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DIENE-TRANSMISSIVE DIELS-ALDER REACTION OF A NEW CROSS-CONJUGATED TRIENE: SELECTIVE FORMATION OF MONO- AND BIS-CYCLOADDUCT

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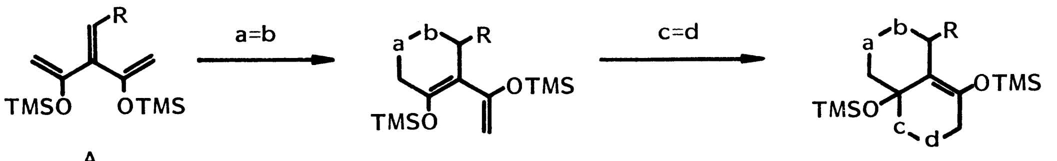
A new activated cross-conjugated triene, 3-(methoxymethylene)-2,4-bis(trimethylsilyloxy)-1,4-pentadiene, was prepared. Its reactions with acetylenic dienophiles resulted in the exclusive formation of mono-cycloadducts, while in the reactions with cyclic olefinic dienophiles such as maleimides and maleic anhydride the mono- and bis-adducts were obtained depending upon the amounts of dienophiles.

The diene-transmissive Diels-Alder reaction of cross-conjugated triene consists of two consecutive cycloaddition reactions, the first one of which offers a diene functionality to the second.1) Of great use as a new synthetic tool is the cross type of diene-transmissive Diels-Alder reaction in which two different dienophiles are orderly incorporated in the bis-cycloadduct. However, the reaction of 3-benzylidene-2,4-bis(trimethylsilyloxy)-1,4-pentadiene A (R=Ph) as a cross-conjugated triene has formed the bis-cycloadduct as a major product even when excess of the triene is used,1) indicating that the newly formed diene of mono-cycloadduct B (R=Ph) is more highly activated by the two silyloxy substituents than either of two dienes in the starting triene. The cross type of diene-transmissive Diels-Alder reaction may be achieved by the use of a new cross-conjugated triene A with a diene-activating substituent (e.g. R=OMe): The first cycloaddition reaction with a dienophile a=b is accelerated by the substituent R leading to the predominant formation of mono-cycloadduct B that then reacts with another dienophile c=d to give the cross bis-cycloadduct C.



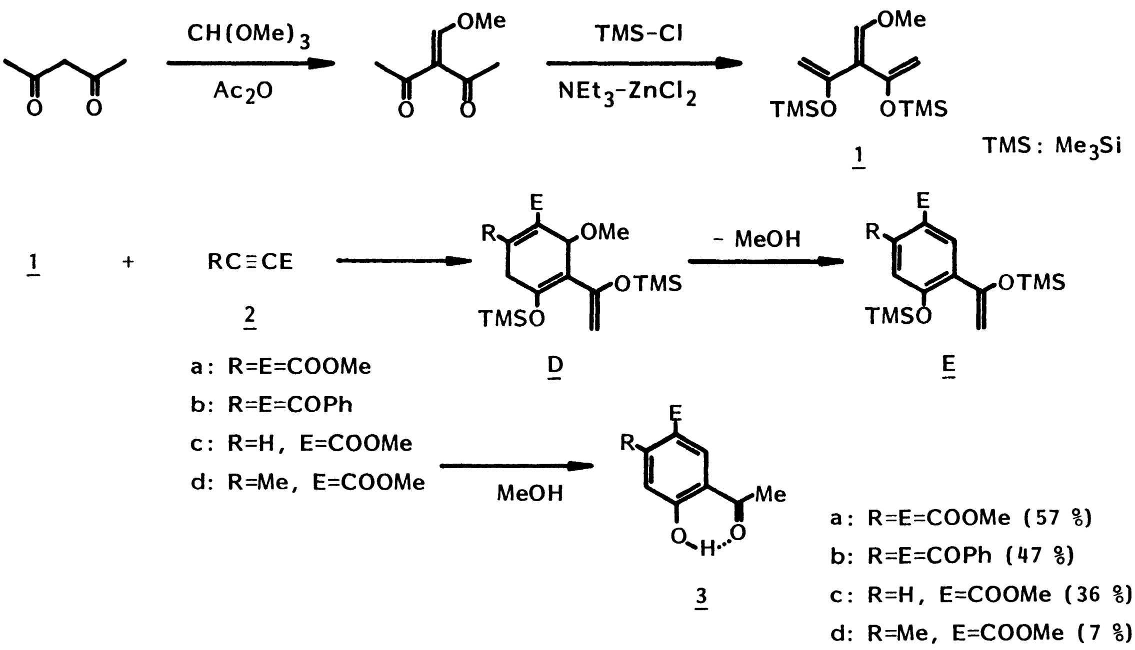
A B C

Cross bis-cycloadduct

R : diene-activating substituent
a=b: the first dienophile
c=d: the second dienophile

In order to open the way to the cross type of diene-transmissive Diels-Alder reaction, a new activated cross-conjugated triene, 3-(methoxymethylene)-2,4-bis(trimethylsilyloxy)-1,4-pentadiene 1, was synthesized and its cycloaddition reactions with acetylenic and olefinic dienophiles were first investigated. The reactions with acetylenes exclusively produced the mono-aduucts, while the mono-and bis-adducts were selectively obtained in the reactions with cyclic olefins depending upon the amounts of dienophiles used.

