Structure and Conformations of Monoacyl and Diacyl 1,2,4-Triazolidine-3,5-diones

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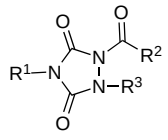
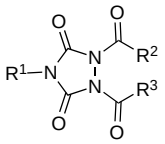
A series of monoacyl and diacyl 1,2,4-triazolidine-3,5-diones substituted at position 4 with either a phenyl or a *tert*-butyl group was prepared. Both acetyl and benzoyl groups were utilized as the acyl substituents. The diacylated compounds containing one or two acetyl groups were somewhat unstable to moisture. The acylated compounds were studied by ^{1}H, ^{13}C and ^{15}N NMR spectroscopy and X-ray crystallography to determine if they were acylated on nitrogen or ring carbonyl oxygen. The results indicated that the acylations occurred on nitrogen. The NMR spectra and molecular modeling computations were used to assign conformations to several of the diacylated compounds.

Introduction

Numerous examples of 1,2,4-triazolidine-3,5-diones substituted at positions 1, 2, and 4 are known. However, only a few monoacylated and diacylated derivatives have been reported.[1−4] Recently we observed that 4-alkyl- and 4-aryl-substituted monoacylated and diacylated 1,2,4-triazolidine-3,5-diones are potent hypolipidemic agents in rodents, both in lowering serum cholesterol and serum triglycerides.[5−7] It is important to know the exact position(s) of the acyl substituents on the triazolidinedione ring. The acyl groups can conceivably be substituted either on the ring nitrogen atoms (**I** and **II**) (N-acylated), the ring carbonyl oxygen atoms (**III** and **IV**) (O-acylated), or in the case of the diacylated compounds on both nitrogen and oxygen (**V**) (N,O-diacylated). This situation is similar to that which existed with the monoacylated and diacylated 3,5-pyrazolidinediones and for which we demonstrated by X-ray analysis and ^{15}N NMR spectroscopy that the acylations occurred exclusively on the ring nitrogen atoms.[8] In the present study a series of monoacylated and diacylated 4-phenyl- and 4-*tert*-butyl-1,2,4-triazolidine-3,5-diones were prepared and studied by ^{1}H, ^{13}C, and ^{15}N NMR spectroscopy and molecular modeling in order to determine the site(s) of acylation and in the instances of the diacylated compounds the preferred conformations of their acyl substituents.



I



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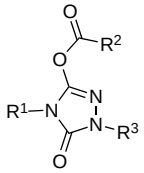

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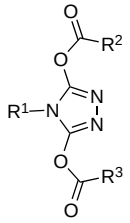

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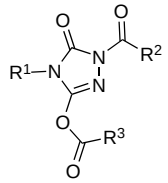

V

Results and Discussion

The mono- and diacylated 1,2,4-triazolidine-3,5-diones that were studied are shown in Table 1. The monoacylated compounds **2**[9] , **3**, and **8** were prepared by reacting **1** or **7** with a 50% excess of the appropriate carboxylic acid anhydride in methylene chloride at room temperature for 24−48 h. Compound **9** could not be prepared in this manner. Reaction of **7** with benzoic anhydride gave only the dibenzoylated product **11**. Reaction of **7** with benzoyl chloride in the presence of pyridine produced **9** in low yield and **11** as the major product. The diacetylated derivatives **4**[9] and **10** were formed by the reactions of **1** and **7**, respectively, with an excess of both acetic anhydride and lead diacetate trihydrate. The dibenzoylated product **5** was produced in high yield from **1** and

