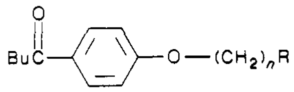
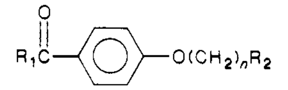
Table I. Photokinetic Data for *p*-Alkenoxyvalerophenones[a]



ketone[b]	n	R	Φ[c]	$k_q\tau$, M	$1/\tau$[d,e]	k_H[e]	k_d[e]	k_{CT}[e,f]
VP	0	CH_3[g]	0.17	4100	2.4	0.4	2.0	
VP_11	1	$CH{=}CH_2$	0.15	3700	2.7	0.4	2.0	0.3
VP_12	2	$CH{=}CHMe$	0.14	3300	3.1	0.4	2.0	0.7
VP_13	3	$CH{=}CMe_2$	0.045	1600	6.2	0.3	2.0	4.0
VP_21	2	$CH{=}CH_2$	0.003	110	91	0.3	2.0	89
VP_22u	2	$C(Me){=}CH_2$	0.0037	82	122	0.4	2.0	120
VP_22s	2	*cis*-$CH{=}CHCH_3$	0.0016					240[h]
VP_23	2	$CH{=}CMe_2$	0.0002					1800[h]
VP_31	3	$CH{=}CH_2$	0.06	2050	4.9	0.3	2.0	2.6
VP_33	3	$CH{=}CMe_2$	0.04	1110	9.0	0.4	2.0	6.5
VP_41	4	$CH{=}CH_2$	0.16	4350	2.3	0.4	1.9	0.1
VP_91	9	$CH{=}CH_2$	0.17	4400	2.3	0.4	1.9	0.1

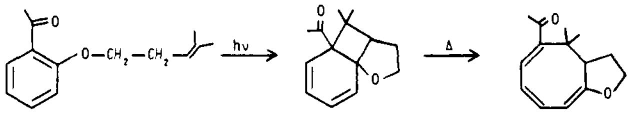
[a] 0.01 M in CH_3CN, 313-nm excitation. [b] In VP_ny, y = number of alkyl groups on double bond. [c] Formation of *p*-alkoxyacetophenone. [d] $k_q = 1 \times 10^{10}\ M^{-1}\ s^{-1}$. [e] Units of $10^6\ s^{-1}$. [f] Sum of intra- and intermolecular quenching by alkenyl group. [g] *p*-Methoxyvalerophenone. [h] Calculated simply from quantum yield ratios.

Scheme I



$R_1 = CH_3CH_2CH_2CH_2,\ CH_3$ $n = 1\text{-}4,\ 9$
$R_2 = CH{=}CH_2,\ cis\text{-}CH{=}CHCH_3,\ C(CH_3){=}CH_2, CH{=}C(CH_3)_2$

of the double bond to the benzene ring in high chemical yield and low to moderate quantum yield. Spectroscopic inspection of samples irradiated at 313 nm to varying conversions indicates that the primary photoproducts are acylbicyclo[4.2.0]octadienes.[19] Heating or GC separation (200 °C column) of these photoproducts results in quantitative rearrangement to yellow cyclooctatrienes[20] (yield = 70%, Φ = 0.05 from *p*-VP_21; 100%, 0.3 from *o*-VP_21). The cyclooctatrienes are expected thermolysis products of the bicyclo[4.2.0]octadienes. We are actively studying the structures and chemistry of the initial photoadducts more fully and shall report thereon shortly.



ortho—AP_23

These studies demonstrate that triplet as well as singlet benzenes undergo highly regiospecific intramolecular CT interactions with nearby double bonds that lead to cycloaddition products. The observed product structures indicate that the double bond adds 1,2 to the benzene ring, as has been observed for several benzonitriles.[21,22] That a π,π^* triplet is reacting is indicated by the nonreactivity of *p*-(3–butenoxy)benzophenone. Unlike the situation with excited singlets, the major addition mode appears to be stepwise and revertible, resulting in double bond isomerization. The predominance of ortho addition agrees with the CT nature of the overall excited-state interaction as well as with its triplet character.[23] The difference in state selectivity is best emphasized by the report that neither $PhOCH_2CH_2CH{=}CH_2$ nor *p*-$CH_3COPh(CH_2)_3CH{=}CH_2$ gives significant yields of cycloadducts upon 254-nm irradiation.[2]

Acknowledgment. This work was supported by NSF Grant CHE 85-06703.