The activated triene 1 was prepared by the trimethylsilylation of 3-(methoxymethylene)-2,4-pentanedione[2] which is readily available from 2,4-pentanedione and methyl orthoformate: The methoxymethylenepentanedione (0.03 mol) and chlorotrimethylsilane (0.12 mol) were heated in dry benzene at 40-50 °C for 24 h in the presence of triethylamine (0.13 mol) and zinc chloride (0.002 mol), the salt precipitated was filtered off, and the filtrate was distilled under a reduced pressure to give a colorless liquid (bp 72 °C/1.8 mmHg) in 82% yield. The triene 1 can be stored safely in the absence of moisture.



Scheme 1.

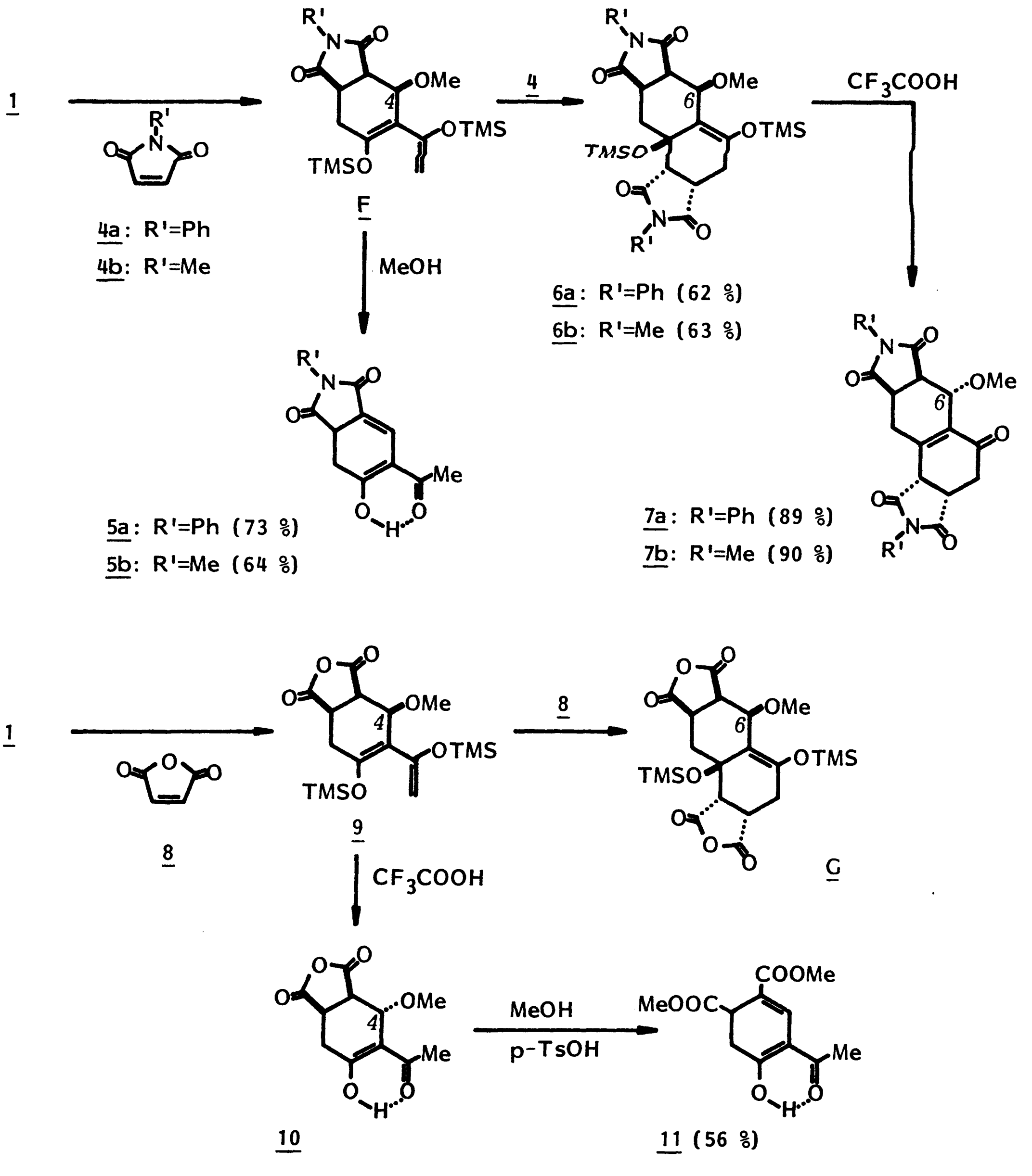
The reaction of 1 with two equivalents of dimethyl acetylenedicarboxylate 2a in benzene at room temperature for 24 h and the work up with methanol afforded the mono-adduct 3a (mp 77 °C) whose structure was determined on the basis of the spectral data as well as the elemental analysis.[3,4] The exclusive formation of mono-adduct 3a is very much contrast to the predominant formation of bis-adduct in the reaction of phenyl-substituted triene A (R=Ph).[1a] This reaction involves the formation of mono-cycloadduct D, the methanol elimination induced by aromatization of D leading to E, and finally the desilylation of E into the isolated product 3a (Scheme 1). The ^{1}H-NMR analysis of the above reaction showed that both the intermediates D and E were actually participating in the reaction, and that the methanol elimination from D occurred even at room temperature.

