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New Cyclization Mode of [*N*-(Diarylmethyleneamino)carbonimidoyl]ketenes: Synthesis of 9*H*-Pyrazolo[3,2-*b*][1,3]benzoxazines

Natalia A. Lisowskaya,*[a] Mateo Alajarin,[b] and Pilar Sanchez-Andrada*[b]

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The thermal decarbonylation of methyl 3-acyl-1-[*o*-bromophenyl(phenyl)methyleneamino]-4,5-dioxo-4,5-dihydro-1*H*-pyrrole-2-carboxylates **2a** and **2b** gave the novel methyl 3-acyl-9-hydroxy-9-phenyl-9*H*-pyrazolo[3,2-*b*][1,3]benzoxazine-2-carboxylates **4a** and **4b**, the structures of which were determined by X-ray crystallography. The proposed mechanism for this conversion, involving the [*N*-(*o*-bromo-α-phenylbenzylideneamino)carbonimidoyl]ketenes **5** and the mesomeric betaines **6** as intermediates, has been investigated by ab initio and DFT calculations.

Introduction

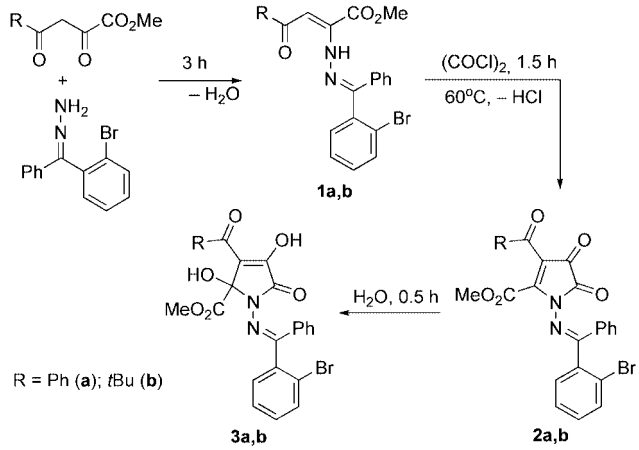
Carbonimidoylketenes are useful reactive intermediates for designing novel heterocyclic constructions by intramolecular cyclizations,[1,2] dimerizations[3] or interaction with nucleophiles[4] and dienophiles.[1,5] The thermal cheletropic decarbonylation of polyfunctionalized pyrrole-2,3(1*H*)-diones is a convenient method for the generation of these ketenes. Variation of the substituents on the pyrrole ring results in the formation of new imidoylketenes and widens their potential for new types of transformations.

In earlier studies some of us had demonstrated that [*N*-(diphenylmethyleneamino)carbonimidoyl]ketenes unexpectedly dimerize – via azomethine imines of the 5-oxo-2,5-dihydropyrazole-1-(methylium)-2-ide type – into substituted dipyrazolo[1,2-*a*;1′,2′-*d*][1,2,4,5]tetrazines.[6] We therefore became intrigued by pursuing the generation of new functionalized [*N*-(methyleneamino)carbonimidoyl]ketenes, seeking for different reaction outcomes.

Here we describe the synthesis of the new 1*H*-pyrrole-2,3-dione derivatives **2a** and **2b** (Scheme 1), which on thermolysis afford the carbonimidoylketenes **5** (Scheme 2), together with the first examples of their intramolecular cyclization, via the azomethine imines **6**, into the novel methyl 3-acyl-9-hydroxy-9-phenyl-9*H*-pyrazolo[3,2-*b*][1,3]benzoxazine-2-carboxylates **4a** and **4b**, the structures of which were determined by X-ray crystallography. The proposed mechanism for the overall conversion of the imidoylketenes **5** into the pyrazolo[3,2-*b*][1,3]benzoxazines **4** has been approached by ab initio and DFT calculations.

Results and Discussion

In designing an efficient route for the preparation of 1*H*-pyrrole-2,3-diones, we chose methyl esters of 4-substituted 2-[*o*-bromophenyl(phenyl)methylene]hydrazino-4-oxo-2-butenoic acids **1a** and **1b** – prepared in 71 and 57% yields from methyl 4-phenyl- and 4-*tert*-butyl-2,4-dioxobutyrates and *o*-bromobenzophenone hydrazone – as appropriate starting materials. Treatment of **1a** and **1b** with oxalyl chloride gave the corresponding methyl 3-acyl-1-[*o*-bromophenyl(phenyl)methyleneamino]-4,5-dioxo-4,5-dihydro-1*H*-pyrrole-2-carboxylates – the 1*H*-pyrrole-2,3-diones **2a** and **2b** – in 30 and 28% yields (Scheme 1). The spectroscopic charac-



Scheme 1. Synthesis of 1*H*-pyrrole-2,3-diones **2a** and **2b**.

