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Chemistry of 1,5-Diketones: II.* Specificity of Transformations of Polycyclic 1,5-Diketones in Acid Media

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Abstract—2-(1,3-Diaryl-3-oxopropyl)cyclohexan-1-ones underwent carbo- and heterocyclization in a mixture of acetic acid with acetic anhydride in the presence of perchloric acid. The transformation of 2-(1,3-diaryl-3-oxopropyl)cyclohexan-1-ones into 2,4-diaryl-5,6,7,8-tetrahydrochromenylium salts was shown to involve intermediate 2,4-diarylbicyclo[3.3.1]non-2-en-9-ones. The structure of 2,4-diaryl-substituted bicyclo[3.3.1]non-2-en-9-ones and products of their reactions with halogens and hydroxylamine hydrochloride was confirmed by ^1H and ^{13}C NMR spectroscopy.

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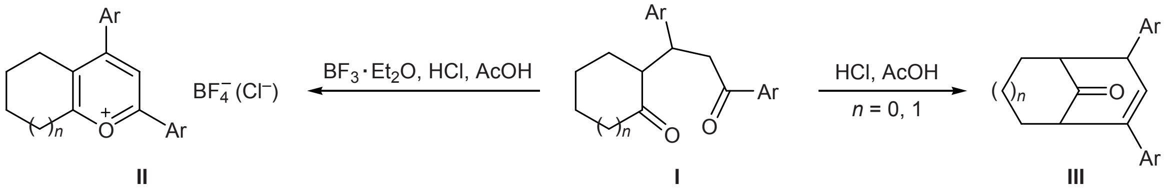
We previously reported [1] on the halogenation of acyclic 1,5-diketones and their fused analogs. In continuation of our studies on the properties of 1,5-dicarbonyl compounds we examined their behavior in acid media. It is known that 2-(1,3-diaryl-3-oxopropyl)-cyclohexan-1-ones **I** under acidic conditions undergo intramolecular heterocyclization to give tetrahydrochromenylium salts and that their carbocyclization produces bridged bicyclic ketones. For example, diaryl-substituted 1,5-diketones **I** react with boron trifluoride–ether complex or with dry hydrogen chloride in acetic acid, yielding tetrahydrochromenylium tetrafluoroborates or chlorides, respectively [2, 3]. Bicyclo-[3.2.1]oct-2-en-8-ones and bicyclo[3.3.1]non-2-en-9-ones were formed as the major products when 2-(1,3-diaryl-3-oxopropyl)cyclopentan- and -cyclohexan-1-ones were heated in boiling acetic acid in the presence of hydrochloric acid [4, 5] (Scheme 1).

By heating 2-(1,3-diaryl-3-oxopropyl)cyclohexan-1-ones **Ia**–**Ic** with perchloric acid in a mixture of acetic acid and acetic anhydride we obtained for the first time mixtures of the corresponding 2,4-diaryl-5,6,7,8-tetrahydrochromenylium perchlorates **IIa**–**IIc** and 2,4-diarylbicyclo[3.3.1]non-2-en-9-ones **IIIa**–**IIIc** at different ratios (Scheme 2, see table). The reaction at low temperature gives mainly bicyclononenones **IIIa** and **IIIb**; raising the temperature to 100°C reduces the yield of compounds **III**, while the yield of chromenylium salts **II** attains 60%.

It was presumed previously [6] that tetrahydrochromenylium salts are formed in reactions of 2-(1,3-diaryl-3-oxopropyl)cyclohexan-1-ones with acid reagents through intermediate tetrahydrochromenes [6]. Our results suggest that the process under study is mediated by bicyclo[3.3.1]non-2-en-9-ones **III**. In fact, compounds **IIIa** and **IIIb** were converted into the corresponding tetrahydrochromenylium perchlorates **IIa** and **IIb** in almost quantitative yield on heating in AcOH–Ac$_2$O in the presence of HClO$_4$. A probable mechanism involves protonation of the

Scheme 1.



