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Dialkylation of Acetophenones and Acetophenone Ethylene Ketals with 1,8-Bis(trimethylsilyl)-2,6-octadiene (BISTRO). Semi-Empirical SCF Studies of α-Methoxy-α-methylbenzyl Cations

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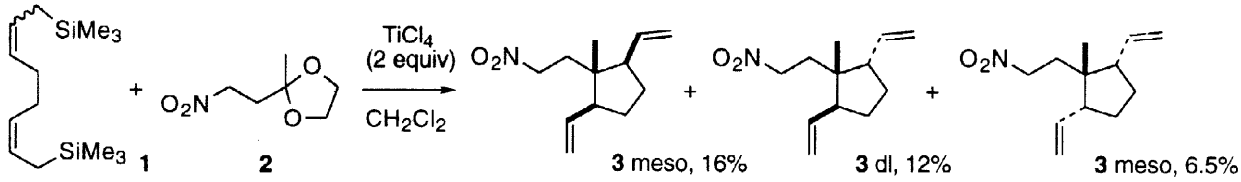
Abstract: Titanium tetrachloride mediated dialkylation of acetophenones or acetophenone ethylene ketals by 1,8-bis(trimethylsilyl)-2,6-octadiene (BISTRO) leads to a mixture of *dl* and *meso* 1-alkyl-1-phenyl-2,5-divinylcyclopentanes. Better yields are observed with *p*-bromoacetophenone and *m*-methoxyacetophenone.

Introduction

In connection with our interest in steroid synthesis,[1] we have recently reported on a new strategy for the synthesis of 1,1-disubstituted-2,5-divinylcyclopentanes which involves the addition of 1,8-bis(trimethylsilyl)-2,6-octadiene **1** (BISTRO) to various electrophilic reagents.[2] In particular, 1-methyl-1-(2-nitroethyl)-2,5-divinylcyclopentanes **3** were generated by treatment of 4-nitro-2-butanone ethylene ketal **2** with BISTRO **1**.[1a] Unfortunately, this substitution reaction gave an inseparable mixture of the three possible diastereomers **3** in moderate yields and quite low diastereoselectivity.[3]



In contrast, addition of BISTRO to α-diketone diketals (*cis*-6-alkyl-1-methyl-2,5,7,10-tetraoxabicyclo[4.4.0]decanes) in the presence of titanium tetrachloride and 4 molar equivalents of nitromethane led to 2,3-diallyl-2,3-dialkyl-1,4-dioxanes with very high diastereoselectivity involving an invertive ("S_N2-like") substitution.[2e]

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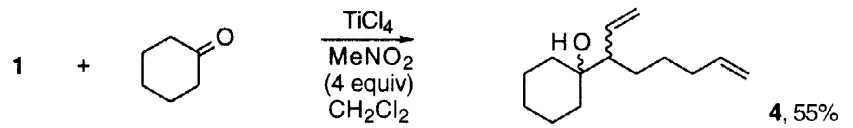
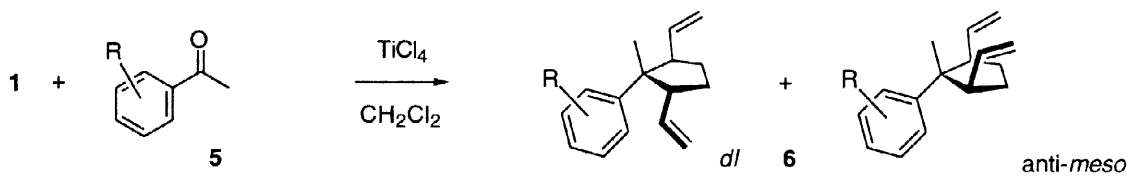
Results

As an extension of this methodology, we report here the addition of BISTRO to acetophenones and acetophenone ethylene ketals. In an earlier study, we noted the poor reactivity of aliphatic ketones such as cyclohexanone which gave the monoalkylated product **4** instead of expected cyclopentane derivatives.



4, 55%

In contrast, dialkylation of acetophenones **5** afforded the expected mixtures of *dl*- and anti-*meso*-1,3-divinylcyclopentanes **6** in moderate to excellent yields (Table 1). The presence of nitromethane (4 molar equiv) increases the yield of the reaction (**5e**, entry 6 and 7).[4]



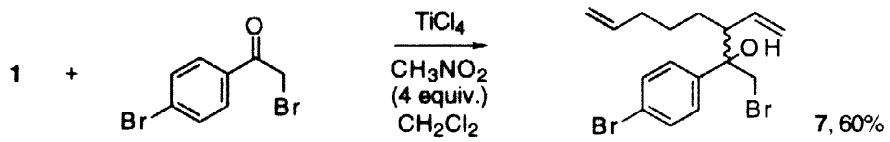
a, R = H; **b**, R = *p*-MeO; **c**, R = *m*-MeO; **d**, R = *o*-MeO; **e**, R = *p*-Br

BISTRO is actually a mixture of the (*Z*, *Z*)-isomer (ca. 50%) and the (*Z*, *E*)-isomer (ca. 40%).[5] We have recently shown that if sodium is used instead of lithium during the reductive dimerization of butadiene, it is possible to obtain BISTRO as a mixture of mainly the (*Z*,*Z*)-isomer (80 %). When this predominantly (*Z*,*Z*) mixture is involved in the reaction with **5c**, the yield of the condensation is much lower (30 % for **6c**) than with the usual BISTRO (entry 4, 95 %). This result emphasizes the better reactivity of the (*Z*, *E*)-isomer of BISTRO compared to the (*Z*, *Z*) one. This phenomenon was confirmed by the better yields obtained with an excess of the usual BISTRO (2.5 equiv) which was formed using lithium.

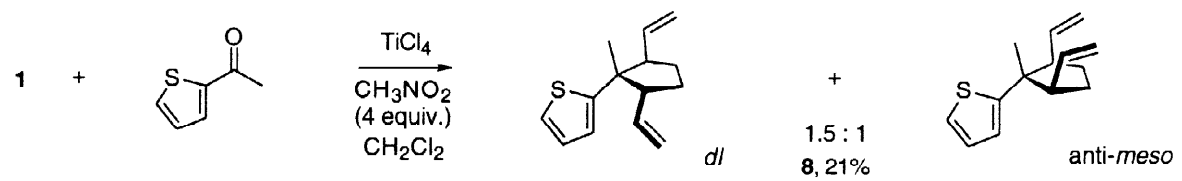
Table 1. Reaction of BISTRO (1) with Acetophenones 5.