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Table 1. Monoacyl and Diacyl 1,2,4-Triazolidine-3,5-diones Studied

compound	R^1	R^2	R^3
1	Ph	H	H
2	Ph	Me	H
3	Ph	Ph	H
4	Ph	Me	Me
5	Ph	Ph	Ph
6	Ph	Ph	Me
7	t-Bu	H	H
8	t-Bu	Me	H
9	t-Bu	Ph	H
10	t-Bu	Me	Me
11	t-Bu	Ph	Ph
12	t-Bu	Ph	Me

a 50% excess of benzoic anhydride in the presence of a stoichiometric quantity of sodium benzoate and as the minor product when the reaction was carried out in the absence of sodium benzoate. In the former instance the sodium benzoate apparently functioned as a base to catalyze the addition of the second benzoyl group. However, the reaction of **1** and **7**, respectively, with excess benzoic anhydride in the presence of excess lead diacetate trihydrate gave only the mixed diacylated products **6** and **12**. In these instances the acetate anion apparently functioned in a dual capacity, i.e. as a base to catalyze diacylation and as a nucleophile in its reaction with benzoic anhydride to produce the mixed anhydride which added the acetyl substituent to the triazolidine ring.

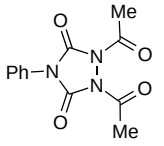
The monoacylated compounds **2**, **3**, **8**, and **9** and the dibenzoylated compounds **5** and **11** were stable to moisture. The diacylated compounds **4**, **6**, **10**, and **12** were unstable to moisture. These compounds decomposed slowly on storage and more rapidly when directly exposed to water in solution as shown by HPLC analysis. This behavior is analogous to that displayed by 1,2-diacyl-3,5-pyrazolidinediones and 2-benzoyl-3,5-isoxazolidinediones which decompose by hydrolysis of their *N*-acyl ring substituents in the presence of atmospheric moisture.[8,9]

The ^{1}H and ^{13}C NMR spectral data of compounds **1**−**12** in DMSO-d_6 are given in Tables 2 and 3. The spectra of the diacylated compounds **4**, **6**, **10**, and **12** which contain at least one acetyl group contained weak signals that could be attributed to the presence of hydrolysis products of the compounds.

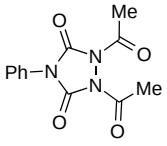
When the NMR solutions were allowed to stand for ten weeks, the extent of hydrolysis gradually increased as the compounds reacted with the small amount of water that had been absorbed by the solutions. Thus compound **4** had undergone 6% hydrolysis after ten weeks and contained both the monoacylated derivative **2** and acetic acid. Compound **6** was 7% hydrolyzed and contained **2**, **3** (trace), and benzoic acid. In a similar manner the solution of compound **10** contained 42% of **8** plus acetic acid, and the solution of compound **12** contained 41% of **8**, 1% of **9**, benzoic acid, and acetic acid (trace). When the NMR solutions of the compounds were heated to 140 °C for 30 min, the hydrolyses were 70−96% complete.

The ^{15}N NMR spectra (Table 4) of compounds **1** and **7** in DMSO-d_6 showed their protonated nitrogens at δ −232.8 and δ −235.4, respectively, and their nonprotonated nitrogens at δ −204.7 and δ −205.5, respectively, relative to external nitric acid. The nitrogens at ring position 2 (NH) of the four monoacylated derivatives appeared at δ −222.2 to δ −230.4. The ring nitrogens at position 4 of all of the acylated compounds appeared as weak-intensity peaks at δ −200.7 to δ −208.8 except for compounds **5** and **11** where they absorbed at δ −225.5 and δ −229.2, respectively. In all instances the nonprotonated nitrogens at ring positions 1 or 1 and 2 of the acylated compounds absorbed at δ −174.2 to δ −186.1. The latter absorptions are in the same chemical shift region as the other nitrogen atoms in the ring. These nitrogens have chemical shifts that are consistent with "pyrrole-like" nitrogens.[10] If the substitutions had occurred on the carbonyl oxygen atoms, the nitrogens would be "pyridine-like" and would appear 50−200 ppm farther downfield than was observed. Therefore, the ^{15}N NMR data indicate that the acylations gave the N-acylated 1,2,4-triazolidine-3,5-diones **I** and **II** and not the O-acylated products **III** and **IV**.[11]