The similar reactions with dibenzoylacetylene 2b, methyl propiolate 2c, and methyl 2-butynoate 2d under reflux in benzene (24 h for 2b, 48 h for 2c and 2d) gave the corresponding mono-adducts 3b (mp 189-190 °C), 3c (mp 99-99.5 °C), and 3d (mp 70 °C), no trace of bis-adducts having been formed in all cases. The high regioselectivity in the reactions with unsymmetrical acetylenes 2c and 2d is comparable to that reported previously.[1a]

The reaction of 1 with an equivalent of N-phenylmaleimide 4a in dry benzene at room temperature for 20 h and the treatment with methanol precipitated the mono-adduct 5a (mp 227 °C) whose structure was confirmed by the spectral data.[5] This product 5a was also accompanied with the elimination of methanol. On the other hand, the reaction with two equivalents of 4a at 50 °C for 20 h and the addition of hexane to the mixture precipitated the bis-cycloadduct 6a (mp 188-190 °C) which was then desilylated into the bis-adduct 7a (mp 148-150 °C) with a catalytic amount of trifluoroacetic acid in benzene (Scheme 2). The stereochemical assignment of 6a was based on the high stereoselectivity of the reaction of phenyl-substituted triene A (R=Ph) with olefinic dienophiles,[1b] the high endo selectivity observed in the cross type of reaction of 1,[6] as well as the spectral data.[7] During the desilylation of 6a, the configuration at the 6-position was inverted giving the thermodynamically more stable bis-adduct 7a,[8] whose structure was confirmed by the spectral data,[9] probably through an elimination-addition mechanism.

Similarly the mono-adduct 5b (mp 186 °C), bis-cycloadduct 6b (mp 185-187 °C), and bis-adduct 7b (mp 180-182 °C) were obtained in the reactions of 1 with N-methylmaleimide 4b.

Maleic anhydride 8 was found so reactive toward 1 that the reaction with an equivalent of 1 without solvent was completed in a few minutes at room temperature, the mono-cycloadduct 9 (bp 180 °C/1 mmHg (bulb-to-bulb)) being isolated by a vacuum distillation. The treatment of 9 with trifluoroacetic acid in benzene gave the desilylated anhydride 10 (mp 117-118 °C) in which the configuration at the 4-position was again inverted. As both the mono-cycloadduct 9 and the desilylated adduct 10 have an



Scheme 2.

anhydride ring which tends to open up in the presence of moisture or protic solvent, the anhydride 10 was esterified into the stable diester 11 (mp 92-92.5 °C). This compound 11 was also obtained directly from the esterification of the reaction mixture between 1 and 8 in 56% yield. The structures of 9, 10, and 11 were determined on the basis of the spectral data.[10] Although the reaction of 1 with two equivalents of 8 formed the bis-cycloadduct G, its purification as well as the conversion into a more stable derivative was unsuccessful.[11]

As a conclusion, in the reactions with the triene 1 acetylenic dienophiles afford only the mono-adducts since the elimination of methanol from the mono-cycloadduct occurs faster than the second cycloaddition reaction. On the other hand, cyclic olefinic dienophiles provide both the mono- and bis-cycloadducts depending upon the amount of dienophile, showing that the cross type of diene-transmissive Diels-Alder reaction will be realized by employing these olefins as the first dienophiles.