Entry	Acetophenone	Reaction condition	Yield **6** (%)	*dl* : *meso*
1	**5a**	**1**, 2.5 eq.; $TiCl_4$, 1.2 eq.; 20 °C; 22 h.	50	1.38 : 1
2	**5b**	**1**, 2.5 eq.; $TiCl_4$, 1.2 eq.; CH_3NO_2, 4 eq.; 20 °C; 36 h.	40	1.63 : 1
3	**5c**	**1**, 2.5 eq.; $TiCl_4$, 1.2 eq.; 20 °C; 13 h.	78	1 : 2.33
4	**5c**	**1**, 2.5 eq.; $TiCl_4$, 1.4 eq.; CH_3NO_2, 4 eq.; 20 °C; 16 h.	95	1 : 1
5	**5d**	**1**, 2.4 eq.; $TiCl_4$, 1.2 eq.; CH_3NO_2, 4 eq.; 20 °C; 20 h.	18	1.5 : 1
6	**5e**	**1**, 2.5 eq.; $TiCl_4$, 1.2 eq.; 20 °C; 21 h.	39	1.32 : 1
7	**5e**	**1**, 2.5 eq.; $TiCl_4$, 1.2 eq.; CH_3NO_2, 4 eq.; 20 °C; 21 h.	81	1.32 : 1

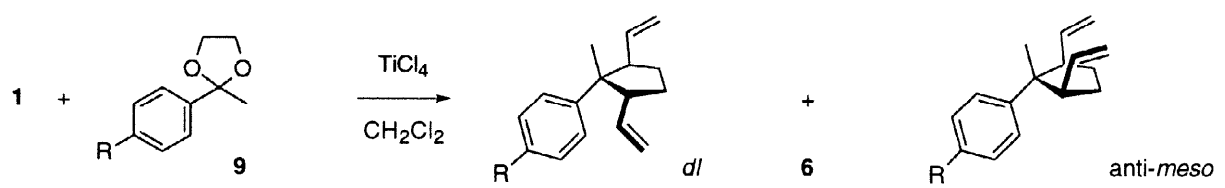
The addition reaction of BISTRO with 4-bromophenacyl bromide provides only the alcohol **7** arising from a monoalkylation followed by a protolysis of the second allylsilane moiety. This unexpected result could be related to a steric and/or an electronic substituent effect.



Among several alkylarylketones that have been reacted with BISTRO such as α-tetralone or acetylfurane, only the 2-acetylthiophene has led to the expected divinylcyclopentanes **8** in a low yield (absence of nitromethane decreases the yield of **8** to 8%).



In contrast, the dialkylation of acetophenone ethylene ketals **9** mostly occurred with good to excellent yields (Table 2).

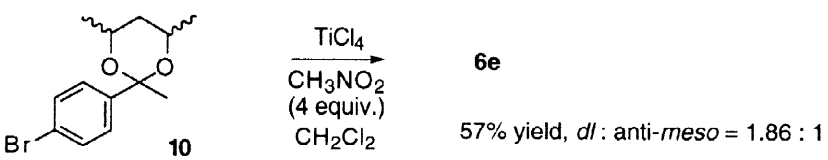


a, R = H; **b**, R = MeO; **e**, R = Br; **f**, R = Me; **g**, R = NO_2

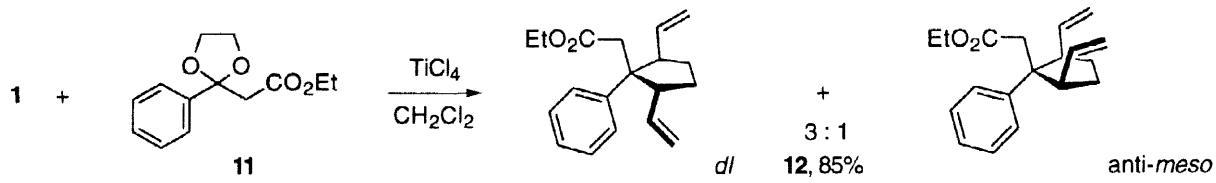
Table 2. Reaction of BISTRO (1) with Acetophenone Ethylene Ketals 9.

Entry	Acetoph. ethyl. ketal	Reaction condition	Yield **6** (%)	*dl* : *meso*
1	**9a**	**1**, 2.5 eq.; $TiCl_4$, 2.0 eq.; –90 °C, 0.5 h.; –50 °C, 48 h.	71	1.86 : 1
2	**9b**	**1**, 2.5 eq.; $TiCl_4$, 2.0 eq.; –90 °C, 0.5 h.; 20 °C, 38 h.	21	2.12 : 1
3	**9e**	**1**, 3.0 eq.; $TiCl_4$, 2.4 eq.; –90 °C, 0.5 h.; –50 °C, 20 h.	91	1.86 : 1
4	**9e**	**1**, 2.5 eq; $TiCl_4$, 2.4 eq; CH_3NO_2, 4 eq; –90 °C, 0.75 h.; –50 °C, 17 h	81	1.94 : 1
5	**9f**	**1**, 2.5 eq.; $TiCl_4$, 2.0 eq.; –90 °C, 0.5 h.; 20 °C, 17 h.	62	2.33 : 1
6	**9g**	**1**, 2.5 eq.; $TiCl_4$, 2.4 eq.; –90 °C, 1 h.	25	3 : 1

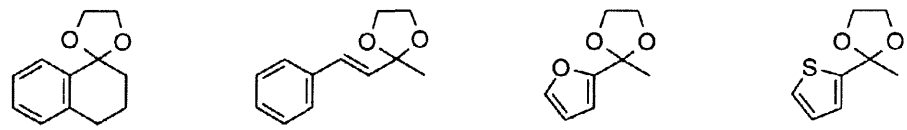
The 4,6-dimethyl-1,3-dioxane ketal **10** reacted with BISTRO with a lower yield than the corresponding ethylene ketal **9e**. The diastereoselectivity of both reactions is nevertheless the same.



Interestingly, the ethylene ketal **11** gives rise to a versatile ester **12**.



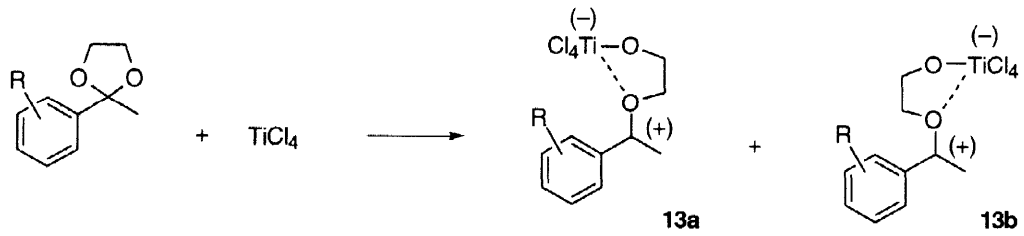
In contrast, ethylene ketals shown below do not react with BISTRO.



