Structure and Thermal Isomerization of the Adducts Formed in the Reaction of Cyclohexyl Isocyanide with Dimethyl Acetylenedicarboxylate[1]

H. Junjappa,[2a] M. K. Saxena,[2a] D. Ramaiah,[2b] B. B. Loharay,[2a] N. P. Rath,[2c] and M. V. George*,[2a,b,d,e]

Photochemistry Research Unit, Regional Research Laboratory (CSIR), Trivandrum 695 019, India, Department of Chemistry, University of Missouri−St. Louis, Missouri 63121, Department of Chemistry, Indian Institute of Technology, Kanpur 208 016, India, Radiation Laboratory, University of Notre Dame, Notre Dame, Indiana 46556, and Jawaharlal Nehru Centre for Advanced Scientific Research, Bangalore 560 064, India

Received July 21, 1998

Reaction of cyclohexyl isocyanide (**1d**) with dimethyl acetylenedicarboxylate (DMAD) gave a mixture of products such as the cyclopenta[*b*]pyridine derivatives **14** (28%) and **19** (1%), the azaspirononatriene derivative **13** (2%), and the azabicyclononatriene **16** (3%). Interestingly, **14** on refluxing in xylene for 3 h gave exclusively **13** (92%), whereas when the reaction was continued for 6 h, a mixture of **13** (85%) and **19** (9%) was formed. In a separate reaction, when **13** was heated in a sealed tube at 200 °C for 1 h, **19** was isolated in 63% yield. Activation energies for the thermal isomerization of **14** to **13** and **13** to **19** have been found to be 19.4 and 16.7 kcal/mol, respectively. Hydrogenation of **13** and **14** gave a mixture of the tetrahydro derivatives, **22** and **23**, in each case. The structures of **13**, **14**, **16**, **19**, **22**, and **23** were established unambiguously through X-ray crystallographic analysis.

Introduction

In view of our general interest in the reaction of 1,3-dipolar systems, we have examined the reaction of a nucleophilic carbene such as cyclohexyl isocyanide with dimethyl acetylenedicarboxylate (DMAD), a reaction in which potential 1,3- and 1,5-dipolar intermediates could be involved. Reactions of aliphatic and aromatic isocyanides with ketones[3,4] and acetylenic compounds[5−12] have been investigated in detail. Thus, it has been reported[8,9] that the reaction of several isocyanides with hexafluoro-2-butyne gives interesting cyclopropene derivatives in aprotic solvents, whereas when the reaction is carried out in protic media such as methanol, two different 1:1:1 adducts (isocyanide:acetylene:alcohol), an unsaturated imino ester and a ketenimine, are formed. Suzuki and co-workers[13,14] have shown that complex mixtures of products are formed from the reactions of aromatic isocyanides such as 2,6-dimethylphenyl and 4-bromo-2,6-dimethylphenyl isocyanides with DMAD (Scheme 1). Some of these include the 2:1 adduct **3**, the 3:1 adduct **5**, and the 2:3 adduct **4**. Interestingly, the product **4** has been found to be thermally sensitive and undergoes facile isomerization to give **6**.[13] The reaction of aliphatic isocyanides with various acetylenic substrates has been reported by Winterfeldt and co-workers.[6,7,15,16] Thus, for example, the reaction of *tert*-butyl and cyclohexyl isocyanides (**1c** and **1d**) with DMAD at 0 °C gave a mixture of 1:2 adducts **7c** and **7d**, respectively, whereas the reaction of *tert*-butyl isocyanide with DMAD at −20 °C gave an interesting 2:3 adduct, the bicyclobutane derivative **8c** (Scheme 2). In addition, other products such as the 1:2 adducts were also isolated from this reaction.[6,7,10] The bicyclobutane derivative **8c** formed in this reaction has been found to undergo thermal isomerization to a pentalene derivative **9c** (Scheme 2).[15,16] Our interest in the reaction of cyclohexyl isocyanide with DMAD dates back to 1961, when in some preliminary studies an initially formed 2:3 adduct **14** was isolated.[17] Since then there have been several reports dealing with the reaction of

(1) (a) Dedicated to Professor Dr. Rolf Huisgen. (b) Document No. RRLT-PRU-85 from the Regional Research Laboratory, Trivandrum, and No. NDRL-4078 from the Notre Dame Radiation Laboratory.

