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REACTION OF 4-METHYL-1,2,4-TRIAZOLINE-3,5-DIONE WITH DI AND TRI-SUBSTITUTED STYRENES

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Abstract

2,4,6-Triisopropylstryrene was synthesized in a single step via the Witting Reaction from the corresponding aldehyde. The reaction of three styrene's derivatives, 2,6-dimethylstyrene, 2,4,6-trimethylstyrene, and 2,4,6-triisopropylstyrene with 4-methyl-1,2,4-triazoline-3,5-dione (MeTD) was investigated. These reactions are instantaneous at room temperature and lead to the formation of 2:1 adducts in high yield via double Diels-Alder reactions. In each case the initially formed 1:1 Diels-Alder adduct is extremely reactive, and was not isolated. It readily undergoes the second Diels- Alder reaction with MeTD. These 2:1 adducts weie fully characterized by IR, ^{13}CNMR (off- resonace, INEPT, multiplicity determination sequence techniques), mass spectra, ^{1}HNMR and elemental analysis.

Introduction

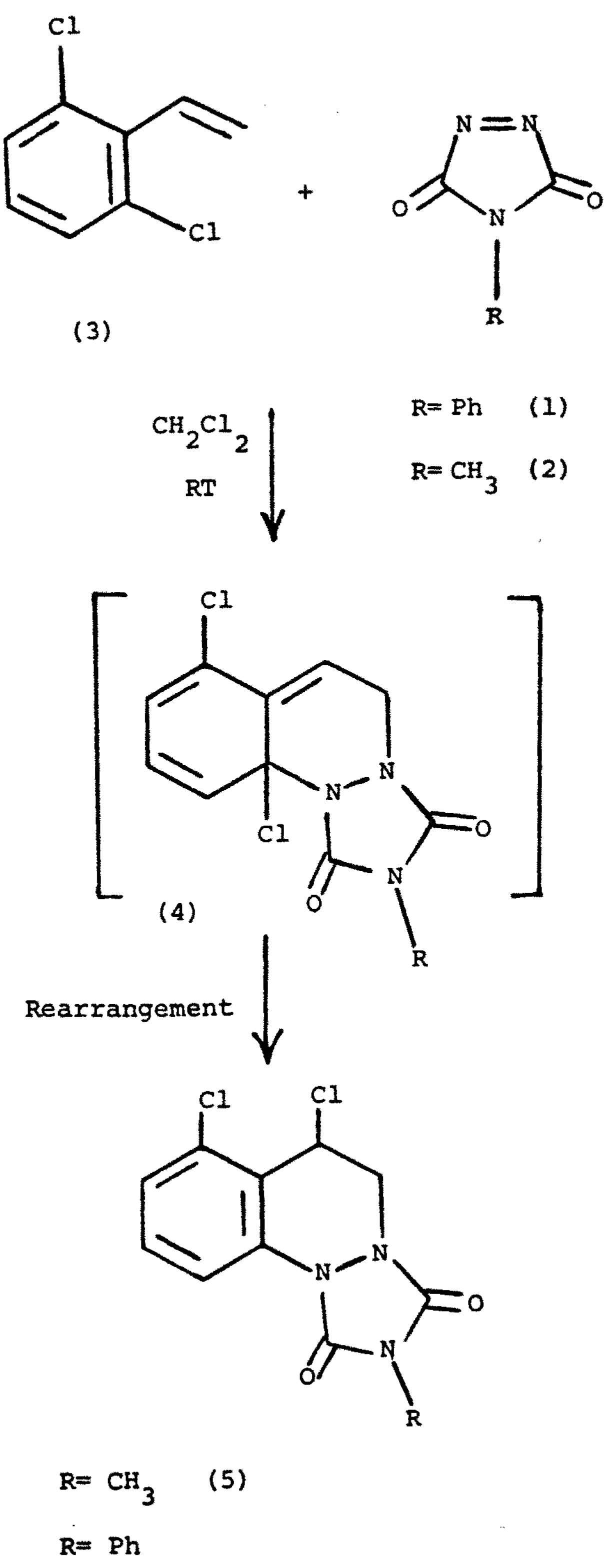
Triazolinediones are extremely reactive dienophiles [1-9] and enophiles [6,9-14] which readily undergo Diels-Alder and Ene reactions with suitable dienes as well as alkenes.

