromatography (SiO_2, 5% ether–hexane) gave 18.24 g (26.43 g, theoretical, 69%) of pure **1**: ^1H NMR ($CDCl_3$) δ 7.25 (s, 1 H), 5.75 (broad s, 1 H), 5.5 (broad s, 1 H), 4.0 (d, J = 1 Hz, 2 H, CH_2O), 2.05 (s, 4 H), 0.8 (s, 9 H), 0.1 (s, 6 H); IR (film) ν_{max} 2955, 2932, 2885, 2858, 2828, 1471, 1253, 1089, 1068, 1005, 837 cm^{-1}; EIMS, m/e 224 (M^+), 167, 149, 135, 121, 107, 91, 89, 75 (base), 59; HRMS, m/e 224.1593, $C_{13}H_{24}OSi$ requires 224.1595.

***N*-Benzoyl-3-aza-[[(*tert*-butyldimethylsilyl)oxy]-methyl]-2-oxabicyclo[2.2.2]oct-5-ene (2) and *N*-Benzoyl-3-aza-5-[[(*tert*-butyldimethylsilyl)oxy]methyl]-2-oxabicyclo-[2.2.2]oct-5-ene (3).** A solution of **1** (1.23 g, 5.47 mmol) and tetra-*n*-butylammonium periodate[16b] (5.47 g, 12.6 mmol) in 10 mL of dry CH_2Cl_2 at 25 °C was treated with benzohydroxamic acid[16a] (1.65 g, 12.1 mmol) in small portions over a period of 1 h.[20] After the addition was complete the reaction mixture was

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poured onto water and extracted with methylene chloride. The combined extracts were dried ($MgSO_4$) and concentrated in vacuo. Chromatography (SiO_2, 50% ether–hexane eluant) afforded 880 mg (1.96 g, theoretical, 45%) of adduct **2** (R_f 0.85, ether) and 310 mg (1.96 g, theoretical, 16%) of **3** (R_f 0.8, ether). **2**: ^1H NMR ($CDCl_3$) δ 7.6–7.15 (m, 5 H), 6.1 (m, 1 H), 4.8 (broad m, 1 H), 4.5 (broad s, 1 H), 4.1 (d, J = 2 Hz, 2 H, CH_2O), 2.1 (m, 2 H), 1.3 (m, 2 H), 0.8 (s, 9 H), 0.1 (s, 6 H); IR (film) ν_{max} 2932, 2895, 2856, 1825, 1641, 1471, 1450, 1390, 1361, 1319, 1253, 1172, 1159, 1088, 939, 898 cm^{-1}; EIMS, m/e 359 (M^+), 302, 222, 210, 194, 179, 165, 105 (base) 91, 77, 75, 57. Anal. Calcd for $C_{20}H_{29}NO_3Si$: C, 66.85; H, 8.08; N, 3.90. Found: C, 67.00; H, 8.30 N, 3.70.

3: ^1H NMR ($CDCl_3$) δ 7.7–7.2 (m, 2 H), 6.2 (dq, J = 7, 2 Hz, 1 H), 4.9 (broad s, 1 H), 4.7 (broad m, 1 H), 4.2 (d, J = 2 Hz, 2 H), 2.1 (m, 2 H), 1.35 (m, 2 H), 0.85 (s, 9 H), 0.1 (s, 6 H); IR (film) ν_{max} 2887, 2865, 2797, 1647, 1437, 1347, 1258, 1190, 1123 cm^{-1}; EIMS, m/e 359 (M^+) 342, 302, 223, 194, 165, 135, 105 (base), 91, 75; HRMS, m/e 359.1892, $C_{20}H_{29}NO_3Si$ requires 359.1915.