[a] Department of Organic Chemistry, Perm State University, 15 Bukireva Str., 614990 Perm, Russian Federation
Fax: +7-3422-396367
E-mail: lisowskaya@mail.ru
[b] Departamento de Química Orgánica, Facultad de Química, Universidad de Murcia, Campus de Espinardo, 30100, Murcia, Spain
Fax: +34-968-364149
E-mail: andrada@um.es
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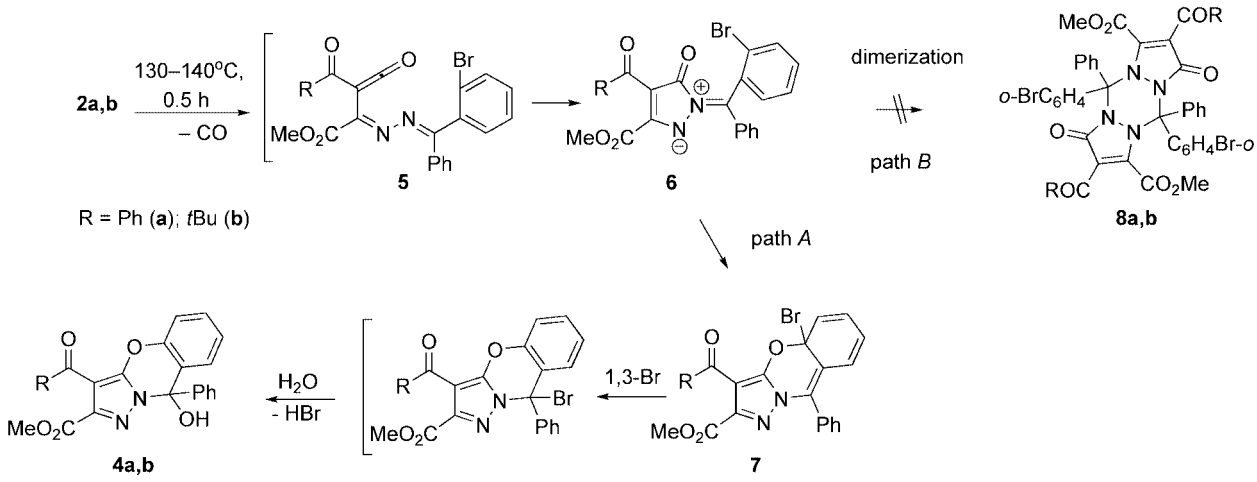


Scheme 2. Thermolysis of 1*H*-pyrrole-2,3-diones **2a** and **2b** and the proposed mechanism of their conversion into **4a** and **4b**.

teristics of compounds **2a** and **2b** are in good agreement with similar data for other 1*H*-pyrrole-2,3-diones.[6,7]

Unfortunately, the quantitative isolation and further application of these new 1*H*-pyrrole-2,3-diones **2a** and **2b** appeared problematic, since they are highly sensitive to moisture and easily hydrolyse to afford the dihydroxy derivatives **3a** and **3b** (27 and 38%). The structure of the model methyl 1-(diphenylmethyleneamino)-2,4-dihydroxy-2,5-dihydro-5-oxo-1*H*-pyrrole-2-carboxylate has been elucidated previously by X-ray crystallography.[8]

The preparative thermolysis of the 1*H*-pyrrole-2,3-diones **2a** and **2b** (130–140 °C, *p*-xylene) resulted in the corresponding methyl 3-acyl-9-hydroxy-9-phenyl-9*H*-pyrazolo-[3,2-*b*][1,3]benzoxazine-2-carboxylates **4a** and **4b** in 82 and 70% yields (Scheme 2). The structure of **4a** was unequivocally established by X-ray analysis (Figure 1).

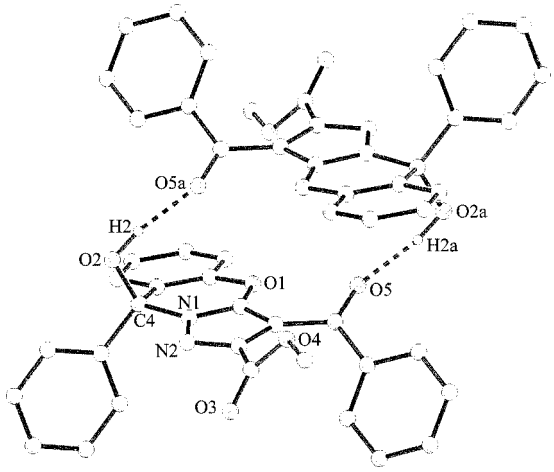


Figure 1. X-ray structure of the dimeric centrosymmetric aggregate of **4a**.

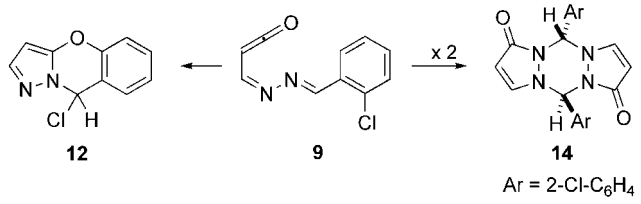
Figure 1 shows a perspective view of the structure of **4a**. The tricyclic fragment of the molecule is flat, the inflection along the O1···C4 line of the central oxazine ring is 11.2°, the deviation from the plane containing the other four atoms is 0.06 Å for atom O1 and 0.17 Å for C4, and the oxazine ring shows an envelope conformation. Remarkably, the molecules exist in the crystal as dimeric centrosymmetric associates, due to strong intermolecular hydrogen bonds [O2–H2···O5 2.749(2) Å, O5···H2 1.81(2) Å, O2–H2 0.95(2) Å, the angle at H2 is 166(2)°].

