in the catalyzed reaction of methyl acrylate and piperylene.[7,8] In this case the steric hindrance mentioned above is obviously impossible since the acyclic diene lacks the methylene group under question.

From this analogous behavior of the stereospecificity of the reactions of the cyclic and acyclic dienes we prefer to explain the higher stereoselectivity by a larger π interaction between the unsaturated centers of the addends in the catalyzed reaction than in the uncatalyzed reaction, an explanation which is an extension of the traditional interpretation of the *endo* rule of the Diels–Alder reactions. The dienophile substituents become more electrophilic when complexed with aluminum chloride, and this enhances the rate of condensation (rate effect). At the same time, the complexes orient themselves to the *endo* direction more predominantly by their stronger π interaction with the residual unsaturation of the diene moiety in the transition state (stereochemical effect of the catalysis). This explanation closely parallels that proposed by Sauer, *et al.*,[9] for the stereochemistry of various adducts from dienophiles of varying reactivity.

The third consideration, the polarity effect, may also be a factor. It has been shown by an elaborate study by Berson, *et al.*, that the proportion of the *endo* adduct increases with the increasing polarity of the solvent used and this was explained by assuming a larger dipole moment of the *endo* transition state than the *exo.*[10] Our present results of marked preference of the *endo* adducts correspond to that which would be obtained in the reactions in an extremely polar solvent according to the experimental rule by Berson, *et al.*[5] Since the activated complex of the catalyzed reaction will be formed in the vicinity of the local field of aluminum chloride, which polarizes the reactant and solvent molecules, the polarity effect appears to operate in the right direction. It is difficult to rationalize this on a sound basis, however, because the effects of the dipole moments of the *endo* and *exo* transition complexes on the rate (which are in favor of the formation of the *endo* adduct), and their balance with the opposing effect of dipole induction energy, are subject to substantial uncertainty,[10] particularly in the presence of aluminum chloride.

Experimental Section

Materials.—Cyclopentadiene, bp 40–41°, was obtained by cracking dicyclopentadiene[11] and stored in Dry Ice. Methyl *trans*-crotonate, bp 119–121°, $n^{20}{}_{\mathrm{D}}$ 1.4238, was prepared by esterification of freshly recrystallized *trans*-crotonic acid. Dimethyl maleate, bp 97.5° at 18 mm, and diethyl maleate, bp 118° at 16 mm, were prepared by treating maleic anhydride with the corresponding alcohols in the presence of concentrated sulfuric acid. Methyl acrylate and methyl methacrylate were prepared as described previously.[2] Solvents were purified in the usual way and were anhydrous.

Reactions.—To a suspension of anhydrous aluminum chloride, 6.0 g, in benzene, 100 ml, was added a dienophile in slight excess of the equimolecular amount, and the mixture was stirred in a thermostat at 30° for a while until all the aluminum chloride dissolved. An equimolecular amount of cyclopentadiene in benzene, 50 ml, was added to the solution in 15 min. After reaction periods of 0.5 and 1 hr (or 1 and 2 hr), 50 ml of the reaction mixture was pipetted out onto 50 ml of water, and the benzene layer was washed until neutral, dried with anhydrous sodium sulfate, and concentrated by evaporation under reduced pressure. The concentrate was analyzed by glpc for the isomer ratio.

For the uncatalyzed reaction higher initial concentrations of the reactants, in the range of 2–2.5 *M*, were convenient to achieve sufficient yields of products within several hours.

Analysis of Products.—The analyses were carried out by glpc with an Ohkura Model 1200 instrument. The determinations of the products from methyl methacrylate employed a 2.7 m × 5 mm ϕ copper column packed with 10 wt % 1,2,3-tris(β-cyanoethoxy)propane on Diasolid M (Nihon Chromato Ind., Co. Ltd.) at 85°. The same column packed with 10 wt % Carbowax 6000 on Diasolid M (the same supplier) was used for all others: at 100° for the acrylate and crotonate reaction products; at 180° for the maleate reaction products. The flow rate of helium gas was about 80 ml/min in all cases.

The assignment of the glpc peaks to the *endo* or *exo* isomer was made by comparison of the observed and literature values of the isomer ratio of the uncatalyzed reaction under the same reaction conditions. The agreement between them (Table I) leaves no doubt about this procedure. In the case of diethyl maleate analogy with the methyl ester was resorted to for the identification of the glpc peaks. The *exo* isomer elutes faster than the *endo* and clear separation of the isomers was achieved in all instances.