***N*-(Methoxycarbonyl)-3-aza-6-[[(*tert*-butyldimethylsilyl)oxy]methyl]-2-oxabicyclo[2.2.2]oct-5-ene (4) and *N*-(Methoxycarbonyl)-3-aza-5-[[(*tert*-butyldimethylsilyl)oxy]methyl]-2-oxabicyclo[2.2.2]oct-5-ene (5).** A solution of **1** (328 mg, 1.46 mmol) and tetra-*n*-butylammonium periodate[16b] (1.46 g, 3.37 mmol) in 5 mL of dry methylene chloride at 25 °C was treated with methyl *N*-hydroxycarbamate[16c] (293 mg, 3.22 mmol) in small portions over a period of 1 h. After the addition was complete the reaction mixture was poured onto water and extracted with methylene chloride. The combined extracts were dried ($MgSO_4$) and concentrated in vacuo. Chromatography (PCTLC, SiO_2, 50% ether–hexane) afforded 329 mg (457 mg theoretical, 72%) of a mixture of **4** and **5**. The mixture of **4** and **5** (100 mg, 0.32 mmol) in 2 mL of dry tetrahydrofuran was treated with tetra-*n*-butylammonium fluoride (0.48 mL of 1.0 M in THF) and allowed to stir at 25 °C for 30 min. Chromatography (PCTLC, 1 mm SiO_2, 50% ether–hexane) afforded 32 mg (64 mg theoretical, 50%) of *N*-(methoxycarbonyl)-3-aza-6-(hydroxymethyl)-2-oxabicyclo[2.2.2]oct-5-ene [^1H NMR ($CDCl_3$) δ 6.3 (dq, J = 6, 2 Hz, 1 H), 4.65 (m, 2 H), 4.15 (d, J = 2 Hz, 2 H), 3.7 (s, 3 H), 2.6 (broad s, 1 H, OH), 2.15 (m, 2 H), 1.40 (m, 2 H); IR (film) ν_{max} 3449, 3019, 2974, 2957, 2943, 1703, 1444, 1371, 1342, 1317, 1269, 1215, 1082, 1045, 754 cm^{-1}; EIMS, m/e 199 (M^+), 164, 110, 91, 79 (base), 67; HRMS, m/e 199.0814, $C_9H_{13}NO_4$ requires 199.0844] and 10 mg (64 mg theoretical, 16%) of *N*-(methoxycarbonyl)-3-aza-4-(hydroxymethyl)-2-oxabicyclo[2.2.2]oct-4-ene [^1H NMR ($CDCl_3$) δ 6.2 (dq, J = 6, 2 Hz, 1 H), 4.65 (m, 2 H), 4.15 (d, J = 2 Hz, 2 H), 3.64 (s, 3 H), 2.10 (m, 2 H), 1.40 (m, 2 H); IR (film) ν_{max} 3460, 3020, 2938, 2828, 1700, 1425, 1370, 1343, 1288, 1260, 1205, 1095, 1040 cm^{-1}; EIMS, m/e 199 (M^+), 164, 132, 108, 91, 79 (base), 67; HRMS, m/e 199.0813, $C_9H_{13}NO_3$ requires 199.0844].

Methyl *N*-Benzoyl-3-aza-2-oxabicyclo[2.2.2]oct-5-ene-6-carboxylate (7) and Methyl *N*-Benzoyl-3-aza-2-oxabicyclo[2.2.2]oct-5-ene-5-carboxylate (8). A solution of **6** (666 mg, 4.82 mmol) and tetra-*n*-propylammonium periodate[16b] (2.990 g, 7.95 mmol) at 25 °C in 10 mL of dry methylene chloride was treated with benzohydroxamic acid[16a] (991 mg, 7.24 mmol) in small portions over a period of 1 h. After the addition was complete the reaction mixture was poured onto water and extracted with methylene chloride. The combined extracts were dried ($MgSO_4$) and concentrated in vacuo. Chromatography (SiO_2, 50% ether–hexane) afforded 612 mg (1.31 g theoretical, 47%) of adduct **7** and 207 mg (1.31 g theoretical, 16%) of **8**. **7**: ^1H NMR ($CDCl_3$) δ 7.75–7.25 (m, 6 H), 5.25 (m, 2 H), 3.75 (s, 3 H), 2.25 (m, 2 H), 1.5 (m, 2 H); IR (film) ν_{max} 2949, 1720, 1651, 1578, 1448, 1439, 1371, 1315, 1267, 1232, 1161, 1099 cm^{-1}; EIMS, m/e 273 (M^+), 137, 105 (base) 77, 57; HRMS, m/e 273.0990, $C_{15}H_{15}NO_4$ requires 273.1000. **8**: ^1H NMR ($CDCl_3$) δ 7.75–7.25 (m, 6 H), 5.55 (broad s, 1 H), 4.90 (m, 1 H), 3.75 (s, 3 H), 2.35 (m, 2 H), 1.50 (m, 2 H); IR (film) ν_{max} 2951, 1720, 1651, 1628, 1578, 1448, 1439, 1375, 1336, 1313, 1265, 1228, 1211, 1159, 1095 cm^{-1}; EIMS, m/e 273 (M^+), 243, 137, 105 (base), 77. Anal. Calcd for $C_{15}H_{15}NO_4$: C, 65.92; H, 5.53; N, 5.13. Found: C, 65.53; H, 5.60; N, 5.10.

