

Electrophilic Substitution Reactions of Benz[*a*]indeno[1,2,3-*cd*]azulene

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The title compound (**2**) was prepared through the photochemical transformation of several triptycene derivatives. Electrophilic substitution reactions of **2** took place primarily at the 6-position: the Vilsmeier reaction gave the 6-formyl derivative in good yield; bromination afforded the 6-bromo derivative, accompanied by a small amount of the 6,11-dibromo compound; nitration yielded mainly the 6-nitro compound, with the 8-nitro derivative as a minor product. However, Friedel-Crafts type reactions did not give any acyl derivatives. Structures of the reaction products were confirmed by their NMR spectra.

Many non-benzenoid aromatics such as azulene, cyclopropenone, tropolone, etc., have been reported in the literatures,<sup>1</sup> and many compounds in this family possess characteristic features. In particular, the electronic spectra of these compounds appear in the visible to near-infrared region.<sup>2</sup> Therefore, these substances qualify as possible candidates for some of the so-called "new materials" such as those used in photoelectronic devices. However, many of them are rather unstable, and some are difficult to synthesize. For example, cyclopenta[*cd*]azulene (**1**)<sup>3</sup> is an intriguing compound; its alkyl derivatives are synthesized from 4-alkylazulene derivatives by a fairly easy procedure, but these are also unstable. The highly unsaturated nature of the double bonds at C<sub>1</sub>-C<sub>2</sub> and C<sub>3</sub>-C<sub>4</sub> is responsible for the high reactivities of these compounds.<sup>4</sup> On the other hand, the title compound, benz[*a*]indeno[1,2,3-*cd*]azulene (**2**),<sup>5</sup> is stable since both of the reactive double bonds of **1** are protected by benzo anneration. Although **2** is readily obtainable from commercially available anthracene derivatives, its chemical properties are practically unknown. In this report, electrophilic substitution reactions of **2** are presented as the most fundamental feature of such hydrocarbons, and complete analyses of the NMR spectra of the obtained derivatives are also reported.

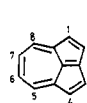
Our plan was to synthesize **2** in a short process from more readily available anthracene derivatives, and to improve the yield of **2**. The first trial involved the dehydrogenating-isomerization of norcaradiene derivative (**3**),<sup>6</sup> an isomer of triptycene, by several dehydrogenation reagents such as dichlorodicyanobenzoquinone (DDQ), but these attempts resulted in the formation of benzo[*a*]fluoranthene.<sup>7</sup> Secondly, we attempted to implement a modified version of Iwamura's method for the photochemical transformation of several bridgehead-substituted triptycenes. Iwamura reported synthesis of **2** from 9-(benzoyloxy)triptycene (**4**) in a good yield (ca. 70%).<sup>5</sup> We used 9-bromoanthracene (**5**) and 9-chloroanthracene (**6**), which were readily available from anthracene by one-step halogenation.<sup>8</sup>

Table I. Yield of Benz[*a*]indeno[1,2,3-*cd*]azulene (**2**)

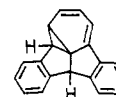
reactant	yield, <sup>a</sup> %	reactant	yield, <sup>a</sup> %
<b>4</b>	82.3	<b>9</b>	20.3 (29.4)
<b>8</b>	15.9 (29.8)	<b>10</b>	84.3

<sup>a</sup> Yield in parentheses is obtained when the reaction is carried out in the presence of Et<sub>3</sub>N.

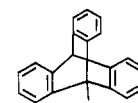
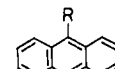
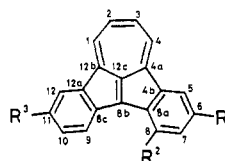
In addition, 9-acetoxyanthracene (**7**)<sup>9</sup> was used as a starting substance. 9-Bromotriptycene (**8**),<sup>10</sup> 9-chlorotriptycene (**9**),<sup>11</sup> and 9-acetoxytriptycene (**10**)<sup>11</sup> were prepared by the reactions of the above 9-substituted anthracenes with benzyne according to the known procedure.<sup>12</sup> Photochemical transformation of the triptycenes to **2** was carried out by irradiation using a low-pressure mercury lamp in cyclohexane (Table I). The yield of **2** from **4** was greater than that of reported by Iwamura.<sup>13</sup>



1



3



2: R <sup>1</sup> = R <sup>2</sup> = R <sup>3</sup> = H	5: R = Br	8
11: R <sup>1</sup> = Br, R <sup>2</sup> = R <sup>3</sup> = H	6: R = Cl	9
12: R <sup>1</sup> = R <sup>3</sup> = Br, R <sup>2</sup> = H	7: R = OAc	10
13: R <sup>1</sup> = NO <sub>2</sub> , R <sup>2</sup> = R <sup>3</sup> = H	R = O <sup>  </sup> CPh	4
14: R <sup>1</sup> = R <sup>3</sup> = H, R <sup>2</sup> = NO <sub>2</sub>		
15: R <sup>1</sup> = CHO, R <sup>2</sup> = R <sup>3</sup> = H		
16: R <sup>1</sup> = NH <sub>2</sub> , R <sup>2</sup> = R <sup>3</sup> = H		

Electrophilic substitution reactions of **2** proceeded smoothly except for the Friedel-Crafts type reactions.