(2) (a) Department of Chemistry, Indian Institute of Technology, Kanpur 208016, India. (b) Photochemistry Research Unit, Regional Research Laboratory (CSIR), Trivandrum 695019, India. (c) Department of Chemistry, University of Missouri-St. Louis, MO 63121. (d) Radiation Laboratory, University of Notre Dame, Notre Dame, IN 46556. (e) Jawaharlal Nehru Centre for Advanced Scientific Research, Bangalore 560 064, India.

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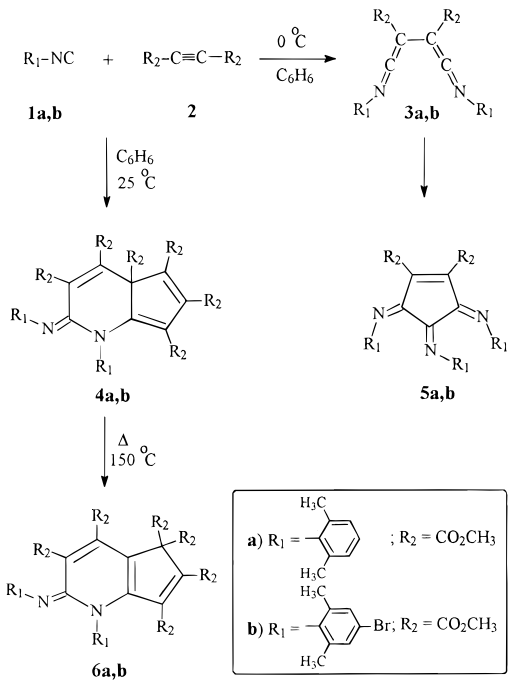
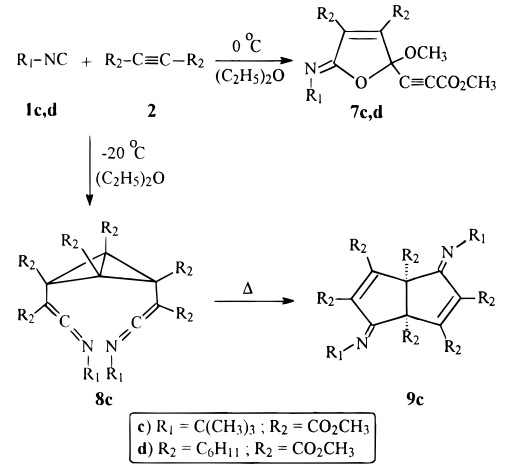
10.1021/jo981427f CCC: $15.00
Published on Web 12/04/1998

Scheme 1



Scheme 2



isocyanides with DMAD,[13−16] and other substrates.[18,19] Some of these involve the formation of 1,3-dipolar species as primary intermediates. The reactions of 1,3- and 1,4-dipolar species with different dipolarophiles have been extensively used in the synthesis of numerous heterocycles.[20] Herein we present the results of our studies dealing with the reaction of cyclohexyl isocyanide with DMAD, the isolation of different cycloadducts, and the thermal isomerization of some of the adducts.

Results and Discussion

1. Reaction of Cyclohexyl Isocyanide (1d) with Dimethyl Acetylenedicarboxylate (DMAD). The reaction of **1d** with DMAD (in a 2:3 ratio) in diethyl ether at ca. 5−10 °C gave a mixture of the cyclopenta[*b*]-pyridine derivatives **14** (28%) and **19** (1%), the azaspirononatriene **13** (2%), and the azabicyclononatriene derivative **16** (3%) (Scheme 3). In contrast, when the reaction was carried out with 1:2, 1:3, and 1:4 ratios of isocyanide and DMAD under identical conditions, only **14** could be isolated, along with some unreacted DMAD, in each case. Interestingly, when the adduct **14** was heated for 3 h in xylene at ca. 130 °C, it underwent isomerization to give **13** in quantitative yields, whereas when **14** was refluxed for 6 h, a mixture of **13** (85%) and another isomer **19** (9%) was formed. Similarly, compound **13**, on heating at ca. 200 °C for 1 h, gave 63% of isomer **19**.

Treatment of **14** with perchloric acid gave a perchlorate salt, **17a** (Scheme 3). The same salt was obtained on treatment of **13** with perchloric acid, suggesting that **14** undergoes initial isomerization to **13**, which then is converted to **17a**. Treatment of **13** with hydrobromic acid likewise gave the hydrobromide **17b**. The structure of **17b** was confirmed through X-ray crystallographic analysis by Gougoutas and Saenger,[21] using a crystal provided by us.

