

from a Facile Condensation of Dibenzoylethylene with Arylacetonitriles

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Several novel bicyclo[2.2.2]lactones were synthesized from a facile one-pot reaction by the condensation of dibenzoylethylene and an arylacetonitrile in basic medium. The reaction proved to be convenient and gives high yield. The structure of the reaction products was established on the basis of their proton and carbon-13 nuclear magnetic resonance, and infrared spectral data as well as their elemental analysis.

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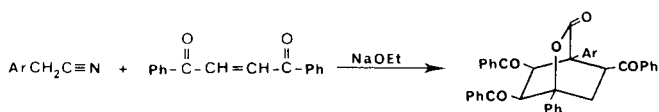
Since it was first reported around the beginning of the century, a huge amount of literature has appeared on the different aspects of the chemistry of *trans*-dibenzoyl-ethylene. It has been reported to undergo condensation with *o*-phenylenediamine [1,3], to cycloadd to 1,3-dipoles as nitrilimine, azomethinimine, ethyl diazoacetate, sulfonium ylides and heteroaromatic *N*-ylides [4,8], to photoisomerize to the *cis*-isomer and undergo photochemical transformations [9-12], to undergo Michael additions and cyclizations [13-18] and to cyclize reductively to substituted furan [19-21], to mention just a few examples. However, little is known about the reaction of *trans*-dibenzoyl-ethylene (DBE) with carbanions and enolates. Therefore, and as a part of our continuous interest in the reaction of active methylene compounds with α,β -Michael acceptors [22-27], we have studied the reaction of DBE with the carbanions derived from arylacetonitriles.

work-up and recrystallization from acetic acid or acetic acid-water mixtures afforded the title compounds **3a-i** shown in Scheme 1. These bicyclic lactones **3a-i** namely 1-phenyl-4-aryl-5,6,8-tribenzoyl-2-oxabicyclo[2.2.2]octan-3-ones crystallized as white solids and in high yields. The structures of the bicyclic lactones **3a-i** were supported by their consistent ir, ^1H nmr, ^{13}C nmr spectra and their correct elemental analyses.

The 1:2 stoichiometry of the reaction of cyanides **1a-i** with DBE **2** was revealed by the ^1H nmr spectra of the lactones **3a-i** and the presence of the correct molecular ion in the mass spectra for some of the latter compounds [28]. Similar reactions that take place with similar stoichiometry are well known [29,30].

The ir spectra of the bicyclic products **3a-i** display

Scheme 1



Compound	Ar
3a	4-Br-C ₆ H ₄
3b	4-Cl-C ₆ H ₄
3c	3-Cl-C ₆ H ₄
3d	4-F-C ₆ H ₄
3e	4-CH ₃ -C ₆ H ₄
3f	3-CH ₃ -C ₆ H ₄
3g	2,4-Cl ₂ -C ₆ H ₃
3h	2,6-Cl ₂ -C ₆ H ₃
3i	1-naphthyl

Arylacetonitriles **1a-i** underwent a smooth reaction at room temperature with DBE, **2**, in 1:2 molar ratio in dry ether using sodium ethoxide as the base. The yellow or light brown precipitates were formed which upon acidic