(1) (a) *Methoden der Organische Chemie*; Bd. 5, 2c: Carbo-cyclische  $\pi$ -Elektronen System; Asao, T., Ed.; G. Theme Verlag: Stuttgart, 1985. (b) Kagaku Sosetsu No. 15, *Chemistry of Novel Aromatic Systems*; Chemical Society of Japan; Tokyo Daigaku Shuppan Kai: Tokyo, 1977, and references cited therein.

(2) For example, azuleno[1,2-*b*]azulenes possess absorption bands in the near-infrared region (ca. 1250 nm). Toda, T.; Shimazaki, N.; Mukai, T.; Kabuto, C. *Tetrahedron Lett.* **1980**, *21*, 4001.

(3) (a) Hafner, K.; Schneider, J. *Justus Liebigs Ann. Chem.* **1959**, *624*, 37. (b) Hafner, K.; Pelster, P.; Patzelt, H. *Ibid.* **1961**, *650*, 80. (c) Hafner, K.; Bangert, K. B. *Ibid.* **1961**, *650*, 98. (d) Anderson, A. G.; Anderson, R. G.; Hollands, G. J. *Org. Chem.* **1965**, *30*, 235.

(4) (a) Hafner, K.; Fleischer, R. *Angew. Chem.* **1970**, *82*, 217. (b) Hafner, K.; Meinhardt, K.-P.; Richarz, W. *Ibid.* **1974**, *86*, 235. (c) Diehl, H.; Hafner, K. *Ibid.* **1976**, *88*, 124.

(5) Kawada, Y.; Takada, H.; Iwamura, H. *Tetrahedron Lett.* **1980**, *21*, 181.

(6) (a) Walsh, T. D. *J. Am. Chem. Soc.* **1969**, *91*, 515. (b) Turro, N. J.; Tobin, M.; Friedman, L.; Hamilton, J. B. *Ibid.* **1969**, *91*, 516.

(7) Campbell, N.; Marks, A. *J. Chem. Soc.* **1951**, 2941.

(8) Norhebel, D. C. *Organic Syntheses*; Wiley: New York, 1973; collect. Vol. V, p 206.

(9) Fieser, L. F.; Putnam, S. T. *J. Am. Chem. Soc.* **1947**, *69*, 1038. (10) Bartlett, P. D.; Cohen, S. G.; Cotman Jr., J. D.; Kronblum, N.; Landry, J. R.; Lewis, S. E. *J. Am. Chem. Soc.* **1950**, *72*, 1003.

(11) Theilacker, W.; Beyer, K. H. *Chem. Ber.* **1961**, *98*, 428.

(12) Fieser, L. F. *Organic Experiments*; Maruzen: Tokyo, 1965; pp 315-317.

(13) Although the yields of photochemical transformation of the bromo- and chlorotriptycenes are not significantly improved, 9-haloanthracenes are obtainable in good yield directly from anthracene,<sup>8</sup> and the yields of 9-halotriptycenes (45-46% from the haloanthracenes) are better than those of 9-acyloxy derivatives (34-36%) from the corresponding 9-(acyloxy)anthracenes. Therefore, 9-halotriptycenes may optionally be used in place of 9-(acyloxy)anthracenes, in light of the fact that the synthesis of the 9-acyloxy derivatives from anthracene is a multistep process. For example, 9-(benzoyloxy)anthracene: Roitt, I. M.; Waters, W. A. *J. Chem. Soc.* **1952**, 2695.

Table II.  $^1\text{H}$  NMR Chemical Shifts ( $\delta$ , ppm) and Coupling Constants (Hz) for Benz[*a*]indeno[1,2,3-*cd*]azulenes in  $\text{CDCl}_3$ 