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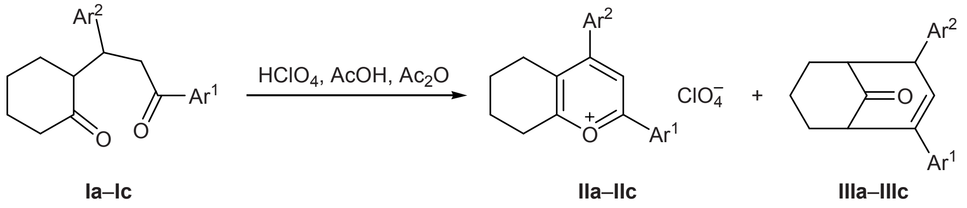
* For communication I, see [1].

Scheme 2.



$$\mathbf{IIa–IIc} \xrightarrow{HClO_4,\ AcOH,\ Ac_2O,\ 100°C} \mathbf{IIIa–IIIc}$$

$Ar^1 = Ar^2 = Ph$ (**a**); $Ar^1 = Ph$, $Ar^2 = 4\text{-}MeOC_6H_4$ (**b**); $Ar^2 = 4\text{-}MeOC_6H_4$, $Ar^2 = Ph$ (**c**).

carbonyl group in ketone **III**, opening of the unsaturated carbocycle, and subsequent heterocyclization to hexahydrochromene **B**. Deprotonation of **B** gives tetrahydrochromene **C** (Scheme 3), and the latter is transformed into tetrahydrochromenylium salt according to the known mechanism [6]. If the substituent at the double bond (Ar^1) in bicyclo[3.3.1]non-2-en-9-one **III** possesses electron-donating properties, the salt formation is hindered because of positive charge delocalization in carbenium ion **A**.

Although bridged unsaturated ketone **III** (n = 0, $Ar^1 = Ar^2$ = Ph) was synthesized for the first time as early as almost 100 years ago [7] by passing hydrogen chloride through a solution of 2-(3-oxo-1,3-diphenylpropyl)cyclopentan-1-one in alcohol, published data on the structure and reactivity of such bicyclic systems are very scarce. As noted in [5], bicycloalkenones like **III** having more than five carbon atoms in the ring are stable. The structure of ketones **III** was determined on the basis of the IR data [8, 9], and the position of the double C=C bond was proved by ^{1}H NMR spectroscopy [10]. Such reactions of ketone **III** as hydrogenation over palladium catalyst [8], reduction with lithium tetrahydridoaluminate [9], and reaction with hypophosphorous acid [10] were reported.

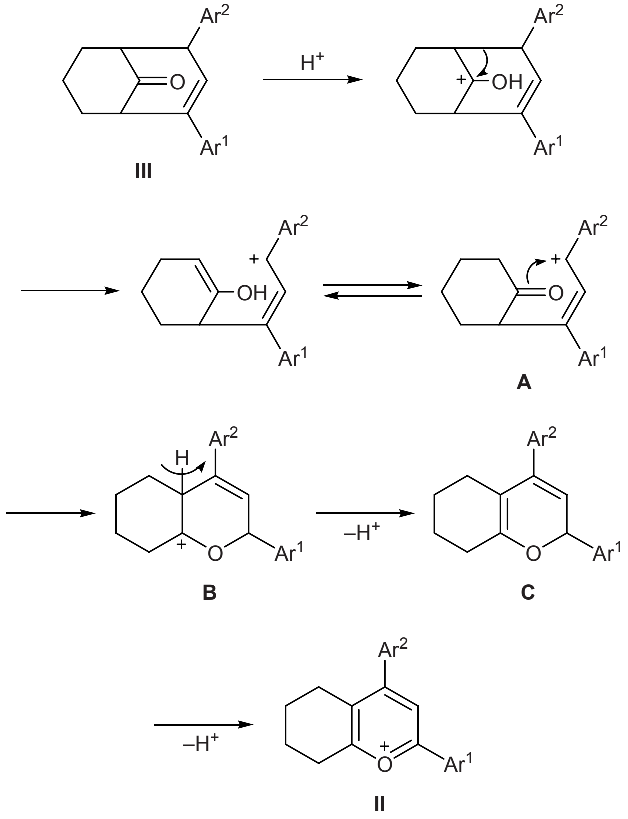
Yields of hetero- and carbocyclization products from carbonyl compounds **Ia**–**Ic**, **IIIa**, and **IIIb**