Methyl *N*-(Methoxycarbonyl)-3-aza-2-oxabicyclo[2.2.2]oct-5-ene-6-carboxylate (9) and Methyl *N*-(Methoxycarbonyl)-3-aza-2-oxabicyclo[2.2.2]oct-5-ene-5-carboxylate (10). A solution of **6** (435 mg, 3.15 mmol) and tetra-*n*-butylammonium periodate[16b] (3.15 g, 7.28 mmol) in 10 mL of dry dimethylformamide at 25 °C was treated with a solution of methyl *N*-hydroxycarbamate[16c] (631 mg, 6.94 mmol) in 2 mL of DMF dropwise via a syringe pump (3 h). After the addition was complete the reaction mixture was poured onto water and extracted with methylene chloride. The combined extracts were dried ($MgSO_4$) and concentrated in vacuo. Chromatography (PCTLC, 2 mm SiO_2, 50% ether–hexane) afforded 219 mg (715 mg theoretical, 30%) of adduct **9** (R_f 0.5, ether) and 80 mg (715 mg theoretical, 11%) of **10** (R_f 0.45, ether). **9**: ^1H NMR ($CDCl_3$) δ 7.37 (dd, J = 6, 2 Hz, 1 H), 5.25 (m, 1 H), 4.9 (m, 1 H), 3.75 (s, 3 H), 3.7 (s, 3 H), 2.2 (m, 2 H), 1.4 (m, 2 H); IR (film) ν_{max} 2955, 1745, 1716, 1633, 1441, 1379, 1348, 1313, 1267, 1230, 1209, 1194, 1161, 1076, 1059, cm^{-1}; EIMS, m/e 227 (M^+), 196, 178, 153, 137 (base), 105, 91, 79; HRMS, m/e 227.0801, $C_{10}H_{13}NO_5$ requires 227.0732. **10**: ^1H NMR ($CDCl_3$) δ 7.30 (dd, J = 6, 2 Hz, 1 H), 5.25 (m, 1 H), 4.8 (m, 1 H), 3.85 (s, 3 H), 3.75 (s, 3 H), 2.25 (m, 2 H), 1.5 (m, 2 H); IR (film) ν_{max} 2955, 1722, 1632, 1441, 1377, 1342, 1317, 1267, 1228, 1209, 1194, 1161, 1115, 1097, 1058 cm^{-1}; EIMS, m/e 227 (M^+)8 196, 178, 153, 137 (base), 105, 91, 79; HRMS, m/e 227.0796, $C_{10}H_{13}NO_5$ requires 227.7932.

Chemical Correlation of 2 and 7 via 14. *N*-Benzoyl-3-aza-6-(hydroxymethyl)-2-oxabicyclo[2.2.2]oct-5-ene (11). A solution of **2** (170 mg, 0.47 mmol) in 5 mL of dry THF was treated with a solution of tetra-*n*-butylammonium fluoride[19] in dry THF (0.56 mL of 1.0 M in THF, 0.56 mmol) and allowed to stir at 25 °C for 15 min. The reaction mixture was concentrated in vacuo and chromatography (SiO_2, ethyl acetate eluant) afforded 85 mg (115 mg, theoretical 74%) of *N*-benzoyl-3-aza-6-(hydroxymethyl)-2-oxabicyclo[2.2.2]oct-5-ene (**11**): mp 143 °C (CH_2Cl_2–hexane, 1:1); ^1H NMR ($CDCl_3$) δ 7.7–7.25 (m, 5 H), 6.35 (dq, J = 6, 2 Hz, 1 H), 5.05 (broad m, 1 H), 4.75 (m, 1 H), 4.25 (d, J = 2 Hz, 2 H), 2.25 (m, 2 H), 1.5 (m, 2 H); ^{13}C NMR δ 168.5 (s, *C*OPh), 145.0 (s, =*C*CH_2OH), 134.5 (s, aryl C-1), 130.8 (d, aryl C-4), 128.6 and 128.1 (two d, aryl C-2/C-3), 124.6 (d, olefinic, =CH), 73.3 (d, CHON), 61.8 (t, CH_2OH), 49.6 (d, CHNO), 23.8 and 22.3 (two t, CH_2); IR (film) ν_{max} 3400, 2932, 2862, 2824, 1635, 1576, 1446, 1365, 1354, 1313, 1296, 1275, 1238, 1174, 1143, 1115, 1078, 1068, 1049, 1022, 976 cm^{-1}; EIMS, m/e 245 (M^+), 209, 137, 123, 105 (base), 91, 77, 51. Anal. Calcd for $C_{14}H_{15}NO_3$: C, 68.57; H, 6.12; N, 5.71. Found: C, 62.18; H, 6.50; N, 5.63.