position	2	11	12	13	14	15	16
1	8.44, dd (5.7, 3.3)	8.47, m	8.43, dd (5.7, 3.0)	8.62, m	8.50–8.58, m	8.60, m	8.25–8.38, m
2	7.90, dd (5.7, 3.3)	7.94, m	7.96, dd (5.7, 3.0)	8.10, m	7.96–8.10, m	8.05, m	7.74–7.86, m
3	7.90, dd (5.7, 3.3)	7.92, m	7.96, dd (5.7, 3.0)	8.08, m	7.96–8.10, m	8.05, m	7.74–7.86, m
4	8.44, dd (5.7, 3.3)	8.41, m	8.43, dd (5.7, 3.0)	8.59, m	8.50–8.58, m	8.60, m	8.25–8.38, m
5	8.32, dt (7.8, 0.9)	8.39, d (1.8)	8.41, dd (1.8, 0.6)	9.09, d (2.1)	8.41, dd (7.5, 1.2)	8.77, dd (1.5, 1.2)	7.69, d (2.1)
6	7.40, td (7.8, 0.9)				7.36, dd (8.1, 7.5)	10.14, s (CHO)	3.84 (2 H), b s ( $\text{NH}_2$ )
7	7.68, td (7.8, 0.9)	7.75, dd (8.1, 1.8)	7.77, dd (8.1, 1.8)	8.50, dd (8.7, 2.1)	8.24, dd (8.1, 1.2)	8.13, dd (8.1, 1.5)	7.09, dd (8.4, 2.1)
8	8.04, dt (7.8, 0.9)	7.87, d (8.1)	7.83, dd (8.1, 0.6)	7.94, d (8.7)		8.06, d (7.5)	7.87, d (8.4)
9	8.04, dt (7.8, 0.9)	7.99, dt (7.5, 0.9)	7.83, dd (8.1, 0.6)	8.01, dt (7.2, 1.2)	7.98, dd (9.0, 0.9)	8.04, dt (7.5, 1.2)	8.00, d (7.5)
10	7.68, td (7.8, 0.9)	7.69, td (7.5, 0.9)	7.77, dd (8.1, 1.8)	7.73, td (7.2, 1.2)	7.69, td (9.0, 1.2)	7.72, td (7.5, 1.2)	7.67, td (7.5, 0.9)
11	7.40, td (7.8, 0.9)	7.42, td (7.5, 0.9)		7.48, td (7.2, 1.2)	7.42, td (7.5, 0.9)	7.46, td (7.5, 1.2)	7.39, td (7.5, 0.9)
12	8.32, dt (7.8, 0.9)	8.32, dt (7.5, 0.9)	8.41, dd (1.8, 0.6)	8.35, dt (7.2, 1.2)	8.28, dt (7.5, 1.2)	8.34, dt (7.5, 1.2)	8.25–8.38, m

Bromination of **2** with bromine in dichloromethane afforded 65% of the 6-bromo derivative (**11**) accompanied by 10% of the 6,11-dibromo compound (**12**). Treatment of **2** with *N*-bromosuccinimide (NBS) also gave 67% of **11** and 15% of **12** in refluxing dichloromethane solution. But in the presence of benzoyl peroxide with NBS, it gave many products by HPLC analysis, and any bromo derivatives could not be isolated. Although nitration of **2** in a mixed acid medium (concentrated nitric acid and sulfuric acid) failed to yield a nitration product, the use of acetyl nitrate gave two different mononitro compounds: namely, 6-nitro (**13**, 26% yield by HPLC) and 8-nitro derivatives (**14**, 9% yield). A single product, the 6-formyl derivative (**15**), was obtained in 84% yield by formylation with Vilsmeier's reagent. All attempts at Friedel-Crafts type acylation of **2** failed and resulted in the recovery of **2**: where acetyl chloride, acetic anhydride, and trifluoroacetic anhydride were used as the acylating reagents, and the reactions were carried out with or without aluminum chloride.

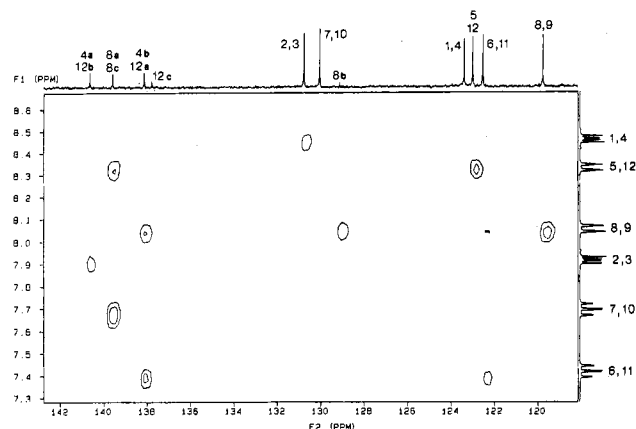
Reduction of **13** with hydrochloric acid and iron gave the 6-amino derivative (**16**), and the subsequent Sandmeyer reaction of **16** afforded **11**.

Regioselectivities of **2** toward these cationoid reagents are nicely in accord with the electron density calculated by the PPP method.<sup>14</sup> the highest electron density is at the 6-position and the second highest is at the 8-position. The main products of the reactions are  $\text{C}_6$  derivatives.<sup>15</sup>

Charge-transfer complexes of **2** with tetracyanoethylene and tetracyanoquinodimethane were reported by Iwamura and co-workers.<sup>5</sup> The complexes show weak absorption bands in the near-infrared region (TCNQ complex;  $\lambda_{\text{max}}$  1015 nm) where tailing reaches to 1200 nm. The electronic spectra of **2** and of the substitution products possess weak and broad absorption bands also in the near infrared region (up to 900 nm,  $\epsilon$  is on the order of  $10^2$ ). When **2** was treated with 1,3,5-trinitrobenzene and with 2,4,7-trinitrofluorenone, it gave 1:1 complexes, the electronic spectra of which appear in almost the same region as **2** itself. Thus, further investigation is needed in order to find more suitable compounds to form charge-transfer complexes possessing absorptions at longer wavelengths with stronger intensities.