The mechanism of the thermal cheletropic decarbonylation of 1*H*-pyrrole-2,3-dione to afford imidoylketene has recently been addressed computationally, showing the pseudopericyclic nature of the corresponding transition state, by three research groups[9]. Birney's group has also reported experimental support for that mechanism.[9c] Wentrup,[10a] McNab[10b] and Chuche[10c] recently demonstrated beautiful examples of intramolecular cyclization of [*N*-(dimethylamino)carbonimidoyl]ketenes into stable azomethine imines. On the basis of these communications and also of our previous assumptions,[6,7a] we propose the following reasonable mechanism for the conversion of the 1*H*-pyrrole-2,3-diones **2a** and **2b** into the substituted 9-hydroxy-9*H*-pyrazolo[3,2-*b*][1,3]benzoxazines **4a** and **4b**. The thermal cheletropic extrusion of CO from **2a** or **2b** affords the [*N*-(*o*-bromobenzylideneamino)carbonimidoyl]ketenes **5**, which should undergo intramolecular cyclization to produce a particular class (see below) of azomethine imines **6**, further cyclization of which would generate the corresponding pyrazolo[3,2-*b*][1,3]benzoxazines **7**. The conversion of these compounds into the final products **4a** and **4b** could occur by 1,3-sigmatropic migration of the bromine atom and subsequent hydrolysis of the resulting *tert*-alkyl bromide (Scheme 2, path ***A***).

Why did the presence of the bromine atom in the *ortho*-position of one of the phenyl rings of the (diphenyl)methyleneamino moiety in carbonimidoylketenes **5** bring about the production of the products **4a** and **4b**, without the expected dimerization of these ketenes **5** via azomethine imines **6** to furnish substituted pyrazolo[1,2-*a*;1′,2′-*d*][1,2,4,5]-tetrazines **8a** and **8b** (path ***B***) occurring, as in the case[6] of [*N*-(diphenylmethyleneamino)carbonimidoyl]ketenes? To answer this question and for a better understanding of this conversion, we undertook a computational study.

Computational Results

For this computational study we selected [(2-chlorobenzylidene)hydrazono]ketene (**9**) as the simplest system for modelling the ketenes **5** used in the experimental study. We thus carried out an intensive search along the RHF/6-31G* and B3LYP/6-31+G* potential energy surfaces for the transformations of **9** into the tricycle **12** and the dimeric structure **14** (Scheme 3). All energies discussed in the text are free energies at the B3LYP/6-31+G*//B3LYP/6-31+G* level unless otherwise noted. Zero-point vibrational energy corrections have been applied, but not scaled. Relative energies, free energies and the lowest or imaginary frequencies for all structures in Figure 2 and Figure 3 are reported in Table 1, together with the free energy barriers. Geometry-optimized structures at the B3LYP/6-31+G*//B3LYP/6-31+G* level for reactants, intermediates, transition states and products are shown in Figure 2 and Figure 3, while the qualitative reaction profiles are depicted in Figure 4.



Scheme 3. Alternative cyclization modes of the ketenes **9** explored in the theoretical study.

Interestingly, we have found that the two transformations have a common intermediate, the zwitterion **10**, and both proceed via stepwise mechanistic pathways as shown in Scheme 4. Before describing the mechanistic paths, however, we should emphasize the special characteristics of the zwitterionic intermediates **10** (and **6**), which are real heterocyclic mesomeric betaines. Depending on their electronic natures, Ollis classified these compounds into four major classes: conjugated, cross-conjugated, pseudo-cross-conjugated and heterocyclic *N*-ylides.[11] Subdivision on the basis of the isoconjugated equivalents gave four additional subclasses, making a total of 16 distinct structural types of heterocyclic mesomeric betaines, and providing the basis for correlating the chemical reactivities of these compounds with the types of conjugation associated with their π-electron systems. A detailed analysis of the polar intermediates **10** (and **6**) and their resonance forms reveals that these compounds are conjugated mesomeric betaines (CMBs) isoconjugated with an odd non-alternant hydrocarbon anion (CMB-odd-non-AH anion). The few examples of this type of mesomeric betaines reported up to now justify the classification of betaines **10** (and **6**) on the basis of their electronic structures.

According to the discussed mechanistic paths (Scheme 4), the first step for both transformations consists of the electrocyclic ring closure (6 electrons, 5 centres) of the ketene **9**, to produce the mesomeric betaine **10** via the transition structure **TS1**. The calculated barrier is only 1.55 kcal·mol^{-1}, the process being slightly endothermic. The geometry of the forming five-membered ring in **TS1** is