Hydrogenation of **14** in methanol using Raney nickel catalyst gave a mixture of two tetrahydro derivatives, **22** (48%) and **23** (10%) (Scheme 4). Similarly, hydrogenation of **13** in methanol, under analogous conditions, gave a mixture of **22** (74%) and **23** (11%). The structures of the different adducts, **14**, **13**, **16**, **19**, and the reduction products **22** and **23** have been determined on the basis of analytical results and spectral data. Further confirmation of these structures was derived through X-ray crystallographic analysis.[22]

The formation of the 2:3 adducts **14**, **13**, **19** and **16** in the reaction of cyclohexyl isocyanide with DMAD can be rationalized in terms of the pathways shown in Scheme 3. Addition of cyclohexyl isocyanide to the triple bond of DMAD, leading to the formation of the 1,3-dipolar intermediate **10** is well documented in the literature.[8,13−16,23] Subsequent reaction of **10** with DMAD could give rise to a 1,5-dipolar intermediate **11**, which in turn could give rise to the iminocyclopentadiene derivative **15**. The reaction of **15** with the 1,3-dipolar intermediate **10** through a [4 + 6] cycloaddition pathway would result in the formation of the cyclopenta[*b*]pyridine derivative **14**, which is the primary 2:3 adduct. Similar 2:3 adducts have been reported in the reaction of 2,6-dimethylphenyl isocyanide and 4-bromo-2,6-dimethylphenyl isocyanide with DMAD.[13] A bicyclic adduct such as **14** can undergo facile rearrangements, leading to isomeric products. Thus, the facile thermal isomerization of **14**, involving a 1,5-sigmatropic shift, would lead to the azaspiro adduct **13**, which in turn can undergo further 1,5-sigmatropic shifts leading to the more stable adduct **19**. The formation of **19** from **13** may be going through the intermediate dihydropyrindine derivative **18** (Scheme 3). One could also visualize the formation of **19**, directly from **14** through several sequential 1,5-sigmatropic shifts.

The formation of **16**, on the other hand, proceeds through an altogether different route. The 1,5-dipolar

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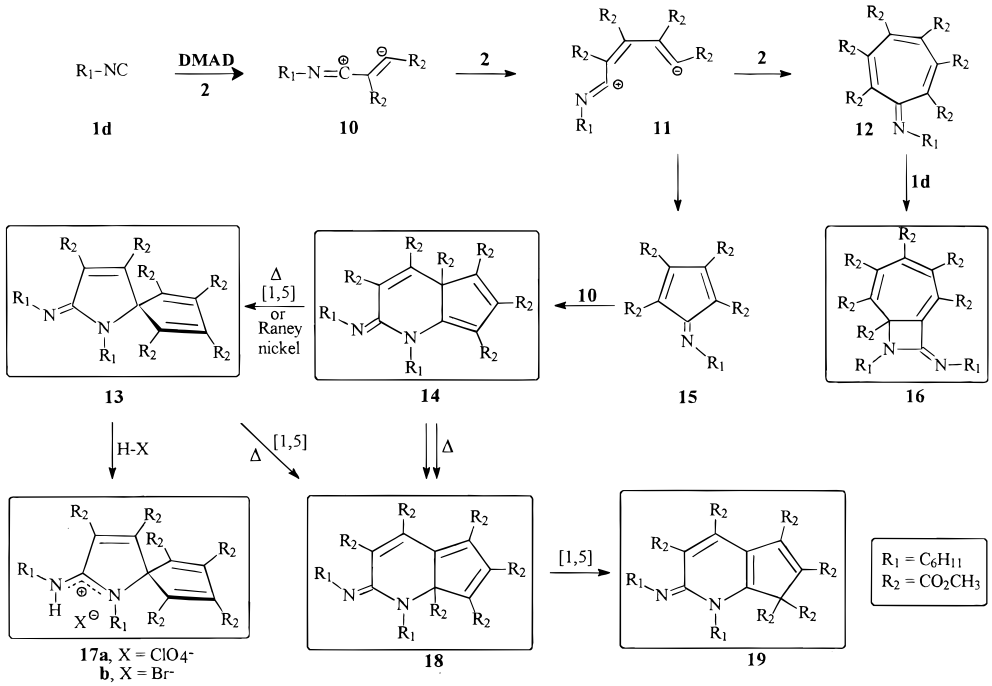
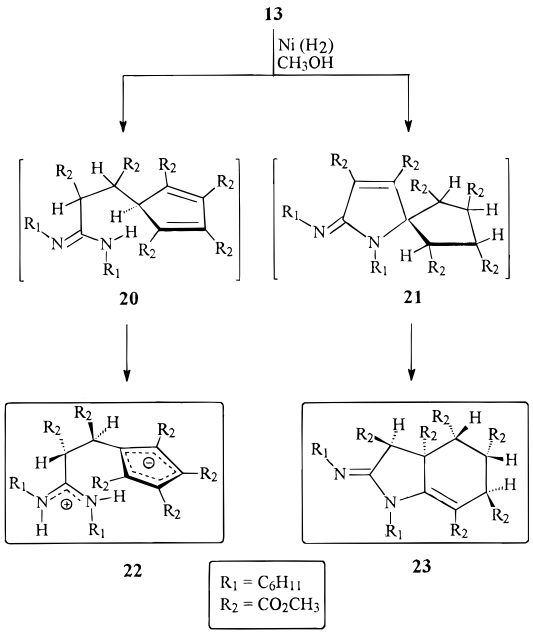
Scheme 3