(14) (a) Murata, S.; Iwamura, H. *Bull. Chem. Soc. Jpn.* 1984, 57, 1697. (b) Sugawara, T.; Iwamura, H. *J. Am. Chem. Soc.* 1985, 107, 1329.

(15) The highest electron density of **2** is at the 8b-position according to Iwamura's calculation.<sup>14</sup> However, if electrophilic attack takes place at the 8b-position, the resultant products should be cycloheptatrienium cation derivatives, which are not good final products. Thus, the reactions occurred at the 6- (or 11-) positions first and at the 8-position as a minor product, even though these positions have the second and third highest electron densities by the calculation. Actually, addition of a proton at  $\text{C}_{8b}$  of **2** and formation of a cycloheptatrienium cation derivative was reported.<sup>14</sup> This process is reversible and the cation forms only in a strongly acidic medium such as trifluoromethanesulfonic acid solution. This is one of the reasons why **2** does not give the nitration products in the strong acid medium, namely that the formed cycloheptatrienium cation is a poor cationoid reagent acceptor.

Figure 1. Long-range heteronuclear COSY spectrum of **2**.Table III.  $^{13}\text{C}$  NMR Chemical Shifts ( $\delta$ , ppm) for Benz[*a*]indeno[1,2,3-*cd*]azulenes

position	2	11	13	15
1	123.3	123.2	125.6	125.2 (or 125.3)
2	130.7	131.1	133.0	131.8 (or 132.2)
3	130.7	130.3	131.8	132.2 (or 131.8)
4	123.3	123.7	126.0	125.3 (or 125.2)
4a	140.6			
4b	138.1			
5	122.9	125.4	118.9	124.5
6	122.5			191.7 (C=O)
7	130.0	132.0	125.4	132.3
8	119.7	120.3	118.8	120.2
8a	139.5			
8b	129.1			
8c	139.5			
9	119.7	119.3	120.1	119.6
10	130.0	129.8	130.9	130.7
11	122.5	122.3	123.7	123.3
12	122.9	122.6	123.4	123.4
12a	138.1			
12b	140.6			
12c	137.7			

The  $^1\text{H}$  NMR spectrum of **2** shows six finely coupled patterns due to its symmetrical structure as is shown on the vertical axis of Figure 1. By means of a COSY experiment (not shown),<sup>16</sup> these signals were correlated to two series: peaks at  $\delta$  8.44 and 7.90 belong to the seven-membered ring of **2**, and the other series,  $\delta$  8.32, 7.40, 7.68, 8.04, belong to six-membered rings. The signals at  $\delta$  8.32 and 8.44 were assigned to be  $\text{H}_5$  ( $\text{H}_{12}$ ) and  $\text{H}_4$  ( $\text{H}_1$ ), respectively, by a NOESY experiment.<sup>17</sup> According to the results, all protons were confirmed as in Table II.

The tertiary carbons of the  $^{13}\text{C}$  NMR spectrum of **2** (horizontal axis of Figure 1) were assigned by means of a

(16) Bax, A.; Freeman, R. *J. Magn. Reson.* 1981, 44, 542.

(17) Jeener, J.; Meier, B. H.; Bachmann, P.; Ernst, R. R. *J. Chem. Phys.* 1979, 71, 4546.

$^{13}\text{C}$ - $^1\text{H}$  heteronuclear COSY experiment (not shown).<sup>18</sup> Figure 1 shows the long-range heteronuclear COSY spectrum of **2**.<sup>19</sup> The quaternary carbon at  $\delta$  138.1 is assigned as  $\text{C}_{4b}$  ( $\text{C}_{12a}$ ), because it couples with  $\text{H}_6$  ( $\text{H}_{11}$ ) and also  $\text{H}_3$  ( $\text{H}_9$ ) through three bonds: the C-H long-range coupling constants of two and four bonds are usually very small in aromatic systems.<sup>20</sup> The signal at  $\delta$  129.1 couples with  $\text{H}_3$  ( $\text{H}_9$ ) and is assigned to be  $\text{C}_{3b}$ . Similarly, peaks at  $\delta$  139.5 and 140.6 are  $\text{C}_{8a}$  ( $\text{C}_{8c}$ ) (which couples with  $\text{H}_5$  and  $\text{H}_7$ ) and  $\text{C}_{4a}$  ( $\text{C}_{12b}$ ) (which correlates to  $\text{H}_3$ ), respectively. Finally,  $\text{C}_{12c}$  appears at  $\delta$  137.7 and the signal corresponds to one carbon by the gated decoupling method. These  $^{13}\text{C}$  NMR assignments of **2** and its derivatives are listed in Table III.