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[7] The term *endo* selectivity is a misnomer in referring to reactions of acyclic dienes but is useful for description, because the formation of *cis*-substituted cyclohexenes is mechanistically analogous to the formation of the *endo* adducts from cyclic dienes. The details of the piperylene–methyl acrylate reaction are under investigation and will be shortly published elsewhere.

[8] It should be noted that this may not deny the explanation for the preferred formation of the *endo* adduct in many examples of the Diels–Alder reactions by the steric hindrance to the *exo* orientation. *E.g.*, the predominant formation of the *endo* adduct from cyclopentene and cyclopentadiene seems to be explained by the steric hindrance, because the overlap interaction between the addends in the transition state is thought to be negligible in this instance.[6]

[9] J. Sauer, H. Wiest, and A. Mielert, *Chem. Ber.*, **97**, 3183 (1964).

[10] See ref 5 for a complete discussion.

[11] R. B. Moffett, "Organic Syntheses," Coll. Vol. IV, John Wiley and Sons, Inc., New York, N. Y., 1963, p 238.

Controlled Oxidation of Organic Compounds with Cerium(IV). II. The Oxidation of Toluenes

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Oxidations of organic compounds with cerium(IV) are potentially interesting since cerium(IV) is an unusually strong, one-electron oxidant. Moreover, unique reactions of cerium(IV) with organic compounds can be expected because of specific coordination properties of the ion with various organic and inorganic ligands. Recently we have reported that ceric ammonium nitrate in 50% aqueous acetic acid converts benzyl alcohols to benzaldehydes in excellent yields.[1] We now wish to report that, under similar conditions, toluenes are oxidized to benzaldehydes.[2] Moreover,

$$\mathrm{ArCH_3} \xrightarrow[\text{50\% aq HOAc}]{\mathrm{Ce(NH_4)_2(NO_3)_6}} \mathrm{ArCHO} \qquad (1)$$

$$\mathrm{ArCH_3} \xrightarrow[\text{HOAc}]{\mathrm{Ce(NH_4)_2(NO_3)_6}} \mathrm{ArCH_2OAc} \qquad (2)$$

in anhydrous acetic acid, ceric ammonium nitrate oxidizes toluenes to benzyl acetates. Yields of the products from oxidation of various toluenes are shown in Table I.

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[1] W. S. Trahanovsky and L. B. Young, *J. Chem. Soc.*, 5777 (1965).

[2] Preliminary communication: Abstracts, 150th National Meeting of the American Chemical Society, Atlantic City, N. J., Sept 1965, p 54S.

TABLE I

OXIDATION OF TOLUENES WITH CERIUM(IV)

		Products, % yield[a]		
Toluene	% HOAc	Benzaldehyde	Benzyl alcohol	Benzyl acetate
$C_6H_5CH_3$	50	36	7	7
p-$CH_3C_6H_4CH_3$	50	73	2	9
p-$ClC_6H_4CH_3$	50	54	19	8
p-$BrC_6H_4CH_3$	50	51	..[b]	..[b]
p-$NO_2C_6H_4CH_3$	50	5	0	0
m-$NO_2C_6H_4CH_3$	50	5	0	0
p-$HOC_6H_4CH_3$	50	(Reaction mixture polymerized)		
p-$NH_2C_6H_4CH_3$	50	(Reaction mixture polymerized)		
p-$CH_3OC_6H_4CH_3$	50	(Reaction mixture polymerized)		
$C_6H_5CH_3$	100	2	2	90
p-$CH_3C_6H_4CH_3$	100	0	0	90
p-$ClC_6H_4CH_3$	100	4	30	36
p-$BrC_6H_4CH_3$[c]	100	20	20	10
p-$NO_2C_6H_4CH_3$	100	0	0	0
p-$CH_3OC_6H_4CH_3$	100	(Reaction mixture polymerized)		

[a] Presumably the benzoic acid accounts for the missing materials. [b] Yields were small and thus not calculated. [c] Starting material (50%) was recovered.

