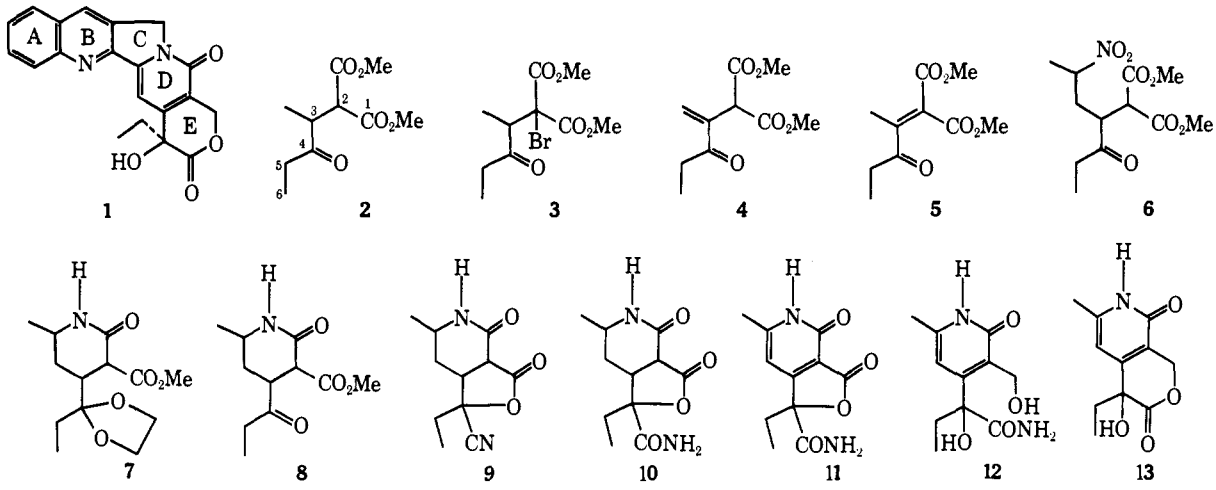


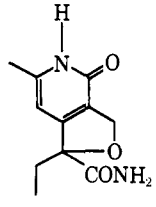
fluxing ether, giving a 90% yield of **6**. Prior to reductive cyclization, the ethylene ketal of **6** was prepared[13] which was then reduced with hydrogen–platinum oxide at 50 psi to give **7** in 50% yield from **6** (crystals from EtOAc–Et_2O, mp 134–136°). Removal of the ketal with trityl fluoroborate[14] in methylene chloride gave **8** as an oil in 90% yield. Treatment of **8** with liquid hydrogen cyanide gave the cyanolactone **9** in 50% yield[1,15] which on hydrolysis in anhydrous HCl–MeOH gave the amide lactone **10** in 98% yield. Dehydrogenation of **10** in the presence of dichlorodicyanoquinone in refluxing dioxane gave a quantitative yield of the pyridone **11** (crystals from MeOH–$CHCl_3$, mp 262–265° dec). Reduction of **11** with lithium borohydride in refluxing THF formed the corresponding diol **12** as a borate ester which was not isolated. Heating **12** with HCl gave the desired camptothecin analog **13** (crystals from CH_2Cl_2, mp 242–243°) in 40% yield from **11**.[16] Compound **13** is a weak but not inactive cytotoxic agent; it is about 1/100th the potency of **1**.[17]

(13) It was found that direct reduction of **6** resulted in formation of the Δ^1-pyrroline *N*-oxide. The 4-oxo moiety of **6** was unreactive under standard ketalization conditions; however, ethylene glycol in the presence of $BF_3 \cdot Et_2O$ at room temperature gave a 90% yield of the desired ketal.

(14) D. H. R. Barton, P. D. Magnus, G. Smith, and D. Zurr, *J. Chem. Soc. D*, 861 (1971).

(15) About 50% unreacted starting material 8 was found which could be readily separated from **9** by chromatography and recycled.

(16) The major by-product in this reaction is the ether



which could be formed either directly from **11** by hydride reduction or during subsequent acid treatment of **12**. This reaction is being further investigated.