Scheme 2

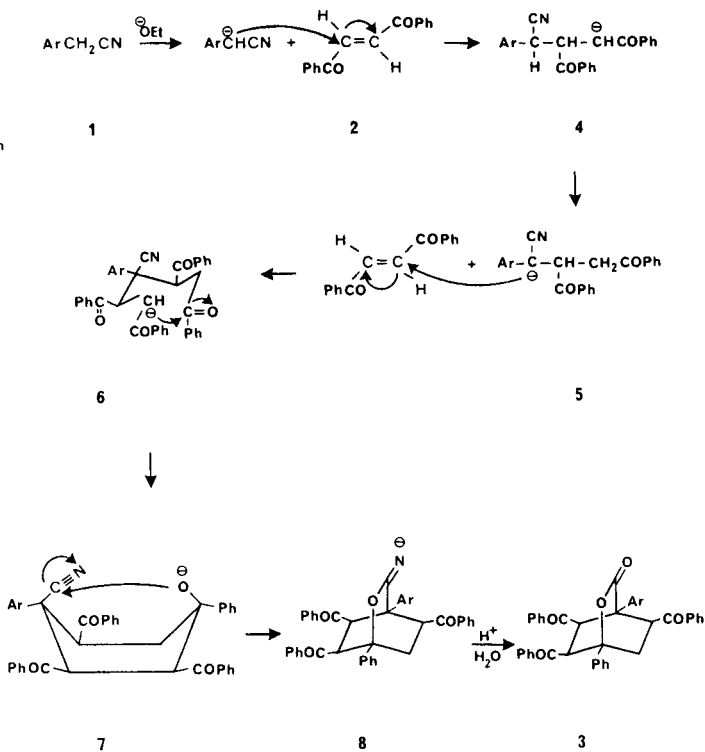




Table 1
Spectral and Analytical Data of Products 3a-i

Product	Ar	¹ H nmr (δ, ppm) deuteriochloroform	ir (potassium bromide, cm ⁻¹)	Molecular Formula	Analysis		
					Calcd./Found C	H	X
3a	4-BrC ₆ H ₄	8.35-8.23 (m, 2H) 7.73-7.01 (m, 18H, d, 2H) 6.57-6.47 (d, 2H) 6.03-5.76 (dd, 1H) 5.21-4.97 (dd, 1H) 4.83-4.70 (d, 1H) 4.11-4.01 (d, 1H) 3.61-3.42 (dd, 1H)	1770, 1665, 1655, 1645, 1590, 1440, 1325, 1245, 1215, 1180, 1040, 1000, 770, 750, 690, 680	C ₄₀ H ₂₉ BrO ₅	71.84	4.36	11.81
					72.09	4.41	12.19
3b	4-ClC ₆ H ₄	8.37-8.25 (m, 2H) 7.88-7.11 (m, 18H) 7.02-6.86 (d, 2H) 6.63-6.53 (d, 2H) 6.04-5.77 (dd, 1H) 5.23-4.99 (dd, 1H) 4.85-4.72 (d, 1H) 4.14-4.04 (d, 1H) 3.63-3.44 (dd, 1H)	1770, 1650, 1590, 1445, 1250, 1220, 1180, 1040, 1000, 775, 760, 700	C ₄₀ H ₂₉ ClO ₅	76.90	4.68	5.60
					76.96	4.90	5.91
3c	3-ClC ₆ H ₄	8.36-8.24 (m, 2H) 7.76-6.54 (m, 22H) 6.04-5.78 (dd, 1H) 5.22-4.97 (dd, 1H) 4.84-4.71 (d, 1H) 4.10-4.00 (d, 1H) 3.62-3.42 (dd, 1H)	1770, 1665, 1650, 1590, 1250, 1210, 1175, 1035, 700, 685	C ₄₀ H ₂₉ ClO ₅	76.90	4.68	5.60
					76.67	4.67	5.84
3d	4-FC ₆ H ₄	8.35-8.21 (m, 2H) 7.72-7.00 (m, 18H) 6.67 (s, 2H) 6.59 (s, 2H) 6.03-5.77 (dd, 1H) 5.21-4.97 (dd, 1H) 4.83-4.70 (d, 1H) 4.13-4.03 (d, 1H) 3.61-3.41 (dd, 1H)	1775, 1660, 1585, 1570, 1260, 1245, 1205, 1170, 1155, 1000, 980, 825, 760, 695	C ₄₀ H ₂₉ FO ₅	78.92	4.81	3.12
					79.13	5.01	3.03
3e	4CH ₃ C ₆ H ₄	8.38-8.23 (m, 2H) 7.75-7.01 (m, 18H) 6.80-6.69 (d, 2H) 6.56-6.45 (dd, 1H) 6.02-5.75 (dd, 1H) 5.19-4.95 (dd, 1H) 4.83-4.70 (d, 1H) 4.08-3.98 (d, 1H) 3.66-3.47 (dd, 1H) 2.08 (s, 3H)	1770, 1670, 1655, 1590, 1570, 1440, 1225, 1175, 1040, 1000, 775, 760, 715, 700, 690	C ₄₁ H ₃₂ O ₅	81.43	5.34	-
					81.63	5.60	-
3f	3CH ₃ C ₆ H ₄	8.38-8.26 (m, 2H) 7.76-6.38 (m, 22H) 6.02-5.75 (dd, 1H) 5.18-4.95 (dd, 1H) 4.82-4.70 (d, 1H) 4.04-3.94 (d, 1H) 3.66-3.47 (dd, 1H) 1.99 (s, 3H)	1775, 1670, 1650, 1590, 1450, 1260, 1240, 1220, 1180, 1050, 770, 710, 700, 690	C ₄₁ H ₃₂ O ₅	81.43	5.34	-
					81.56	5.51	-
3g	2,4-Cl ₂ C ₆ H ₃	8.35-8.22 (m, 2H) 7.74-6.84 (m, 22H) 6.10-5.84 (dd, 1H) 5.22-4.99 (dd, 1H) 4.84-4.72 (d, 1H) 4.42-4.31 (d, 1H) 3.87-3.67 (dd, 1H)	1770, 1670, 1650, 1585, 1570, 1440, 1330, 1210, 1170, 1040, 760, 695, 685	C ₄₀ H ₂₈ Cl ₂ O ₅	72.93	4.29	10.63
					72.80	4.40	10.47

