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REACTION OF CONJUGATED ENONES WITH tert-BUTYLDIMETHYLSILYL TRIFLATE AND INTRAMOLECULAR ANNELATION

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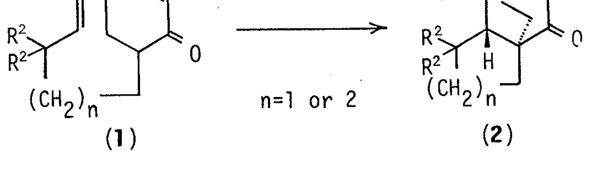
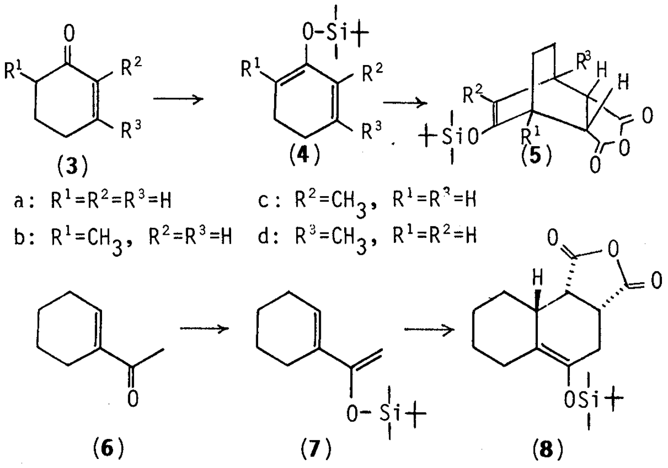
Reaction of 2-cyclohexen-1-ones (**3a-c**) with tert-butyldimethylsilyl triflate and triethylamine gave selectively cross-conjugated dienol ethers (**4a-c**) except 3-methyl-2-cyclohexen-1-one (**3d**). Reaction of 6-(5-ethoxycarbonyl-3,3-dimethyl-4-pentenyl-1)-2-cyclohexen-1-one (**10**) under the same reaction conditions gave rise to annelation affording to tricyclo[5.2.2.0^{1,5}]undecenes (**11**) along with the through-conjugated dienol ether (**12**).

KEYWORDS ——intramolecular double Michael reaction; tert-butyldimethylsilyl triflate; cross-conjugated dienol silyl ether; tricyclo[5.2.2.0^{1,5}]undecene

In the course of our study on the intramolecular double Michael reaction,[1,2] we were interested in the generation of the cross-conjugated silyl dienol ethers from conjugated enones. It is known that such dienes are useful substrates for the Diels-Alder reaction.[3] The formation of cross-conjugated dienolate anions by α'-deprotonation of enones with lithium dialkylamides under kinetically controlled conditions, followed by silylation, is a useful method for the regioselective formation of 2-silyloxy-1,3-dienes from conjugated enones.[4-6] When the reaction was applied to the α,β-unsaturated enone esters (**1**), the double Michael reaction occurred spontaneously affording, in highly stereoselective manner, the tricyclic compound (**2**).[1] We further studied the reaction of conjugated enones with tert-butyldimethylsilyl triflate in the presence of triethylamine[7,8] and here report the findings.



Reaction of 2-cyclohexen-1-ones (**3a-c**) and 1-acetyl-1-cyclohexene (**6**) with 1.1 mole equivalent of *tert*-butyldimethylsilyl triflate and 1.5 mole equivalent of triethylamine in dichloromethane for 5 min at ambient temperature produced quantitatively 2-silyloxy-1,3-dienes (**4a-c**)9) and (**7**),9) respectively. The structures of the products were determined by ^{1}H-NMR spectroscopy5-7) and the Diels-Alder reaction with maleic anhydride. The cycloaddition was carried out in dichloromethane for 16∼24 h at ambient temperature to give the adducts (**5a-c**)9) and (**8**)9) in 74%, 77%, 83%, and 82% overall yields from the corresponding enones, respectively. The endo structures of the the products, each obtained as a single isomer, were deduced on consideration of the reaction mechanism. The formation of the silyl enol ethers (**5a-c**) by the cycloaddition suggested the structure of the cross-conjugated dienol ether, since the through-conjugated dienol ether would give the bicyclo[2.2.2]octane having the silyloxy group at the angular position. On the other hand, 3-methyl-2-cyclohexen-1-one (**3d**) gave a mixture of **4d** and **9**7,9) in a ratio of 5 : 6 under the same reaction conditions as above. Treatment of the mixture with maleic anhydride in dichloromethane for 20 h at room temperature afforded the single adduct (**5d**)9) in 40% overall yield from **3d**.