Discussion

To rationalize the mechanism of the Lewis acid-promoted acetal substitution reaction,[6] synchronous (S_N2-like)[2e,7] or dissociative (S_N1-like)[8] substitution processes have been proposed as well as the involvement of equilibrating ion pairs.[9] For aromatic acetals, the stereoselectivity of the addition of crotylsilane was poor and highly dependent upon both the nature of the para-substituent and the stereochemistry of the crotylsilane.[10,11] It is worth noting that the Hammett plot between logarithms of the diastereomer ratio ln(syn/anti) with Brown-Okamoto's σ^+ values[12] have revealed good linear correlations ($\rho = -1.25$, $r = 0.996$ in the case of *Z*-crotylsilane and $\rho = 1.26$, $r = 0.988$ for *E*-crotylsilane).

In our case, the yields of the addition of BISTRO to acetophenones or acetophenone ethylene ketals are strongly dependent upon the nature of the ring substituent, better results are observed with *m*-MeO (Table 1, entry 4) or *p*-Br (Table 1, entry 7 and Table 2, entry 3). Earlier work concerning the reaction of chiral dioxane acetals with allyltrimethylsilane reported a dramatic rate-retarding effect by the electron-withdrawing para substituents with insignificant effects on the stereoselectivity.[9b] We assume that aromatic ketals are activated by Lewis acids to undergo the C–O bond cleavage, giving the alkoxymethylbenzylic cationic species (oxocarbenium ion) **13**.[13–15] It is well known that an oxocarbocation precursor of the hemiacetal is involved during the acid hydrolysis of acetophenone ketals.[16]



Relatively few studies have been devoted to the conformational preferences of benzylic cations. In a recent work, the crystal structure of the cumyl hexafluoroantimonate(V) has been determined at −124 °C.[17] Some studies have also reported on the dependence of both the ^{13}C chemical shifts and the atomic charges at the *ipso*, *ortho*, *para* positions with the Hammett σ constants and other properties.[18]

Table 3. Optimized Energies, Angles, Bond Lenghts and Charges of α-Methoxy-α-methylbenzyl Cations Calculated using the PM3 Method.

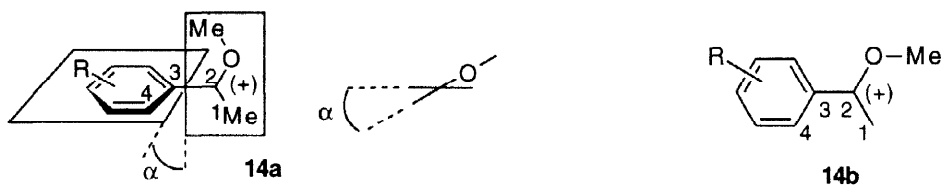
Substituent	σ^+ [a]	k ($l.mol^{-1}.s^{-1}$) [b]	**14a** ΔH_f (kcal/mol)	**14b** ΔH_f (kcal/mol)	relative energies **14a/14b** (kcal/mol)	**14a** angle α [c]	**14a** Charge Q [d]	**14a** LUMO energy (eV)	**14a** C–C distance [e]	**14b** Charge Q [d]	**14b** LUMO energy (eV)	**14b** C–C distance [e]
p-Dimethylamino	–1.7	1.47×10^5	144.75	140.52	4.23	15.6	0.598	–5.536	1.4045	0.531	–5.471	1.4007
p-Amino	–1.3	4.91×10^4	147.63	144.21	3.42	16.6	0.618	–5.667	1.4076	0.551	–5.606	1.4037
p-Hydroxy	–0.92	2.83×10^4	110.67	107.44	3.23	22.5	0.719	–6.145	1.4249	0.646	–6.104	1.4186
p-Methoxy	–0.78	9.40×10^3	116.67	113.66	3.01	21.7	0.708	–6.054	1.4229	0.638	–6.017	1.4164
p-Methyl	–0.31	2.09×10^3	147.99	145.36	2.61	25.2	0.755	–6.238	1.4333	0.682	–6.221	1.4266
m-Methyl	–0.1	1.68×10^3	149.40	147.05	2.35	27.2	0.777	–6.294	1.4390	0.699	–6.291	1.4319
p-Trimethylsilyl	–0.09	–	108.92	106.52	2.40	25.6	0.743	–6.051	1.4375	0.668	–6.034	1.4252
p-Fluoro	–0.07	1.19×10^3	119.11	116.34	2.77	26.4	0.779	–6.491	1.4375	0.705	–6.481	1.4306
Hydrogen	0	9.56×10^2	159.68	157.25	2.43	27.2	0.782	–6.357	1.4391	0.708	–6.353	1.4321
m-Methoxy	0.05	4.53×10^2	121.20	119.11	2.09	28.6	0.791	–6.287	1.4435	0.715	–6.300	1.4362
p-Chloro	0.11	4.07×10^2	153.60	150.86	2.74	25.2	0.757	–6.333	1.4335	0.680	–6.315	1.4266
p-Bromo	0.15	3.79×10^2	170.23	167.74	2.49	27.7	0.783	–6.432	1.4403	0.710	–6.432	1.4332
m-Bromo	0.405	1.56×10^2	170.20	167.70	2.50	27.1	0.789	–6.436	1.4403	0.718	–6.437	1.4335
p-Trimethylammonium	0.41	–	383.66	379.36	4.30	33.2	0.908	–9.461	1.4692	0.856	–9.493	1.4665
p-Trifluoromethyl	0.612	–	10.46	8.16	2.30	29.9	0.821	–6.746	1.4485	0.748	–6.767	1.4419
p-Cyano	0.66	–	201.73	199.17	2.56	28.0	0.797	–6.639	1.4426	0.723	–6.646	1.4357
p-Nitro	0.79	–	164.20	162.00	2.20	30.9	0.834	–6.915	1.4523	0.766	–6.947	1.4462
p-Diazo	1.88	–	465.20	460.55	4.65	35.6	0.938	–10.28	1.4782	0.889	–10.275	1.4774
m-Methoxy(H^+)(**17**)	1.18	–	397.88	393.69	4.19	32.7	0.912	–9.743	1.4684	0.860	–9.761	1.4662
p-Methoxy(H^+)(**18**)	1.50	–	395.14	390.70	4.44	34.5	0.922	–9.736	1.4728	0.871	–9.763	1.4706
p-Methoxy(BF_3)(**19**)[f]	0.33	–	–157.77	–160.95	3.18	28.0	0.731	–5.936	1.4244	0.635	–5.914	1.4193
p-Methoxy($SnCl_4$)(**20**)	–0.38	–	12.44	9.75	2.69	24.0	0.714	–5.803	1.4250	0.626	–5.871	1.4155

[a] Brown-Okamoto's σ^+ values (ref. 12). [b] k : Rate constants of the H^+-catalysed hydrolysis of substituted acetophenone dimethyl ketals (ref. 16c).