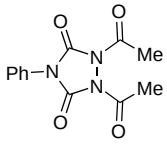
The diacetylated derivative **4** was analyzed by X-ray crystallography.[12] The analysis showed that the compound was acylated on the nitrogen atoms at positions 1 and 2 (i.e. **II**; R^1 = Ph, R^2 = R^3 = Me). Thus the X-ray results confirm the conclusion drawn from the ^{15}N NMR data. There are three limiting N,N-diacetylated conformations for the acetyl groups of compound **4**. They are the *endo,endo*; *endo,exo*; and *exo,exo* N,N-diacetylated conformations. The acetyl groups were in the *endo,endo* conformation. The carbonyl groups were twisted conrotatory out of planarity with the triazolidine ring by an average of 33°. This is comparable to the average conrotatory twisting of 31° that was previously observed for the two acetyl groups in *endo,endo*-1,2-diacetyl-4,4-diethyl-3,5-pyrazolidinedione.[8] The phenyl group at position 4 was twisted out of coplanarity by approximately 80°.



endo, endo



endo, exo



exo, exo

The Tripos Associates SYBYL (version 6.1a) molecular modeling software was used to model the three limiting conformations of **4**. The conformations were built and minimized in vacuo to a gradient of 0.005 kcal/(mol*A) using the Tripos force field and Gasteiger-Marsili charges. The *endo,endo* conformation was predicted to be 1.104 kcal/mol more stable than the *endo,exo* conformation and 8.382 kcal/mol more stable than the *exo,exo* conformation. This prediction is in agreement with the X-ray crystallographic analysis results. The acetyl groups of the *exo,exo* conformation were twisted conrotatory approximately 12° above and below the triazolidine ring to relieve the steric interaction between the two acetyl methyl groups, and the ring itself was twisted out of planarity, showing a ring CNNC torsion angle of −7.6°. The acetyl groups

(10) Levy, G. C.; and Lichter, R. L. *Nitrogen-15 Nuclear Magnetic Resonance Spectroscopy*; John Wiley and Sons: New York, 1979; Chapter 3.

(11) Compounds **10** and **12** showed several weak-intensity resonances which were in agreement with the partial hydrolysis of these compounds that was exhibited in their ^{1}H and ^{13}C NMR spectra.

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Table 2. ^{1}H NMR Spectral Data for Compounds 1−12[a]

H type	1	2	3	4	5	6	7	8	9	10	11	12
t-Bu							1.47	1.57	1.53	1.56	1.51	1.57
CH_3CO		2.49		2.48		2.57		2.43		2.42		2.51
Ph	7.73−7.47	7.43−7.56	7.40−7.84	7.47−7.56	7.43−7.98	7.45−7.97			7.47−7.73		7.44−7.96	7.46−7.99
NH	10.5	10.5	−				9.6	11.6	11.5			

[a] ^{1}H NMR chemical shifts are at 28 °C in DMSO-d_6 relative to internal TMS.

Table 3. ^{13}C NMR Spectral Data for Compounds 1−12[a,b]

C type	1	2	3	4	5	6	7	8	9	10	11	12
t-Bu CH_3							28.11	27.96	27.89	27.91	27.91	27.69
t-Bu quaternary							56.13	57.47	57.49	58.99	57.54	59.00
CH_3		22.74		23.44		23.39		23.21		23.66		23.60
CO (Me)		163.12		164.92		164.52		163.13		165.02		164.48
CO (Ph)			163.11		163.01	164.12			163.15		163.19	164.95
					167.40						167.40	
ring CO (1)		147.33	147.38	148.63	147.32	147.61		148.36	148.08	149.09	148.11	148.89
					150.21						151.71	
ring CO (2)						148.36						148.38
ring CO (NH)	153.98	149.48	150.29				155.91	151.19	151.69			
Ph	126.46	126.53	126.90	127.37	126.90−	127.31			127.72		127.76	128.29
	128.06	128.24	127.82	129.06	133.8	128.23			129.22		128.59	130.74
	129.22	128.74	128.50	129.16	(12 peaks)	128.92			132.17		129.25	132.06
	132.27	130.80	128.95	130.42		129.13			132.95		129.31	134.00
			129.50			130.28					130.86	
			131.10			130.57					132.21	
			132.53			131.77					132.87	
			132.56			133.96					132.99	