(17) Cytotoxicity was determined by the procedures described in *Cancer Chemother. Rep.*, **25**, 1 (1962). The values for **1** and **13** determined at the same time were, respectively, 3×10^{-2} and 4×10^{0}. Potency is determined in terms of the number of micrograms required to give an ED_{50} response; the lower the value, the more potent the compound. The data would indicate that **1** was approximately 100 times more potent than **13**. Allowing for the fact that **13** was racemic and assuming that one of the racemates was inactive, **13** might be regarded as about 1/50th as active as **1** in this assay. The relationship between cytotoxicity and antitumor or antileukemia activity is not, as yet, well established. It is planned to test **13** in P-388 and L-1210 mouse leukemia as soon as a sufficient quantity has been prepared.

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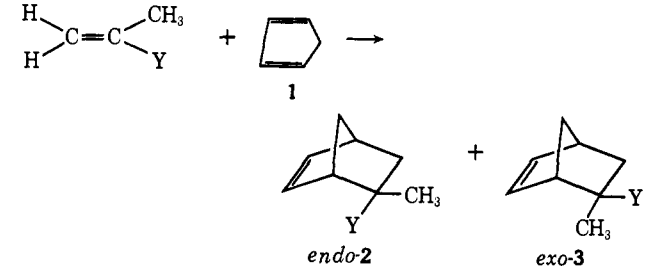
The Role of Attractive Interactions in Endo–Exo Stereoselectivities of Diels–Alder Reactions

Sir:

In the study of Diels–Alder reactions of methyl-substituted dienophiles with cyclopentadiene (**1**), we found that the methyl group shows a greater tendency toward endo orientation than most of the electron-withdrawing polar substituents Y, thereby leading to preferential formation of exo Y adducts (**3**).[1] We



Y = CN, $COOCH_3$, $COCH_3$, CHO, COOH

wish to report evidence that the attractive van der Waals forces between the methyl group in dienophiles and the unsaturated center of dienes play a significant role in the stabilization of the exo Y transition state.

(1) Y. Kobuke, T. Fueno, and J. Furukawa, *J. Amer. Chem. Soc.*, **92**, 6548 (1970).

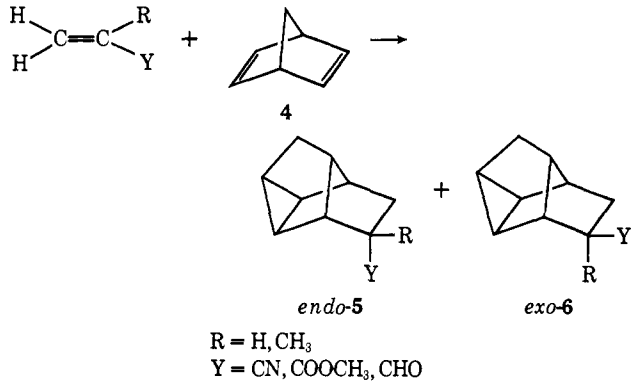
Table I. Relative Endo Selectivities (%)

Dienophile R[a]	Dienophile Y[a]	With 4[b] (150°)	With 1[c] (100°)
H	CN	57.7	55.3
H	$COOCH_3$	81.0	70.5
H	CHO	75.0	70.5
CH_3	CN	25.2	16.2
CH_3	$COOCH_3$	33.8	31.8
CH_3	CHO	23.3	23.6

[a] See Scheme I. [b] Reactions were conducted in neat. Use of *n*-hexane as solvent effects little change in the results. [c] Reference 1.

The homo Diels–Alder reaction of norbornadiene (**4**) with various acrylic and methacrylic compounds[2] gave kinetically controlled endo–exo [2 + 2 + 2] adducts **5** and **6**. The endo–exo stereoselectivities observed are shown in Table I, together with the corresponding selectivity data already reported for the reactions of **1**.[1]

Scheme I

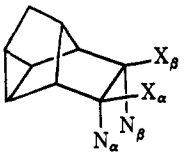


The relative endo–exo percentage of adducts did not vary by more than ±1.0% at different yields ranging from 0.8 to 64%. Moreover, no sign of epimerization was observable when the isomer adducts isolated were heated under the reaction conditions (150°, a few hours). Stereospecificity of the reaction was confirmed with *cis*- and *trans*-crotononitriles, $CH_3CH{=}CHCN$; both the isomeric nitriles gave a mixture of endo and exo adducts which perfectly retain the initial olefin configurations. These results clearly indicate that the addition of olefins to **4** is a stereospecific, kinetically controlled reaction.