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(19) E.g., 1-acetyl-2,2-dimethyl-6-oxatricyclo[$5.4.0^{1,7}.0^{3,7}$]undeca-8,10-diene from *o*-AP_23: ^1H NMR (C_6D_6) δ 5.69 (d of d, 1 H, $J_{11,10} = 9.6$, $J_{9,10} = 5.5$ Hz), 5.51 (d of d, 1 H, $J_{8,9} = 9.6$, $J_{10,9} = 5.5$ Hz), 5.42 (d, 1 H, $J_{10,11} = 9.8$ Hz), 5.33 (d, 1 H, $J_{9,8} = 9.8$ Hz), 3.8–3.6 (m, 2 H, OCH_2), 2.31 (s, 3 H, CH_3CO), 2.47 (d of d, 1 H, $J_{3,4} = 8.2$, $J_{3,4'} = 1.6$ Hz), 1.6–1.4 (m, 2 H, OCH_2CH_2), 1.25, 1.19 (each s, 3 H, CH_3).

(20) E.g., 4-acetyl-11-oxabicyclo[6.3.0]undeca-1,3,5-triene from *p*-AP_21: ^1H NMR ($CDCl_3$) δ 4.24, 4.16 (each m, 1 H, $J_{9,10} = 6.8$ Hz, CH_2O) 1.83, 2.13 (each m, 1 H, $J_{9,10} = 6.3$ Hz, OCH_2CH_2), 3.06 (br m, 1 H, $J_{8,9} \sim J_{8,7} \sim 6.3$ Hz, CH_2CHCH_2), 2.29–2.50 (m, 2 H, $J_{7,8} = 6.3$, $J_{6,7} = 6.8$ Hz, $CHCH_2CH{=}$), 5.92 (d of t, 1 H, $J_{6,7} = 6.8$, $J_{5,6} = 12.5$ Hz, $CH_2CH{=}CH$), 6.27 (d, 1 H, $J_{6,5} = 12.5$ Hz, $CH{=}CHC(COMe){=}$), 7.00 (d, 1 H, $J_{3,2} = 6.8$ Hz, $MeCOC{=}CHCH{=}$), 5.40 (d, 1 H, $J_{2,3} = 6.8$ Hz, $CH{=}CO$), 2.31 (s, 3 H, CH_3CO); UV λ_{max} (hexane) 370 nm (ϵ 4000). IR, MS, and ^{13}C NMR spectra also agree with the proposed structure.

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Conformational Effects on the Regiochemical Metalation of C_5–C_{13} *N*-Benzyllactams

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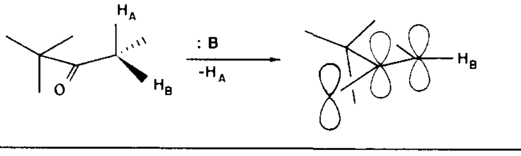
Received February 9, 1987

Although conformational effects have been long known to influence a variety of regiochemical and stereochemical reactions, it has not been until recently that rational approaches to controlling these important transformations have been utilized by the synthetic community. A report recently described the profound effects of conformation in medium rings on the enolization and ultimately the stereochemical outcome of alkylation.[1] An earlier report by Fraser[2] describes the stereoelectronic effect in a twistan-4-one wherein only one of the two α-protons is suitably placed for enolization[3] by base (eq 1).



(1)

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(1) Still, C. W.; Galynker, A. *Tetrahedron* **1981**, *37*, 3981 and references cited therein.

(2) (a) Fraser, R. R.; Champagne, P. J. *J. Am. Chem. Soc.* **1978**, *100*, 657 and references cited therein. (b) Stork, G.; Still, W. C.; Singh, J. *Tetrahedron Lett.* **1979**, 5077.