[a] ^{13}C NMR chemical shifts are at 28 °C in DMSO-d_6 relative to internal TMS. [b] Data for **5** and **11** are for the *endo,exo* conformations.

Table 4. ^{15}N NMR Spectral Data for Compounds 1−12[a]

compound	^{15}N chemical shift, δ
1	−232.8, −204.7
2	−222.2, −200.7, −175.8
3	−222.9, −205.0, −181.2
4	−202.7, −174.2
5	−225.5, −181.6
6	−203.6, −179.8, −174.2
7	−235.4, −205.5
8	−230.1, −206.7, −183.2
9	−230.4, −208.8, −186.1
10	−208.1, −181.3
11	−229.2, −185.0
12	−225.7, −185.0, −180.9

[a] ^{15}N NMR chemical shifts are at 28 °C in DMSO-d_6 relative to external nitric acid.

of the *endo,endo* and *endo,exo* conformations were coplanar with the triazolidine ring. The phenyl groups of all three conformations were twisted by approximately 42° relative to the triazolidine ring. The *endo,endo* conformation was solvated with two layers of DMSO molecules (249 solvent molecules) with the SYBYL Molecular Silverware algorithm in a periodic box using periodic boundary conditions. The solvated molecule was minimized as described above and using minimum periodic boundary conditions. A total of 95500 iterations were required. The minimized system showed the two acetyl carbonyl groups twisted conrotatory 2.7° and 2.4° above and below the ring, respectively. The phenyl group was twisted by 38° relative to the triazolidine ring, and the triazolidine ring itself was twisted out of planarity by 1°. The results indicate that solvation with DMSO leads to a slight twisting of the acetyl groups out of the plane of the triazolidine ring, but the twisting is much less than that which occurs in the crystalline state. The solvation has only a small effect on the twisting of the phenyl group. The slight changes in the torsion angles of the acetyl groups would not be expected to have a significant effect on the NMR spectra of the molecule. It appears that the fast minimizations in vacuo give reasonably good approximations of the geometries of the three limiting conformations of the molecule.

In order to compare the relative stabilities of the three limiting conformations in DMSO solution, each limiting conformation was solvated with one layer of DMSO molecules and minimized as above to a gradient of 0.05 kcal/(mol*A). Under these conditions the relative stabilities of the solvated systems were *endo,exo* (250 solvent molecules) > *endo,endo* (249 solvent molecules) > *exo,exo* (235 solvent molecules). The *endo,exo* system was 37 kcal/mol more stable than the *endo,endo* system and 216 kcal/mol more stable than the *exo,exo* system. In each solvated conformation the acetyl groups were twisted slightly out of planarity with the triazolidine ring. Care must be taken in interpreting the calculated results. It is obvious that the number of solvent molecules involved in each system contributes greatly to its minimized energy, and other factors are undoubtedly operative. Therefore, the calculated order of stability for the solvated conformations is not conclusive, and the ranking of the *endo,endo* and *endo,exo* conformations is in doubt. In any event the barriers to rotation among the three conformations are expected to be low, and all three conformations are expected to contribute to the equilibrium mixture in solution. The NMR spectrum of the molecule would not be effected by the equilibrium composition.