Table 1 (continued)

Product	Ar	¹ H nmr (δ, ppm) deuteriochloroform	ir (potassium bromide, cm ⁻¹)	Molecular Formula	Analysis Calcd./Found		
					C	H	X
3h	2,6-Cl ₂ C ₆ H ₃	8.39-8.26 (m, 2H) 7.79-7.64 (m, 5H) 7.61-7.38 (m, 8H) 7.33-6.77 (m, 8H) 6.11-5.84 (dd, 1H) 5.18-4.91 (dd, 1H, d, 1H) 4.76-4.64 (d, 1H) 4.38-4.18 (dd, 1H)	1770, 1665, 1655, 1590 1570, 1430, 1330, 1210 1175, 1040, 985, 770 760, 700, 690	C ₄₀ H ₂₈ Cl ₂ O ₅	72.93 73.02	4.29 4.25	10.63 10.80
3i	1-naphthyl	8.42-8.27 (m, 2H) 7.90-6.89 (m, 25H) 6.17-5.90 (dd, 1H) 5.22-4.99 (dd, 1H) 4.89-4.68 (dd, 2H) 3.99-3.80 (dd, 1H)	1775, 1670, 1660, 1590 1445, 1250, 1215, 1170 1030, 1000, 775, 700, 685	C ₄₄ H ₃₂ O ₅	82.47 82.28	5.04 5.29	- -

Table 2
¹³C Chemical Shifts of Products 3a-i (δ, ppm)

Product	Ar			Aromatic carbons	Aliphatic carbons
3a	4-BrC ₆ H ₄	201.2, 196.7, 195.1	174.0	143.6 - 121.7	92.7, 62.8, 61.5 53.3, 48.3, 47.3
3b	4-ClC ₆ H ₄	201.1, 196.7, 195.2	174.1	143.4 - 124.0	92.7, 62.8, 61.5 53.3, 48.2, 47.4
3c	3-ClC ₆ H ₄	201.1, 196.6, 195.1	173.8	143.4 - 124.0	92.7, 62.8, 61.5 53.3, 48.5, 47.4
3d	4-FC ₆ H ₄	201.2, 196.7, 195.1	174.3	168.1 - 155.8 143.6 - 114.9	92.6, 62.8, 61.7 53.3, 48.0, 47.5
3e	4CH ₃ C ₆ H ₄	201.4, 196.9, 195.2	174.8	143.7 - 124.1	92.6, 63.2, 61.7 53.6, 48.4, 47.4, 20.7
3f	3-CH ₃ C ₆ H ₄	201.3, 196.7, 195.1	174.7	143.7 - 124.2	92.7, 63.2, 61.7 53.3, 48.8, 47.3, 20.9
3g	2,4-Cl ₂ C ₆ H ₃	201.1, 196.6, 195.2	172.5	143.4 - 124.0	93.0, 63.0, 58.9 52.9, 47.4, 47.3
3h	2,6-Cl ₂ C ₆ H ₃	201.2, 195.4, (two carbons)	171.9	143.7 - 124.0	93.3, 62.7, 58.5 54.9, 46.9, 45.1
3i	1-naphthyl	201.3, 196.8, 195.2	174.4	143.8 - 122.9	92.9, 63.6, 60.6 53.9, 47.5, 46.4