Scheme 4



intermediate **11** could react further with DMAD to give the iminocycloheptatriene derivative **12**. Further reaction of the starting isocyanide **1d** with **12** could give yet another 2:3 adduct, **16**.

Both **14** and **13**, on treatment with Raney nickel in methanol gave a mixture of **22** and **23**, in each case, although in different yields. It is assumed that both **22** and **23** are derived from the common precursor **13**. In the presence of Raney nickel, **14** isomerizes to **13** initially, before it undergoes hydrogenation. This is substantiated by the fact that there was a decrease in the absorption at 420 nm, characteristic of **14** and a corresponding increase in the absorption at 328 nm, characteristic of **13**, when **14** was treated with Raney nickel alone, without hydrogen.

The formation of the tetrahydro derivatives **22** and **23** from **13** upon Raney nickel treatment may proceed through the initially formed intermediates, **20** and **21**, respectively (Scheme 4). Hydrogenation of the pyrrolidine ring of **13** would result in **20**, which subsequently isomerizes to **22**. It has been possible to locate the positions of all the hydrogen atoms through X-ray analysis, and it is interesting to note that **22** exists as a zwitterionic species with the two nitrogens bearing two hydrogen atoms and the positive charge and the cyclopentadiene ring having the negative charge. Hydrogenation of the cyclopentadiene moiety, on the other hand, may lead to **21**, which can undergo further rearrangement in the presence of Raney nickel to give **23**.

Table 1. Rate Constants and Thermodynamic Data of the Thermal Isomerization of 14 to 13 and 13 to 19[a]

thermal isomerization[b]	temp (K)	rate constant, k, 10^{-4} s^{-1}	E_a, kcal/mol	ΔS, eu
14 to **13**	358	0.84	19.4	−25.6
	368	1.74		
	378	3.71		
13 to **19**	413	1.10	16.7	−38.9
	423	1.76		
	428	2.22		

[a] Average of more than two experiments. [b] The thermal isomerization monitoring wavelengths (λ_{max}) are 420 nm for **14** to **13** and 380 nm for **13** to **19**.

2. Thermal Isomerization of 14 to 13 and 13 to 19. The observed rate of isomerization followed first-order kinetics uniformly with different concentrations of **14** at different temperatures in xylene. The progress of the reaction was followed by the decrease in the extinction coefficient at λ_{max} 420 nm (characteristic of compound **14**) as a function of time at a given temperature. Plot of log A versus time gave a straight line, and from the slope, the rate of the reaction was calculated. Table 1 summarizes the kinetic and thermodynamic parameters for the thermal isomerization of **14** and **13**.

The activation energy for this isomerization was found to be 19.4 kcal mol^{-1}, with a large negative entropy

change (−25 eu), which is typical of usual sigmatropic rearrangements.

The kinetic studies on the thermal isomerization of compound **13** to **19** were carried out in *o*-dichlorobenzene. Measurement of λ_{max} at 328 nm did not show gradual decrease in the extinction coefficient but rather a gradual increase in the extinction coefficient along with the development of new peak at λ_{max} 380 nm (characteristic of compound **19**). We have found that the plot of log *A* at λ_{max} 380 nm with time at a given temperature for the initial period (35 min) of isomerization reaction gave a straight line and the slope of which yielded the rate of isomerization of **13** to **19** (Table 1). The activation energy for this process was found to be 16.7 kcal mol^{-1} with a large negative entropy change (−39 eu). This indicates the fact that the isomerization of **13** to **19** is very facile, even though involving several steps.

Experimental Section

The equipment and procedures for melting point determination and spectral recordings are described in earlier papers.[24] Solvents were purified by standard procedures before use. Kinetic experiments were carried out in a constant-temperature bath (±0.1 °C). Xylene and *o*-dichlorobenzene used for kinetic measurements were purified and dried before use.