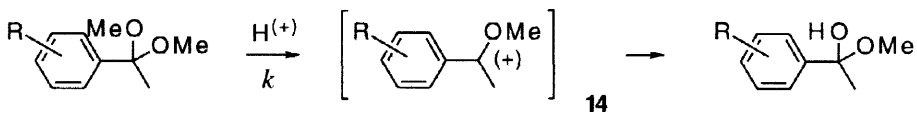
[c] Values of the dihedral angle C(1)-C(2)-C(3)-C(4)(see Fig. 1). [d] Q : total positive charge of the α-methoxy-α-methylcarbenium group. The Mulliken charges are expressed in electron. [e] C(2)-C(3) bond lengths (Å)(see Fig. 1). [f] Calculated using the AM1 method.

With the aim to determine the structure of the transition state for the addition of allylsilane to acetophenones and acetophenone ethylene ketals, we performed semi-empirical calculations for the α-methoxy-α-methylbenzyl cations **14** instead of **13**, using the PM3 method (see Table 3).[19] In principle, the α-methoxy-α-methylbenzyl cation **14** can exist as two conformers **14a** and **14b**. In all cases, **14b** is the most stable, but **14a** can result from a kinetic process of ionization (and in a similar manner, for **13a**). Calculations show that the α-methoxy-α-methylbenzyl cation **14a** is twisted around the C(2)–C(3) bond.[20,21] The dihedral angle C(1)–C(2)–C(3)–C(4) α increases when the phenyl group bears an electron-withdrawing substituent and a linear relationship can be established for α versus σ^+ values of the substituent (Fig. 1).[22] Moreover, the dihedral angle α is related to the total positive charge Q of the α-methoxy-α-methylcarbenium group (Fig. 2). The distribution of the total positive charge between the α-methoxy-α-methylcarbenium moiety and the phenyl group increases from 1.5 : 1 for *p*-dimethylamino group to 9 : 1 for *p*-trimethylammonium group. The atomic charge of the carbocationic center increases with the electron-withdrawing character of the substituent as expected but its value is limited to 0.425. When the substituent exerts a strong electron-withdrawing effect, the other atoms of the methoxymethylcarbenium moiety supply the functional carbon atom.

Figure 1. Structures of the α-methoxy-α-methylcarbocation **14**



The steric shielding due to the interaction between methyl and phenyl groups prevents complete p–π resonance overlap[23] of the phenyl group with the adjacent empty p-orbital. Consequently, *the value of* α *appears as a measurement of the resonance effect stemming from conjugation between the carbocation center and the substituted ring.* As expected, the C(2)–C(3) bond lengths $d_{(C-C)}$ are correlated with σ^+ (Fig. 3). In a similar manner, the energy of the LUMO of **14b** decreases with the values σ^+ (Fig. 4). *So, the nucleophilic attack should be accelerated for the electron-withdrawing groups.*[24] This is confirmed by the rate constants *k* of the H^+-catalysed hydrolysis of substituted acetophenone dimethyl ketals.[16c] Thus, a linear least squares fit was observed for log*k* versus the energy of the LUMO of **14b** (Fig. 5). Interestingly, the rate constants of the reaction of allylsilanes with the ionized benzaldehyde dimethyl acetal decreased for the electron-donating groups. [25]



The ^1H chemical shifts of α-methoxy-α-methylbenzyl cations formed by treatment of acetophenone ketals with fluorosulfonic acid were recorded.[26] A plot of the chemical shift of the methyl group with α is depicted in Fig. 6. Some other computed best-fit line of correlation can be proposed : $d_{C-C} = 0.004\alpha + 1.342$ (r = 0.983)(we note that for $\alpha = 0$, the bond length value (1.34 Å) corresponds to the C=C bond distance)[27] and $\text{Log}k = -1.435\sigma^+ + 2.876$ (r = 0.990).