strong absorption bands at 1770 and 1660-1650 cm⁻¹ which are assigned to the lactone and keto functional groups. The ir spectra show the complete disappearance of the cyano group as well. On the other hand the ¹H nmr spectra of lactones **3a-i** show five aliphatic protons in the range δ 6.2-3.4 ppm in the form of two unresolved double doublets, a double doublet and two doublets assigned to the cyclohexane ring in the bicycles **3a-i**. The aromatic protons integrate correctly for one substituted phenyl and four phenyl groups. Moreover, the completely decoupled ¹³C nmr spectra of lactones **3a-i** indicate the presence of

six sp³-hybridized carbon atoms in the range δ 93.3-45.1 ppm, believed to be those of the cyclohexane ring, in addition to three carbonyl carbons in the range δ 201.3-195.1 ppm, and a fourth carbonyl carbon at around δ 172 ppm assigned to the lactone function. The mass spectra of the lactones **3** recorded displayed the molecular ion as a tiny peak with the benzoyl daughter ion as the base peak.

The ¹H nmr and ir spectral data and elemental analysis of lactones **3a-i** are given in Table 1, while the ¹³C nmr data are summarized in Table 2.

The formation of bicyclic lactones **3a-i** may be explained by the mechanism depicted in Scheme 2. It involves two successive Michael additions followed by two cyclizations. The first step is the conjugate addition of the carbanion generated from the nitrile **1** to DBE **2** to form the enolate **4** which rearranges to the carbanion **5** and adds in turn to a second molecule of the Michael acceptor **2** to afford the intermediate **6**. The latter cyclizes via the nucleophilic 1,6-addition of the carbanion to the carbonyl function five carbons away leading to the cyclic intermediate **7**. Another 1,6-addition of the anion to the cyano group yields the bicyclic intermediate **8**. Protonation and hydrolysis during the acidic work up transform the latter intermediate into the bicyclic product **3**. Reactions reminiscent to the second cyclization are familiar. For example, syn-4-amino-1-cyclohexane carboxylic acid may dehydrate to form a bicyclic lactam [31]. It is worth mentioning that all the products **3a-i** showed one spot in tlc using different solvent systems.

Other likely structures for the products of the reaction of nitriles **1a-i** with DBE **2** were considered and ruled out. For example, the cyclohexanone **9** and/or the lactone **10** would be produced if the mechanism drawn in Scheme 3 were operative. These structures were excluded on the

basis of the ^{13}C nmr and ir spectra of the reaction products which revealed the presence of only three keto groups and a lactone function together with the absence of the two vinylic carbons in the lactone **10**. Moreover, the reaction products gave negative tests for unsaturation with bromine and with potassium permanganate.

EXPERIMENTAL

Melting points were measured on an Electrothermal melting point apparatus and are uncorrected. The ir spectra were recorded as potassium bromide disks using a Pye Unicam SP3-100 spectrophotometer. The ^1H nmr and ^{13}C nmr spectra were run in deuteriochloroform with tetramethylsilane as the internal reference using a Bruker WP 80 SY spectrometer. *trans*-Dibenzoyl ethylene and arylacetonitriles were purchased from Aldrich.

General Procedure for the Reaction of Arylacetonitriles **1a-i** with *trans*-Dibenzoyl ethylene **2**.

The arylacetonitrile **1a-i** (17 mmoles) was added to a suspension of sodium ethoxide (1.33 g, 17 mmoles) in dry ether (100 ml) and was stirred for 5 minutes. DBE, **2**, (4.01 g, 17 mmoles) was then added and stirring was continued for 30 minutes at room temperature. The reaction mixture turned brown and a heavy precipitate formed. The latter was collected by suction filtration and dissolved and recrystallized from glacial acetic acid or acetic acid-water mixture to give products **3a-i**.