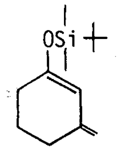
(**3**) (**4**) (**5**)

a: $R^1=R^2=R^3=H$ c: $R^2=CH_3$, $R^1=R^3=H$

b: $R^1=CH_3$, $R^2=R^3=H$ d: $R^3=CH_3$, $R^1=R^2=H$

(**6**) (**7**) (**8**)

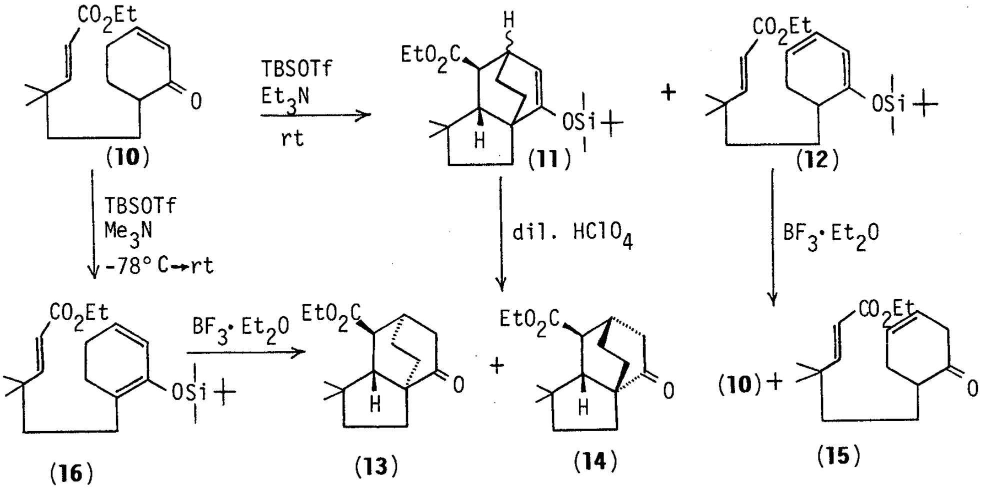
The above method offers a convenient way to synthesize the rather stable cross-conjugated silyl dienol ether by the simple manipulation performed under mild and not so strict anhydrous conditions as in the case of lithium dialkylamide and the silyl chloride.



(**9**)

Surprisingly, when the reaction was applied to 6-(5-ethoxycarbonyl-3,3-dimethyl-4-pentenyl-1)-2-cyclohexen-1-one (**10**),2) two diastereoisomers of the tricyclic compound (**11**) were created. Namely, the reaction of **10** with 1.1 mole equivalent of *tert*-butyldimethylsilyl triflate and 1.5 mole equivalent of triethylamine in dichloromethane for 5 min at ambient temperature formed three products. After medium pressure chromatography on silica gel, tricyclo[5.2.2.0^{1,5}]undecene (**11**)9) was obtained in 37% yield as a mixture of two stereoisomers in the ratio of about 3 : 2 along with the through-conjugated silyl dienol ether (**12**)9) in 45% yield. Treatment of the mixture (**11**) with 10% perchloric acid in tetrahydrofuran for 1 h at ambient temperature, followed by chromatographic separation, gave two ketones (**13**)2) and (**14**)9) in 55% and 33% yields, respectively. On the reaction of boron trifluoride etherate with **12** in dichloromethane for 1 h at room temperature, the conjugated enone (**10**) and the deconjugated enone (**15**)$^{9)}$ were obtained in 54% and 45% yields, respectively.

The formation of the tricyclo[5.2.2.0^{1,5}]undecenes (**11**) could be regarded as an intramolecular double Michael reaction catalyzed by tert-butyldimethylsilyl triflate. The intramolecular Diels-Alder reaction of the cross-conjugated dienol ether could be ruled out for the following reason. The reaction of **10** with tert-butyldimethylsilyl triflate in the presence of excess trimethylamine in dichloromethane at -78°C for 6 h and at room temperature for 1 h gave the cross-conjugated dienol ether (**16**).$^{9)}$ No formation of **11** and **12** was detected on the basis of ^{1}H-NMR analysis. The silyl ether (**16**) was isolated in 37% yield along with the starting enone (**10**) and converted into the mixture of **13** and **14** in low yield when treated with boron trifluoride etherate.