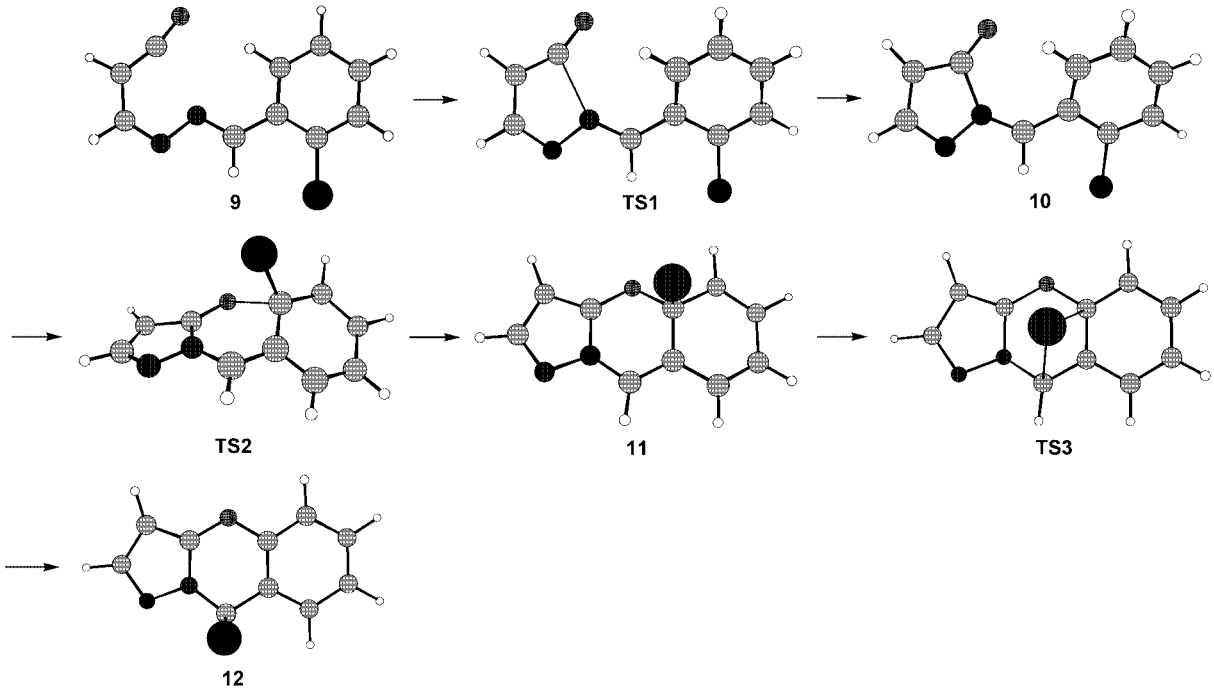


Figure 2. Computer plot of the stationary points found in the transformation of [(2-chloro-benzylidene)hydrazono]ketene (**9**) into tricycle **12** optimized at the B3LYP/6-31+G* level.

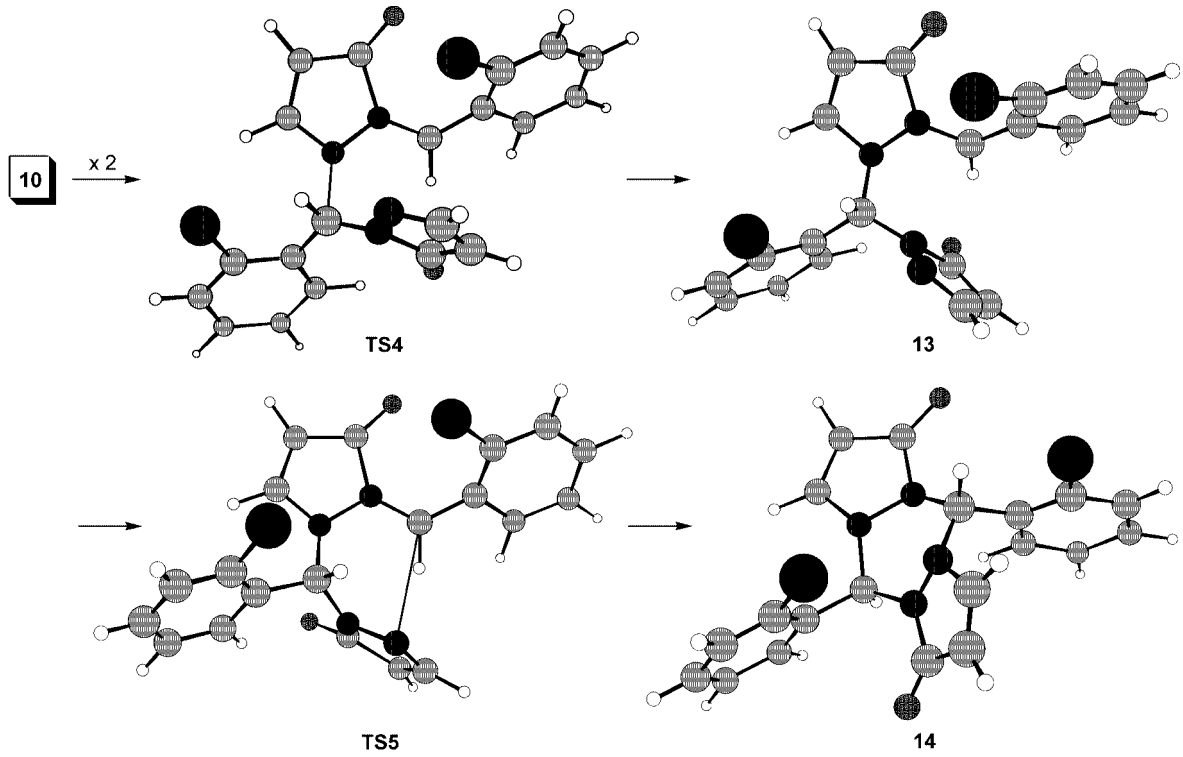


Figure 3. Computer plot of the stationary points found in the transformation of the mesomeric betaine **10** into the tricycle **14** optimized at the B3LYP/6-31+G* level.