The ^{13}C NMR spectra of the dibenzoylated derivatives **5** and **11** showed six carbonyl carbons for each compound. Three were assignable to ring carbonyl carbons, and three were assignable to benzoyl carbonyl carbons. Compound **11** showed two sets of *tert*-butyl group signals in a relative ratio of 83:17 and 12 aromatic carbons. Compound **5** showed 20 aromatic carbons. After the solutions had been stored for ten weeks at room temperature, the minor-intensity set of *tert*-butyl signals and two of the carbonyl signals, one each in the ring carbonyl and

benzoyl carbonyl regions, of **11** had disappeared, and four of the aromatic signals had virtually disappeared. Two of the carbonyl signals and eight of the aromatic signals of **5** were weaker in intensity.

Both **5** and **11** were studied by variable temperature ^{1}H and ^{13}C NMR spectroscopy. Spectra were recorded at 28 °C, 56 °C, 84 °C, 112 °C, 140 °C, and after the samples were cooled back to 28 °C. Compound **11** was stable over the entire temperature range. However, there were significant changes in the appearance of its phenyl hydrogen multiplets in its ^{1}H NMR spectrum beginning at 84 °C and becoming more pronounced at 112 °C. At 28 °C the aromatic region of **11** showed four multiplets at δ 7.96 (d, J = 7.0 Hz), 7.70 (d, J = 7.0 Hz), 7.59 (multiplet, J = 7.0−8.5 Hz), and 7.47 (sextet, 2 overlapping t, J = 8.0 Hz) having relative intensities of 1:1:1:2. At 112 °C the two downfield doublets were slightly broadened, and the peaks at δ 7.59 and δ 7.47 were broad distorted multiplets. The ^{13}C NMR spectra remained relatively unchanged to 84 °C. At 112 °C one ring carbonyl, one benzoyl carbonyl, and the minor intensity set of *tert*-butyl group signals were missing. In the aromatic region four of the signals were considerably weaker. At 140 °C the four weak aromatic signals were virtually gone, and the remaining eight signals were very near their original positions. On cooling the sample back to 28 °C the spectrum was virtually unchanged from that at 140 °C. Compound **5** exhibited similar behavior. At 112 °C its ^{13}C NMR spectrum showed only four carbonyl carbons and 12 primary aromatic carbons. At 140 °C and after cooling the sample back to 28 °C all the weak intensity aromatic resonances had disappeared.

Compound **11** was subjected to both the Systematic Search and Simulated Annealing routines in SYBYL in order to determine its limiting conformations. Only conformations involving the orientations of the benzoyl groups were considered. Conformations involving mirror images or orientations of the *tert*-butyl group were ignored. The Simulated Annealing routine utilized the Tripos force field and Gasteiger-Marsili charges. The SYBYL default settings were used. The resulting conformations were minimized in vacuo as described above. One *exo,exo* conformation, two *endo,exo* conformations, and two *endo,endo* conformations were found. The *exo,exo* conformation was lowest in energy being 2.678 and 3.739 kcal/mol, respectively, lower in energy than the *endo,exo* conformations and 3.169 and 3.411 kcal/mol, respectively, lower in energy than the *endo,endo* conformations. The two OCNN torsion angles between the benzoyl carbonyls and the triazolidine ring of the *exo,exo* conformation were twisted conrotatory 13° above and below the plane of the ring, respectively. The planes of the two benzene rings were both twisted conrotatory 42.4° relative to the triazolidine ring such that the two benzene rings were situated one on top of the other and nearly parallel to each other. The benzene rings were 2.870 Å apart at their ipso carbons and 3.600 Å apart at their *para* carbons. The benzoyl carbonyls of the more stable of the two *endo,exo* conformations were both rotated conrotatory 12° relative to the plane of the triazolidine ring, and the planes of the aromatic rings were twisted such that the angle between them was 70°, i.e. they were nearly perpendicular to each other, and their angles relative to the plane of the triazolidine ring were 130° (*exo*) and 119° (*endo*), respectively. In the more stable of the two *endo,endo* conformations the carbonyl groups were rotated conrotatory by 8° above and below the plane of the triazolidine ring. The planes of the benzene rings were rotated approximately 58° relative to the triazolidine ring.