Initial compound no.	Temperature, °C	Product (yield, %)	
Ia	0	**IIa** (0)	**IIIa** (16)
Ia	20	**IIa** (10)	**IIIa** (73)
Ia	100	**IIa** (27)	**IIIa** (63)
Ib	20	**IIb** (43)	**IIIb** (34)
Ib	100	**IIb** (60)	**IIIb** (10)
Ic	100	**IIc** (14)	**IIIc** (64)
IIIa	100	**IIa** (90)	–
IIIb	100	**IIb** (92)	–

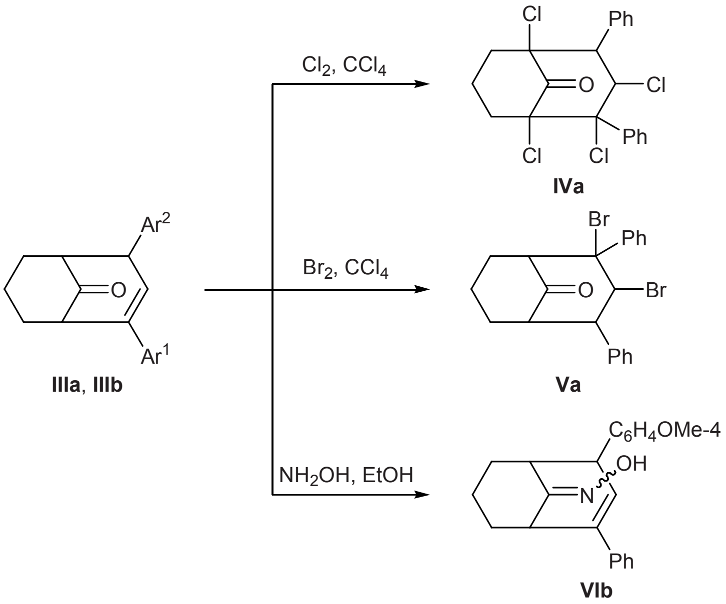
The spectral parameters of compounds **IIIa**–**IIIc** were consistent with the assumed structure.

We also examined the relative reactivities of different reaction centers in unsaturated ketones **IIIa** and **IIIb** toward electrophilic and nucleophilic reagents. Halogenation of compound **IIIa** with chlorine or bromine in carbon tetrachloride at room temperature smoothly afforded the corresponding halogen-substituted bicyclononanones **IVa** and **Va**, indicating that the bicyclic skeleton is stable under these conditions. By

Scheme 3.



Scheme 4.



treatment of ketone **IIIb** with hydroxylamine in ethanol we obtained oxime **VIb** (Scheme 4). The structure of halogenated ketones **IVa** and **Va** and oxime **VIb** was confirmed by the IR and ^{13}C NMR spectra.

EXPERIMENTAL

The ^{1}H and ^{13}C NMR spectra were recorded on a Bruker MSL-400 spectrometer from solutions in chloroform-*d* or DMSO-d_6 using hexamethyldisiloxane as internal reference. The IR spectra were measured on a Specord M-80 spectrometer from samples dispersed in mineral oil or hexachlorobutadiene. The progress of reactions and the purity of products were monitored by thin-layer chromatography on Silufol UV-254 plates using hexane–diethyl ether–chloroform (4 : 1 : 1) as eluent; spots were detected by treatment with iodine vapor. Initial 1,5-diketones **Ia**–**Ic** were synthesized according to the procedure described in [4].