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References

1) a) O. Tsuge, E. Wada, and S. Kanemasa, Chem. Lett., 1983, 239; b) O. Tsuge, E. Wada, and S. Kanemasa, Chem. Lett., 1983, 1525.

2) L. Claisen, Justus Liebigs Ann. Chem., 297, 1 (1897).

3) All the new compounds reported herein provided satisfactory elemental analyses.

4) 3a: IR (KBr) 1720, 1645 cm^{-1} (C=O); ^{1}H-NMR ($CDCl_3$) δ2.67 (3H, s, MeCO), 3.87, 3.90 (each 3H, s, OMe), 7.02, 8.27 (each 1H, s, ArH), 12.50 ppm (1H, s, OH); Mass m/e 252 (M^+).

5) 5a: IR (KBr) 1765, 1710-1610 cm^{-1} (C=O, C=C); ^{1}H-NMR ($CDCl_3$) δ2.25 (3H, s, MeCO), 2.64 (1H, dd, J=16.2, 14.4 Hz, CH_2), 3.07 (1H, dd, J=16.2, 7.1 Hz, CH_2), 3.73 (1H, ddd, J=14.4, 7.1, 2.4 Hz, CH), 7.20-7.50 (6H, m, ArH, =CH), 16.00 ppm (1H, s, OH); Mass m/e 283 (M^+).

6) O. Tsuge, S. Kanemasa, H. Sakoh, and E. Wada, Chem. Lett., 1984, the following paper.

7) 6a: IR (KBr) 1775, 1705 (C=O), 1250, 845 cm^{-1} (Me_3Si); ^{1}H-NMR ($CDCl_3$) δ0.19, 0.25 (each 9H, s, Me_3Si), 2.48-3.80 (8H, m, CH_2, CH), 3.20 (3H, s, OMe), 4.91 (1H, d, J=3.5 Hz, 6-H), 7.00-7.52 ppm (10H, m, ArH); Mass m/e 632 (M^+).

8) The Dreiding model inspection shows the compound 7a would be less hindered than the iosmer with the other configuration at the 6-position.

9) 7a: IR (KBr) 1775, 1720-1660 cm^{-1} (C=O); ^{1}H-NMR ($CDCl_3$) δ2.45-3.92 (8H, m, CH_2, CH), 3.12 (3H, s, OMe), 5.10 (1H, d, J=4.0 Hz, 6-H), 7.10-7.60 ppm (10H, m, ArH); Mass m/e 470 (M^+).

10) 9: IR (neat) 1860, 1785 (C=O), 1250, 850 cm^{-1} (Me_3Si); ^{1}H-NMR ($CDCl_3$) δ0.24 (18H, s, Me_3Si), 2.48 (1H, dd, J=16.5, 10.0 Hz, CH_2), 2.85 (1H, dd, J=16.5, 7.5 Hz, CH_2), 3.12 (1H, dd, J=10.0, 3.5 Hz, 3a-H), 3.17 (3H, s, OMe), 3.47 (1H, ddd, J=10.0, 10.0, 7.5 Hz, 7a-H), 4.37, 4.63 (each 1H, d, J=1.0 Hz, $=CH_2$), 4.65 ppm (1H, d, J=3.5 Hz, 4-H); Mass m/e 384 (M^+).

10: IR (KBr) 1850, 1785, 1770, 1600 cm^{-1} (C=O); ^{1}H-NMR ($CDCl_3$) δ2.20 (3H, s, MeCO), 2.54 (1H, dd, J=16.5, 9.0 Hz, CH_2), 2.96 (1H, dd, J=16.5, 8.0 Hz, CH_2), 3.14 (3H, s, OMe), 3.26 (1H, dd, J=11.0, 3.0 Hz, 3a-H), 3.61 (1H, m, 7a-H), 4.70 (1H, d, J=3.0 Hz, 4-H), 15.80 ppm (1H, s, OH); Mass m/e 240 (M^+).

11: IR (KBr) 1725, 1690, 1610 cm^{-1} (C=O); ^{1}H-NMR ($CDCl_3$) δ2.14 (3H, s, MeCO), 2.71 (1H, dd, J=17.5, 7.0 Hz, CH_2), 2.94 (1H, dd, J=17.5, 3.2 Hz, CH_2), 3.64, 3.77 (each 3H, s, COOMe), 3.94 (1H, dd, J=7.0, 3.2 Hz, CH), 7.54 (1H, s, =CH), 15.94 ppm (1H, s, OH); Mass m/e 254 (M^+).

11) The reaction mixture obtained from 1 and two equivalents of 8 in deuteriobenzene (at 40 °C for 4 h) showed the clear ^{1}H-NMR spectrum of bis-cycloadduct G: δ3.00 (s, OMe), 4.75 ppm (d, J=3.5 Hz, 6-H).

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