The *exo,exo* and the more stable of the *endo,exo* and *endo,endo* conformations of **11** were solvated in SYBYL with one layer of DMSO molecules and minimized to a gradient of 0.05 kcal/(mol*A) as described above. The relative energies of the minimized solvated systems were *endo,exo* (187 solvent molecules) > *exo,exo* (188 solvent molecules) > *endo,endo* (183 solvent molecules). The *endo,exo* system was 11 kcal/mol more stable than the *exo,exo* system and 72 kcal/mol more stable than the *endo,endo* system. The torsion angles between the acetyl carbonyl groups and the triazolidine ring for the conformations were comparable to those calculated for the nonsolvated conformations. In **11** the calculated relative order of stability of the solvated conformations is more likely to be accurate than those of **4** in that the conformation predicted to be most stable had one fewer molecule of solvation than did the second most stable conformation.

The NMR data of **11** are in agreement with both the calculated order of stability of its solvated conformations and the molecular modeling geometries obtained for it. The ^{13}C NMR carbonyl region of the *endo,exo* conformation would be expected to show two triazolidine ring and two benzoyl group carbonyl peaks, and the aromatic region would show eight aromatic resonances. The *exo,exo* and *endo,endo* conformtions would be expected to show two peaks each in the carbonyl region because of the symmetry that is present in them. Additionally the *exo,exo* conformation would show six and the *endo,endo* conformation would show four aromatic carbons assuming rapid rotation about the phenyl to carbonyl bonds in the latter conformation.[13] The data does not support the presence of the *exo,exo* conformation. Initially both the *endo,exo* and the *endo,endo* conformations were present with the former conformation being the major component. On standing at room temperature for ten weeks or upon heating to 112 °C, all of the *endo,endo* conformation converted to the *endo,exo* conformation. The barrier to rotation back to the *endo,endo* conformation was apparently sufficiently high that this rotation did not occur. The torsional barrier into and out of the *exo,exo* conformation is likely prohibitively high because of steric factors, and this conformation is not observed. Separate signals for the two aromatic rings are clearly visible in the ^{1}H NMR spectrum of the *endo,exo* conformation at 28 °C. The two doublets at δ 7.96 and δ 7.70 represent the *ortho* hydrogens, the multiplet at δ 7.59 corresponds to the *para* hydrogens, and the overlapping triplets at δ 7.47 correspond to the *meta* hydrogens of the respective rings. The cause of the changes in the ^{1}H NMR spectrum at the higher temperatures is not readily clear. One possibility is that an interconversion between the *endo,exo* conformation and its equivalent *exo,endo* conformation is taking place.

The variable temperature NMR spectra of **5** were similar to those of **11**. These results are consistent with

(13) It has been suggested that simultaneous "rocking" of the amide carbonyl bonds of the *exo,exo* conformation would lead to four rather than six aromatic carbons in its ^{13}C NMR spectrum. While this is a possibility, the close proximity of the "stacked" benzene rings in this conformation would be expected to lead to an observable anisotropic (ring-current) effect in its ^{1}H NMR spectrum. Since the aromatic chemical shift range observed in **12**, which would not show this anisotropic effect, is virtually identical to that of **11**, it can be concluded that the *endo,endo* conformation of **11** is not present in DMSO solution.

the presence of a mixture of *endo,exo* and *endo,endo* conformations in the original sample. At approximately 112 °C or on standing at room temperature the *endo,endo* comformation converted to the more stable *endo,exo* conformation.