Reaction of 2-(1,3-diaryl-3-oxopropyl)cyclohexan-1-ones Ia–Ic with perchloric acid. Perchloric acid (d = 1.69 g/cm^3), 0.7 ml (0.012 mol), was added under continuous stirring to a mixture of 0.005 mol of compound **Ia**–**Ic**, 5.5 ml of glacial acetic acid, and 1 ml of acetic anhydride. The mixture was stirred at room temperature or on heating until the conversion of the initial diketone was complete, evaporated by half, and poured into 150 ml of diethyl ether. The precipitate was filtered off, washed with diethyl ether, and dried. We thus isolated 2,4-diaryl-5,6,7,8-tetrahydrochromenylium perchlorates **IIa**–**IIc**. Perchlorate **IIa** was identified by the melting point [11]. The filtrate was evaporated, and the precipitate of bicyclo[3.3.1]non-2-en-9-one **IIIa**–**IIIc** was filtered off, washed with ethanol, and dried. The yields are given in table.

4-(4′-Methoxyphenyl)-2-phenyl-5,6,7,8-tetrahydrochromenylium perchlorate (IIb). Red crystals, mp 196–198°C (reprecipitated from $CHCl_3$ into Et_2O). IR spectrum, ν, cm^{-1}: 2936 (CH_2), 2855 (OCH_3), 1540 (pyrylium), 1092 (ClO_4^-). Found, %: C 61.94; H 5.40; Cl 8.10. $C_{23}H_{23}ClO_7$. Calculated, %: C 61.82; H 5.19; Cl 7.93.

2-(4′-Methoxyphenyl)-4-phenyl-5,6,7,8-tetrahydrochromenylium perchlorate (IIc). Red–brown crystals, mp 204–206°C (reprecipitated from $CHCl_3$ into Et_2O). IR spectrum, ν, cm^{-1}: 2938 (CH_2), 2855 (OCH_3), 1540 (pyrylium), 1090 (ClO_4^-). Found, %: C 62.24; H 5.30; Cl 8.00. $C_{23}H_{23}ClO_7$. Calculated, %: C 61.82; H 5.19; Cl 7.93.

2,4-Diphenylbicyclo[3.3.1]non-2-en-9-one (IIIa). Colorless crystals, mp 144.5–145.5°C (from AcOH–Ac_2O, 5 : 1). IR spectrum, ν, cm^{-1}: 2947 (CH_2), 1712 (C=O), 1657 (C=C). ^{1}H NMR spectrum, δ, ppm: 2.58–2.81 m (6H, CH_2), 5.51 s (1H, 4-H), 7.70–6.90 m (10H, H_{arom}), 7.86 s (1H, 3-H). ^{13}C NMR spectrum, δ_C, ppm: 16.91 (C^7), 29.84 (C^8), 31.74 (C^6), 47.72 (C^5), 48.70 (C^1), 49.95 (C^4), 125.61 (C^3), 126.53–128.48 (C_{arom}), 140.46 (C^2), 212.9 (C^9). Found, %: C 87.62; H 7.11. $C_{21}H_{20}O$. Calculated, %: C 87.50; H 6.94.

4-(4′-Methoxyphenyl)-2-phenylbicyclo[3.3.1]-non-2-en-9-one (IIIb). Colorless crystals, mp 171–

172°C (from AcOH–Ac_2O, 5:1). IR spectrum, ν, cm^{-1}: 2934 (CH_2), 2852 (OCH_3), 1715 (C=O), 1654 (C=C). ^1H NMR spectrum, δ, ppm: 2.21–1.30 m (6H, CH_2), 3.97 s (3H, OCH_3), 6.32 s (1H, 4-H), 7.76 s (1H, 3-H), 8.77–8.12 m (9H, H_{arom}). ^{13}C NMR spectrum, δ_C, ppm: 17.02 (C^7), 29.71 (C^8), 31.74 (C^6), 47.76 (C^5), 48.78 (C^1), 49.87 (C^4), 59.92 (CH_3), 125.5–128.5 (C_{arom}), 126.24 (C^3), 140.56 (C^2), 158.93 ($C^{4'}$), 213.12 (C^9). Found, %: C 83.82; H 7.51. $C_{22}H_{22}O_2$. Calculated, %: C 82.88; H 6.96.