X-ray crystal analysis[10] confirmed the structure of this alcohol.

14 from 2. A stirred solution of *N*-benzoyl-3-aza-6-(hydroxymethyl)-2-oxabicyclo[2.2.2]oct-5-ene (**11**, 1.647 g, 6.72 mmol) prepared as described above in 5 mL of dry CH_2Cl_2 at 0 °C was treated with activated MnO_2 (16.47 g, 10 weight equiv) in small portions and the slurry was allowed to stir at 25 °C for 1 h. The reaction mixture was filtered through Celite and the filtrate concentrated in vacuo. Chromatography (SiO_2, ether eluant) afforded 1.26 g (1.63 g theoretical, 77%) of *N*-benzoyl-3-aza-2-oxabicyclo[2.2.2]oct-5-ene-6-carboxaldehyde (**12**): ^1H NMR ($CDCl_3$) δ 9.45 (s, 1 H), 7.75–7.25 (m, 6 H), 5.45 (m, 1 H), 5.25 (m, 1 H), 2.35 (m, 2 H), 1.5 (m, 2 H); IR (film) ν_{max} 1687, 1647, 1618, 1578, 1448, 1367, 1327, 1277, 1178, 945, 906, 785, 754, 704, 665 cm^{-1}; EIMS, m/e 243 (M^+), 137, 105 (base), 77. Anal. Calcd for $C_{14}H_{13}NO_3$: C, 69.14;, H, 5.35; N, 5.76. Found: C, 69.09; H, 5.60; N, 5.80.

A solution of **12** (1.26 g, 5.18 mmol) in 3 mL of dry mesitylene and 5 mL of condensed 1,3-butadiene in a resealable Carius tube was heated in sand-packed lead pipe by using a heating mantle at 130–140 °C for 48 h. The reaction tube was cooled to −78 °C and the contents transferred to a round-bottom flask and concentrated in vacuo. Chromatography (SiO_2, 50% ether–hexane eluant) afforded 1.25 g (1.54 g theoretical, 81%) of the Diels–Alder adduct **13** as a single stereoisomer: ^1H NMR ($CDCl_3$) δ 9.35 (s, 1 H), 7.75–7.25 (m, 5 H), 5.90 (m, 2 H), 4.50 (broad m, 1 H), 4.10 (broad s, 1 H), 2.25–1.00 (m, 9 H); ^{13}C NMR ($CDCl_3$) δ 201.5 (d, CHO), 167 (s, *C*OPh), 136 (s, aryl C-1), 130.6, 130.3, 128.3, 128.0, 125.8 (five d, aryl C-2, C-3, and C-4 and *C*H=*C*H), 75.5 (d, HCON), 54.9 (s, *C*CHO), 52.5 (d, CHNO), 36.5 (d, CH), 27.0, 25.9, 24.1 and 22.9 (four t, four CH_2); EIMS, m/e 297 (M^+), 149, 135, 123, 105 (base), 95, 77, 71, 57. Anal. Calcd for $C_{18}H_{19}NO_3$: C, 72.72; H, 6.39; N, 4.71. Found: C, 73.10; H, 6.70; N, 4.78.

2,4-DNP of **13**: mp 248 °C. Anal. Calcd for $C_{24}H_{23}N_5O_6$: C, 60.37; H, 4.85; N, 14.67. Found: C, 59.98; H, 4.99; N, 14.30.