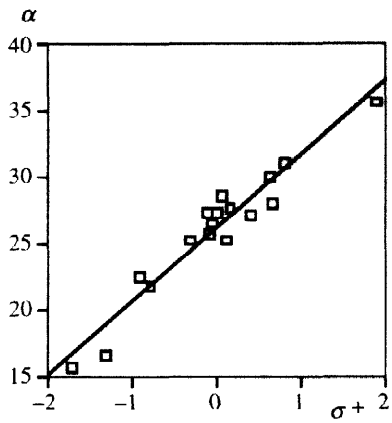


Fig. 1: $\alpha = 5.569\sigma^+ + 26.142$
r = 0.963

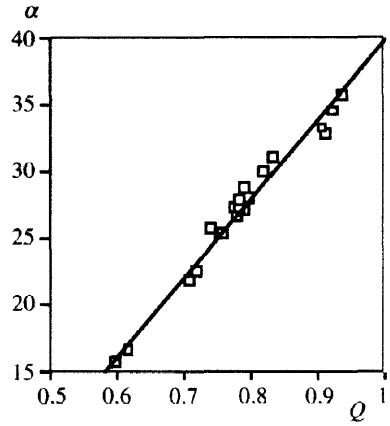


Fig. 2: $\alpha = 0.017Q + 0.328$
r = 0.989

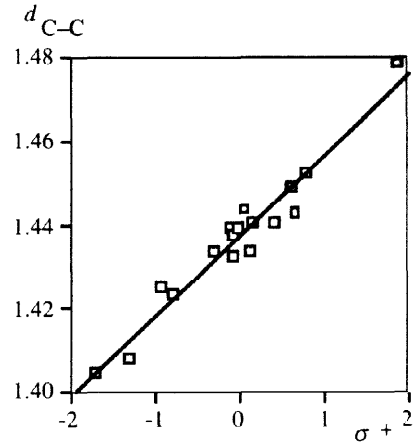


Fig. 3: $d_{C-C} = 0.019\sigma^+ + 1{,}437$
r = 0.972

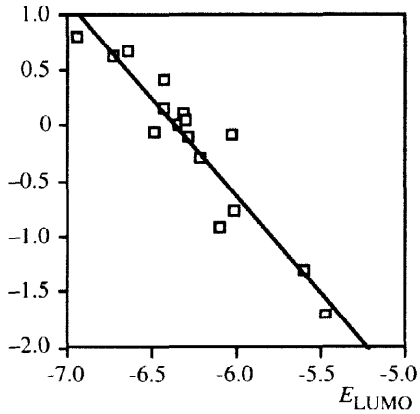


Fig. 4: $E_{Lumo} = -0.509\sigma^+ - 6.35$
r = 0.944

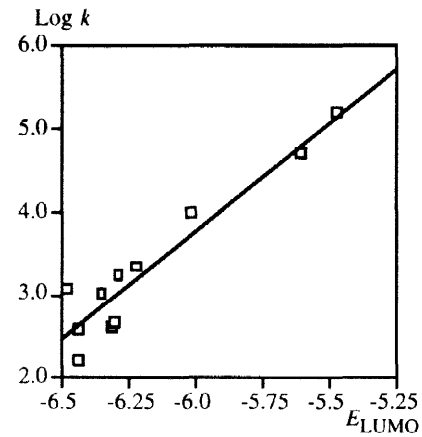


Fig. 5: $\text{Log}k = 2.6E_{Lumo} + 19.34$
r = 0.948

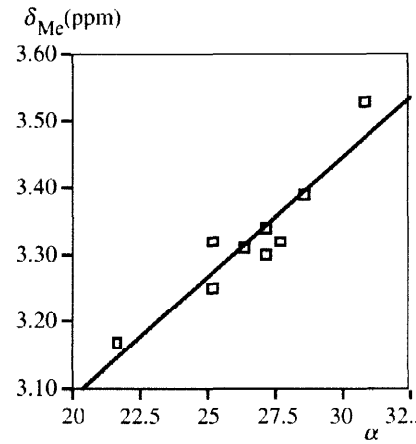
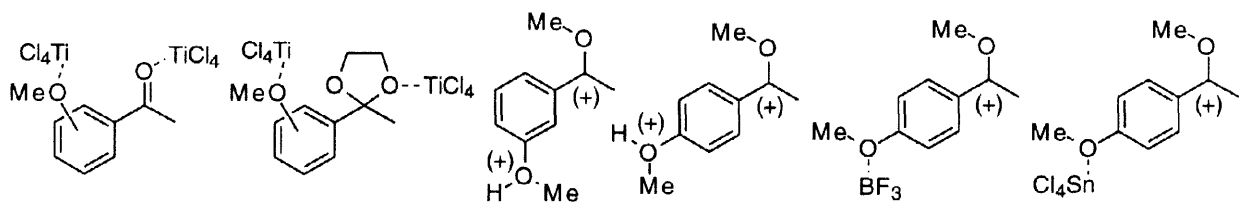


Fig. 6: $\delta_{Me} = 0.036\alpha + 2.37$
r = 0.933

The $TiCl_4$-mediated addition of BISTRO to methoxyacetophenone and methoxyacetophenone ethylene ketal could actually involve the methoxy-complexed reagents **15** and **16**, respectively. The agreement observed in the correlation of α and σ^+ suggests that α values resulting from calculations of the structures **17-20** may be used in equation $\alpha = 5.569\sigma^+ + 26.142$ (Fig. 1) to calculate tentative σ^+ constants for protonated, BF_3 or $SnCl_4$-complexed methoxy group.[28] We have found the following values: *m*-methoxy-(H^+), $\sigma^+ = 1.18$; *p*-methoxy-(H^+), $\sigma^+ = 1.50$; *p*-methoxy-(BF_3), $\sigma^+ = 0.33$; *p*-methoxy-($SnCl_4$), $\sigma^+ = -0.38$.[29] Thus, protonation of methoxy group attached to the ring induced a strong electron-withdrawing effect. In contrast, we note the weak effect resulting from the complexation of the *p*-methoxy group with BF_3 (calculated with the AM1 method) or $SnCl_4$. Moreover, the energy of the LUMO was higher after complexation (see Table 3) and this should reduce the reactivity.



15 **16** **17** **18** **19** **20**

The high reactivity of *p*-bromoacetophenone and *m*-methoxyacetophenone towards BISTRO can be explained by a favorable balance between the rate of the ionization step and the rate of the reaction with BISTRO (relatively low LUMO levels of the corresponding α-alkoxy-α-methylbenzyl cations).

In conclusion, we have described a two step stereoselective synthesis of aryldivinylcyclopentanes from 1,3-butadiene in high yields. These compounds are of high synthetic potential, particularly as precursors of 13-arylsteroids [synthesis of 11-methoxycarbonyl-13-(3-*p*-bromophenyl)-17-vinylgona-1,3,5(10)-trienes].[30] Moreover, we have found a correlation between the calculated value of the angle α and σ^+. Thus, the σ^+ values of unusual substituents can be tentatively calculated.

Experimental Section

General. ^1H (200 MHz) and ^{13}C NMR (50 MHz) spectra were recorded on a Bruker AC 200 spectrometer in $CDCl_3$ solutions. Chemical shifts (δ) are reported in ppm with tetramethylsilane as internal standard. IR spectra were recorded on a Perkin-Elmer 1600 spectrophotometer. Flash chromatography was performed on silica gel (Merk 60 GF_{254} 230-400 mesh) and TLC on silica gel (Merck 60 F_{254}). The *dl-meso* ratio was determined first. by ^1H NMR and confirmed by GC (Carlo-Erba GC 6000 Vega Series).

Computational Methods. Computer modeling was carried out with the Hyperchem program (version 5.0) from Hypercube, Inc. on a PC equipped with a 200 MHz Pentium-Pro. Structures were minimized with the following parameters: PM3 or AM1 basic set; restricted Hartree-Fock (RHF) level; minimization algorithm, until the rms energy gradient was less than 0.001 kcal/mol.Å; accelerated convergence.

Materials. All solvents were distilled before used, CH_2Cl_2 and $CHCl_3$ from P_2O_5, MeOH under $Mg(OMe)_2$. **1,8-Bis(trimethylsilyl)-2,6-octadiene (BISTRO) (1)** was prepared according to the previously described procedure.[5a] **Ethylene Ketals (9-11)** were prepared from the commercially available ketones at reflux of anhydrous chloroform in the presence of an excess of ethylene glycol [(±)-2,4-pentanediol for **10**] and a catalytic amount of *p*-toluenesulfonic acid using a Dean-Stark trap.