2-(4′-Methoxyphenyl)-4-phenylbicyclo[3.3.1]non-2-en-9-one (IIIc). Colorless crystals, mp 128.5–129°C (from AcOH–Ac_2O, 5:1). IR spectrum, ν, cm^{-1}: 2940 (CH_2), 2855 (OCH_3), 1710 (C=O), 1660 (C=C). ^1H NMR spectrum, δ, ppm: 1.36–2.09 m (6H, CH_2), 3.53 s (3H, OCH_3), 6.52 s (1H, 4-H), 7.49 s (1H, 3-H), 7.26–7.57 m (9H, H_{arom}). ^{13}C NMR spectrum, δ_C, ppm: 17.26 (C^7), 29.74 (C^8), 31.63 (C^6), 47.61 (C^5), 48.82 (C^1), 49.76 (C^4), 54.85 (CH_3), 126.16–130.53 (C_{arom}), 136.9 (C^3), 141.0 (C^2), 158.9 ($C^{4'}$), 213.0 (C^9). Found, %: C 83.16; H 6.86. $C_{22}H_{22}O_2$. Calculated, %: C 82.88; H 6.96.

2,4-Diphenyl-5,6,7,8-tetrahydrochromenylium perchlorate (IIa). Perchloric acid, 1.2 g (0.7 ml, 0.012 mol), was added dropwise to a solution of 1.44 g (0.005 mol) of compound **IIIa** in a mixture of 5.5 ml of glacial acetic acid and 1.1 ml of acetic anhydride. The mixture was heated for 14 h at 100°C, evaporated by half, and poured into 50 ml of diethyl ether. The precipitate was filtered off, washed with diethyl ether, and dried. Yield 90%; the product was identified by the melting point [11].

1,2,3,5-Tetrachloro-2,4-diphenylbicyclo[3.3.1]nonan-9-one (IVa). A solution of 1.5 g (0.0052 mol) of compound **IIIa** in carbon tetrachloride was saturated with gaseous chlorine over a period of 3.5 h at room temperature. The solution was cooled, and the precipitate was filtered off. Yield 1.0 g (43%), colorless crystals, mp 98–99°C (from *i*-PrOH). IR spectrum, ν, cm^{-1}: 2940 (CH_2), 1720 (C=O), 680–630 (C–Cl). ^{13}C NMR spectrum, δ_C, ppm: 26.14 (C^7), 30.41 (C^8), 30.49 (C^6), 39.66 (C^5), 40.31 (C^1), 46.31 (C^4), 51.34 (C^3), 51.45 (C^2), 128.47–136.84 (C_{arom}), 201.10 (C^9). Found, %: C 56.88; H 4.84; Cl 31.93. $C_{21}H_{18}Cl_4O$. Calculated, %: C 58.91; H 4.24; Cl 33.12.

2,3-Dibromo-2,4-diphenylbicyclo[3.3.1]nonan-9-one (Va). A solution of 3.7 ml (1.2 g, 0.0076 mol) of bromine in 7 ml of carbon tetrachloride was added dropwise over a period of 0.5 h under stirring at room temperature to a solution of 2.0 g (0.0064 mol) of compound **IIIa** in carbon tetrachloride. The solution was partially evaporated and cooled, and the precipitate was filtered off. Yield 2.0 g (64%), colorless crystals, mp 167.5–168°C (from EtOH). IR spectrum, ν, cm^{-1}: 2955 (CH_2); 1722 (C=O); 691, 520 (C–Br). Found, %: C 56.88; H 4.80; Br 36.13. $C_{21}H_{20}Br_2O$. Calculated, %: C 56.28; H 4.50; Br 35.66.

4-(4′-Methoxyphenyl)-2-phenylbicyclo[3.3.1]non-2-en-9-one oxime (VIb). A solution of 0.25 g (0.8 mmol) of compound **IIIb** and 0.14 g (2.1 mmol) of hydroxylamine hydrochloride in 10 ml of anhydrous ethanol was heated for 3.5 h on a boiling water bath. The solution was cooled, and the precipitate was filtered off. Yield 0.15 g (58%), colorless crystals, mp 214–215°C (from EtOH). IR spectrum, ν, cm^{-1}: 2920 (CH_2); 2860, 2840 (NOH); 1620 (C=C); 1040 (OCH_3). Found, %: N 3.65. $C_{21}H_{23}NO$. Calculated, %: N 4.20.

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