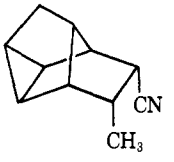
(2) Homo Diels–Alder reactions of norbornadiene with this class of dienophiles have already been reported by R. C. Cookson, J. Dance, and J. Hudec, *J. Chem. Soc.*, 5416 (1964), but stereochemical configurations of the adducts remain ambiguous.

The endo–exo configuration of adducts was determined by the comparison of their nmr spectra. The nmr spectra of *cis*-crotononitrile adducts **7** and **8** gave two doublets of equal intensities centered at 3.03 ppm for **7** and a doublet at 3.01 ppm for **8**, both assignable to the proton α to the cyano group.[3] The well-established angular dependence of coupling constants for bicyclic compounds[4] permits us an unequivocal assignment that **7** and **8** are endo and exo adducts, respectively. This characteristic coupling pattern was applied to other acrylic adducts, where endo and exo α protons

Table II. Nmr Spectra and Some Physical Properties of Some Isomeric Addenda



				α-H		CH_3			
N_α	X_α	N_β	X_β	δ	J, Hz	δ	J, Hz	Bp, °C (P, mm)	$n^{20}D$
CN	H	H	H	2.88	q 4.7			109 (8)	1.5066
H	CN	H	H	2.78	d of d 9.0, 5.2			107 (8)	1.5050
CN	CH_3	H	H			1.35	s	108 (8)	1.4980
CH_3	CN	H	H			1.50	s	105.5 (8)	1.4960
CN	H	CH_3	H	3.03	d of d 11.4, 5.0	1.27	d 7.2	110 (7)	1.5036
H	CN	H	CH_3	3.01	d 8.8	1.15	d 7.2	108 (7)	1.5040
CN	H	H	CH_3	2.2–2.4	br	1.04	d 7.1	106 (9)	1.4965
H	CN	CH_3	H	2.5–2.6	br	1.20	d 7.0	105 (9)	1.4950



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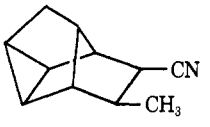

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appeared as double doublets and multiplets through the coupling with bridgehead as well as vicinal endo and exo protons, respectively. The above assignment also established the lower field shift of the *endo*-methyl resonance of **7** as compared to the *exo*-methyl of **8**.[5] This last tendency, which was generally observable for methyl and carbomethoxy resonances of other crotonic adducts, was applied to the stereochemical assignment of methacrylic addenda.[6] Table II records some of the nmr data along with some characterizations of isomeric addenda.

The most obvious structural distinction between **1** and **4** is the lack of methylene hydrogens in **4**. Since the bridgehead 1,4 protons of **4** are lifted up far above the olefinic plane, **4** will experience little steric repulsion at its exo side.[7] Importantly, Table I demonstrates

(3) The spectral assignment of these low-field signals was firmly established by the fact that the signals at 2.78 and 2.88 ppm of acrylonitrile adducts disappear in the acrylonitrile-*1-d* adducts.

(4) Different couplings of endo ($J \cong 0$) and exo (J = 3.0–5.0 Hz) protons with the adjacent bridgehead hydrogen are observed for many bicyclic compounds: P. Laszlo and P. von R. Schleyer, *J. Amer. Chem. Soc.*, **86**, 1171 (1964), and references cited therein.

(5) The lower field shift of the *endo*-methyl signal is a result of the cross-ring in-plane deshielding effect of the three-membered ring. The relative magnitudes of the shifts for the *endo*- and *exo*-methyl groups are the reverse of those found for the norbornene and norbornane systems.