Table 1. Relative energies with zero-point vibrational energy corrections (kcal·mol^{-1}), low or imaginary frequencies [cm^{-1}] and relative free energies (kcal·mol^{-1}) for the stationary points found in the conversions **9** →**12** and **9** →**14** calculated at the B3LYP/6-31+G* theoretical level, together with the free energy barriers[a] (kcal·mol^{-1}).

Structure	Relative energy	Low frequencies	Relative free energy	Free energy barriers	
9	0.00	17.7	0.00	$\Delta G^{\neq}_1$	1.55
TS1	0.69	–99.6	1.55	$\Delta G^{\neq}_2$	24.63
10	–0.19	9.3	0.19	$\Delta G^{\neq}_3$	4.00
TS2	22.08	–414.2	24.83	ΔGrx*n*12	–18.13
11	3.66	75.8	6.27	$\Delta G^{\neq}_4$	26.32
TS3	7.82	–144.0	10.27	$\Delta G^{\neq}_5$	2.84
12	–20.60	60.9	–18.13	ΔGrx*n*14	–8.55
TS4	10.32	–221.0	26.71		
13	4.04	19.3	20.59		
TS5	5.89	–54.0	23.43		
14	–25.92	19.8	–8.55		

[a] See Figure 4 for the notation of energy barriers.

planar, and the electronic motions correspond to the attack of the lone pair of the nitrogen atom N1 on the LUMO plane of the ketene component, both placed in the molecular plane. NBO analysis of **TS1** thus shows bonding between the N1 lone pair and the π*C5–O9 natural localized orbital, the second order perturbation energy associated with this donation being $E(2)_{LpN\rightarrow\pi^*C5-O9}$ = 55.1 kcal·mol^{-1}. Furthermore, the magnetic characteristics of **TS1** have been analyzed by computation of the NICS values along the *z*-axis perpendicular to the molecular plane, the ring critical point being the intersection point as defined by Bader.[12] The low absolute computed NICS values reveal the nonaromatic character of **TS1**, the NICS value computed at the ring critical point and the maximum NICS value being –1.97 and –4.07 ppm·mol^{-1} respectively. These features (i.e., the low energy barrier of the conversion **9** →**10**, the planar and nonrotatory geometry[13] of **TS1**, and their nonaromatic characters) are indicative of a *pseudopericyclic*[14] process.

The mesomeric betaine **10** can evolve by two alternative stepwise pathways, which we have denoted as *A* and *B* in Scheme 4, to give **12** or **14**, respectively. In path *A* the intermediate **10** undergoes a 6π-electrocyclic ring closure via the transition structure **TS2** to produce tricycle **11**, which is finally transformed into **12** by a [1,3]-Cl shift[15] through the transition structure **TS3** (see Figure 2). The energy barrier associated with the transformation **10**→**11** is 24.6 kcal·mol^{-1}, while that corresponding to the conversion

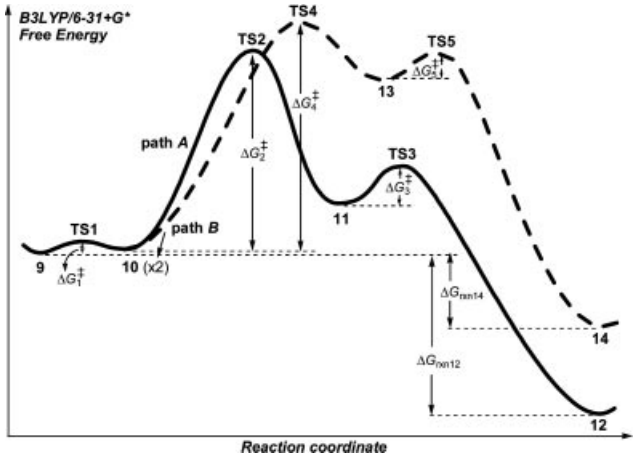


Figure 4. Qualitative reaction profiles at the B3LYP/6-31+G* level for the alternative modes of cyclization of ketene **9** (path *A* and path *B*) to give **12** and **14**, respectively.

of **11** into **12** is only 4 kcal·mol^{-1}. The overall process of the transformation of the ketene **9** into **12** is exothermic by 18.13 kcal·mol^{-1} (see Table 1).

The alternative mode of cyclization of ketene **9** considered in this study (path *B*) occurs through dimerization of mesomeric betaine **10**. The computational calculations predict that this process is not concerted but takes place in two steps. In the first one the formation of a σ-C–N bond occurs via the transition structure **TS4** through the attack of nitrogen (N2) on the iminium carbon atom (C6) of a second molecule, providing the polar dimeric structure **13**, which finally cyclizes to the dimer **14** via **TS5** (see Figure 3). The computed barriers were 26.3 and 2.84 kcal·mol^{-1}, respectively (see Table 1), and the overall transformation **9** → **13** is calculated to be exothermic by 8.55 kcal·mol^{-1}.