### Experimental Section

All melting points are uncorrected. Mass, IR, and electronic spectra were recorded on a Hitachi M-80 (direct inlet), a JASCO IR-G (KBr pellets), and a Hitachi U-3400 apparatus ( $\text{CH}_2\text{Cl}_2$ ), respectively. The HPLC analyses were carried out using a column (4 mm i.d., 20 cm) containing LiChrosorb RP-18 (7  $\mu\text{m}$ ), and MeOH as mobile phase. The column (20 mm i.d., 30 cm) containing LiChroprep RP-18 (25-40  $\mu\text{m}$ ) was used for preparative HPLC. The NMR spectra were measured using a Varian VXR-300 spectrometer ( $\text{CDCl}_3$ ).

**Synthesis of Benz[a]indeno[1,2,3-*cd*]azulene (2).** **General Procedure.** Argon was bubbled through a solution of 9-substituted triptycene (3.2 mmol) in cyclohexane (1.6 L) for 2 h at room temperature. Then, if necessary, triethylamine (5 drops) was added. The solution was irradiated under argon for 10 h with a low-pressure mercury lamp (10 W) in a quartz vessel. Upon evaporation of the solvent, the residue was chromatographed on  $\text{SiO}_2$  (40 mm i.d., 25 cm) with hexane. The crude product from the green band on the column was recrystallized from EtOH, giving brown needles of **2** (the yield is summarized in Table I): mp 198–200 °C dec (lit.<sup>5</sup> mp 200–201 °C, dec); UV-vis  $\lambda_{\text{max}}$  784 (sh, log  $\epsilon$  1.19), 695 (2.15), 639 (2.18), 585 (sh, 2.12), 500 (3.44), 491 (3.46), 466 (3.49), 391 (4.09), 371 (4.04), 353 (3.97), 342 (3.92), 296 (sh, 4.69), 285 (4.71), 273 (4.77), 244 nm (sh, 4.30); mass (70 eV)  $m/z$  252 ( $\text{M}^+$ ), 224, 125.

**Charge-Transfer Complexes of 2.** Hydrocarbon **2** and an acceptor (1.1 mol equiv to **2**) were refluxed in  $\text{CHCl}_3$  and cooled to crystallize the corresponding CT complex.

**2-1,3,5-Trinitrobenzene:** mp 219 °C dec; UV-vis  $\lambda_{\text{max}}$  899 (sh, log  $\epsilon$  1.23), 786 (sh, 1.92), 703 (sh, 2.15), 637 (2.21), 599 nm (sh, 2.18). Anal. Calcd for  $\text{C}_{20}\text{H}_{12}\text{C}_6\text{H}_3\text{N}_3\text{O}_6$ : C, 67.10; H, 3.25; N, 9.03. Found: C, 67.09; H, 3.08; N, 8.97.

**2-2,4,7-Trinitro-9-fluorenone:** mp 230–231 °C dec; UV-vis  $\lambda_{\text{max}}$  776 (sh, log  $\epsilon$  2.06), 699 (sh, 2.29), 639 (2.33), 592 nm (sh, 2.30). Anal. Calcd for  $\text{C}_{20}\text{H}_{12}\text{C}_{13}\text{H}_9\text{N}_3\text{O}_7$ : C, 69.84; H, 3.02; N, 7.41. Found: C, 69.84; H, 2.95; N, 7.37.

**Reaction of Norcaradiene Derivative 3 with DDQ.** A mixture of **3**<sup>5</sup> (50 mg, 0.20 mmol) and DDQ (57 mg, 0.25 mmol) in PhH (5 mL) was refluxed for 5 h. After treatment with aqueous  $\text{NaHCO}_3$  (5%), the reaction mixture was chromatographed on  $\text{SiO}_2$  with hexane to afford benzo[a]fluoranthene (45 mg, 90%): mp 140–142 °C (lit.<sup>7</sup> mp 145–146 °C); UV-vis  $\lambda_{\text{max}}$  422, 364, 301, and 259 nm; mass (70 eV)  $m/z$  252 ( $\text{M}^+$ ).

**Bromination of 2.** To an ice-cooled solution of **2** (50 mg, 0.2 mmol) in  $\text{CH}_2\text{Cl}_2$  (10 mL) was added a solution of  $\text{Br}_2$  (32 mg, 0.2 mmol) in  $\text{CH}_2\text{Cl}_2$  (1 mL) over a period of 15 min. The resulting mixture was stirred at room temperature for an additional 3 h and quenched with aqueous  $\text{Na}_2\text{S}_2\text{O}_3$  (5%, 10 mL). After percolating on a short column of  $\text{SiO}_2$  (PhH), the crude products were separated by means of HPLC. The first eluate gave **2** (4 mg, 8%). The second eluate afforded **11** (43 mg, 65%): mp 184.0–185.5 °C (dec, from EtOH); UV-vis  $\lambda_{\text{max}}$  784 (sh, log  $\epsilon$  2.01), 701 (2.22), 645 (2.25), 596 (sh, 2.19), 493 (3.52), 468 (3.56), 390 (4.11), 370 (4.08), 352 (4.03), 299 (sh, 4.69), 281 (4.85), 246 nm (sh, 4.33); mass (20 eV)  $m/z$  332, 330 ( $\text{M}^+$ ), 251 ( $\text{M}^+ - \text{Br}$ ), 225. Anal. Calcd for

$\text{C}_{20}\text{H}_{11}\text{Br}$ : C, 72.53; H, 3.35. Found: C, 72.25; H, 3.19.