The reaction of PhTD (4- phenyl- substituted 1,2,4-triazoline-3,5-dione) (1) with styrene at room temperature was reported to yield a double Diels-Alder adduct [2]. However, a reinvestigation of this reaction by G.B. Butler and coworkers [15] demonstrated that the Diels-Alder Ene adduct was the predominate product in a 2:1 ratio. The reaction of MeTD (4- methyl- substituted 1,2,4-triazoline-3,5-dione) (2) with styrene was also investigated. This reaction leads to the formation of a mixture of double Diels-Alder and Diels-Alder Ene adducts in a 1:2 ratio.

We have reported [16] that PhTD (1) and MeTD (2) undergo reaction with 2,6- dichlorostyrene (3) at room temperature (Scheme I). These reactions are extremely fast at room temperature. The first step of the reaction is the formation of a reactive intermediate (4) via a [4+2] Diels-Alder reaction. The second step is an allylic type rearrangement of chlorine atom which rearomatizes the benzene ring. Although this reactive intermediate (4) can undergo a second Diels- Alder reaction, a double Diels-Alder adduct was not isolated. The structure of adduct (5) was determined via X-ray diffraction analysis of a single crystal.

Keywords: 1,2,4- triazoline- 3,5- dione; Rearrangement

Scheme I



The above results prompted us to examine the reaction of di and tri-alkyl substituted (2,4 and 6 positions) of styrene with MeTD.

Results and Discussion

The reaction of MeTD (2) with 2,6-dimethylstyrene (6) was performed in methylene chloride at room temperature. Upon addition of the pink color solution of MeTD to a methylene chloride solution of 2,6-dimethyl styrene, a colorless solution was formed. At the end of the reaction, solvent was removed and a white solid was obtained. Since this white solid was pure, further purification was not necessary (Scheme II).

The elemental analysis of the white solid is in agreement with 1:2 adducts (9). The first step of the reaction is the formation of reactive intermediate (7) via a [4+2] Diels-Alder reaction. This intermediate further reacts with another molecule of the MeTD to yield the 1:2 adduct (9) by [4+2] Diels- Alder reaction. The intermediate (7) can also undergo an allylic type rearrangement via methyl migration in order to restore the aromatic character to the benzene ring. But, the second Diels-Alder reaction is very fast and such an allylic type rearrangement did not occur.

