

$\exp(1178/(RT))$ ,  $n(p\text{-CH}_3) = 7555 \exp(-6092/(RT))$ , and  $n(m\text{-Cl}) = 228 \exp(-5067/(RT))$ . The variation in the preexponential terms for  $n$  appears unexpected; VanArtsdalen found  $n = 1016 \exp(-5381/(RT))$  for toluene. For the series  $p\text{-CH}_3$ , H, and  $m\text{-Cl}$ , we have the smooth trend of  $\log(A_{\text{HBr}}/A_{\text{Br}_2}) = 3.87, 3.01, \text{ and } 2.36$ . All data of Table II give good Hammett plots vs.  $\sigma^+$ .

From eq 8,  $\Delta H(m\text{-Cl}) - \Delta H(p\text{-CH}_3) = 1178 + 6092 - 5067 = 2.2 \text{ kcal/mol}$ . The benzyl C-H bond in  $m$ -chlorotoluene is stronger than that in  $p$ -xylene by 2.2 kcal/mol, and we estimate the uncertainty at  $\pm 0.6$ . This result is in agreement with Pryor's recent report of a difference of 1.9 kcal/mol.<sup>20</sup> Two independent methods lead to virtually the same result. The substituent effect is in the direction predicted.<sup>10</sup> As with phenols,<sup>21</sup> Hammett correlations for benzyl hydrogen abstraction by radicals should not be interpreted solely on the basis of "polar effects" in the transition state.<sup>10,22,23</sup>

**Registry No.**  $p$ -Xylene, 106-42-3;  $m$ -chlorotoluene, 108-41-8; hydrogen bromide, 10035-10-6; bromine, 7726-95-6.

**Supplementary Material Available:** The derivation of eq 10; for run 9, the spectrophotometer chart, the FORTRAN program for the numerical method and output, and the plot of  $(1/\text{rate})$  vs.  $[\text{HBr}]/[\text{Br}_2]$  (7 pages). Ordering information is given on any current masthead page.

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(24) The complex  $(\text{HBr}\cdot\text{Br}_2)$  may be present; eq 8 would still be valid, with  $k_4$  and  $k_4'$  referring to reaction with complex. No complex expected at dilutions of Table I.

## Regioselectivity in the Addition of Carbanions to (1,4-Dimethoxynaphthalene)tricarboonylchromium. A New Entry into Anthracyclinone Synthesis

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One of the fascinating aspects of the reaction of carbon nucleophiles with substituted arenes coordinated to  $\text{Cr}(\text{CO})_3$  is the high regioselectivity of the addition often encountered.<sup>1-7</sup> Theoretical analysis<sup>4,8,9</sup> as well as carefully designed experiments<sup>4,6</sup> have demonstrated the interplay of electronic and steric factors<sup>10</sup>

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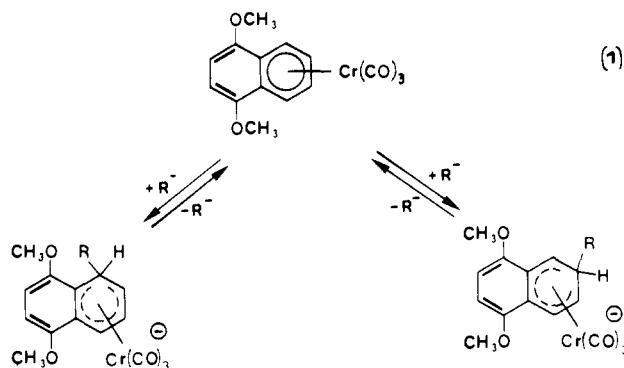
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in this reaction. Naphthalenetricarboonylchromium (**1**) exhibits a particularly high  $\alpha$  regioselectivity (>98%) with a range of nucleophiles of different size and reactivity.<sup>21</sup> It has been pointed out<sup>8</sup> that conformational effects of the  $\text{Cr}(\text{CO})_3$  group cannot account for the observed regioselectivity (the  $\text{Cr}(\text{CO})_3$  adopts a staggered conformation<sup>12</sup>); however, a correlation with the LUMO coefficient of the free arene has been suggested.<sup>2,13</sup>