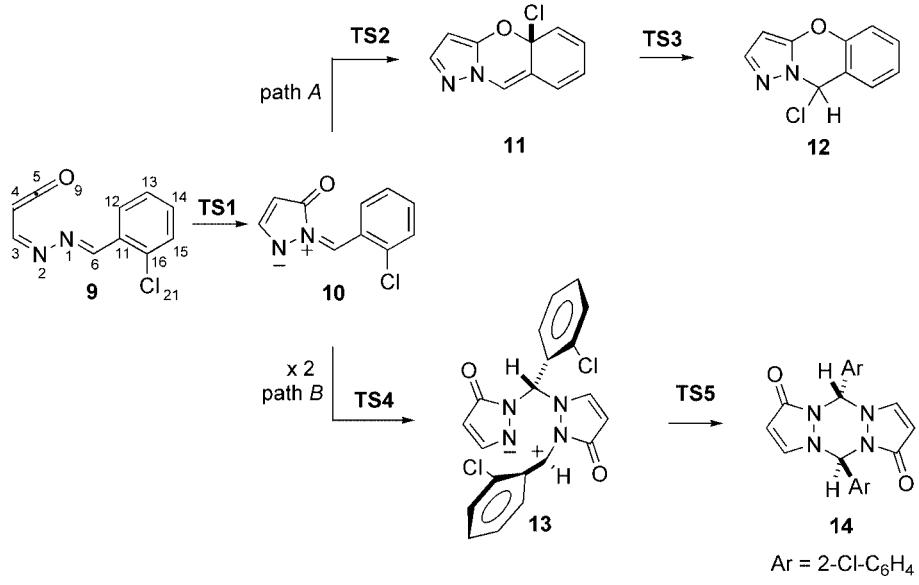
From the free energy barriers calculated for the two alternative modes of cyclization of the ketene **9**, this theoretical approach predicts that the tricycle **12** should be both the kinetically and thermodynamically controlled product (see Figure 4), the limiting rate step being the 6π-electrocyclic ring closure transforming the mesomeric betaine **10** into the tricycle **11**. Although the barrier for the conversion of **10** into the dimeric intermediate **13** is not much higher, so the formation of **14** should be an accessible process (especially so in view of the high temperature used in the experimental study), the lower thermodynamic stability of **14** in relation to **12**, together with the entropic acceleration of the intramolecular cyclization process in comparison with the intermolecular dimerization, explain why only the formation of **12** should be observed.

Conclusion

In summary, we have demonstrated here that the presence of a bromine atom in the *ortho*-position of one of the phenyl rings of the [*N*-(diphenylmethyleneamino)carbonimidoyl]ketenes **5** allows for their conversion into the fascinating 9*H*-pyrazolo[3,2-*b*][1,3]benzoxazines **4**, instead of the expected dimeric dipyrazolo[1,2-*a*;1′,2′-*d*][1,2,4,5]-tetrazines **8**. The computational study reveals that the two alternative cyclization modes have a common intermediate – the mesomeric betaines **6**, formed from the electrocyclic ring closure (6 electrons, 5 centres) of the imidoylketenes in a process of pseudopericyclic nature – and offers a rational explanation for the exclusive formation of tricycles **12**.

Computational Methods

The molecular orbital calculations were carried out with Gaussian 03.[16] Geometry optimizations were attempted first at the RHF/6-31G* level[17] and then with the B3LYP[18] functional with the 6-31+G* basis set. Frequency calculations verified the identity of each stationary point as



Scheme 4. Mechanistic pathways found for the transformation of the ketene **9** into **12** and **14**.

a minimum or as transition state. Second-order perturbation analyses were achieved by the NBO (Natural Bond Orbital) method.[19] NICS (Nucleus-Independent Chemical Shifts) values were obtained at the B3LYP/6-31+G*//B3LYP/6-31+G* level with the GIAO (Gauge-Independent Atomic Orbital) method.[20]

Experimental Section

General: The ^{1}H NMR spectra were recorded in [D$_6$]DMSO and $CDCl_3$ solutions with HMDS as the internal standard with a Bruker DPX 400 (400 MHz) spectrometer. The IR spectra were recorded in Nujol mulls with a UR-20 spectrometer. The melting points are uncorrected. TLC analyses were run on SILUFOL UV-254 plates. Solvents were dried by standard methods.

X-ray Crystallography: The unit cell parameters were measured on a KM-4 (KUMA DIFFRACTION) four-cycle automatic detector with χ-geometry (graphite monochromatized Mo-K_α, radiation, ω-2θ scan mode, $3.5 < 2\theta < 54.02°$). In total, 3989 independent reflections were measured. No correction for absorption was applied ($\mu = 0.096$ mm^{-1}). The structure was determined by a direct statistic method with subsequent series of calculations of electronic density maps. The hydrogen atoms' positions were calculated from geometrical terms. The atom hydrogen at O2 was revealed by differential analysis. The final anisotropic specification of non-hydrogen atoms gave $R_1 = 0.0393$, $wR_2 = 0.1063$ for 2339 reflections with $I > 2\sigma(I)$ and $R_1 = 0.1065$, $wR_2 = 0.1177$ for all 3989 reflections. GOF = 9.895. All final calculations were performed by using the Shelx97 program.[21]