1-Phenyl-4-(4-bromophenyl)-5,6,8-tribenzoyl-2-oxabicyclo[2.2.2]octan-3-one **3a**.

This compound was prepared in a yield of 80% (4.6 g), mp 220-222°.

1-Phenyl-4-(4-chlorophenyl)-5,6,8-tribenzoyl-2-oxabicyclo[2.2.2]octan-3-one **3b**.

This compound was prepared in a yield of 75% (4.1 g), mp 226-228°.

1-Phenyl-4-(3-chlorophenyl)-5,6,8-tribenzoyl-2-oxabicyclo[2.2.2]octan-3-one **3c**.

This compound was prepared in a yield of 82% (4.4 g), mp 219-220°.

1-Phenyl-4-(4-fluorophenyl)-5,6,8-tribenzoyl-2-oxabicyclo[2.2.2]octan-3-one **3d**.

This compound was prepared in a yield of 49% (2.5 g), mp 211-212°.

1-Phenyl-4-(4-tolyl)-5,6,8-tribenzoyl-2-oxabicyclo[2.2.2]octan-3-one **3e**.

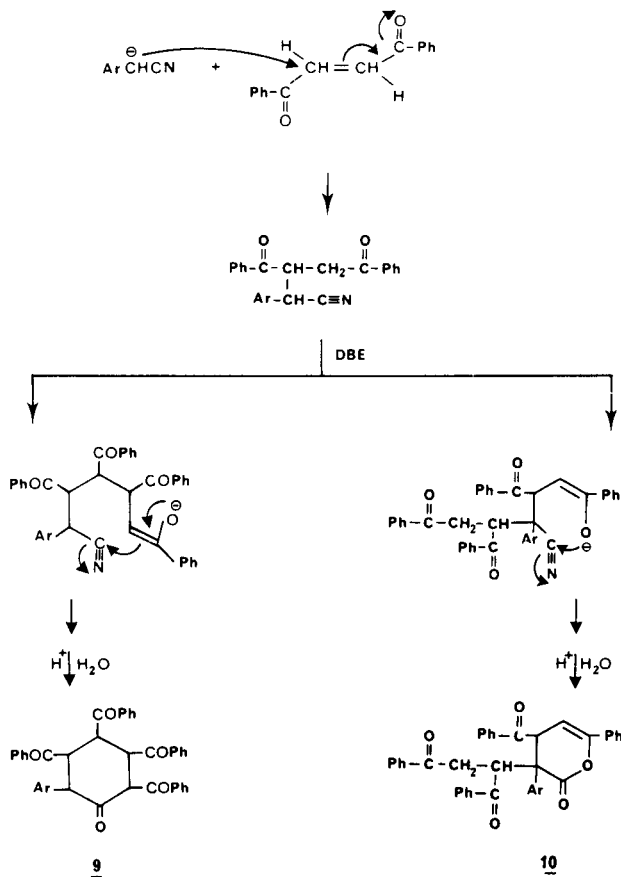
This compound was prepared in a yield of 65% (3.4 g), mp 219-220°.

1-Phenyl-4-(3-tolyl)-5,6,8-tribenzoyl-2-oxabicyclo[2.2.2]octan-3-one **3f**.

This compound was prepared in a yield of 77% (4.0 g), mp 203-204°.

1-Phenyl-4-(2,4-dichlorophenyl)-5,6,8-tribenzoyl-2-oxabicyclo[2.2.2]octan-3-one **3g**.

Scheme 3



This compound was prepared in a yield of 80% (4.5 g), mp 232-233°.

1-Phenyl-4-(2,6-dichlorophenyl)-5,6,8-tribenzoyl-2-oxabicyclo[2.2.2]octan-3-one **3h**.

This compound was prepared in a yield of 74% (4.2 g), mp 228-229°.

1-Phenyl-4-(1-naphthyl)-5,6,8-tribenzoyl-2-oxabicyclo[2.2.2]octan-3-one **3i**.

This compound was prepared in a yield of 71% (3.9 g), mp 223-224°.

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