In this communication we consider the question of regioselectivity in (1,4-dimethoxynaphthalene)tricarboonylchromium (**2**).<sup>15,16</sup> We expected that superposed on the factors governing regioselectivity in **1** steric and electronic effects due to the OMe groups may become apparent in the reactions of **2**. The data listed in Table I suggest that these effects do, in fact, dominate regiochemistry under conditions of kinetic control.

In a typical reaction, complex **2** (1.5 mmol) was added as a solid to a solution (10 mL of THF,  $-78^\circ\text{C}$ ) of the carbanion (1.05 equiv) prepared according to standard procedures. After dropwise addition of hexamethylphosphoric triamide (HMPT, 4 mL)<sup>17</sup> the mixture was stirred for the time and at the temperature indicated in Table I. The solution was then recooled to  $-78^\circ\text{C}$ , treated with iodine (9 mmol in 10 mL of THF), and left to warm up overnight. Isolation by conventional procedures yielded the substituted naphthalenes.

Steric effects are evident under conditions favoring kinetic control of the addition. The small nucleophile 2-lithioacetonitrile yields predominantly the  $\alpha$  substitution product **3** (entries 1 and 2) whereas the sterically more demanding 2-lithio-2-methylpropionitrile gives under analogous conditions predominantly  $\beta$  addition (entries 3-5). With the latter, conversion is virtually complete after 1 h at  $-50^\circ\text{C}$ . Consequently, the different product distribution observed on increasing reaction time and/or temperature (entries 4-6) is indicative of a rearrangement to the thermodynamically favored  $\alpha$  addition intermediate. Presumably this transfer occurs via dissociation of the carbanion as depicted in eq 1. On the basis of the observed slow exchange of (benz-



ene)tricarboonylchromium between carbanions, reversibility of nucleophilic attack on  $\text{Cr}(\text{CO})_3$ -coordinated arenes has been

(10) Regioselectivity of nucleophilic attack appears to be governed by a number of factors—such as charge polarization induced by the conformation adopted by the  $\text{Cr}(\text{CO})_3$  group, coefficient size of the lowest energy arene-centered unoccupied molecular orbital, reactivity of the nucleophile, and steric demands of arene substituent and nucleophile.

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(13) Extended Hückel MO calculations on monosubstituted arene  $\text{Cr}(\text{C}-\text{O})_3$  complexes indicate the lowest arene-centered unoccupied MO to be qualitatively very similar to the LUMO of the free arene.<sup>9,4</sup> Examination of the frontier orbitals of naphthalene and the valence orbitals of  $\text{Cr}(\text{CO})_3$ <sup>14,8</sup> suggests an analogous situation in this complex—thereby providing a rationale for the  $\alpha$  regioselectivity of nucleophilic attack.

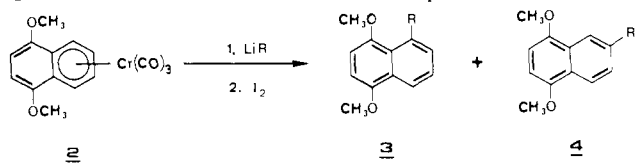
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(16) Substituents on naphthalene have a strong directing effect on the coordination behavior of the arene. Thus, 1,4-dimethoxynaphthalene reacts with  $\text{Cr}(\text{CO})_6$  regiospecifically to yield the complex with the  $\text{Cr}(\text{CO})_3$  group coordinated to the nonsubstituted ring.

(17) Complex **2** forms a suspension in the reaction mixture, on addition of HMPT at  $-60^\circ\text{C}$ ; a homogeneous solution is formed after 30 min.

