A new method for the preparation of 2,3-cycloalkeno-5,6-cycloalkeno-4H-pyran-4-ones

Fan Xu, Xueqin Cao, Zhengbai Cao* and Lei Zou

Department of Chemistry, Suzhou University, Suzhou 215006, China

Abstract

Several 2,3-cycloalkeno-5,6-cycloalkeno-4H-pyran-4-ones, such as 2,3,5,6-bicyclopenteno-4H-pyran-4-one and 1,2-dihydronaphtho[3,4-b]cyclopenteno[1,2-e]-4H-pyran-4-one, were synthesized conveniently by the reaction of a cyclic ketone enamine and diacylchloride. This reaction allows a new method for preparation of these compounds, which may be the precursors for the synthesis of some useful heterocycles. © 2000 Elsevier Science Ltd. All rights reserved.

Keywords: cyclic ketone enamine; diacylchloride; 2,3-cycloalkeno-5,6-cycloalkeno-4H-pyran-4-one; preparation.

The Stork reaction, with its generality and wide-ranging applicability, is covered thoroughly in several reviews.[1,2] The reaction of ketone or aldehyde enamines with alkyl halides furnishes alkylated products,[3] while with acid chlorides gives acylated products.[4] Many other different types of products can also be isolated. For example, application of the Stork reaction to the enamine of N-benzyl-4-piperidone with diketene forms azachromone,[5] while the enamine of benzocyclopentanone with o-acetoxybenzoyl chloride gives benzopyran-4-one.[6] Furthermore, 1,3,5-triketone and its cyclized derivative 2,3,5,6-bicycloalkeno-4H-pyran-4-one can be obtained by the reaction of two equivalents of cyclic ketone enamine with phosgene.[7] Hünig reported that bi(1,3-diketone) was formed by the reaction of diacylchloride with cyclopentanone enamine (1:2 mole ratio).[8] Recently, we found that when hexanedioylchloride reacted with 1-piperidino-cyclohexene (1:1 mole ratio), 2,3-cyclohexeno-5,6-cyclopenteno-4H-pyran-4-one (**3b**) was obtained. This method has not to the best of our knowledge been reported, and the symmetric or asymmetric 2,3-cycloalkeno-5,6-cycloalkeno-4H-pyran-4-ones can be synthesized easily. In this paper, this approach was adopted for the preparation of six 2,3-cycloalkeno-5,6-cycloalkeno-4H-pyran-4-ones,[9] which were characterized by conventional IR, ^{1}H NMR and elemental analyses. Herein, we wish to report our preliminary results.

---

* Corresponding author. Fax: 86-512-5112371; e-mail: orglab@suda.edu.cn
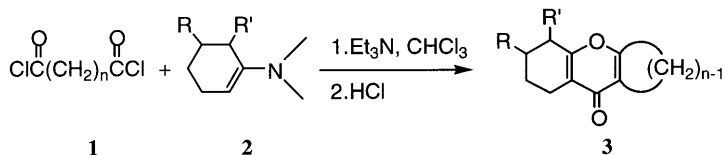
In a typical experimental procedure, a mixture of cyclic enamine (1.0 equiv.), diacylchloride (1.1 equiv.) and triethylamine (2.0 equiv.) in chloroform was refluxed for several hours. After hydrolysis with 3N hydrochloric acid for 2 h, the organic layer was separated and then the solvent was removed by distillation. The product was purified by column chromatography on silica to give the desired product. The results are listed in Table 1.

Using different cyclic enamines or different diacylchlorides, the 4H-pyran-4-ones may be symmetrical or asymmetrical. Only hexanedioylchloride and heptanedioylchloride were successfully used in this method. When pentanedioylchloride or octanedioylchloride were used, the 4H-pyran-4-one derivative could not be obtained.

From Table 1 we can conclude: (1) the skeleton of the cyclic ketone is preserved in the product, (2) the self-condensation takes place inside diacylchloride forming a new carbon ring, and (3) the number of carbon atoms of the new ring is one less than that of diacylchloride. The