Table I. Alkylation of Lactams **1** to α-Alkyl (**4**) and/or α′-Alkyl (**5**) Derivatives

1 ring size	*n*	RX[a]	% **4**[b]	% **5**[b]	total yield % (**4** + **5**)[c]
5	1	MeI	99.5	0.5	78
6	2	MeI	99.5	0.5	84
7	3	MeI	0.5	99.5	86
7	3	MeI	0.5	99.5	86
7	3	*n*-BuI	0.5	99.5	91
7	3	allyl Br	0.5	99.5	89
7	3	$PhCH_2Br$	0.5	99.5	96
8	4	MeI	0.5	99.5	40
8	4	*n*-BuI	0.5	99.5	45
8	4	allyl Br	0.5	99.5	57
8	4	$PhCH_2Br$	0.5	99.5	83
9	5	*n*-BuI	24.5	75.5	90
9	5	allyl Br	25.0	75.0	83
9	5	$PhCH_2Br$	21.0	79.0	63
10	6	allyl Br	87.0	13.0	80
11	7	allyl Br	99.5	0.5	56
13	9	allyl Br	50	50	83

[a] Metalation was performed in THF at −78 °C with 1.1 equiv of *t*-BuLi. The electrophile (4.0 equiv) was added after 10 min at −78 °C. [b] Ratios determined by HPLC with hexane–ethyl acetate as eluent. Detection limits were ±0.25%. Separation of **4** and **5** was performed in every case by using flash or radial chromatography, and each was characterized by NMR. [c] Remainder of material was starting lactams, **1**.

We now report that a series of *N*-benzyllactams **1** with ring sizes varying from 5–11 to 13 have been examined with respect to their site of metalation (α to carbonyl and/or α to nitrogen) and show variations which we conclude are due to their conformations. Furthermore, molecular mechanics calculations were performed on these systems and appear to be generally consistent with the experimental results (vide infra).

The lactams **1**[4,5] were treated with *tert*-butyllithium (THF, −78 °C), and the resulting lithiated intermediates **2** and **3** were treated with alkyl halides, affording products **4** and **5** (Table I). For the five- and six-ring lactams, metalation and alkylation gave, as expected, exclusively **4** whereas the seven- and eight-ring lactams gave only alkylated products (**5**) derived from metalation at the benzyl group (**3**). Metalation–alkylation of the nine-ring lactam gave a 3–4:1 mixture with benzyl alkylation predominating whereas the 10-ring lactam led to an 87:13 ratio of alkylated material favoring **4**. Of further surprise was the fact that the 11-ring lactam led to exclusive enolate alkylation while the 13-ring lactam gave a 1:1 ratio of both products **4** and **5**. This unusual trend of regiochemical results was confirmed as being the result of kinetic deprotonation since equilibration (i.e., proton transfer) did not become a factor until the temperatures were raised (ca. −20 °C).

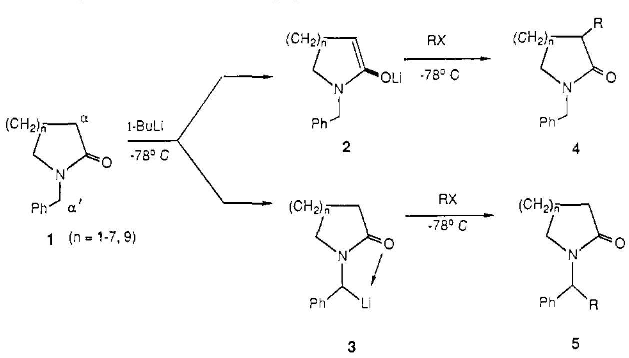
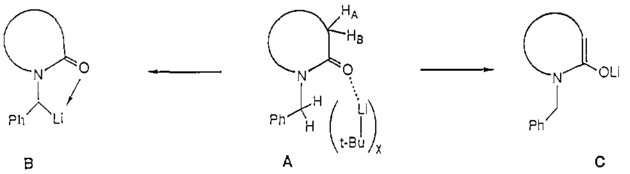


Table II. Steric Energy (kcal/mol) of the Lowest Energy Conformer

O=C—C—H angle	ring size 11	6	10	13	9	7	8
model 1							
90 ± 5°	0.0		1.8	0.0			
90 ± 10°	0.0	0.0	1.6	1.3		4.0	
90 ± 15°	0.0	0.0	1.6	0.9		4.0	3.2
90 ± 20°	0.0	0.0	1.6	0.9		4.0	3.2
90 ± 25 °	0.0	0.0	1.1	0.7	1.9	2.4	3.2
90 ± 30°	0.0	0.0	0.0	0.7	0.4	0.0	3.2
model 2							
90° restraint	0.05	0.09	1.79	1.26	2.21	2.25	3.5i
enolization, %	>99	>99	87	50	25	<1	<1