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9) All new compounds gave satisfactory IR ($CHCl_3$), ^{1}H-NMR ($CDCl_3$), MS and high-resolution MS data. Characteristic data are recorded as follows. **4a**, ^{1}H-NMR δ:0.10(6H, s), 1.00(9H, s), 2.10 - 2.30(4H, m), 4.80(1H, m, C_1-H), 5.70 - 5.90(2H, m, C_3- and C_4-H). **4b**, ^{1}H-NMR δ:0.10(6H, s), 0.90(6H, s), 1.65(3H, s), 2.10(4H, br s), 5.60(2H, m, C_3 and C_4-H), **4c**, ^{1}H-NMR δ:0.10(6H, s), 0.90(9H, s), 1.08(3H, br s), 2.10(4H, br s), 4.80(1H, m, C_1-H), 5.55(1H, m, C_4-H). **4d**, ^{1}H-NMR δ:0.10(6H, s), 0.85(9H, s), 1.80(3H, br s), 4.66(1H, m), 5.40(1H, m). **9**, ^{1}H-NMR δ:0.15(6H, s), 0.91(9H, s), 4.50(2H, s), 5.44(1H, s). **7**, ^{1}H-NMR δ:0.13(6H, s), 0.93(9H, s), 1.43 - 1.83(4H, m), 1.96 - 2.26(4H, m), 4.05 and 4.20(each 1H, each s, $=CH_2$), 6.10(1H, m, C_2-H). **5a**, IR νmax: 1870, 1780(C=O), 1635 cm^{-1}(C=C); ^{1}H-NMR δ:4.96(1H, dd, J=1 and 7 Hz). **5b**, mp 122 - 126°C; IR νmax: 1860, 1780(C=O), 1625 cm^{-1}(C=C); ^{1}H-NMR δ: 4.90(1H, d, J=7 Hz). **5c**, mp 86.5 - 87.5°C; IR νmax: 1865, 1785(C=O), 1675 cm^{-1}(C=C); ^{1}H-NMR δ: 1.60(3H, s). **5d**, mp 112 - 113.5°C; IR νmax: 1865, 1780(C=O), 1635 cm^{-1}(C=C); ^{1}H-NMR δ: 1.45(3H, s), 4.60(1H, d, J=1 Hz). **8**, mp 89 - 91°C; IR νmax: 1860, 1782(C=O), 1685 cm^{-1}(C=C). **11**, IR νmax: 1720(C=O), 1625 cm^{-1} (C=C); ^{1}H-NMR δ : 0.10(6H, s), 0.90(9H,s), 3.80 - 4.20(2H, m), 4.70 and 4.90(1H, each d, each J=6 Hz). **12**, IR νmax: 1700(C=O), 1640 cm^{-1}(C=C); ^{1}H-NMR δ:0.10(6H, s), 0.86(9H, s), 0.96(6H, s), 1.15(3H, t, J=7 Hz), 4.00(2H, q, J=7 Hz), 4.85(1H, d, J=6 Hz), 5.10-5.70(2H, m), 5.46(1H, d, J=16 Hz), 6.67(1H, d, J=16 Hz). **14**, IR νmax: 1725, 1720 cm^{-1}(C=O); ^{1}H-NMR δ: 0.66(3H, s), 0.94(3H, s), 1.27(3H, t, J=7 Hz), 4.16(2H, q, J=7 Hz). **15**, IR νmax: 1708 - 1715 cm^{-1}(C=O); ^{1}H-NMR δ:1.10(6H, s), 1.30(3H, t, J=6.5 Hz), 2.80(2H, br s), 4.05(2H, q, J=6.5 Hz), 5.57(1H, d, J=15 Hz), 5.70(2H, br s), 6.73(1H, d, J=15 Hz). **16**, IR νmax: 1710(C=O), 1645 cm^{-1}(C=C); ^{1}H-NMR δ: 0.10(6H, s), 0.96(9H, s), 1.10(6H, s), 1.32(3H, t, J=7 Hz), 4.13(2H, q, J=7 Hz), 5.60(1H, d, J=16 Hz), 5.62(2H, br s), 6.80(1H, d, J=16 Hz).

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