CCDC-262743 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Methyl 2-[(*o*-Bromophenyl)phenylmethylenehydrazino]-4-oxo-4-phenyl-2-butenoate (1a): A solution of methyl benzoylpyruvate[22] (1.00 g, 4.85 mmol) and *o*-bromobenzophenone hydrazone (1.33 g, 4.85 mmol) in dry benzene (50 mL) was heated at reflux for 1.5 h in a flask fitted with a Dean–Stark trap and then cooled. The crude precipitate was isolated by filtration and recrystallized from a benzene/hexane (1:1) mixture to give product **1a** (1.60 g, 71%) as lemon yellow crystals, m.p. 119–120 °C. ^{1}H NMR (400 MHz, [D$_6$]-DMSO): δ = 12.52 (s, 1 H, N*H*), 7.54–7.89 (m, 14 H, Ar*H*), 4.51 (s, 1 H, C*H*), 3.67 (s, 3 H, OMe) ppm. IR (nujol): $\tilde{\nu}$ = 3200 (NH), 1760 (O–C=O), 1625 (C^4=O), 1580 (C=C, C=N) cm^{-1}. $C_{24}H_{19}BrN_2O_3$ (463.32): calcd. C 62.22, H 4.13, Br 17.25, N 6.05; found C 62.24, H 4.11, Br 17.27, N 6.07.

Methyl 2-[(*o*-Bromophenyl)phenylmethyleneamino]-4-*tert*-butyl-4-oxo-2-butenoate (1b): This compound was prepared from methyl pivaloylpyruvate[22] (1.00 g, 5.37 mmol) and *o*-bromobenzophenone hydrazone (1.48 g, 5.34 mmol) by the method described above for **1a**. Compound **1b** (1.36 g, 57%) was obtained as yellow crystals, m.p. 146–148 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 11.94 (s, 1 H, N*H*), 7.24–7.82 (m, 9 H, Ar*H*), 5.06 (s, 1 H, C*H*), 4.45 (s, 3 H, OMe), 1.06 (s, 9 H, *t*Bu) ppm. IR (nujol): $\tilde{\nu}$ = 3470 (NH), 1740 (O–C=O), 1625 (C^4=O), 1570 (C=C, C=N) cm^{-1}. $C_{22}H_{23}BrN_2O_3$ (443.33): calcd. C 59.60, H 5.23, Br 18.02, N 5.42; found C 59.61, H 5.21, Br 18.02, N 5.40.

Methyl 3-Benzoyl-1-[(*o*-Bromophenyl)phenylmethyleneamino]-4,5-dihydro-4,5-dioxo-1*H*-pyrrole-2-carboxylate (2a): A solution of oxalyl chloride (0.19 mL, 2.27 mmol) in dry chloroform (1 mL) was added dropwise to a solution of **1a** (1.00 g, 2.15 mmol) in dry chloroform (5 mL). The reaction mixture was heated for 1.5 h, the chloroform (2 mL) was then evaporated off, and dry hexane was added (1 mL). A precipitate separated from the resulting solution and was filtered off to give product **2a** (0.33 g, 30%) as a deep red solid, m.p. 111–113 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.22–7.92 (m, 14 H, Ar*H*), 3.68 (s, 3 H, OCH_3) ppm. IR (nujol): $\tilde{\nu}$ = 1725 (O–C=O, C^5=O), 1715 (C^4=O), 1670 (C^3–C=O) cm^{-1}. $C_{26}H_{17}BrN_2O_5$ (517.33): calcd. C 60.36, H 3.31, Br 15.45, N 5.42; found C 60.38, H 3.30, Br 15.47, N 5.41.

Methyl 1-[(*o*-Bromophenyl)phenylmethyleneamino]-3-pivaloyl-4,5-dihydro-4,5-dioxo-1*H*-pyrrole-2-carboxylate (2b): This compound was prepared from **1b** (1.00 g, 2.25 mmol) and oxalyl chloride (0.20 mL, 2.37 mmol) by the method described above for **2a**. Compound **2b** (0.31 g, 28%) was obtained as a deep red solid, m.p. 104–106 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.34–7.70 (m, 9 H, Ar*H*), 3.75 (s, 3 H, OMe) 1.13 (s, 9 H, *t*Bu) ppm. IR (nujol): $\tilde{\nu}$ = 1745 (O–C=O, C^5=O), 1670 (C^4=O, C^3–C=O) cm^{-1}. $C_{24}H_{21}BrN_2O_5$ (497.34): calcd. C 57.96, H 4.26, Br 16.07, N 5.63; found C, 57.94, H 4.27, Br 16.05, N 5.63.