Other workers have reported that cerium(IV) oxidizes toluenes to benzaldehydes; however, their methods do not involve mild conditions suitable for the oxidation of toluenes to one product in good yield. Some early German patents[3] reported that ceric oxide in 60% sulfuric acid oxidizes toluene, *p*-chlorotoluene, *p*-nitrotoluene, and *o*-nitrotoluene to the corresponding aldehyde. No procedures or yields were given. *p*-Xylene was converted to *p*-tolualdehyde with electrolytically regenerated ceric sulfate in aqueous sulfuric acid solutions.[4] However, an excess of *p*-xylene was used and the highest yield reported was only 8%.

Under our reaction conditions, which are milder and more suitable for the oxidation of organic compounds, certain toluenes are oxidized cleanly and in good yield to one product. For example, *p*-xylene produced a 73% yield of *p*-tolualdehyde in 50% aqueous acetic acid and a 90% yield of *p*-methylbenzyl acetate in anhydrous acetic acid (no products resulting from the oxidation of both methyl groups were observed). Unfortunately, toluenes with strongly electron-withdrawing substituents such as the nitro group are inert toward oxidation and toluenes with strongly electron-donating substituents such as the methoxy group polymerize. However, other methods of oxidizing toluenes have disadvantages and in favorable cases cerium(IV) oxidation is the most convenient method. The Étard reaction[5] is experimentally tricky and the use of chromium trioxide in acetic anhydride leads to the geminal diacetate which must subsequently be hydrolyzed to the aldehyde.[6] Lead tetraacetate in acetic acid oxidizes toluenes to benzyl acetates,[7] but yields are moderate and the reagent is difficult to handle. Schmidt and Schmidbaur have reported that trimethylsilyl chromate oxidizes toluene to benzyl alcohol; however, they have given no experimental procedure or yield.[8] Other methods of oxidizing toluenes are multistep procedures and involve mono- or dihalogenation to the benzyl[9] or benzal[10] halide. The benzyl halide can then be hydrolyzed to the benzyl alcohol or oxidized to the benzaldehyde by various methods.[11] Hydrolysis of the benzal halides gives benzaldehydes.[10]

The oxidation of toluenes to benzaldehydes in 50% aqueous acetic acid probably proceeds through the benzyl alcohol since the alcohol is present in small amounts at the end of the reaction and benzyl alcohols are oxidized to benzaldehydes very rapidly under these conditions.[1] The mechanism of the oxidation of toluenes to benzyl alcohols by monomeric cerium(IV) species could involve either two one-electron oxidations as shown in Scheme I or one two-electron oxidation as shown in Scheme II.[12] Although the existence of cerium(II) in aqueous solution has never been reported, the high yield of one product in certain cases favors a mechanism such as the two-electron-oxidation mechanism, which does not involve radicals. Indeed, some free-radical reactions are clean, but, in this case, one would expect free radicals to attack the products, especially toward the end of the reaction. Another possible mechanism which obviates radicals is a two-electron-oxidation reaction involving polymeric cerium species. Cerium(IV) does tend to form polymers presumably involving cerium–oxygen–cerium bonds.[13]

SCHEME I

$$ArCH_3 + Ce^{+4} \longrightarrow ArCH_2\cdot + Ce^{+3} + H^+ \qquad (3)$$

$$ArCH_2\cdot + Ce^{+4} \longrightarrow ArCH_2^+ + Ce^{+3} \qquad (4)$$

$$ArCH_2^+ + H_2O \longrightarrow ArCH_2OH + H^+ \qquad (5)$$

SCHEME II

$$ArCH_3 + Ce^{+4} \longrightarrow ArCH_2^+ + Ce^{+2} + H^+ \qquad (6)$$

$$ArCH_2^+ + H_2O \longrightarrow ArCH_2OH + H^+ \qquad (5)$$

$$Ce^{+4} + Ce^{+2} \longrightarrow 2Ce^{+3} \qquad (7)$$

The oxidation of the *p*-halotoluenes in anhydrous acetic acid is of special interest since a large amount of the corresponding benzyl alcohol and benzaldehyde was produced. Moreover, *p*-bromobenzyl acetate was submitted to the reaction conditions and gave only 14% *p*-bromobenzaldehyde (no *p*-bromobenzyl alcohol observed) at a rate slower than the rate of oxidation of *p*-bromotoluene. Thus the benzyl alcohol seems to be produced directly from the toluene and benzaldehyde from the benzyl alcohol. The difference in products

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(3) Farbwerke vorm. Meister, Lucius and Brüning, German Patents 158,609 (1902) and 174,238 (1903); *Chem. Zentr.*, [I] **76**, 840 (1905); [II] **77**, 1297 (1906).