Starting Materials. Cyclohexyl isocyanide (**1d**), bp 56−58 °C (11 mm),[25] dimethyl acetylenedicarboxylate (**2**, DMAD), bp 95−98 °C (19 mm),[26] and Raney nickel catalyst[27] were prepared by reported procedures.

Reaction of Cyclohexyl Isocyanide (1d) with Dimethyl Acetylenedicarboxylate (DMAD). To a solution of **1d** (4.36 g, 0.04 mol) in anhydrous diethyl ether (100 mL) at around 5−10 °C was added, in portions, an ethereal solution (100 mL) of DMAD (12.18 g, 0.085 mol) over a period of 2 h with constant stirring. After the addition was over, the reaction mixture was allowed to stand at room temperature for 2 h, and then the ether was distilled off on a water bath to give a sticky dark red mass. It was cooled and triturated with ethanol (15 mL) and kept in the refrigerator overnight to give 3.6 g (28%) of hexamethyl 1-cyclohexyl-2-(cyclohexylimino)-1*H*-cyclopenta[*b*]-pyridine-3,4,4a,5,6,7(2*H*)-hexacarboxylate (**14**), mp 156−157 °C, after recrystallization from ethanol: IR ν_{max} (KBr) 1738, 1708 cm^{-1}; UV λ_{max} (methanol) 214 nm (ϵ, 19050), 424 (10000); ^{1}H NMR ($CDCl_3$) δ 1.1−1.95 (20H, m), 2.41 (1H, m), 3.21 (1H, m), 3.67 (3H, s), 3.69 (3H, s), 3.75 (3H, s), 3.77 (3H, s), 3.79 (3H, s), 3.93 (3H, s); ^{13}C NMR (CDCl3) δ 23.73, 23.74, 25.35, 25.62, 26.25, 26.63, 28.60, 30.48, 32.81, 33.79, 51.64, 51.73, 52.32, 52.47, 53.72, 60.56, 65.03, 66.23, 106.89, 118.23, 127.98, 139.65, 142.36, 152.33, 160.56, 161.22, 161.76, 162.65, 164.14, 164.56, 165.10; mass spectrum, *m/e* (relative intensity) 644 (M^+, 100), 585 (9), 374 (6). Anal. Calcd for $C_{32}H_{40}N_2O_{12}$: C, 59.62; H, 6.25; N, 4.34. Found: C, 59.99; H, 6.27; N, 4.38.

The mother liquor, after removal of the solid, was chromatographed over alumina. Elution of the column with a mixture (1:1) of benzene and petroleum ether gave 130 mg (1%) of hexamethyl 1-cyclohexyl-2-(cyclohexylimino)-1,2-dihydro-7*H*-cyclopenta[*b*]pyridine-3,4,5,6,7,7-hexacarboxylate (**19**), mp 197−198 °C: IR ν_{max} (KBr) 1780, 1710 cm^{-1}; UV λ_{max} (methanol) 252 nm (ϵ, 10000), 384 (25120), 440 (5100); ^{1}H NMR ($CDCl_3$) δ 1.1−1.9 (18H, m), 2.75−2.95 (4H, m), 3.76 (3H, s), 3.77 (3H, s), 3.78 (6H, s), 3.80 (3H, s), 3.89 (3H, s); ^{13}C NMR ($CDCl_3$) δ 24.31, 25.26, 25.80, 29.44, 33.44, 51.84, 52.05, 52.50, 53.58, 57.24, 65.99, 68.07, 107.79, 113.04, 120.52, 135.89, 141.53, 146.15, 157.70, 161.40, 163.82, 164.20, 164.77, 166.11; mass spectrum *m/e* (relative intensity) 644 (M^+, 14), 480 (48), 471 (74). Anal. Calcd for $C_{32}H_{40}N_2O_{12}$: C, 59.62; H, 6.25; N, 4.53. Found: C, 59.59; H, 6.27; N, 4.53.