The data in Table I can be explained on the basis of conformational preference of the protons α to the carbonyl. In the five- and six-ring lactams, the initial coordination[6] of *tert*-butyllithium to the carbonyl oxygen (A) is followed by removal of H_A or H_B, provided that one of these protons is approximately 90° to the plane of the carbonyl group.[7] In the five- and six-ring lactams, this condition is essentially fulfilled based upon the well-known conformation of these ring systems. However, for seven, eight, and larger rings, the minimum conformational energy may not allow H_A or H_B to assume this alignment, and thus metalation of the benzylic proton is kinetically favored, furnishing the benzyl-lithiated intermediate B.



In support of this rationalization on the regiochemical metalation, molecular mechanics calculations on all the ring systems (except the five-ring system) were performed using the Allinger MM-2 force field.[8] The experimental work on the 5–8-, 11-, and 13-ring lactams was carried out *prior* to the calculations, whereas the calculations on the 9- and 10-ring systems were performed *prior* to the actual metalations.

To search for a possible relationship between the site of deprotonation and the conformations of the lactams, a global conformational search was conducted at 60° torsion angle resolution for the 6–10-membered lactams and at 120° resolution for the 11- and 13-membered lactams.[9] After energy minimization a number of unique, low-energy conformers were found.

To develop a crude model for the relative rates of enolization vs. benzylic metalation, we make the assumption that the rate of benzylic metalation is independent of lactam ring size. If this rate is indeed constant, then the relative rates of enolization might be correlated with certain properties of the O=C—C—H system as suggested above. The simplest model (model 1, Table II) is one based only on the ground-state O=C—C—H dihedral angle[2b]

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(3) These requirements for enolization were first set forth over 30 years ago by Corey, who introduced the term "stereoelectronic effect" (Corey, E. J.; Sneen, R. A. *J. Am. Chem. Soc.* **1956**, *78*, 6229).

(4) The *N*-benzyllactams were prepared from the lactams (95–99%) by treatment with KH–TMEDA (1.2 equiv) and benzyl chloride (1.1 equiv) in THF at 25 °C.

(5) The lactams (5–9- and 13-membered rings) are commercially available from Aldrich. The 10- and 11-membered lactams were prepared according to: Olah, G. A.; Fung, A. P. *Synthesis* **1979**, 537. The cyclodecanone was prepared according to: Burpitt, R. D.; Thweatt, J. G. *Org. Synth. Collect.* 1973; *Vol. 5*, 277.

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(7) Wolfe, S.; Schlegel, H. B.; Csizmadia, I. G.; Bernardi, F. *Can. J. Chem.* **1975**, *53*, 3365.

(8) The MM2(85) force field employed was kindly supplied by Professor N. L. Allinger and included a preliminary parameter set for amides.

(9) The conformational searches were conducted on the *N*-methyllactams assuming either 60° or 120° dihedral angle resolution as indicated in the text for all X–C(sp3)–C(sp3)–X torsional arrays. X–C(sp2)–C(sp3)–X and X–N(sp2)–C(sp3)–X linkages used 60° resolution in all cases, and the amide linkage was allowed to be either s-cis or s-trans. All structures were minimized to a final gradient of 10^{-3} kJ/Å, were compared for duplication by least-squares superimposition, and were verified as true minima by vibrational frequency calculation.

and favors enolization with structures in which this angle approximates 90°. Table II gives the steric energy (kilocalories per mole, relative to global minimum) of the lowest energy conformer with said dihedral angle within the angular window specified.

As expected, structures having low-energy conformers with α-hydrogens close to 90° are the ones most prone to enolization. However, the relationship is qualitatively correct for the data only with the 25° angular window. A slightly smaller window (20°) makes the nine-ring prediction exclusively benzylic metalation (vs. experimental 25% enolization), and a slightly larger window (30°) makes the seven-ring prediction exclusively enolization (vs. experimental <1% enolization). Thus, the sensitivity of the results to the precise window size renders this model problematic.