General Procedure for the Addition of BISTRO (1) to Ketones. Ketone (1.5 mmol) in 3 ml of anhydrous CH_2Cl_2 and 2.5 eq. of BISTRO (**1**) in 6 ml of anhydrous CH_2Cl_2 were successively added at -70 °C to a stirred solution of 1.2 eq. of $TiCl_4$ and 4 eq. of CH_3NO_2 (when indicated) in 4-5 ml of anhydrous CH_2Cl_2 under argon. The resulting solution was allowed to warm to room temperature. After stirring at 20 °C, for between 13 to 36 hours, depending on the reactivity of the ketone, the reaction was quenched by adding an excess of a saturated NH_4Cl aqueous solution. The mixture was decanted and the aqueous layer was extracted twice with CH_2Cl_2. The combined organic layers were washed with a saturated $NaHCO_3$ aqueous solution and water, dried over $MgSO_4$ and evaporated under reduced pressure to give an oil which was purified by flash chromatography on silica gel (petroleum ether/ether).

1-(Octa-1,7-dien-3-yl)-cyclohexanol (4). Reaction of cyclohexanone following the general procedure gave **4**, 55 %. IR (neat) 3462, 3073, 1639, 999, 964, 910 cm^{-1}; ^1H NMR δ 5.88-5.50 (2H, m), 5.16-4.88 (4H, m), 2.09-1.10 (17H, m); ^{13}C NMR δ 139.0, 138.8, 117.7, 114.3, 72.4, 55.5, 33.8, 34.9, 34.7, 27.3, 25.9, 21.8.

1-Methyl-1-phenyl-2,5-divinylcyclopentane (6a). Reaction of acetophenone **5a** following the general procedure gave **6a**, 50 %, *dl* : *meso* = 1.38 : 1; IR (neat) 3076, 1638, 1377, 1247, 997, 910, 756, 699 cm^{-1}; ^1H NMR δ 7.39-7.10 (5H, m), 5.90 (1H, ddd, *J* = 17.5, 10.3, 7.5 Hz, *dl*), 5.64 (2H, ddd, *J* = 17.2,

10.5, 6.8 Hz, *meso*), 5.32 (1H, ddd, J = 18.8, 10.4, 7.9 Hz, *dl*), 5.15-4.65 (4H m), 3.20-3.10 (1H, m, *dl*), 2.91-2.84 (2H, m, *meso*), 2.63-2.55 (1H, m, *dl*), 2.13-1.92 (2H, m), 1.91-1.62 (2H, m), 1.27 (3H, s, *dl*), 1.03 (3H, s, *meso*); ^{13}C NMR δ 146.6 (*dl*), 146.1 (*meso*), 141.1, 139.7, 138.1, 128.0, 127.8, 127.4, 126.4, 125.5, 115.3, 115.2, 113.4, 56,3 (*dl*), 54.9 (*meso*), 51.7 (*dl*), 51.6 (*meso*), 48.8 (*dl*), 29.1 (*dl*), 28.3 (*dl*), 26.9 (*meso*), 24.2 (*dl*), 13.4 (*meso*). Anal. Calcd for $C_{16}H_{20}$: C, 90.51; H, 9.49. Found: C, 90.61; H, 9.39.

1-Methyl-1-(4-methoxyphenyl)-2,5-divinylcyclopentane (6b). Reaction of 4-methoxyacetophenone **5b** (in the presence of nitromethane) following the general procedure gave **6b**, 40 %, *dl* : *meso* = 1.63 : 1; IR (neat) 3075, 1636, 1293, 1184, 1038, 910, 828 cm^{-1}; ^{1}H NMR δ 7.28-7.16 (2H, m), 7.04-6.77 (2H, m), 5.88 (1H, ddd, J = 17.4, 10.3, 7.6 Hz, *dl*), 5.64 (2H, ddd, J = 17.2, 10.5, 6.7 Hz, *meso*), 5.32 (1H, ddd, J = 17.2, 10.2, 7.9 Hz, *dl*), 5.13-4.66 (4H, m), 3.77 (3H, s, *meso*), 3.76 (3H, s, *dl*), 3.18-3.00 (1H, m, *dl*), 2.90-2.72 (2H, m, *meso*), 2.62-2.49 (1H, m, *dl*), 2.11-1.88 (2H, m), 1.87-1.56 (2H, m), 1.23 (3H, s, *dl*), 0.99 (3, s, *meso*); ^{13}C NMR δ 157.4 (*meso*), 157.2 (*dl*), 141.2 (*meso*), 139.7 (*dl*), 138.5, 138.1 (*dl*), 128.2, 127.3, 115.2 (*meso*), 113.2 (*dl*), 113.0 (*dl*), 56.2 (*dl*), 54.84, 50.9, 49.0 (*dl*), 29.0, 28.31, 26.72, 24.2 (*dl*), 13.5 (*meso*). Anal. Calcd for $C_{17}H_{22}O$: C, 84.25; H, 9.15. Found: C, 84.19; H, 9.22.

1-Methyl-1-(3-methoxyphenyl)-2,5-divinylcyclopentane (6c). Reaction of 3-methoxyacetophenone **5c** (in the presence of nitromethane) following the general procedure gave **6c**, 95 %, *dl* : *meso* = 1 : 1; IR (neat) 3075, 1637, 1604, 1256, 1050, 909 cm^{-1}; *meso*: ^{1}H NMR δ 7.25-7.17 (1H, m), 6.97-6.86 (2H, m), 6.74-6.61 (1H, m), 5.65 (2H, ddd, J = 17.2, 10.5, 6.7 Hz), 5.19-4.65 (4H, m), 3.79 (3H, s), 2.91-2.80 (2H, m), 2.10-1.86 (2H, m), 1.85-1.60 (2H, m), 1.01 (3H, s); ^{13}C NMR δ 159.4, 148.1, 138.2, 128.8, 119.0, 115.4, 113.3, 110.3, 55.1, 54.9, 51.7, 26.9, 13.6. *dl* : ^{1}H NMR δ 7.21 (1H, m), 6.97-6.81 (2H, m), 6.73-6.66 (1H, m), 5.90 (1H, ddd, J = 17.6, 10.3, 7.6 Hz), 5.35 (1H, ddd, J = 17.6, 10.1, 7.6 Hz), 5.14-4.67 (4H, m), 3.77 (3H, s), 3.16-3.05 (1H, m), 2.64-2.54 (1H, m), 2.15-1.86 (2H, m), 1.85-1.58 (2H, m), 1.25 (3H, s); ^{13}C NMR δ 159.2, 148.0, 141.1, 139.8, 128.6, 120.1 , 115.2), 114.3, 113.4, 110.1, 56.2, 55.1, 51.7, 48.9, 29.1, 28.2, 24.3. Anal. Calcd for $C_{17}H_{22}O$: C, 84.25; H, 9.15. Found: C, 84.15; H, 9.20.