(4) R. Ramaswamy, M. S. Venkatachalapathy, and H. V. K. Udupa, *Bull. Chem. Soc. Japan*, **35**, 1751 (1962).

(5) R. C. Fuson, "Reactions of Organic Compounds: A Textbook for the Advanced Student," John Wiley and Sons, Inc., New York, N. Y., 1962, pp 208–209.

(6) (a) S. V. Lieberman and R. Connor, "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1943, p 441; (b) T. Nishimura, *Org. Syn.*, **36**, 58 (1956).

(7) G. W. K. Cavill and D. H. Solomon, *J. Chem. Soc.*, 3943 (1954).

(8) M. Schmidt and H. Schmidbaur, *Angew. Chem.*, **70**, 704 (1958).

(9) G. H. Coleman and G. E. Honeywell, "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1962, p 443.

(10) (a) See ref 9, p 89; (b) W. L. McEwen, "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1962, p 133.

(11) L. F. Fieser and M. Fieser, "Advanced Organic Chemistry," Reinhold Publishing Corp., New York, N. Y., 1961, pp 816–819.

(12) The possibility of a two-electron oxidation was suggested by Professor R. Pettit.

(13) F. A. Cotton and G. Wilkinson, "Advanced Inorganic Chemistry," Interscience Publishers, Inc., New York, N. Y., 1962, p 886.

from the hydrocarbon toluenes and the halo-substituted toluenes could be a result of a change in mechanism. Possibly there is a change from a one- to a two-electron oxidation or possibly the halogen may complex directly with cerium(IV). The mechanisms of these oxidations are currently being investigated.

Experimental Section

Materials.—*p*-Methoxytoluene was prepared from *p*-cresol and dimethyl sulfate,[14] bp 172–173° (740 mm), lit.[15] bp 176–177.5° (753 mm). All other toluenes and the benzaldehydes were commercial materials purified by standard methods when necessary. *p*-Methylbenzyl alcohol was obtained from the saponification of *p*-methylbenzyl acetate (Columbia Organic) and was recrystallized from heptane, mp 57.0–59.5°, lit.[16] mp 61°. The other benzyl alcohols were obtained from commercial sources and other workers. The benzyl acetates were prepared by acetylation of the alcohols by acidic acetic acid. Purity of all compounds was checked by vapor phase chromatography (vpc) and nuclear magnetic resonance (nmr). The reagent grade ceric ammonium nitrate (from Matheson Coleman and Bell and G. F. Smith and Co.) was used without further purification.

Vpc analyses were conducted on an Aerograph Model 202 gas chromatograph (Wilkens Instrument and Research, Inc.) fitted with dual thermal conductivity detectors. A 6 ft × $^1/_4$ in. column packed with 20% SF-96 on 60–80 Chromosorb W was used at column temperatures from 100 to 200°.

Product Studies in 50% Aqueous Acetic Acid.—To 2 mmoles of the toluene was added 8–16 mmoles of 0.5 M ceric ammonium nitrate in 50% aqueous acetic acid. The solution (or mixture) was heated on a steam bath until it was pale yellow (*ca.* 15–30 min). A quantity of 100 μl of standard, ethyl *n*-butyrate, was added. The solution was added to 25 ml of water in a separatory funnel and the mixture was extracted with 25 ml of ether. The ether layer was separated and washed with enough 1.5 N potassium hydroxide to neutralize all the acetic acid. The ether solution was dried over magnesium sulfate and analyzed by vpc. Products were identified by vpc peak enhancement using authentic samples. The relative thermal conductivities and distribution ratios (between the ether and aqueous phases) of standard and aldehydes were determined by adding 2 mmoles of the aldehyde and 100 μl of ethyl *n*-butyrate to the appropriate amount of 0.5 M solution of ceric ammonium nitrate in 50% aqueous acetic acid which had been reduced to a cerium(III) solution by adding a small amount of ethyl alcohol and heating on a steam bath until colorless. The solution was worked up as previously described and the vpc peak areas of standard and aldehyde were obtained. The yields of alcohol and acetate were calculated by making the assumption that the relative thermal conductivities and distribution ratios of the aldehyde, alcohol, and acetate are the same.