Table I. Reactions of Carbanions with Complex 2



entry	carbanion LiR	time, h/ temp, °C	product mixture <sup>a</sup> , %		combined yield, <sup>b</sup> %
			3	4	
1	LiCH <sub>2</sub> CN	1/-50	75 <sup>c</sup>	25 <sup>c</sup>	34 <sup>c</sup>
2	LiCH <sub>2</sub> CN	30/-20	100	0	72
3	LiC(CH <sub>3</sub> ) <sub>2</sub> CN	0.5/-60	22	78	69
4	LiC(CH <sub>3</sub> ) <sub>2</sub> CN	1/-40	27	73	84
5	LiC(CH <sub>3</sub> ) <sub>2</sub> CN	2/0	47	53	76
6	LiC(CH <sub>3</sub> ) <sub>2</sub> CN	46/0	97 <sup>c</sup>	3 <sup>c</sup>	72 <sup>c</sup>
7	LiCH <sub>2</sub> COO- <i>t</i> -Bu	1/0	67	33	89
8	LiCH <sub>2</sub> COO- <i>t</i> -Bu	48/0	>98 <sup>c</sup>	<2 <sup>c</sup>	84 <sup>c</sup>
9	LiC(CH <sub>3</sub> )S(CH <sub>2</sub> ) <sub>3</sub> S	1/0	0	100	61
10	LiC(CH <sub>3</sub> )S(CH <sub>2</sub> ) <sub>3</sub> S	48/0	0	100	71

<sup>a</sup> All compounds were isolated and independently characterized. Their IR, <sup>1</sup>H NMR (360 MHz), and mass spectra are in full agreement with the assigned structures. The product ratios are based on isolated material (unless otherwise noted). <sup>b</sup> The percentage yields refer to isolated (column chromatography) material after separation into 3 and 4 (unless otherwise indicated). <sup>c</sup> Ratio determined by <sup>1</sup>H NMR integration, combined yields refer to mixtures of 3 and 4.

considered extremely slow below 0 °C.<sup>18</sup> Furthermore, product distributions resulting from reactions with substituted-benzene complexes were reported to be invariant to changes in reaction time and temperature (0.5 min at -78 °C to 24 h at 25 °C), strongly suggesting kinetic control of the reaction.<sup>2</sup> In contrast, in reactions of 2 reversibility of the addition to the kinetically favored intermediate depends largely on the nature of the anion. Irreversible β addition is only observed with 2-lithio-2-methyl-1,3-dithiane (entries 9 and 10). The different behavior of the sulfur-stabilized carbanion compared to the ester enolate (entries 7 and 8) and the cyano-stabilized carbanions (entries 1-6) may simply reflect the difference in the pK<sub>a</sub> value of the conjugate acid.

The regioselective β attack of methylthioanion can be interpreted in terms of steric and electron-pair repulsion between the incoming anion and the methoxy group. In a synthetic application this reaction provides the key step in a short and novel route to the daunomycinone precursor 1,4-dimethoxy-6-acetyl-tetralin (6)<sup>19</sup> (Scheme I).

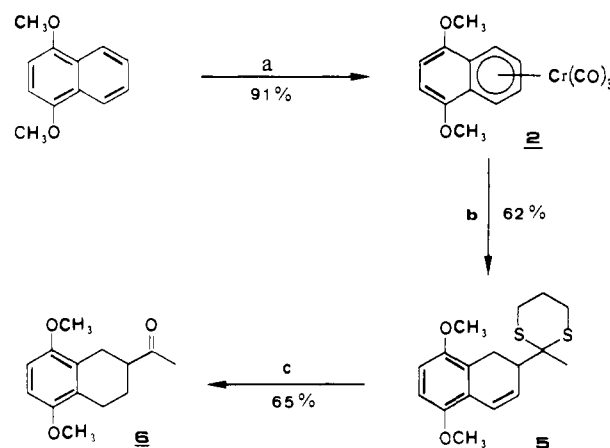
Starting with 1,4-dimethoxynaphthalene, regioselective<sup>16</sup> introduction of the Cr(CO)<sub>3</sub> group was achieved in 91% yield by a procedure described previously.<sup>11</sup> Reaction of 2 with 2-lithio-2-methyl-1,3-dithiane in THF/HMPPT followed by protonation<sup>20</sup> of the intermediate and decomplexation (Ce(IV)) resulted in nucleophilic addition of the masked-carbonyl function with reduction of one double bond to yield, after chromatography on silica gel and crystallization (ether/hexane), the dihydronaphthalene 5 (mp 102 °C, 62%). Dithiane hydrolysis followed by hydrogenation yielded a 5:1 mixture of the desired product 6 and its aromatic counterpart (78% yield).