Conclusion

The acylations of 4-substituted 1,2,4-triazolidine-3,5-diones occur exclusively on the ring nitrogen atoms. There is no evidence that either *O*-acyl, *O*,*O*-diacyl, or *N*,*O*-diacyl groups were present in any of the compounds. The diacylated structures containing one or two acetyl groups were somewhat unstable to hydrolysis, and the hydrolyses were largely complete on heating to 140 °C. The diacetylated derivative **4** exists in the *endo,endo* conformation in the solid state, but the identity of the preferred conformation in DMSO solution is uncertain. The dibenzoylated derivatives **5** and **11** exist primarily in the *endo,exo* conformation in DMSO solution at 28 °C. It does not appear that the *endo,exo* conformation converts to the *endo,endo* and/or *exo,exo* conformations on heating.

Experimental Section

General. Melting points are uncorrected. HPLC analyses were carried out on a Whatman ODS-2 reverse-phase HPLC column. Elemental analyses were performed by Desert Analytics, Tucson, AZ. NMR spectra were obtained in DMSO-d_6 at 28 °C. The ^{1}H NMR spectra were recorded with a 5 mm ^{1}H probe operating at 499.843 MHz. The proton 90° pulse was 10.0 μs. The spectral width was 8000.0 Hz, the relaxation delay was 1.000 s, and the acquisition time was 1.892 s. The ^{13}C NMR spectra were recorded with a 5 mm probe operating at 125.697 MHz. The carbon 90° pulse was 8.0 μs. The spectral width was 25000.0 Hz, the relaxation delay was 0.200 s, and acquisition time was 1.300 sec. TMS was the internal reference standard for both the ^{1}H and ^{13}C NMR spectra. The ^{15}N NMR spectra were recorded with a 10 mm probe operating at 50.653 MHz. The spectral width was 23242.3 Hz, the relaxation delay was 6.900 s, and the acquisition time was 0.705 s. External nitric acid was the reference standard.

The 1,2-unsubstituted urazoles **1** and **7** were purchased from the Aldrich Chemical Co. and Lancaster Synthesis, Inc., respectively. Compounds **2**, **4**, **8** (mp 103−104.5 °C, lit. mp 117−119 °C[6]), and **10** were prepared as previously reported.[6,7]

1-Benzoyl-4-phenyl-1,2,4-triazolidine-3,5-dione (3) and 1,2-Dibenzoyl-4-phenyl-1,2,4-triazolidine-3,5-dione (5). To a solution of benzoic anhydride (10.2 g, 45 mmol) in CH_2Cl_2 (150 mL) was added 4-phenyl-1,2,4-triazolidine-3,5-dione (**1**) (5.30 g, 30 mmol). The mixture was allowed to stir at rt for 48 h. The mixture was filtered to give a white solid. Recrystallization of the solid from absolute EtOH gave 3.3 g (39%) of pure **3**: mp 211−213 °C; IR (Nujol) 1784 (m), 1714 (s), 1682 cm^{-1} (s). Anal. Calcd for $C_{15}H_{11}N_3O_3$, C 64.05, H 3.94, N 14.94. Found: C 63.81, H 3.76, N 14.81.

The CH_2Cl_2 solution was washed with 10% Na_2CO_3 (3 × 50 mL), dried ($MgSO_4$), and evaporated under reduced pressure to yield a white solid. Recrystallization of the solid from EtOH/acetone (50:50) gave 1.3 g (16%) of pure **5**: mp 272−273 °C; IR (Nujol), 1797 (m), 1754 (s), 1724 (s), 1704 cm^{-1} (s). Anal. Calcd for $C_{22}H_{15}N_3O_4$: C 68.56, H 3.92, N 10.90. Found: C 68.52, H 3.80, N 10.90. Compound **5** was alternately prepared in higher yield (44%) by reacting **1** (5.30 g, 30 mmol) and benzoic anhydride (20.3 g, 90 mmol) in the presence of sodium benzoate (8.64 g, 60 mmol) in CH_2Cl_2 (150 mL) at rt for 20 h.