Table 1
Formation of 2,3-cycloalkeno-5,6-cycloalkeno-4H-pyran-4-ones

Entry	Diacylchloride	Enamine	Product	Yield [a](%)
3a				27
3b	$ClC(CH_2)_4CCl$			29
3c				30
3b'				30(76[b])
3d	$ClC(CH_2)_5CCl$			32(84[b])
3e				32(85[b])
3f				29

a. Isolated yield
b. HPLC yield

above conclusions can be explained by a mechanism similar to a Dieckmann reaction. We think the first step of this reaction, taking the preparation of **3a** as an example in Scheme 1, is the self-condensation of the diacylchloride forming 2-carbonyl cyclopentanoyl chloride (A), which is an electrophile. Following that, the enamine (B), which is a nucleophile, attacks the exocyclic carbonyl group giving 1,3,5-triketone (C) after hydrolysis. Then the triketone is enolized and loses water to form the final product (D). Using this mechanism, the product of reaction of hexanedioylchloride with 1-piperidino-cyclohexene must be the same as that of heptane-dioylchloride with 1-piperidino-cyclopentene. The hypothesis was completely confirmed by experiments (Entries **3b** and **3b′**). Further reaction of cyclic enamines with pentanedioylchloride or octanedioylchloride failed, proving the possibility that the self-condensation did not occur owing to the existence of ring strain. The further study of the mechanism is in progress.

Scheme 1.
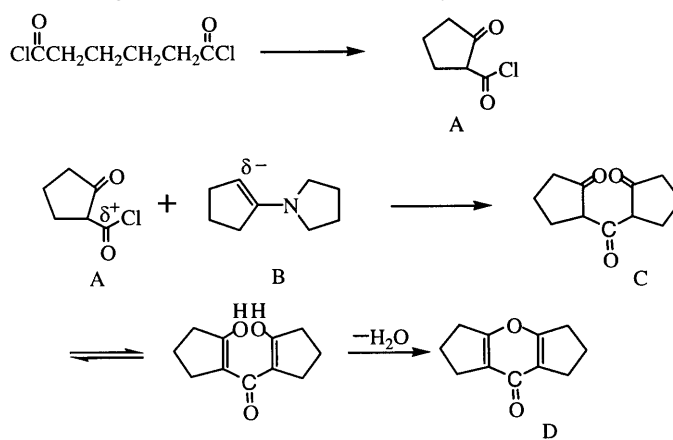
The crystal structures of compounds **3a** and **3c** are presented in Figs. 1 and 2.
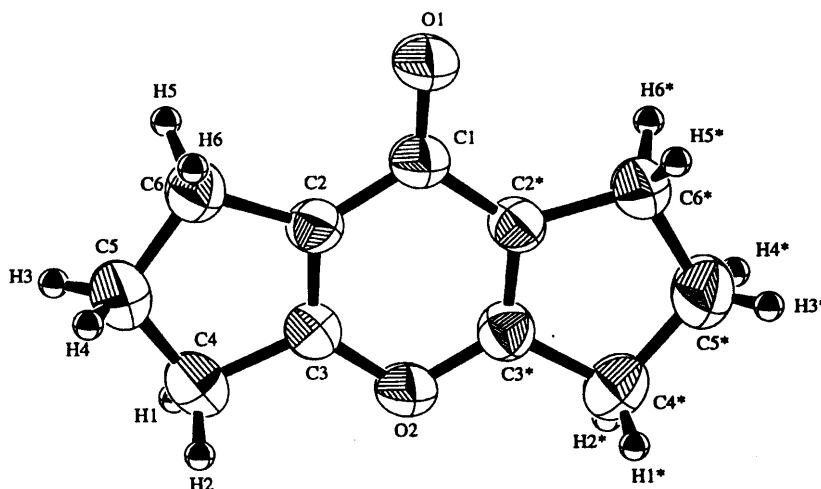

Figure 1. Crystal structure of **3a**

2,3-Cycloalkeno-5,6-cycloalkeno-4*H*-pyran-4-ones can be easily transformed into some useful derivatives. For example, xanthone (**4d**) was obtained from compound **3d** by catalytic dehydrogenation with Pd–C catalyst at atmospheric pressure in 70% yield.[10]
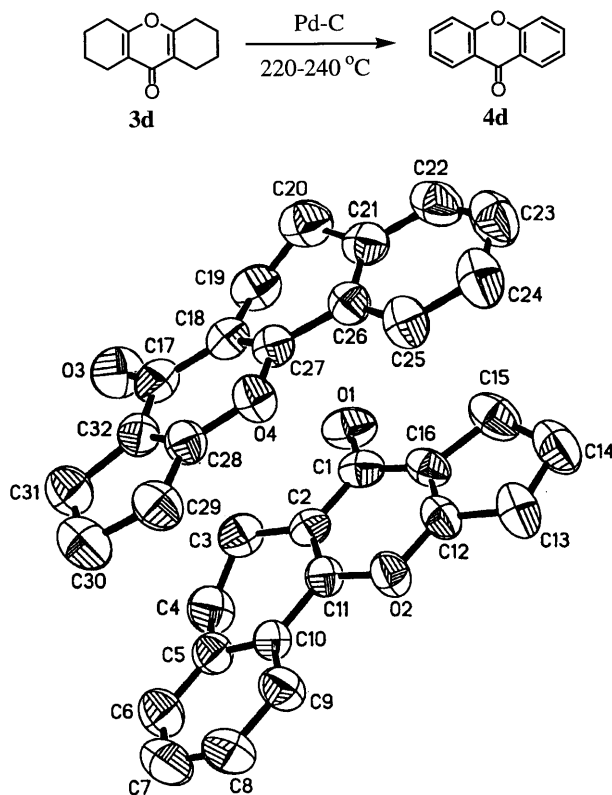
Figure 2. Crystal structure of **3c**