In summary, the results presented indicate the delicate balance that exists among the factors affecting regioselectivity and reversibility of the addition of carbanions to complex 2. Further

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(20) In contrast to the cyclohexadienyl Cr(CO)<sub>3</sub> anions where protonation necessitates treatment with an excess of strong acid (e.g., CF<sub>3</sub>COOH),<sup>18</sup> protonation of our intermediate occurs readily to yield, as the sole product, the desired isomer 5. In general, protonation and oxidation steps were carried out in one operation with 3 equiv of Ce<sup>IV</sup> in aqueous THF.

Scheme I<sup>a</sup>

<sup>a</sup> All reactions were carried out under nitrogen. Key: (a) Bu<sub>2</sub>O/hexane (10/1), THF (1 mL), Cr(CO)<sub>6</sub>, reflux 3 days; (b) (i) LiC(CH<sub>3</sub>)S(CH<sub>2</sub>)<sub>3</sub>S, THF/HMPA (9/1), 0 °C, 60 h; (ii)

Ce(NH<sub>4</sub>)<sub>2</sub>(NO<sub>3</sub>)<sub>6</sub> (3 equiv), THF/H<sub>2</sub>O (9:1), -78 °C → room temperature, 12 h; (c) (i) *N*-chlorosuccinimide (4 equiv), AgNO<sub>3</sub>, collidine, 25 °C, 2 min, saturated aqueous Na<sub>2</sub>SO<sub>3</sub>, saturated aqueous NaHCO<sub>3</sub>, CH<sub>2</sub>Cl<sub>2</sub>; (ii) H<sub>2</sub> (1 atm), Pd/C (10%), room temperature.

mechanistic and synthetic studies along these lines are in progress in our laboratory.

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**Registry No.** 2, 12111-66-9; 3 (R = CH<sub>2</sub>CN), 87555-39-3; 3 (R = C(CH<sub>3</sub>)<sub>2</sub>CN), 87555-40-6; 3 (R = CH<sub>2</sub>COO-*t*-Bu), 87555-41-7; 4 (R = CH<sub>2</sub>CN), 87555-42-8; 4 (R = C(CH<sub>3</sub>)<sub>2</sub>CN), 87555-43-9; 4 (R = CH<sub>2</sub>COO-*t*-Bu), 87555-44-0; 4 (R = C(CH<sub>3</sub>)S(CH<sub>2</sub>)<sub>3</sub>S), 87555-45-1; 5, 87566-96-9; 6, 33654-68-1; LiCH<sub>2</sub>CN, 20428-58-4; LiC(CH<sub>3</sub>)<sub>2</sub>CN, 50654-53-0; LiCH<sub>2</sub>COO-*t*-Bu, 41850-36-6; LiC(CH<sub>3</sub>)S(CH<sub>2</sub>)<sub>3</sub>S, 27969-97-7.

## Aldol Reaction of Silyl Enol Ethers with Aldehydes under Neutral Conditions<sup>1</sup>

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The aldol reaction, usually carried out with base or acid as the catalyst, is one of the most fundamental reactions in organic chemistry.<sup>2</sup> In recent years, the development of new methods for the directed aldol reaction has seen rapid growth in relation to control of acyclic stereochemistry.<sup>2a,3</sup> Several important un-

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