1-Methyl-1-(2-methoxyphenyl)-2,5-divinylcyclopentane (6d). Reaction of 2-methoxyacetophenone **5d** (in the presence of nitromethane) following the general procedure gave **6d**, 18 %, *dl* : *meso* = 1.5 : 1; IR (neat) 3073, 1637, 1291, 1237, 1179, 1030, 997, 908 cm^{-1}; ^{1}H NMR δ 7.35-7.11 (2H, m), 6.92-6.78 (2H, m), 6.01 (1H, ddd, J = 17.6, 10.3, 7.3, *dl*), 5.62 (2H, ddd, J = 17.0, 10.3, 6.6 Hz, *meso*), 5.30 (1H, ddd, J = 17.6, 10.3, 7.3 Hz, *dl*), 5.22-4.54 (4H, m), 3.82 (3H, s, *meso*), 3.78 (3H, s, *dl*), 3.72-3.65 (1H, m), 3.23-3.07 (1H, m), 2.12-1.87 (2H, m), 1.80-1.58 (2H, m), 1.28 (3H, s, *dl*), 1.01 (3H, s, *meso*); ^{13}C NMR δ 157.4 (*meso*), 157.2 (*dl*), 142.1, 140.5, 139.9, 135.5, 129.7, 127.8, 127.3, 127.0, 120.4, 119.9, 115.4, 114.2, 111.9, 111.6, 110.7, 55.1, 54.7, 52.7 (*dl*), 49.2 (*meso*), 48.4 (*dl*), 29.1, 27.3, 27.2, 20.6 (*dl*), 15.0 (*meso*). Anal. Calcd for $C_{17}H_{22}O$: C, 84.25; H, 9.15. Found: C, 84.32; H, 9.28.

1-Methyl-1-(4-bromophenyl)-2,5-divinylcyclopentane (6e). Reaction of 4-bromoacetophenone **5e** (in the presence of nitromethane) following the general procedure gave **6e**, 81 %, *dl* : *meso* = 1.32 : 1; IR (neat) 3075, 1636, 1007, 912, 822 cm^{-1}; ^{1}H NMR δ 7.42-7.32 (2H, m), 7.24-7.13 (2H, m), 5.84 (1H, ddd, J = 17.5, 10.1, 7.6 Hz, *dl*), 5.60 (2H, ddd, J = 17.0, 10.5, 6.8 Hz, *meso*), 5.28 (1H, ddd, J = 16.5, 9.8, 8.1 Hz, *dl*), 5.12-4.66 (4H, m), 3.12-3.00 (1H, m, *dl*), 2.88-2.72 (2H, m, *meso*), 2.64-2.50 (1H, m, *dl*), 2.14-1.86 (2H, m), 1.85-1.58 (2H, m), 1.23 (3H, s, *dl*), 1.00 (3H, s, *meso*); ^{13}C NMR δ 145.7 (*dl*), 145.3 (*meso*), 140.7, 139.2, 137.7, 128.0, 127.8, 127.4, 126.4, 125.5, 119.6 (*meso*), 119.4 (*dl*), 115.7, 115.5, 113.8, 55.0 (*meso*), 56.2 (*dl*), 51.5 (*meso*), 51.4 (*dl*), 50.0 (*dl*), 29.1 (*dl*), 28.4 (*dl*), 27.0 (*meso*), 24.1 (*dl*), 13.36 (*meso*). Anal. Calcd for $C_{16}H_{19}Br$: C, 65.99; H, 6.58. Found: C, 66.11; H, 6.51.

1-Bromo-2-(4-bromophenyl)-3-vinyl-oct-7-en-2-ol (7). Reaction of 4-bromophenacyl bromide (in the presence of nitromethane) following the general procedure gave **7**; IR (neat) 3545, 1274, 1074, 1007, 921, 854 cm^{-1}; ^1H NMR δ 7.47 (1H, dd, *J* = 3.0, 8.7 Hz), 7.22 (1H, dd, *J* = 1.6, 8.6 Hz), 5.78-5.56 (2H, m), 5.37-5.08 (2H, m), 5.04-4.81 (2H, m), 3.95-3.70 (2H, m), 2.55-2.31 (2H, m), 2.01-1.06 (6H, m); ^{13}C NMR δ 142.5, 140.2, 138.6, 138.5, 137.4, 137.2, 131.2, 131.0, 128.2, 127.5, 121.5, 121.2, 119.1, 118.8, 114.5, 77.0, 76.2, 53.4, 53.2, 45.0, 44.7, 33.5, 33.3, 28.3, 27.7, 26.8, 26.6.

1-Methyl-1-(2-thienyl)-2,5-divinylcyclopentane (8). Reaction of acetyl thiophene (in the presence of $MeNO_2$) following the general procedure gave **8**, 21%, *dl* : *meso* = 1.5 : 1; IR 3076, 1639, 1419, 1377, 1241, 996 cm^{-1}; ^1H NMR δ 7.20-6.99 (1H, m), 6.98-6.89 (1H, m), 6.82-6.79 (1H, m), 5.92-5.63 (3H, m), 5.35 (1H, ddd, *J* = 17.7, 10.1, 8.2 Hz, *dl*), 5.10-4.73 (4H, m), 3.03 (1H, q, *J* = 8.0 Hz , *dl*), 2.85-2.75 (2H, m, *meso*), 2.45 (1H, q, *J* = 7.3 Hz, *dl*), 2.14-1.88 (2H, m), 1.84-1.60 (2H, m), 1.32 (3H, s, *dl*), 1.05 (3H, s, *meso*); ^{13}C NMR δ 152.1, 140.3 (*dl*), 139.1 (*dl*), 137.7 (*meso*), 126.4, 126.2, 123.4, 123.3, 122.7, 122.7, 115.9 (*meso*), 115.4 (*dl*), 114.0 (*dl*), 57.0 (*meso*), 56.9 (*dl*), 52.5 (*dl*), 51.4 (*meso*), 50.9 (*dl*), 29.0, 28.9, 26.8, 25.0 (*dl*), 14.8 (*meso*). Anal. Calcd for $C_{14}H_{18}S$: C, 77.01; H, 8.31. Found: C, 77.19; H, 8.40.

General Procedure for the Addition of BISTRO (1) to Aromatic Ketals: To a stirred solution of 2 or 2.4 eq. of $TiCl_4$ (3 eq. in case of **11** and 4 eq. of CH_3NO_2 in case of **9e**) in 4-5 ml of anhydrous CH_2Cl_2 under argon was added slowly at -60 °C aromatic ketal (1.5 mmol) in 3 ml of anhydrous CH_2Cl_2. The resulting solution was cooled at - 90 °C and 2.5 eq. (3 eq., **9e**) of BISTRO (**1**) in 6 ml of anhydrous CH_2Cl_2 were added. After stirring at -90 °C for 30-45 minutes (1 hour, **9g**), the resulting solution was allowed to warm to -50 °C or room temperature. After stirring at -50 °C for between 17 to 48 hours or at 20 °C for between 17 to 48 hours, depending on the reactivity of the ketal, the reaction was worked up using the procedure described above for aromatic ketones.