(6) All new adducts, both endo and exo, which were isolated by preparative gas chromatography, gave mass, ir, and nmr spectra compatible with the assigned structures.

(7) The lack of steric repulsion at the exo side of **4** was evidenced from its reactions with acrylic compounds having various α-alkyl substituents. Methyl esters of α-isopropyl- and α-*sec*-butylacrylic acids gave mainly

nearly the same endo selectivities for **1** and **4** in the reactions with a given acrylic or methacrylic compound. Both dienes are electroneutral, and thus the type of interactions operative in the determination of endo–exo stereoselectivity should be analogous for the two dienes. The fact that the exo adducts are the predominant products of the reactions of methacrylic dienophiles with both dienes could best be understood by assuming that, in the transition state, the methyl substituent in the dienophile is subject to greater attraction from the diene sp^2 carbons than the unsaturated polar substituents. The attractive force of the methyl group will be of the van der Waals type (dispersion).

Recently, Houk and Luskus[8] have argued against our proposal of the attractive van der Waals interactions of the methyl group, claiming that the stereoselectivity observed for **1**[1] should be taken as an indication of the steric repulsion between the methyl substituent in dienophiles and the apical hydrogens in **1**. They found that 2,5-dimethyl-3,4-diphenylcyclopentadienone (**9**), which has no such apical hydrogen atom, gives major endo adducts in its reactions with methyl methacrylate and crotonate. However, their substrate must be greatly polarized because of the carbonyl group attached to the reaction center. Apparently, the situation introduces an additional complexity to the otherwise straightforward understanding of the stereochemical factors for the reactions of simple, nonpolar diene moieties. Direct comparison of the endo selectivities between **1** and **9** thus cannot be clear-cut evidence against our hypothesis of the van der Waals attractive interaction. Even though the adverse steric effects can often be an important factor to control stereochemical courses, they certainly cannot be a major factor in the reaction of **4** and probably not in the reaction of **1**, either.

In conclusion, we emphasize that cases can exist in which the endo–exo stereoselectivity of Diels–Alder reactions is governed primarily by local London–van der Waals attraction forces.[9] The methyl substituent in dienophiles exhibits rather greater attractive forces than do the unsaturated polar substituents, *e.g.*, CN, $COOCH_3$, and CHO. Polar dienes might well be influenced by dipole–dipole and dipole–induced dipole interactions and cause changes in potential surface of reaction, analyses of which would need more thorough investigations.[8,10]

endo adducts **5**, in contrast to the exo selectivity of the methacrylate. In the case of **1**, the products were mainly exo adducts for all these three dienophiles. Steric repulsions are thought to be an influencing factor only in the reactions of bulky dienophiles, in which bulky alkyl substituents favor the less crowded side; exo in **4** and endo in **1** (Y. Kobuke, T. Sugimoto, T. Shimizu, and J. Furukawa, unpublished data).

(8) K. N. Houk and L. J. Luskus, *J. Amer. Chem. Soc.*, **93**, 4606 (1971)

(9) The same type of attractive interaction is reported to determine the steric course of syn addition of carbenoid to olefins: G. L. Closs and R. A. Moss, *J. Amer. Chem. Soc.*, **86**, 4042 (1964); R. A. Moss, *J. Org. Chem.*, 30, 3261 (1965).

(10) K. L. Williamson, Y. L. Hsu, R. Lacko, and C. H. Youn, *J. Amer. Chem. Soc.*, **91**, 6129 (1969); K. N. Houk, *Tetrahedron Lett.*, 2621 (1970).