Further elution of the column gave 385 mg (3%) of hexamethyl 8-cyclohexyl-9-(cyclohexylimino)-8-azabicyclo[5.2.0]-nona-2,4,6-triene-1,2,3,4,5,6-hexacarboxylate (**16**), mp 183−184 °C, after recrystallization from ethyl acetate: IR ν_{max} (KBr) 1741, 1727, 1714 cm^{-1}; UV λ_{max} (methanol) 264 nm (ϵ, 15850), 365 (9330); ^{1}H NMR ($CDCl_3$) δ 1.0−2.3 (20H, m), 3.3 (1H, m), 3.72 (3H, s), 3.74 (3H, s), 3.76 (3H, s), 3.81 (6H, s), 3.83 (3H, s), 4.20 (1H, m); ^{13}C NMR ($CDCl_3$) δ 23.86, 24.25, 24.49, 25.44, 25.56, 29.14, 30.12, 33.82, 34.00, 51.70, 52.52, 52.62, 52.80, 53.40, 58.89, 59.05, 64.29, 95.31, 123.21, 128.04, 131.00, 133.80, 142.72, 159.10, 163.99, 164.62, 164.77, 164.98, 167.60; mass spectrum *m/e* (relative intensity) 644 (M^+, 43), 562 (66), 480 (10). Anal. Calcd for $C_{32}H_{40}N_2O_{12}$: C, 59.62; H, 6.25; N, 4.34. Found: C, 59.84; H, 6.40; N, 4.26.

Finally, the column was eluted with a mixture (4:1) of benzene and ethyl acetate to give 250 mg (2%) of hexamethyl 1-cyclohexyl-2-(cyclohexylimino)-1-azaspiro[4.4]nona-3,6,8-triene-3,4,6,7,8,9-hexacarboxylate (**13**), mp 136−137 °C, after recrystallization from methanol: IR ν_{max} (KBr) 1755, 1740, 1725 cm^{-1}; UV λ_{max} (methanol) 242 nm (ϵ, 15140), 365 (2570); ^{1}H NMR ($CDCl_3$) δ 1.0−1.8 (18H, m), 1.95−2.17 (2H, m), 2.81−3.01 (1H, m), 3.30 (1H, m), 3.70 (3H, s), 3.75 (6H, s), 3.90 (6H, s), 3.91 (3H, s); ^{13}C NMR ($CDCl_3$) δ 24.31, 25.26, 25.62, 26.28, 28.63, 35.44, 52.23, 52.35, 52.71, 55.25, 57.78, 80.22, 136.07, 138.08, 140.90, 142.04, 148.12, 160.23, 161.10, 162.41, 165.13; mass spectrum *m/e* (relative intensity) 644 (M^+, 100), 553 (8). Anal. Calcd for $C_{32}H_{40}N_2O_{12}$: C, 59.62; H, 6.25; N, 4.53. Found: C, 59.59; H, 6.13; N, 4.45.

The experiment was repeated using 1:2, 1:3, and 1:4 ratios of isocyanide and DMAD, under identical conditions to give 9%, 15%, and 26%, respectively, of **14** as the only isolable product, along with some amounts of the unreacted DMAD, in each case.

Thermal Transformation of 14. A solution of **14** (1.29 g, 2.0 mmol) in dry xylene (25 mL) was refluxed for 3 h under nitrogen atmosphere. The reaction mixture slowly turned blood red. The solvent was removed under vacuum to give a deep red viscous liquid, which was triturated with ethanol to give 1.18 g (92%) of **13**, mp 136−137 °C (mixture mp), after recrystallization from ethanol.

In a separate run when the solution of **14** (3.22 g, 5.0 mmol) in dry xylene (30 mL) was refluxed for 6 h under nitrogen atmosphere, and workup of the reaction mixture as in the earlier case gave 2.75 g (85%) of the red product **13**, mp 136−137 °C (mixture mp). The mother liquor, after removal of the red solid, was concentrated and fractionally recrystallized from methanol to give 300 mg (9%) of **19**, mp 197−198 °C (mixture mp).

Thermal Transformation of 13. A sample of **13** (322 mg, 0.5 mmol) was heated in an oil bath at ca. 200 °C for 1 h in a sealed tube. The reaction mixture was dissolved in ethanol and fractionally recrystallized to give 200 mg (63%) of **19**, mp 198 °C (mixture mp).

Reaction of 14 with Perchloric Acid. To a warm solution of **14** (322 mg, 0.5 mmol) in methanol (5 mL) was added perchloric acid (1 mL) in portions, and the reaction mixture was allowed to stand at room temperature for 6 h. The reaction mixture became colorless. It was diluted with cold water when a colorless solid precipitated out. The solid product was filtered, washed with cold water, and recrystallized from ethanol to give 320 mg (86%) of the perchlorate salt of hexamethyl 1-cyclohexyl-2-(cyclohexylimino)-1-azaspiro[4.4]-nona-3,6,8-triene-3,4,6,7,8,9-hexacarboxylate (**17a**), mp 186−188 °C: IR ν_{max} (KBr) 3331, 1724 cm^{-1}; UV λ_{max} (methanol) 245 nm (ϵ, 28900), 295 (20420); ^{1}H NMR ($CDCl_3$) δ 1.6−2.15 (22H, m), 3.8 (3H, s), 3.9 (6H, s), 4.0 (6H, s), 4.1 (3H, s); ^{13}C