The structure and stereochemistry of **13** was confirmed by X-ray analysis.[10b]

A solution of this Diels-Alder adduct **13** (27 mg, 0.091 mmol) in 0.2 mL of dry dimethylformamide was treated with pyridinium dichromate[21] (102 mg, 0.27 mmol) at 0 °C and the mixture was allowed to stir at room temperature for 9 h. The reaction mixture was poured onto 60 mL of 5% HCl and extracted with ether. The combined extracts were concentrated in vacuo. The crude carboxylic acid was taken up in ether and treated with excess diazomethane at 0 °C, and the mixture was allowed to stir at room temperature overnight. Chromatography (PCTLC, 1 mm SiO_2, 50% ether-hexane eluant) afforded 15 mg (29 mg theoretical, 52%) of **14** as a pale yellow oil: ^1H NMR ($CDCl_3$) δ 7.75-7.25 (m, 5 H), 5.95 (m, 2 H), 4.6 (broad m, 1 H), 4.15 (broad m, 1 H), 3.65 (s, 3 H), 2.8-1.5 (broad m, 9 H); EIMS, m/e 327 (M^+), 131, 105, (base), 91, 77, 68; HRMS, m/e 327.1477, $C_{19}H_{21}NO_4$ requires 327.1469.

14 from 7. A solution of the ester **7** (90 mg, 0.33 mmol) in 1 mL of dry mesitylene and 3 mL of condensed 1,3-butadienes in a resealable Carius tube was heated in a sand-packed lead pipe with a heating mantle at 130-140 °C for 48 h. The reaction tube was cooled to -78 °C and the contents transferred to a round-bottom flask and concentrated in vacuo. Chromatography (SiO_2, 50% ether-hexane) afforded 75 mg (108 mg theoretical, 70%) of pure **14** as a single stereoisomer identical in all respects with material prepared from **2**.

Chemical Correlation of 3 with 8 via 17. 17 from 3. Following the procedure detailed for the conversion of **2** to **14**, **3** afforded **17** in an unoptimized 12% overall yield. **17**: ^1H NMR ($CDCl_3$) δ 7.75-7.25 (m, 5 H), 5.9 (m, 2 H), 4.85 (broad m, 1 H), 3.95 (broad s, 1 H), 3.70 (s, 3 H), 2.8-1.5 (m, 9 H); IR (film) ν_{max} 3044, 3005, 2953, 1734, 1626, 1576, 1452, 1433, 1294, 1279, 1211, 1161, 987 cm^{-1}; EIMS, m/e 327 (M^+), 190, 131, 105 (base), 91, 77; HRMS, m/e 327.1468, $C_{19}H_{21}NO_4$ requires 327.1469.

17 from 8. A solution of **8** (70 mg, 0.256 mmol) in 1 mL of dry mesitylene and 3 mL of condensed 1,3-butadiene in a resealable Carius tube was heated in a sand-packed lead pipe with a heating mantle at 130-140 °C for 48 h. The reaction tube was cooled to -78 °C and the contents transferred to a round-bottom flask and concentrated in vacuo. Chromatography (SiO_2, 50% ether-hexane) afforded 53 mg (83 mg, theoretical, 64%) of pure **17** as a single stereoisomer identical in all respects with material prepared from **3**.

(4α,9β,10β)-4-(Benzoylamino)-9-(methoxycarbonyl)-*cis*-Δ^6-1-octalone Ethylene Ketal (19). A stirred solution of **14** (629 mg, 1.92 mmol) in 9.6 mL of MeOH at room temperature, was treated with 9435 mg of Na/Hg (8%, 15 weight equiv)[22] and allowed to stir for 1.5 h. The reaction mixture was filtered through Celite and the filtrate poured over water and extracted with EtOAc. The combined extracts were dried ($MgSO_4$) and concentrated in vacuo. Chromatography (SiO_2, EtOAc eluant) afforded 425 mg (625 mg, theoretical, 68%) of alcohol **18**: ^1H NMR ($CDCl_3$) δ 7.85-7.25 (m, 5 H), 7.00-6.70 (m, 2 H), 6.0-5.5 (m, 2 H), 4.35-3.9 (m, 1 H), 3.8 (s, 3 H), 3.2-1.75 (m, 8 H); EIMS, m/e 329 (M^+), 297, 269, 230, 208, 180, 158, 148, 132, 122, 105 (base), 91, 77; HRMS, m/e 329.16395, $C_{19}H_{23}NO_4$ requires 329.16257; IR (KBr) ν_{max} 3408, 1720, 1647, 1578, 1487, 1414, 1385, 1346, 1321, 1261, 713, 696, 661, 625 cm^{-1}.