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Photochemistry of Ethylenediaminetetraacetate Complexes. Excited State Reaction Pathways in Cobalt(III) Complexes[1]

Sir:

It has become increasingly evident that triplet sensitizers are powerful tools for characterizing chemically reactive excited states of transition metal complexes.[2-11] Despite the obvious mechanistic potentialities, the photosensitization of oxidation–reduction decomposition of cobalt(III) complexes[2,3,7] has been fraught with sufficient ambiguities[12] that Adamson's radical pair hypothesis[13,14] can still be vigorously defended as the only viable model for cobalt(III) photochemistry.[15,16] A particularly puzzling feature of the photochemistry of cobalt(III) complexes has been the lack of appreciable photochemical reactivity associated with the irradiation of ligand field absorption bands[2,13-15,17-19] contrasted to the significant yields of aquation products frequently observed to accompany irradiation of near-ultraviolet charge transfer to metal (CTTM) absorption bands.[2,13-15] To date, the single quantitative study of the sensitized oxidation–reduction decomposition of a cobalt(III) complex, the reaction which accompanies $Co(NH_3)_6^{3+}$ quenching of the biphenyl phosphorescence,[7] has resulted in a limiting sensitized yield (of Co^{2+}) about four times greater than the yield which results from direct excitation.[7,20] This observation suggests that the product yields resulting from the direct excitation of cobalt(III) complexes may be greatly complicated by inefficient intersystem crossing from the initially populated spectroscopic singlet states to chemically reactive triplet states.

In this communication we report on the direct and sensitized photochemistry of some simple acido–ethylenediaminetetraacetate complexes of cobalt(III), $Co(HEDTA)X^-$ (X = Cl, Br, NO_2).[21] As sensitizer we have chosen $Ru(bipy)_3^{2+}$ whose emission spectroscopy[22] and utility as a sensitizer[9] have been well docu-

(1) Partial support of this research by the National Science Foundation (Grant GP 24053) is gratefully acknowledged.

(2) V. Balzani and V. Carassiti, "The Photochemistry of Coordination Compounds," Academic Press, New York, N. Y., 1970.

(3) A. Vogler and A. W. Adamson, *J. Amer. Chem. Soc.*, 90, 5943 (1968).

(4) S. Chen and G. B. Porter, *ibid.*, **92**, 3196 (1970).

(5) G. B. Porter, *ibid.*, **91**, 3980 (1969).

(6) V. Balzani, R. Ballardini, M. T. Gandolfi, and L. Moggi, *ibid.*, **93**, 339 (1971).

(7) M. A. Scandola and F. Scandola, *ibid.*, **92**, 7278 (1970).

(8) V. S. Sastri and C. H. Langford, *ibid.*, **91**, 7533 (1969).

(9) J. N. Demas and A. W. Adamson, *ibid.*, **93**, 1800 (1971).

(10) P. Natarajan and A. W. Adamson, *ibid.*, **93**, 5599 (1971).

(11) T. L. Kelly and J. F. Endicott, *ibid.*, **94**, 278 (1972).

(12) See especially Chapter 11 in ref 2 and the discussion in ref 7.

(13) A. W. Adamson and A. H. Sporer, *J. Amer. Chem. Soc.*, 80, 3865 (1958).

(14) A. W. Adamson, *Discuss. Faraday Soc.*, **29**, 163 (1960).

(15) A. Vogler and A. W. Adamson, *J. Phys. Chem.*, **73**, 4183 (1969).

(16) R. D. Lindholm and T. K. Hall, *J. Amer. Chem. Soc.*, **93**, 3525 (1971).

(17) Important exceptions are the case of $Co(NH_3)_5NO_2^{2+}$ where direct ligand field excitation leads to reasonably large yields of Co^{2+} and $Co(NH_3)_5ONO^{2+}$,[18] and the case of $Co(NH_3)_5O_2CCH_3^{2+}$ where direct ligand field excitation leads to $Co(NH_3)_4(OH_2)O_2CCH_3^{2+}$.[19]

(18) V. Balzani, R. Ballardini, N. Sabbatini, and L. Moggi, *Inorg. Chem.*, 7, 1398 (1968).

(19) E. R. Kantrowitz, M. Z. Hoffman, and J. F. Endicott, *J. Phys. Chem.*, **75**, 1914 (1971).

(20) M. F. Manfrin, G. Varani, L. Moggi, and V. Balzani, *Mol. Photochem.*, **1**, 387 (1969).

(21) The pK_a of the free glycinate arm of the chelate is about 6, and thus it was always protonated under the conditions of our study.

(22) J. N. Demas and G. A. Crosby, *J. Mol. Spectrosc.*, **26**, 72 (1968).