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NMR ($CDCl_3$) δ 24.24, 24.86, 25.17, 25.57, 29.66, 32.67, 53.47, 53.81, 54.22, 55.87, 135.35, 136.15, 145.48, 159.43, 159.62, 161.44, 161.45. Anal. Calcd for $C_{32}H_{41}N_2O_{16}Cl$: C, 51.50; H, 5.78; N, 4.51. Found: C, 51.81; H, 5.76, N, 4.06.

Reaction of 13 with Perchloric Acid. To a solution of **13** (322 mg, 0.5 mmol) in methanol (5 mL) was added perchloric acid (1 mL) in small portions. The reaction mixture became colorless after 6 h. It was then diluted with cold water, when a thick colorless solid precipitated. The product was recrystallized from ethanol to give 330 mg (89%) of the same perchlorate salt, **17a**, mp 186−188 °C (mixture mp).

Reaction of 13 with Hydrobromic Acid. To a solution of **13** (644 mg, 1.0 mmol) in methanol (5 mL) was added hydrobromic acid (2 mL), and the reaction mixture was allowed to stand at room temperature for 12 h. It was then poured on crushed ice. The solid product that precipitated out was filtered, washed with cold water, and recrystallized from methanol to give 720 mg (99%) of the hydrobromide salt of hexamethyl 1-cyclohexyl-2-(cyclohexylimino)-1-azaspiro[4.4]-nona-3,6,8-triene-3,4,6,7,8,9-hexacarboxylate (**17b**),[18] mp 156−157 °C: IR ν_{max} (KBr) 1724, 1650 cm^{-1}; UV λ_{max} (methanol) 246 nm (ϵ, 13490), 300 (5250). Anal. Calcd for $C_{32}H_{41}N_2O_{12}$-Br: C, 52.95; H, 5.56; N, 3.86. Found: C, 52.90; H, 5.74; N, 3.82.

Catalytic Hydrogenation of 14 in Methanol. To a solution of **14** (515 mg, 0.8 mmol) in methanol (30 mL) was added freshly prepared Raney nickel catalyst (1.0 g), and the reaction mixture was shaken in hydrogen atmosphere at 80 psi for 32 h. The catalyst was filtered and washed with an additional amount of methanol (20 mL). The filtrate was concentrated under vacuum, and the resultant viscous mass was chromatographed over silica gel. Elution with a mixture (1:1) of benzene and petroleum ether gave 52 mg (10%) of hexamethyl 1-cyclohexyl-2-(cyclohexylimino)-3a*H*-indole-3,-3a,4,5,6,7-hexacarboxylate **23**, mp 193−194 °C, after recrystallization from methanol: IR ν_{max} (KBr) 3320, 1740, 1700 cm^{-1}; UV λ_{max} (methanol) 260 nm (ϵ, 36770), 352 (31940); ^1H NMR ($CDCl_3$) δ 0.8−2.3 (20H, m), 2.6−3.1 (2H, s), 3.35 (1H, d, J = 9 Hz), 3.7 (3H, s), 3.8 (6H, s), 3.9 (7H, s), 4.0 (3H, s), 4.65 (1H, d, J = 2 Hz), 4.71 (1H, s); ^{13}C NMR ($CDCl_3$) δ 24.15, 25.58, 26.00, 26.50, 26.75, 27.49, 27.64, 34.35, 41.62, 42.32, 43.41, 49.62, 51.70, 52.25, 52.48, 52.63, 52.81, 53.98, 54.39, 58.74, 59.39, 61.45, 90.32, 99.83, 149.40, 150.29, 167.64, 167.77, 169.63, 170.37, 170.73, 174.10; mass spectrum (chemical ionization) m/s 649 (MH^+, 100). Anal. Calcd for $C_{32}H_{44}N_2O_{12}$: C, 59.25; H, 6.79; N, 4.32. Found: C, 59.44; H, 6.42; N, 4.54.