A stirred solution of the alcohol **18** (21.5 mg, 0.06 mmol) in 0.3 mL CH_2Cl_2 at 0 °C was treated with PCC[23] (28 mg, 0.13 mmol) and allowed to stir at room temperature for 1.5 h. The reaction mixture was filtered through Celite and the filtrate poured onto 10% HCl and extracted with EtOAc. The combined extracts were dried ($MgSO_4$) and concentrated in vacuo. Chromatography (SiO_2, EtOAc eluant) afforded 15 mg (21 mg theoretical, 71%) of the desired ketone: ^1H NMR ($CDCl_3$) δ 7.8-7.3 (m, 5 H), 6.25-5.95 (m, 1 H), 5.75-5.6 (m, 2 H), 5.0-4.5 (m, 1 H), 3.85 (s, 3 H), 3.0-2.0 (m, 9 H); IR (KBr) ν_{max} 3302, 1718, 1633, 1551, 1242, 1226 cm^{-1}; EIMS, m/e 327 (M^+), 267, 205, 174, 147, 122, 105 (base), 77; HRMS, m/e 327.14674, $C_{19}H_{21}NO_4$ requires 327.14693.

A solution of the ketone (300 mg, 0.91 mmol) in 15 mL of benzene containing 0.1 mL (1.8 mmol, 2 equiv) of ethylene glycol and 17 mg (0.091 mmol, 0.1 equiv) of *p*-TsOH, was allowed to reflux for 6 h with azeotropic removal of water. The crude mixture was then poured over water and extracted with EtOAc. The combined extracts were dried ($MgSO_4$) and concentrated in vacuo. Chromatography (PCTLC, 1 mm, EtOAc eluant) gave 282 mg (340 mg theoretical, 83%) of ketal **19**: ^1H NMR ($CDCl_3$) δ 7.7-7.25 (m, 5 H), 6.85-6.6 (m, 1 H), 5.85-5.4 (m, 2 H), 4.35-4.00 (m, 1 H), 3.8 (m, 4 H), 3.65 (s, 3 H), 3.0-1.5 (m, 9 H); IR (film) ν_{max} 3450, 3025, 2975, 2900, 1720, 1660, 1520, 1480, 1460, 1440, 1260 cm^{-1}; EIMS, m/e 371 (M^+), 326, 250, 200, 191, 105 (base), 86, 77. Anal. Calcd for $C_{21}H_{25}NO_3$: C, 67.90; H, 6.78; N, 3.77. Found: C, 67.52; H, 6.90; N, 3.79.

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Supplementary Material Available: Full details of the X-ray structure determination of **13** (13 pages). Ordering information is given on any current masthead page.

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(22) Sodium amalgam (8%) was purchased from City Chemical Corp., New York. Reduction with aluminum amalgam (20 mol, THF-H_2O 10:1, 60 °C, 10 h) afforded **18** (63%) and recovered **14**.

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Reduction of Schiff Bases with Isopropyl Alcohol and Aluminum Isopropoxide in the Presence of Raney Nickel[1]

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The reduction of several *N*-alkyl and *N*-aryl ketimines to the corresponding secondary amines is described. The reaction, which generally proceeds in high yield, is effected by isopropyl alcohol and aluminum isopropoxide in the presence of Raney nickel. In the absence of the nickel catalyst, that is, under the Meerwein-Ponndorf-Verley conditions, the reaction takes a different route and *N*-isopropylamines are formed at preference to the direct reduction products. Without the aluminum alkoxide the reduction proceeds only for a small percentage. This reaction, besides offering a new method for the synthesis of secondary amines, represents the first example where the couple aluminum alkoxide/Raney nickel is used in catalytic transfer hydrogenation reactions.

We have been interested for many years in the system alcohol, aluminum alkoxide, and Raney nickel as alkylating agent of indoles,[2,3] pyrroles,[3] and amines.[4] In particular, in a recent paper,[1] we described some mechanistic aspects

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