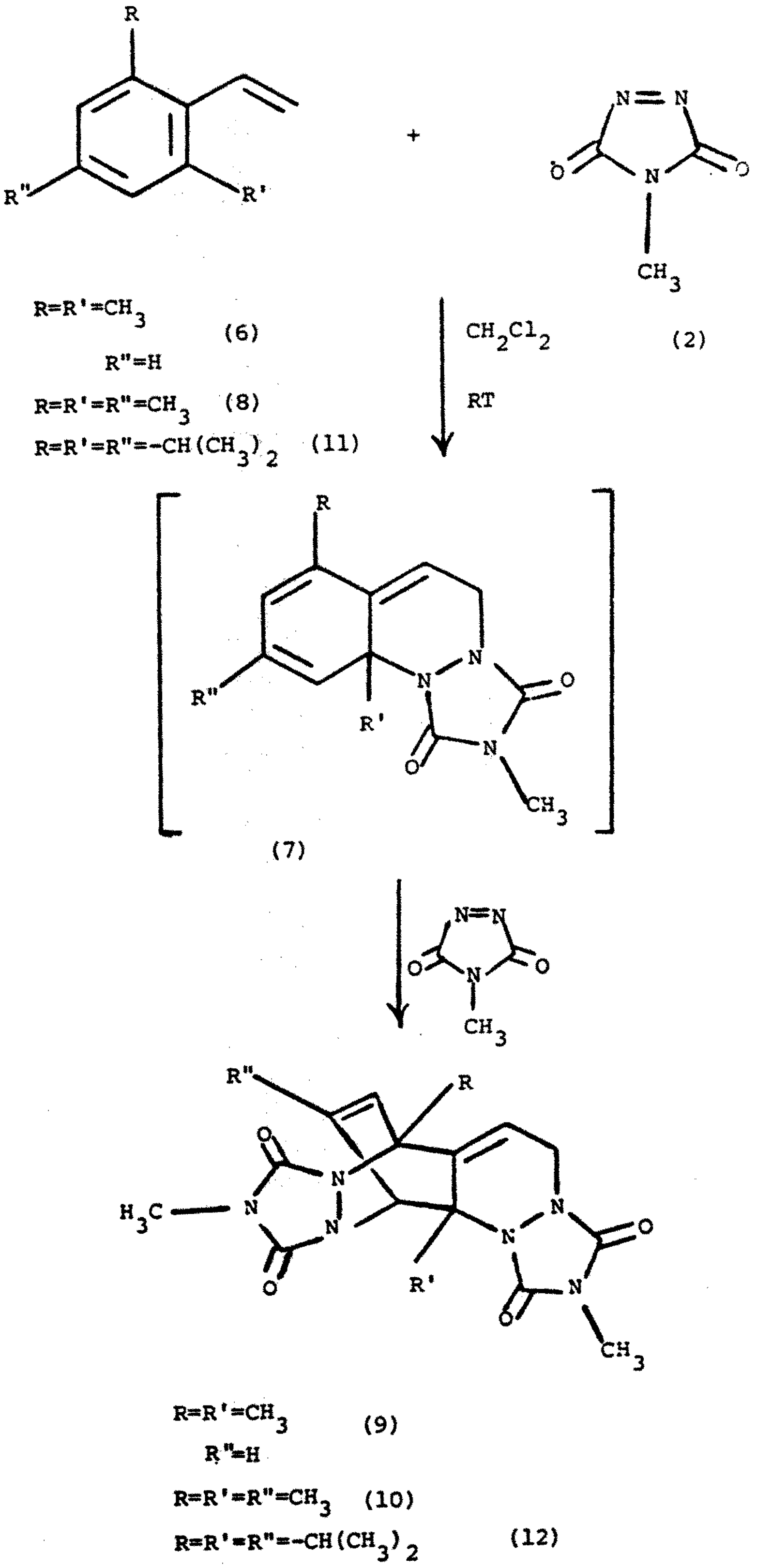
The ^{1}H-NMR spectrum of compound (9) (Fig.1) showed peaks at 1.30, 2.10, 2.96 and 3.10 ppm which were assigned to the four types of CH_3 protons. Peaks at 4.33 ppm (two quartetes) were assigned to the methylene protons. Peaks at 6.38 ppm were assigned to the vinyl and bridge protons.

The ^{13}C-NMR spectrum of compound (9) (Fig.2) showed peaks at 17.30, 20.91, 25.00 and 25.34 ppm which were assigned to the four types of CH_3 carbons. Peaks at 151.81, 153.76, 155.13 and 156.34 ppm were assigned to the four types of carbonyl carbons. All other peaks are in agreement with the proposed structure (9). The off-resonance and multiplicity determination sequence (CH, CH_3, positive; CH_2, C, negative) ^{13}C-NMR spectrum (Fig 2b,c) were used for the assignment of

CH_2, CH and $-\overset{|}{\underset{|}{C}}-$ carbons.

2,4,6-Trimethylstyrene (8) undergoes reaction with MeTD (2) (Scheme II) when a methylene chloride solution of MeTD is added dropwise to a methylene chloride solution of compound (8) (1:1 mole ratio). The

Scheme II



R
R"
R'
+
N=N
O
N
O
CH_3
$R=R'=CH_3$
(6)
R"=H
$R=R'=R"=CH_3$ (8)
$R=R'=R"=-CH(CH_3)_2$ (11)
CH_2Cl_2
RT
(2)
(7)
H_3C
(9)
$R=R'=R"=CH_3$ (10)
$R=R'=R"=-CH(CH_3)_2$ (12)