The third eluate yielded **12** (8 mg, 10%): mp 229.0–231.5 °C (dec, from EtOH); UV-vis  $\lambda_{\text{max}}$  795 (sh, log  $\epsilon$  2.01), 710 (2.21), 653 (2.23), 610 (sh, 2.17), 501 (3.49), 470 (3.51), 389 (4.10), 368 (4.09), 351 (4.03), 321 (sh, 4.37), 299 (sh, 4.73), 287 (4.91), 249 nm (sh, 4.32); mass (20 eV)  $m/z$  413, 411, 409 ( $\text{M}^+$ ), 332, 330 ( $\text{M}^+ - \text{Br}$ ), 250 ( $\text{M}^+ - 2\text{Br}$ ), 125.

A solution of **2** (25 mg, 0.1 mmol) and NBS (18 mg, 0.1 mmol) in  $\text{CH}_2\text{Cl}_2$  (10 mL) was refluxed for 16 h and gave **2** (trace), **11** (22 mg, 67%), and **12** (6 mg, 15%) by treatment similar as above.

**Nitration of 2.** To a solution of **2** (25 mg, 0.1 mmol) in acetic anhydride (15 mL) at room temperature was added acetyl nitrate (0.2 mmol) prepared prior to use by adding  $\text{HNO}_3$  to cold acetic anhydride. After being stirred for 3 h, the reaction mixture was poured into aqueous NaOH (5%, 200 mL), stirred, and extracted with  $\text{CH}_2\text{Cl}_2$  (100 mL). The extract was passed through a short column ( $\text{SiO}_2$ , PhH) to give a mixture of **13** and **14** as a red-violet eluate: HPLC analysis indicated that the experiment yielded **13** (retention volume, 6.7 mL; 26%) and **14** (7.7 mL; 9%).

The mixture was chromatographed on a silica gel column (30 mm i.d., 30 cm) with  $\text{CCl}_4$  to afford **13** (5 mg, 17%): mp 203–204 °C dec; IR, 1595, 1320  $\text{cm}^{-1}$ ; UV-vis  $\lambda_{\text{max}}$  834 (sh, log  $\epsilon$  1.74), 751 (sh, 2.27), 668 (sh, 2.50), 612 (sh, 2.59), 518 (4.05), 490 (sh, 3.96), 418 (3.78), 394 (sh, 3.98), 369 (4.55), 354 (4.45), 296 (4.58), 287 (sh, 4.57), 255 (sh, 4.49), 249 nm (sh, 4.47); mass (20 eV)  $m/z$  297 ( $\text{M}^+$ ), 251 ( $\text{M}^+ - \text{NO}_2$ ). Anal. Calcd for  $\text{C}_{20}\text{H}_{11}\text{NO}_2$ : C, 80.79; H, 3.73; N, 4.71. Found: C, 80.79; H, 3.82; N, 4.59.

The second eluate yielded **14** (2 mg, 7%): mp 208.5–210.0 °C dec; IR, 1598, 1338, 1320, 1306  $\text{cm}^{-1}$ ; UV-vis  $\lambda_{\text{max}}$  734 (sh, log  $\epsilon$  2.08), 663 (sh, 2.32), 612 (sh, 2.41), 500 (3.86), 386 (4.14), 367 (4.09), 339 (4.03), 272 (4.69), 244 nm (sh, 4.48); mass (70 eV)  $m/z$  297 ( $\text{M}^+$ ), 251 ( $\text{M}^+ - \text{NO}_2$ ). Anal. Calcd for  $\text{C}_{20}\text{H}_{11}\text{NO}_2$ : C, 80.79; H, 3.73; N, 4.71. Found: C, 80.71; H, 3.48; N, 4.69.

**Vilsmeier Reaction of 2.** To cold *N,N*-dimethylformamide (0.73 g, 10 mmol) was added dropwise  $\text{POCl}_3$  (1.53 g, 10 mmol), and the mixture was stirred for 1 h. During the course of the reaction, the temperature was elevated from cold to room temperature. A solution of **2** (126 mg, 0.5 mmol) in DMF (10 mL) was added to the mixture and stirred at room temperature for 2 h and then for an additional 10 h at 65–70 °C. After addition of ice-water (200 mL), the reaction mixture was extracted with  $\text{CH}_2\text{Cl}_2$  (100 mL, 8 times), evaporated to dryness, and recrystallized from benzene to yield **15** (118 mg, 84%): mp 202.0–203.5 °C dec; IR, 1670  $\text{cm}^{-1}$ ; UV-vis  $\lambda_{\text{max}}$  757 (sh, log  $\epsilon$  2.18), 675 (2.38), 625 (2.44), 580 (2.41), 507 (3.83), 477 (3.80), 397 (2.59), 380 (sh, 3.92), 349 (4.63), 340 (sh, 4.60), 292 nm (4.73); mass (20 eV)  $m/z$  280 ( $\text{M}^+$ ), 251 ( $\text{M}^+ - \text{CHO}$ ), 125. Anal. Calcd for  $\text{C}_{21}\text{H}_{12}\text{O}$ : C, 89.98; H, 4.32. Found: C, 89.87; H, 4.15.