A second model (model 2) attempts to assess the ease of enolization by measuring the excess steric energy necessary to attain the stereoelectronically preferred 90° O=C—C—H alignment. We used an arbitrarily large 1000 kJ/mol and 1-fold torsional restraint to force the α-hydrogens of each conformer to approximate the desired 90° torsion angle, and the resulting minimized energies (relative to the global minimum) of the lowest energy structures thus found are summarized in Table II.

With model 2, the correlations with experiment are rather good given the simplistic nature of our treatment. Furthermore, the results are not strongly dependent on the precise magnitude of the torsional restraint. Finally, we would like to note that application of this model to the twistanone system[2a] gives an excess strain of only 0.3 kcal/mol for the kinetically more acidic (by 290:1) hydrogen and 7.4 kcal/mol for the less acidic one.

Acknowledgment. We thank the National Science Foundation for financial support.

Formation of 1,3,4,5-Tetraphenyl-2,6,7-trioxabicyclo[3.2.1]oct-3-ene from the Ozonolysis of 1,2,3,4-Tetraphenyl-1,3-cyclopentadiene. First [3 + 4] Addition of a Carbonyl Oxide Moiety to an α,β-Unsaturated Carbonyl Group

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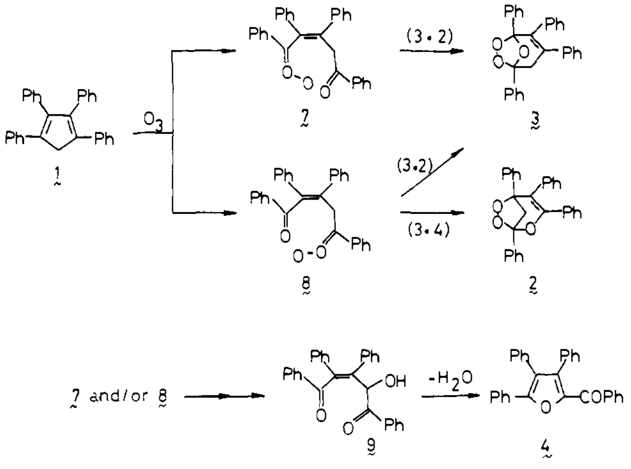
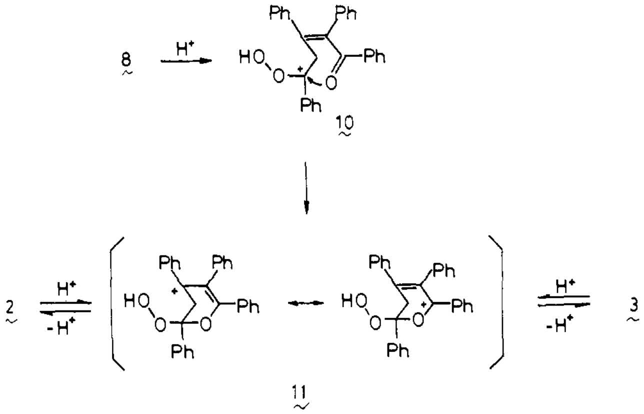
Received March 16, 1987

Carbonyl oxides, being key intermediates in the ozonolysis of olefins, have attracted much attention.[1] The most well-known feature of their chemistry is the 1,3-dipolar cycloaddition to a carbonyl group affording 1,2,4-trioxolane (final ozonide). It is therefore surprising that only one clear-cut example is known, to our knowledge, for the reaction of carbonyl oxide with α,β-unsaturated carbonyl compound: the ozonolysis of 2,3-di-*tert*-butyl-1,3-butadiene on polyethylene, which proceeds via formaldehyde oxide and *tert*-butyl 1-*tert*-butylvinyl ketone, yields 3-*tert*-butyl-3-(1-*tert*-butylvinyl)-1,2,4-trioxolane in good yield.[1f] If a formal [3 + 4] addition of carbonyl oxide to α,β-unsaturated carbonyl could occur instead of a [3 + 2] addition, a 1,2,4-trioxacyclohept-5-ene would be produced in place of the isomeric 3-vinyl-1,2,4-trioxolane. We report herein that this is certainly observed in the ozonolysis of 1,2,3,4-tetraphenyl-1,3-cyclopentadiene (**1**).[2,3]