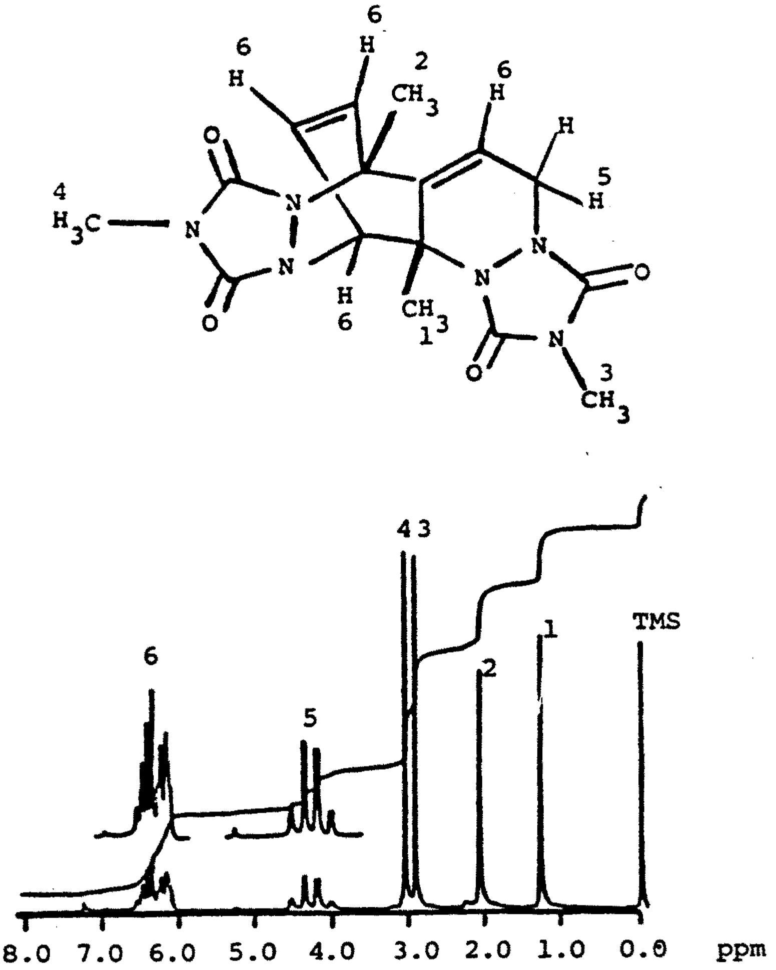


Figure 1. ^{1}H-NMR (100 MHZ) spectrum of compound (9) in $CDCl_3$ at 25°C.

reaction is fast at room temperature and a white solid was obtained after removal of the solvent. Although the reaction was performed based on 1:1 molar ratio, the elemental analysis of the white solid is in agreement with 1:2 adduct (10). This adduct was generated from double Diels-Alder reactions.

The ^{13}C-NMR spectrum of compound (10) (Fig.3) showed peaks at 16.62, 20.08, 20.77, 24.24 and 24.93 ppm which were assigned to the five types of CH_3 carbons. Peaks at 151.66, 153.73, 155.12 and 156.23 ppm were assigned to the four types of carbonyl carbons. All other peaks are in agreement with the proposed structure (10). The off-resonance ^{13}C-NMR (Fig. 3b) was used for the assignment of CH_2, CH and $-\overset{|}{\underset{|}{C}}-$ carbons.

2,4,6-Triisopropylstyrene (11) is not commercially available. This compound has been synthesized [17] by the Grignard reaction of methyl magnesium iodide with 2,4,6-triisopropylbenzaldehyde followed by dehydration of the alcohol on $KHSO_4$. We prepared this compound (10) in a single step via the Witting reaction from the corresponding aldehyde in high yield. Thus methyltriphenylphosphonium bromide was allowed to react with methyllithium in ether solution to give a yellowish suspension. To this suspension, a solution of 2,4,6-triisopropylbenzaldehyde was added dropwise. The product (11) was obtained as a colorless liquid via vacuum distillation.