Product Studies in Anhydrous Acetic Acid.—A quantity of 4–10 mmoles of ceric ammonium nitrate was added to a solution of 2 mmoles of toluene in enough glacial acetic acid to make the ceric ion concentration 0.5 M if all the ceric ammonium nitrate had dissolved. The mixture was refluxed until the orange solid turned white and the liquid pale yellow (*ca.* 10–45 min). The mixture was worked up and analyzed as previously described.

Oxidation of *p*-Bromobenzyl Acetate.—A quantity of 4 mmoles of ceric ammonium nitrate was added to 2 mmoles of *p*-bromobenzyl acetate in 8 ml of glacial acetic acid. The mixture was refluxed until pale yellow (73 min) and worked up and analyzed as described above. Only *p*-bromobenzaldehyde and *p*-bromobenzyl acetate were detected in the ratio 14:86.

Acknowledgment.—We thank Dr. E. J. Geels and Professor G. A. Russell for some of the benzyl alcohols used in this study and the donors of the Petroleum Research Fund, administered by the American Chemical Society, for partial support of this research.

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[14] G. S. Miers and F. D. Hager, "Organic Syntheses," Coll. Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1941, p 58.

[15] J. K. Marsh, *J. Chem. Soc.*, **125**, 418 (1924).

[16] D. Davidson and M. Weiss, "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1962, p 590.

Synthesis of Adenine by Oligomerization of Hydrogen Cyanide

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Oró and Kimball[1] have reported that purines, especially adenine, are formed under presumed primitive earth conditions. By heating a solution of hydrogen cyanide in aqueous ammonia for one to several days at moderate temperatures (27–100°), they obtained 0.3–0.5% of adenine.

This communication reports on the oligomerization of hydrogen cyanide to synthesize the pentamer, adenine, under similar conditions. It was found that adenine and 4,5-dicyanoimidazole were synthesized simultaneously by heating a solution of hydrogen cyanide in liquid ammonia for 10 to 20 hr at elevated temperatures. The yields of adenine and 4,5-dicyanoimidazole were 15 and 10%, respectively, based on hydrogen cyanide used.

The marked improvement of the yield was considered to be due to the following reasons. It has been well known that hydrogen cyanide is polymerized explosively in the presence of base such as ammonia. In liquid ammonia,[2] however, hydrogen cyanide is considered to exist in stable dissociated form at room temperature, and even at higher temperatures formamidine, one carbon unit to be condensed with presumed hydrogen cyanide trimer or its amidine derivatives, could exist much more stably than in aqueous ammonia. As a matter of fact, hydrogen cyanide dissolved in the excess of liquid ammonia was stored without any change at 15° for 2 months.

It is noteworthy that the yield of adenine is markedly improved in liquid ammonia as compared to the aqueous system reported by Oró. This simple method is considered to be a highly attractive one to synthesize adenine and 4,5-dicyanoimidazole. In this connection it would be interesting to study the reaction mechanism. More details will be reported at a later date.

Experimental Section

Hydrogen cyanide (4 ml), dried over phosphorus pentoxide, and 10 ml of liquid ammonia, dried over sodium, were placed in a small pressure tube and heated at 120° for 20 hr. Then the volatile materials were removed from the reaction mixture under reduced pressure. The residual dark brown solid was extracted with hot water. The paper chromatogram of the aqueous solution developed by the solvent system, *n*-propyl alcohol–ammonium hydroxide–water (20:12:3 v/v), showed two spots (R_f 0.84 and 0.45) under ultraviolet light. The R_f value of 0.45 corresponds to that of adenine and 0.84 to that of 4,5-dicyanoimidazole.

The excised spots were extracted with 0.1 N hydrochloric acid and the yields of adenine (15%) and 4,5-dicyanoimidazole (10%) were determined by the ultraviolet absorbance of the acidic solution.

The crude adenine was isolated by evaporating the aqueous extract under reduced pressure to dryness. Sublimation at 210–

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[1] J. Oró and A. P. Kimball, *Arch. Biochem. Biophys.*, **94**, 217 (1961).

[2] L. F. Audrieth and J. Kleinberg, "Non-aqueous Solvents," John Wiley and Sons, Inc., New York, N. Y., 1953, p 77.