2-Acetyl-1-benzoyl-4-phenyl-1,2,4-triazolidine-3,5-dione (6). To a mixture of **1** (5.30 g, 30 mmol) and powdered $Pb(OAc)_2 \cdot 3H_2O$ (22.8 g, 60 mmol) in CH_2Cl_2 (200 mL) was added benzoic anhydride (33.9 g, 150 mmol). The mixture was allowed to stir at rt for 48 h and filtered, and to the filtrate was added concd HCl (5 mL). The filtrate was washed with water (3 × 100 mL) and 10% Na_2CO_3 (3 × 75 mL), dried ($MgSO_4$), and evaporated under reduced pressure to give a viscous light-tan oil. The oil was stirred with absolute EtOH (60 mL) to precipitate a white solid that was filtered to yield 3.65 g (38%) of **6** as a white solid. Recrystallization of the solid from absolute EtOH gave 3.3 g (39%) of pure **6**: mp 145.5−146 °C; IR (Nujol) 1814 (m), 1753 (s), 1715 cm^{-1} (s). Anal. Calcd for $C_{17}H_{13}N_3O_4$: C 63.15, H 4.05, N 13.00. Found: C 62.95, H 3.96, N 12.95.

1-Benzoyl-4-*tert*-butyl-1,2,4-triazolidine-3,5-dione (9) and 1,2-Dibenzoyl-4-*tert*-butyl-1,2,4-triazolidine-3,5-dione (11). To a mixture of 4-*tert*-butyl-1,2,4-triazolidine-3,5-dione (**7**) (2.00 g, 12.7 mmol) and pyridine (1.50 g, 19 mmol) in CH_2Cl_2 (70 mL) was added benzoyl chloride (1.79 g, 12.7 mmol). The mixture was stirred at rt for 20 h. The resulting solution was washed with 10% HCl (2 × 30 mL) and 10% Na_2CO_3 (3 × 30 mL). The carbonate washings were acidified (HCl) to produce a white precipitate that was removed by filtration to yield 0.17 g (5%) of **9**. Recrystallization from cyclohexane gave pure **9**: mp 131−133 °C (lit.[6] mp 96−98 °C); IR (Nujol), 3144 (m), 1791 (m), 1722 (s), 1682 cm^{-1}(s). Anal. Calcd for $C_{13}H_{15}N_3O_3$: C 59.76, H 5.79, N 16.08. Found: C 59.68, H 5.83, N 16.03.

The CH_2Cl_2 solution was dried ($MgSO_4$) and evaporated under reduced pressure to yield 1.30 g (56%) of **11**. Recrystallization from EtOH/acetone (70:30) gave pure **11**: mp 244.5−245 °C; IR (Nujol), 1796 (m), 1738 (s), 1728 (s), 1698 cm^{-1} (s). Anal. Calcd for $C_{20}H_{19}N_3O_4$: C 65.74, H 5.24, N 11.50. Found: C 65.77, H 5.02, N, 11.28. When the reaction was carried out with a 50% molar excess of benzoyl chloride, the yield of **11** was increased to 82%.

2-Acetyl-1-benzoyl-4-*tert*-butyl-1,2,4-triazolidine-3,5-dione (12). To a mixture of **7** (1.00 g, 6.37 mmol) and powdered $Pb(OAc)_2 \cdot 3H_2O$ (4.83 g, 12.7 mmol) in CH_2Cl_2 (100 mL) was added benzoic anhydride (4.32 g, 19.1 mmol). The mixture was allowed to stir at rt for 42 h, filtered, washed with water (3 × 50 mL) and 10% Na_2CO_3 (3 × 50 mL), dried ($MgSO_4$), and evaporated under reduced pressure to yield 1.35 g (70%) of **12** as a white solid. Recrystallization of the solid from absolute EtOH gave pure **12**: mp 164−166 °C; IR (Nujol) 1806 (m), 1742 (s), 1711 cm^{-1} (s). Anal. Calcd for $C_{15}H_{17}N_3O_4$: C 59.39, H 5.65, N 13.85. Found: C 59.59, H 5.61, N 13.66.

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