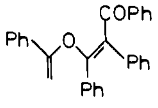
Scheme I



Scheme II



The reaction of **1** with 1 equiv of ozone in methylene chloride afforded a mixture of two isomeric peroxides **2** and **3** in 27% yield, the **2**:**3** ratio being 3:7 (Scheme I).[4] In good agreement with this assignment, treatment of the cyclic peroxide **2** with triphenylphosphine gave a mixture of the ketone **5**[5] and the diketone **6** in yields of 45% and 35%, respectively, while only the diketone **6**[6]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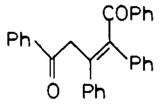
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[1] (a) Bailey, P. S. *Ozonation in Organic Chemistry*; Academic: New York, 1982; Vol. 2. (b) Kuczkowski, R. L. *Acc. Chem. Res.* **1983**, *16*, 42. (c) Kuczkowski, R. L. In *1,3-Dipolar Cycloaddition Chemistry*; Padwa, A., Ed.; Wiley: New York, 1984; Vol. 2. (d) Kumar, S.; Murray, R. W. *J. Am. Chem. Soc.* **1984**, *106*, 1040. (e) Keul, H.; Kuczkowski, R. L. *Ibid.* **1984**, *106*, 5370. (f) Griesbaum, K.; Volpp, W.; Greinert, R. *Ibid.* **1985**, *107*, 5309. (g) Nakamura, N.; Nojima, M.; Kusabayashi, S. *Ibid.* **1986**, *108*, 4671. (h) Bunnelle, W. H.; Schlemper, E. O. *Ibid.* **1987**, *109*, 612.

[2] In the concerted cycloaddition of a 4π-electron 1,3-dipole to a dipolarophile having 4π electrons, [3 + 4] addition is thermally disallowed by orbital symmetry and, consequently, the alternative [3 + 2] mode is always preferred.[3a] Very recently, however, Huisgen discovered that the addition of thiocarbonyl ylide to tetracyanoethylene, which proceeds stepwise, provides the [3 + 4]-addition product together with the [3 + 2]-addition product.[3b]

[3] (a) Crabb, J. N.; Storr, R. C. In *1,3-Dipolar Cycloaddition Chemistry*; Padwa, A., Ed.; Wiley: New York, 1984; Vol. 2. (b) Huisgen, R.; Mloston, G.; Langhals, E. *J. Am. Chem. Soc.* **1986**, *108*, 6401; *J. Org. Chem.* **1986**, *51*, 4087.

[4] **2**: mp 125–127 °C (from methanol); ^{1}H NMR δ 3.63 (d, J = 11 Hz, 1 H), 4.17 (d, J = 11 Hz, 1 H), 7.50–9.00 (m, 20 H); ^{13}C NMR δ 51.415 (1 C, C-8), 87.449 (1 C, C-5), 107.779 (1 C, C-1), 118.751 (1 C, C-4), 126.280–136.550 (24 C), 150.375 (1 C, C-3); mass spectrum, *m/e* 418 (M$^+$). Anal. Calcd for $C_{29}H_{22}O_3$: C, 83.23; H, 5.26. Found: C, 83.27; H, 5.29. **3**: mp 116–119 °C (from methanol); ^{1}H NMR δ 3.63 (d, J = 18 Hz, 1 H), 4.03 (d, J = 18 Hz, 1 H), 7.50–8.70 (m, 20 H); ^{13}C NMR δ 42.111 (1 C, C-4), 108.506 (1 C, C-5 or C-1), 109.032 (1 C, C-1 or C-5), 125.886–139.570 (26 C); mass spectrum, *m/e* 418 (M$^+$). Anal. Calcd for $C_{29}H_{22}O_3$: C, 83.23; H, 5.26. Found: C, 83.27; H, 5.29.

[5] **6**: mp 124–126 °C (from methanol); ^{1}H NMR δ 4.44 (d, J = 3 Hz, 1 H), 4.79 (d, J = 3 Hz, 1 H), 6.90–7.65 (m, 18 H), 7.89–8.16 (m, 2 H); IR 1660, 1640, 1600, 1490, 1442, 1312, 1263, 1214, 1175, 1116, 1070, 1011 cm^{-1}. Anal. Calcd for $C_{29}H_{22}O_2$: C, 86.57; H, 5.47. Found: C, 86.62; H, 5.41.

[6] Rio, G.; Fellion, Y. *Tetrahedron Lett.* **1962**, 1213.

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