Acknowledgements

References

1. Hickmott, P. W. *Tetrahedron* **1982**, *38*, 1975; Hickmott, P. W. *Tetrahedron* **1982**, *38*, 3363.
2. Hickmott, P. W. *Tetrahedron* **1984**, *40*, 2989.
3. Whitesell, J. K.; Whitesell, M. A. *Synthesis* **1983**, 517.
4. Inukai, T.; Yoshizawa, R. *J. Org. Chem.* **1967**, *32*, 404.
5. Belsky, I. *Tetrahedron Lett.* **1970**, 4597.
6. Gorlitzer, K. *Arch. Pharmaz.* **1975**, *81*, 308.
7. Belsky, I. *Tetrahedron* **1972**, *28*, 771.
8. Hünig, S.; Lendle, W. *Chem. Ber.* **1960**, *93*, 913.
9. Compound **3a**: mp 119–120°C; elemental analysis: calcd for $C_{11}H_{12}O_2$: C, 74.97; H, 6.86. Found: C, 74.92; H, 6.73. ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 2.05$–2.15 (m, 4H), 2.70–2.78 (m, 4H), 2.81–2.89 (m, 4H). **3b**: mp 64–65°C; elemental analysis: calcd for $C_{12}H_{14}O_2$: C, 75.76; H, 7.42. Found: C, 75.63; H, 7.44. ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 1.59$–2.10 (m, 6H), 2.40–2.58 (m, 4H), 2.65–2.85 (m, 4H). **3c**: mp 109–110°C; elemental analysis: calcd for $C_{16}H_{14}O_2$: C, 80.65; H, 5.92. Found: C, 80.45; H, 5.80. ^{1}H NMR (400 MHz, CD_3COCD_3): $\delta = 2.65$–2.78 (m, 4H), 2.82–3.08 (m, 4H), 3.20–3.33 (m, 2H), 7.32–7.85 (m, 4H). **3b′**: mp 64–65°C; elemental analysis: calcd for

$C_{12}H_{14}O_2$: C, 75.76; H, 7.42. Found: C, 75.83; H, 7.52. **3d**: mp 126.5–127°C; elemental analysis: calcd for $C_{13}H_{16}O_2$: C, 76.44; H, 7.90. Found: C, 75.94; H, 7.89. ^{1}H NMR (400 MHz, CDCl$_3$): $\delta = 1.66$–1.83 (m, 8H), 2.44–2.47 (m, 4H), 2.49–2.53 (m, 4H). **3e**: mp 62–63°C; elemental analysis: calcd for $C_{14}H_{18}O_2$: C, 77.03; H, 8.31. Found: C, 77.09; H, 8.44. ^{1}H NMR (400 MHz, CDCl$_3$): $\delta = 1.25$ (d, $J = 6.8$, 3H), 1.64–1.78 (m, 8H), 2.41–2.55 (m, 6H), 2.66–2.79 (m, 1H). **3f**: mp 117–118°C; elemental analysis: calcd for $C_{17}H_{16}O_2$: C, 80.92; H, 6.39. Found: C, 81.01; H, 6.35. ^{1}H NMR (400 MHz, CDCl$_3$): $\delta = 1.68$–1.94 (m, 4H), 2.46–2.72 (m, 4H), 2.79–2.92 (m, 4H), 7.15–7.80 (m, 4H).

10. Compound **4d**: mp 178–180°C; elemental analysis: calcd for $C_{13}H_8O_2$: C, 79.58; H, 4.11. Found: C, 79.75; H, 4.11. ^{1}H NMR (400 MHz, CDCl$_3$): $\delta = 7.37$–8.36 (m, 8H).