**Attempted Friedel-Crafts Reaction of 2.** To a mixture of acetic anhydride (51 mg, 0.5 mmol) and  $\text{AlCl}_3$  (106 mg, 0.8 mmol) in  $\text{CH}_2\text{Cl}_2$  (10 mL) was added **2** (63 mg, 0.25 mmol) in  $\text{CH}_2\text{Cl}_2$  (10 mL), and the reaction mixture was refluxed for 7 h. After the usual workup, a quantitative amount of **2** was recovered.

Another experiment involved the reaction of **2** (63 mg, 0.5 mmol) with trifluoroacetic anhydride (53 mg, 0.25 mmol) and  $\text{AlCl}_3$  (180 mg, 1.35 mmol) in  $\text{CH}_2\text{Cl}_2$  (20 mL) under refluxing for 3 h; the compound isolated was **2** (53 mg, 85%).

**Reduction of 13.** To a solution of **13** (70 mg, 0.24 mmol) in DME (5 mL) were added powdered Fe (0.56 g, 0.01 g-atom), EtOH (50 mL), and HCl (4 M, 3 mL) with stirring under reflux conditions. After refluxing for 1 h, the mixture was neutralized with aqueous  $\text{NaHCO}_3$  (5%) and extracted with  $\text{CH}_2\text{Cl}_2$  (150 mL). The crude product was chromatographed on  $\text{SiO}_2$  (40 mm i.d., 5 cm) with PhH to give **16** (48 mg, 75%) as dark brown crystals (from  $\text{CH}_2\text{Cl}_2$ ): mp 195.5–197.5 °C dec; IR 3370  $\text{cm}^{-1}$ ; UV-vis  $\lambda_{\text{max}}$  749 (log  $\epsilon$  2.13), 685 (2.17), 516 (3.40), 489 (3.45), 463 (sh, 3.31), 395 (4.08), 375 (4.13), 360 (4.03), 305 (sh, 4.64), 291 (4.92), 245 nm (sh, 4.26); mass (20 eV)  $m/z$  267 ( $\text{M}^+$ ), 239. Anal. Calcd for  $\text{C}_{20}\text{H}_{13}\text{N}$ : C, 89.86; H, 4.90; N, 5.24. Found: C, 89.77; H, 4.73; N, 5.10.

**Sandmeyer Reaction of 16.** A solution of aqueous HBr (48%, 0.5 mL) and  $\text{H}_2\text{O}$  (0.5 mL) was added to **16** (5 mg, 0.02 mmol) in DME (0.5 mL) at –20 °C. After diazotization by adding aqueous  $\text{NaNNO}_2$  (3%), a large excess of  $\text{Cu}_2\text{Br}_2$  (140 mg) was added and the reaction mixture was warmed gradually to 60 °C. Upon treatment in the usual manner, the residue was chromatographed

(18) Bax, A. J. *Magn. Reson.* 1983, 53, 517.

(19) Wynants, C.; Hallenga, K.; van Binst, G.; Michel, A.; Zanen, J. J. *Magn. Reson.* 1984, 57, 93.

(20) Weigert, F. J.; Roberts, J. D. *J. Am. Chem. Soc.* 1967, 89, 2967.

(SiO<sub>2</sub>, 17 mm i.d., 3 cm, hexane), and the green band on the column yielded a small amount of product. Its <sup>1</sup>H NMR spectrum was identical with that of 11 obtained by bromination of 2.

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**Registry No.** 2, 4670-86-4; 2-1,3,5-trinitrobenzene, 124581-61-9; 2-2,4,7-trinitro-9-fluorenone, 124581-62-0; 3, 22674-47-1; 4, 74067-57-5; 8, 15364-55-3; 9, 793-40-8; 10, 97733-14-7; 11, 124581-63-1; 12, 124581-64-2; 13, 124581-65-3; 14, 124581-66-4; 15, 124581-67-5; 16, 124581-68-6; benzo[*a*]fluoroanthene, 203-33-8.