1-Methyl-1-(4-methylphenyl)-2,5-divinylcyclopentane (6f). Reaction of 4-methylacetophenone ethylene ketal **9f** following the general procedure gave **6f**, 62 %, *dl* : *meso* = 2.33 : 1; IR (neat) 3075, 1636, 997, 910, 815 cm^{-1}; ^1H NMR δ 7.27-7.05 (4H, m), 5.90 (1H, ddd, *J* = 17.3, 10.3, 7.7 Hz, *dl*), 5.66 (2H, ddd, *J* = 17.2, 10.6, 6.8 Hz, *meso*), 5.35 (1H, ddd, *J* = 17.3, 10.3, 7.7 Hz, *dl*), 5.15-4.67 (4H, m), 3.20-3.05 (1H, m, *dl*), 2.95-2.84 (2H, m, *meso*), 2.65-2.58 (1H, m, *dl*), 2.31 (3H, s, *meso*), 2.30 (3H, s, *dl*), 2.15-1.86 (2H, m), 1.85-1.54 (2H, m), 1.26 (3H, s, *dl*), 1.02 (3H, s, *meso*); ^{13}C NMR δ 143.6 (*dl*), 143.1 (*meso*), 141.3, 139.9, 138.3, 135.0 (*meso*), 134.8 (*dl*), 128.7 (*meso*), 128.5 (*dl*), 127.3 (*dl*), 126.3 (*meso*), 115.3, 115.1, 113.3, 54.9 (*meso*), 51.4 (*dl*), 51.3 (*meso*), 56.3 (*dl*), 48.9 (*dl*), 29.1 (*dl*), 28.4 (*dl*), 26.9 (*meso*), 24.3 (*dl*), 21.0, 13.5 (*meso*). Anal. Calcd for $C_{17}H_{22}$: C, 90.20; H, 9.80. Found: C, 90.15; H, 9.72.

1-Methyl-1-(4-nitrophenyl)-2,5-divinylcyclopentane (6g). Reaction of 4-nitroacetophenone ethylene ketal **9g** following the general procedure gave **6g**, 25 %, *dl* : *meso* = 3.0 : 1; IR (neat) 3054, 1637, 1007, 912, 822 ^1H NMR δ 8.11-8.02 (2H, m), 7.46-7.36 (2H, m), 5.91-5.70 (1H, m, *dl*), 5.64-5.41 (2H, m, *meso*), 5.31-5.16(1H, m, *dl*), 5.12-4.61 (4H, m), 3.19-3.02 (1H, m, *dl*), 2.92-2.72 (2H, m, *meso*), 2.69-2.55 (1H, m, *dl*), 2.30-1.10 (4H, m), 1.24 (3H, s, *dl*), 1.04 (3H, s, *meso*); ^{13}C NMR δ 154.9 (*dl*), 154.5 (*meso*), 145.8 (*meso*), 145.8 (*dl*), 140.2, 138.6, 137.2, 128.3, 127.4, 123.1, 122.9, 116.3, 116.2, 114.4, 56.6 (*dl*), 55.5 (*meso*), 52.5 (*meso*), 52.3 (*dl*), 49.1 (*dl*), 29.3, 28.4, 27.4, 24.0 (*dl*), 13.4 (*meso*). Anal. Calcd for $C_{16}H_{19}NO_2$: C, 74.68; H, 7.44; N, 5.44. Found: C, 74.72; H, 7.48; N, 5.37.

1-Ethoxycarbonylmethyl-1-phenyl-2,5-divinylcyclopentane (12). Reaction of **11** following the general procedure gave **12**, 85 %, *dl* : *meso* = 3.0 : 1; IR (neat) 1736, 1172, 1034, 913, 701 ^1H NMR δ 7.43-7.14 (5H, m), 6.00-5.83 (1H, m), 5.39-5.21 (1H, m, *dl*), 5.10-4.94 (4H, m), 4.07-3.84 (2H, m), 3.47

(2H, d J = 13.6 Hz, *meso*), 3.02 (1H, 1/2 AB J = 16.8 Hz, *dl*), 2.60 (1H, 1/2 AB J = 16.8 Hz, *dl*), 3.10 (1H, m, *dl*), 2.65 (1H, m, *meso*), 2.53-2.18 (4H, m, *dl*), 2.11-1.48 (4H, m), 1.07-0.97 (3H, m); ^{13}C NMR δ 171.5, 171.2, 144.9, 142.7, 140.8, 139.4, 138.3, 127.7, 127.5, 127.4, 126.4, 125.8, 125.7, 115.8, 115.5, 115.0, 53.9, 53.6, 53.2, 50.0, 40.7, 35.4, 29.6, 28.8, 27.0, 13.9, 13.8. Anal. Calcd for $C_{19}H_{24}O_2$: C, 80.24; H, 8.51. Found: C, 80.31; H, 8.57.

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22. The σ^+ value for the *p*-trimethylammonium group (0.41) appears to be out of line and this substituent has been discarded. Since the trimethylammonium substituent cannot supply electrons conjugatively, its σ^+ value (0.41) should not be less positive than its σ value (0.82).

23. (a) In molecular mechanics, the dihedral potential function is: $V_{dihedral} = V_0/2(1 - \cos\alpha)$, see: Allinger, N. L. *Adv. Phys. Org. Chem.* **1976**, *13*, 1–82. (b) PM3-calculated rotation barrier of **14b** (R = H), 8.15 kcal/mol [$\alpha = 0$ °, $\Delta H_f = 157.25$ Kcal/mol; $\alpha = 90$ °, $\Delta H_f = 165.40$ Kcal/mol] or **14b** (R = NMe_2), 16.28 kcal/mol [$\alpha = 0$ °, $\Delta H_f = 140.52$ Kcal/mol; $\alpha = 90$ °, $\Delta H_f = 156.8$ Kcal/mol].

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27. The calculated C(2)–C(3) bond length (1.404 Å with the PM3-method, 1.406 Å with AM1-method) in cumyl cation was close to the experimental value (1.41(2) Å), see ref. 17.

28. The semi-empirical PM3 SCF-MO method is not extended to titanium.

29. For a gas-phase basicity measurements of 4X-acetophenones, see: Dell'Erba, C.; Mugnoli, A.; Noto, R.; Novi, M.; Occhiucci, G.; Petrillo, G.; Sancassan, F.; Spinelli, D. *Tetrahedron* **1997**, *53*, 731–738.

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