Continued elution of the column with a mixture (1:4) of ethyl acetate and benzene gave 248 mg (48%) of tetramethyl 5-[3-(cyclohexylamino]-3-(cyclohexylimino)-1,2-bis(methoxycarbonyl)-2-propenyl]-1,3-cyclopentadiene-1,2,3,4-tetracarboxylate (**22**), mp 213−214 °C, after recrystallization from ethyl acetate: IR ν_{max} (KBr) 3410, 1750, 1730, 1715 cm^{-1}; UV λ_{max} (methanol) 227 nm (ϵ, 17400), 301 (14500); ^1H NMR ($CDCl_3$) δ 0.71−2.2 (20H, m), 2.9−3.4 (2H, m), 3.55 (3H, s), 3.65 (3H, s), 3.70 (3H, s), 3.72 (3H, s), 3.80 (3H, s), 3.87 (3H, s), 3.90−4.4 (1H, m), 5.4 (2H, q, J = 12 Hz), 6.51 (1H, d, J = 8 Hz, D_2O-exchangeable), 8.9 (1H, d, J = 8 Hz, D_2O-exchangeable); ^{13}C NMR ($CDCl_3$) δ 24.31, 24.42, 24.67, 24.99, 29.29, 30.69, 33.21, 33.60, 42.28, 47.19, 50.71, 51.07, 51.55, 51.79, 52.35, 53.52, 54.76, 109.82, 113.89, 116.18, 123.34, 159.42, 166.74, 167.10, 168.56, 169.75, 170.66, 173.01; mass spectrum m/e (relative intensity) 648 (M^+, 4), 280 (39), 199 (52), 67 (100). Anal. Calcd for $C_{32}H_{44}N_2O_{12}$: C, 59.20; H, 6.80; N, 4.32. Found: C, 59.40; H, 6.70; N, 4.57.

Catalytic Hydrogenation of 13 in Methanol. To a solution of **13** (644 mg, 1.0 mmol) in methanol (50 mL) was added Raney nickel catalyst (1.0 g), and the reaction mixture was shaken in the presence of hydrogen at 70 psi for 24 h. The catalyst was filtered and washed with an additional amount of methanol (20 mL). The filterate was concentrated under vacuum, and the products were chromatographed over silica gel. Elution with a mixture (1:4) of ethyl acetate and benzene gave 72 mg (11%) of **23**, mp 193−194 °C (mixture mp), after recrystallization from ethyl acetate.

Continued elution of the column with a mixture (1:1) of benzene and ethyl acetate gave 478 mg (74%) of **22**, mp 213-214 °C (mixture mp), after recrystallization from ethyl acetate.

Kinetic Measurements. A degassed solution of **14** in xylene (4.3×10^{-5} M) was placed in a 250 mL flask, covered with a septum, and maintained at the desired temperature. Aliquots of this solution were removed at different time intervals to glass vials, and the reaction, in each case, was quenched by dipping it in ice-bath. The absorbance was measured, and the change in absorbance with respect to time was plotted to give a straight line. The value of the rate constant was evaluated using standard equations, and it was found that the reaction followed first-order kinetics. Measuring the rate constants at three different temperatures and plotting the values of log k versus $1/T$ gave a straight line. The values of the activation energy (E_a) and entropy change (ΔS) were evaluated using standard equations.

Similarly, a degassed solution of **13** in *o*-dichlorobenzene (4.5×10^{-5}) was subjected to kinetics studies as in the earlier case. The values for rate constants and Arrhenius parameters for the conversion of **14** to **13** and **13** to **19** are presented in Table 1.

X-ray Structure Determination of 13, 14, 16, 19, 22, and 23. Crystals of **13**, **14**, **16**, **19**, **22**, and **23** were subjected to X-ray crystallographic analysis, employing a Siemens R3 automated four circle diffractometer. Data reduction and structure solution were achieved by SHELXTL-PLUS structure solution package.[28] Full details on the crystal and molecular structures will be published elsewhere.[22]

Acknowledgment. The authors thank Professor Dr. Rolf Huisgen for helpful discussions and Dr. Klaus Herbig for partial experimental assistance. We (D.R. and M.V.G.) thank the Council of Scientific and Industrial Research, Government of India, the Regional Research Laboratory (CSIR), Trivandrum, the Department of Chemistry, Indian Institute of Technology, Kanpur, India, (H.J., M.K.S., B.B.L., and M.V.G.), the University of Missouri-St. Louis (N.P.R.) and Jawaharlal Nehru Centre for Advanced Scientific Research, Bangalore 560 012, India (M.V.G.), and the Office of Basic Energy Sciences of the U. S. Department of Energy (M.V.G. (in part)) for financial support of this work.

Supporting Information Available: ORTEP diagrams of structures and copies of ^1H and ^{13}C NMR spectra of compounds **13**, **14**, **16**, **19**, **22**, and **23**, and a kinetics plot (22 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

JO981427F

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