## Secondary $\alpha$ -Deuterium Isotope Effects in the Formation of Imines

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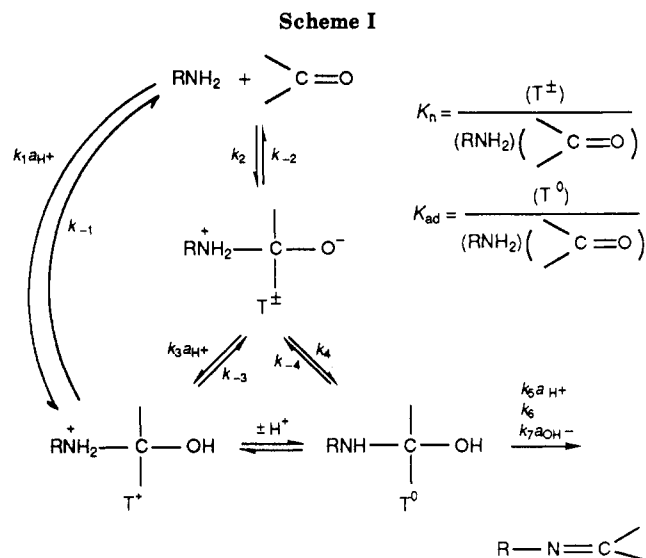
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Kinetic  $\alpha$ -deuterium isotope effects,  $k_D/k_H$ , for hydronium ion catalyzed addition ( $k_1 a_{H^+}$ ) of semicarbazide ( $pK_a = 3.86$ ) to *m*-bromobenzaldehyde and *p*-nitrobenzaldehyde, and of methoxyamine ( $pK_a = 4.73$ ) and hydroxylamine ( $pK_a = 6.15$ ) to *m*-bromobenzaldehyde, are near 1.14 and independent of the nature of both the nucleophile and the benzaldehyde employed. The corresponding values for the uncatalyzed reaction ( $k_2$ ) of *m*-bromobenzaldehyde with several nucleophiles decrease from 1.30 to 1.16 when the nucleophile is changed from semicarbazide to hydroxylamine. For the addition of semicarbazide,  $k_D/k_H$  decreases from 1.14 to 1.11 as the benzaldehyde is varied from *m*-bromobenzaldehyde to *p*-nitrobenzaldehyde. Values of  $k_D/k_H$  for the hydronium ion catalyzed process, which converts the zwitterionic intermediate  $T^\pm$  to  $T^+$  ( $K_n k_3 a_{H^+}$ ), are near 1.21 for the reaction of several nucleophiles with all the benzaldehydes studied. The isotope effect observed for the uncatalyzed formation of the carbinolamine intermediate  $T^0$  ( $K_n k_4$ ) suggests a dependence on the nature of the nucleophile and the benzaldehyde. These results indicate that the extent of carbon-nitrogen bond formation in the transition state for addition of the nucleophiles to the carbonyl group is a function of the reactivity of the reagents and the catalysts.

The reaction of nitrogen nucleophiles with carbonyl compounds occurs in two general stages: formation of a carbinolamine addition intermediate followed by carbinolamine dehydration to yield the imine product.<sup>2-3</sup> Carbinolamine formation occurs by at least three separate routes<sup>4-6</sup> as shown in Scheme I, concerted addition of amine and protonation of the carbonyl oxygen atom ( $k_1 a_{H^+}$ ), a stepwise route involving trapping by proton transfer of a dipolar compound formed by addition of amine to the carbonyl group ( $k_2$  followed by  $K_n k_3 a_{H^+}$  or  $K_n k_4$ ), and a "spectator" mechanism involving preassociation of acid catalyst with the carbonyl oxygen.<sup>7</sup> Subsequent carbinolamine dehydration may occur via acid-catalyzed, pH-independent, and base-catalyzed pathways ( $k_5 a_{H^+}$ ,  $k_6$ ,  $k_7 a_{OH^-}$ ).

Consequently, by appropriate choice of experimental conditions, a single set of compounds can be employed to probe the transition-state structure for several different steps. As a specific set of reactants, we have chosen substituted benzaldehydes as the carbonyl component and semicarbazide, methoxyamine, phenylhydrazine, and hy-



droxylamine as the amines. This permits study of the effect of variation of both substrate and nucleophile on the transition-state structure. Moreover, since the addition step for these reactants can be either pH-independent or hydronium ion catalyzed, the relationship between catalysis and transition-state structures may also be probed. This paper reports  $\alpha$ -deuterium isotope effects for these reactions as a function of the structure of carbonyl component, amine, and acid catalysis.

### Experimental Section

**Materials.** Analytical grade reagent inorganic salts were used without further purification. Glass-distilled water was used

(1) Fellow of the Fundação de Amparo à Pesquisa do Estado de São Paulo.

(2) Jencks, W. P. *Prog. Phys. Org. Chem.* 1964, 2, 63-128.

(3) Jencks, W. P. *Catalysis in Chemistry and Enzymology*; McGraw-Hill: New York, 1969.

(4) Sayer, J. H.; Pinsky, B.; Schonbrunn, A.; Washtien, W. *J. Am. Chem. Soc.* 1974, 96, 7988-8009.

(5) Rosenberg, S. M.; Silver, S. M.; Sayer, J. H.; Jencks, W. P. *J. Am. Chem. Soc.* 1974, 96, 7986-98.

(6) Abrams, W. R.; Kallen, R. G. *J. Am. Chem. Soc.* 1976, 98, 7777-89.

(7) Sayer, J. H.; Edman, C. *Ibid.* 1979, 101, 3010-16.

(8) Equation 1 is taken from ref 4 and does not include the spectator mechanism.<sup>5</sup> The formulation provided is adequate to account for all results presented herein.