Methyl 3-Benzoyl-1-[(*o*-bromophenyl)phenylmethyleneamino]-2,4-dihydroxy-2,5-dihydro-5-oxo-1*H*-pyrrole-2-carboxylate (3a): The residual solution remaining after the synthesis of compound **2a** was allowed to interact with air moisture for 1 h. The resulting solid was filtered off and recrystallized from chloroform/hexane (1:1) to give product **3a** (0.31 g, 27%) as a light yellow solid, m.p. 154–156 °C. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 11.86 (br. s, 1 H, C^4–O*H*), 7.01–8.12 (m, 15 H, Ar*H* + C^2–O*H*), 3.85 (s, 3 H, OMe) ppm. IR (nujol): $\tilde{\nu}$ = 3420, 3190 (OH), 1760, 1700 (O–C=O, C^5=O), 1670 (C^3–C=O) cm^{-1}. $C_{26}H_{19}BrN_2O_6$ (535.34): calcd. C 58.33, H 3.58, Br 14.93, N 5.23; found C 58.35, H 3.55, Br 14.95, N 5.23.

Methyl 1-[(*o*-Bromophenyl)phenylmethyleneamino]-3-pivaloyl-2,4-dihydroxy-2,5-dihydro-5-oxo-1*H*-pyrrole-2-carboxylate (3b): The residual solution remaining after the synthesis of compound **2b** was allowed to interact with air moisture for 0.5 h. The resulting solid was filtered off and recrystallized from chloroform/hexane (1:1) to give product **3b** (0.44 g, 38%) as a light yellow solid, m.p. 129–130 °C. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 12.64 (br. s, 1 H, C^2–O*H*), 7.70–7.35 (m, 10 H, Ar*H* + C^3–O*H*), 3.75 (s, 3 H, OMe), 1.14 (s, 9 H, *t*Bu) ppm. IR (nujol): $\tilde{\nu}$ = 3420, 3190 (OH), 1750 (O–C=O, C^5=O), 1630 (C^3–C=O) cm^{-1}. $C_{24}H_{23}BrN_2O_6$ (515.35): calcd. C 55.93, H 4.50, Br 15.50, N 5.44; found C 55.94, H 4.52, Br 15.53, N 5.44.

Methyl 3-Benzoyl-9-hydroxy-9-phenyl-9*H*-pyrazolo[3,2-*b*][1,3]benzoxazine-2-carboxylate (4a): A solution of **2a** (1.00 g, 1.93 mmol) in dry *p*-xylene (2 mL) was heated at 138–140 °C for 0.5 h and then cooled. The precipitated solid was isolated by filtration and then recrystallized from toluene to give compound **4a** (0.68 g, 82%) as colourless crystals, m.p. 180–182 °C. ^{1}H NMR (400 MHz, [D$_6$]-DMSO): δ = 8.41 (s, 1 H, O*H*), 7.87–7.17 (m, 14 H, Ar*H*), 3.51 (s, 3 H, OMe) ppm. ^{13}C NMR (100.6 MHz, [D$_6$]DMSO): δ_C = 187.03 (C=O), 161.66 (COO), 146.94, 145.98, 142.73, 142.40, 137.92, 133.25, 130.38, 128.87, 128.79, 128.61, 128.45, 128.40, 128.35, 128.28, 128.23, 126.40, 125.40, 124.16, 116.12, 102.36, 84.70 (C^9–O*H*), 51.93 (OMe) ppm. IR (nujol): $\tilde{\nu}$ = 3345 (OH), 1730 (O–C=O), 1620 (C^3–C=O) cm^{-1}. MS: *m*/*z* (%) = 426 [*M*]$^+$ (12), 349 [*M* – Ph]$^+$ (22), 317 (34), 289 (24), 181(61). $C_{25}H_{18}N_2O_5$ (426.42): calcd. C 70.42, H, 4.25, N 6.57; found C, 70.42, H 4.24, N 6.59.

Methyl 9-Hydroxy-9-phenyl-3-pivaloyl-9*H*-pyrazolo[3,2-*b*][1,3]benzoxazine-2-carboxylate (4b): This compound was prepared from **2b** (1.00 g, 2.20 mmol) by the method described above for **2a**. Com-

pound **4b** (0.57 g, 70%) was obtained as colourless crystals; m.p. 153–155 °C. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 8.37 (s, 1 H, O*H*), 7.48–7.25 (m, 9 H, Ar*H*), 3.73 (s, 3 H, OMe), 1.26 (s, 9 H, *t*Bu) ppm. ^{13}C NMR (100.6 MHz, [D$_6$]DMSO): δ = 202.55 (C=O), 162.00 (COO), 146.06, 143.52, 142.65, 141.78, 130.37, 129.31, 128.73, 128.60, 128.25, 126.08, 125.34, 124.09, 116.09, 102.81, 84.75 (C^9–O*H*), 52.05 (OMe), 44.27, 25.95 (Me) ppm. IR (nujol): $\tilde{\nu}$ = 3385 (OH), 1750 (O–C=O), 1650 (C^3–C=O) cm^{-1}. MS: *m*/*z* (%) = 349 [*M* – *t*Bu]$^+$ (13), 105 (80), 77 (16). $C_{23}H_{22}N_2O_5$ (406.43): calcd. C 67.97, H 5.46, N 6.89; found C 67.99, H 5.45, N 6.90.

Supporting Information (see also the footnote in the first page of this article): Table S1, including the chief electronic and energetic features for all stationary points discussed in the text. Cartesian coordinates of local minima and transition structures discussed in the text, the corresponding computer plots showing selected geometrical parameters, and selected orbital interactions of the NBO analysis.

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