The ^{1}H-NMR and ^{13}C-NMR spectra (Fig. 4,5) of

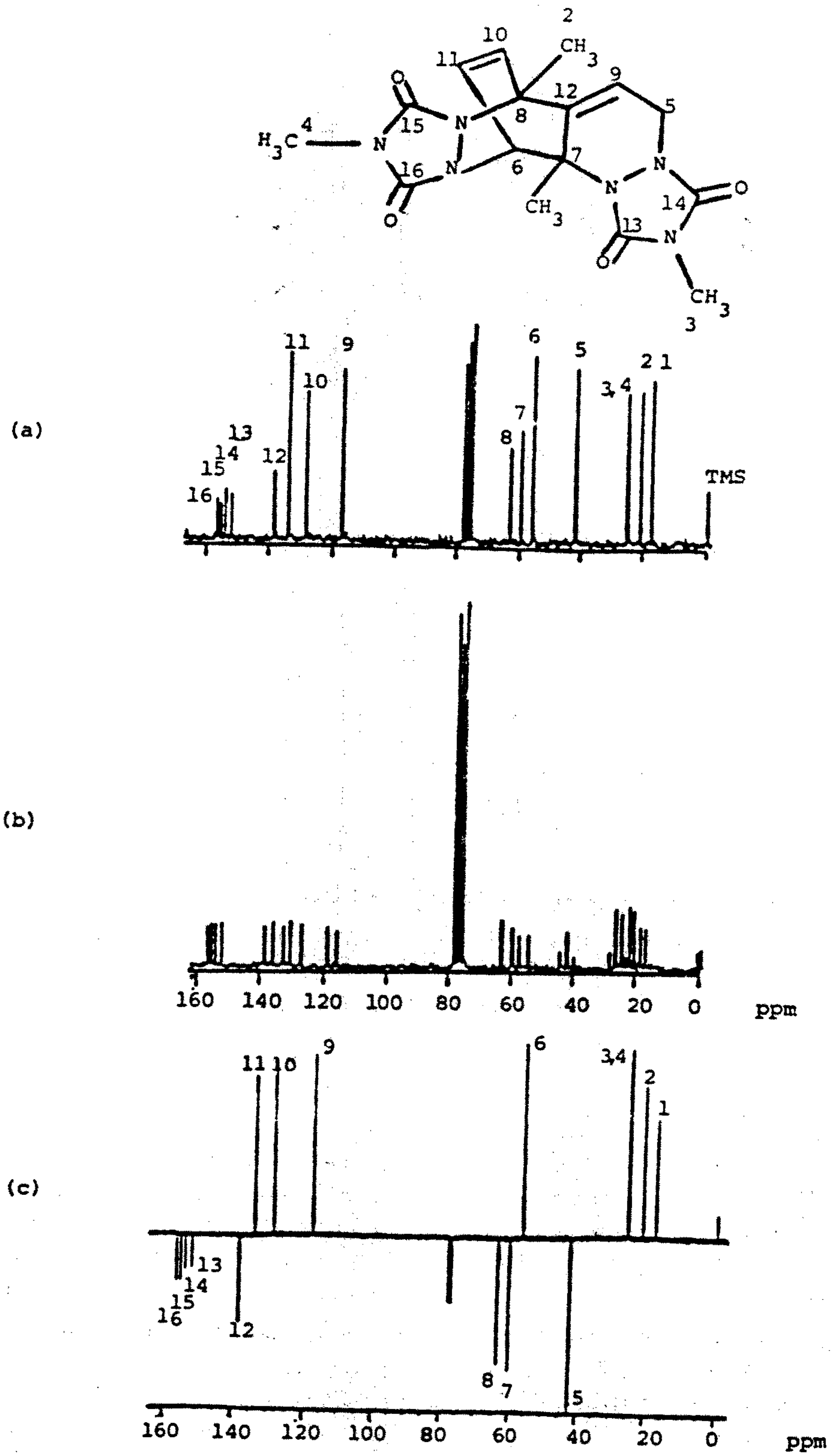


Figure 2. ^{13}C-NMR spectrum of compound (9) in $CDCl_3$ at 25°C. (a) complete decoupled (25 MHZ), (b) off-resonance (25 MHZ), (c) multiplicity determination sequence (CH, CH_3, positive; CH_2, C, negative) (125 MHZ).

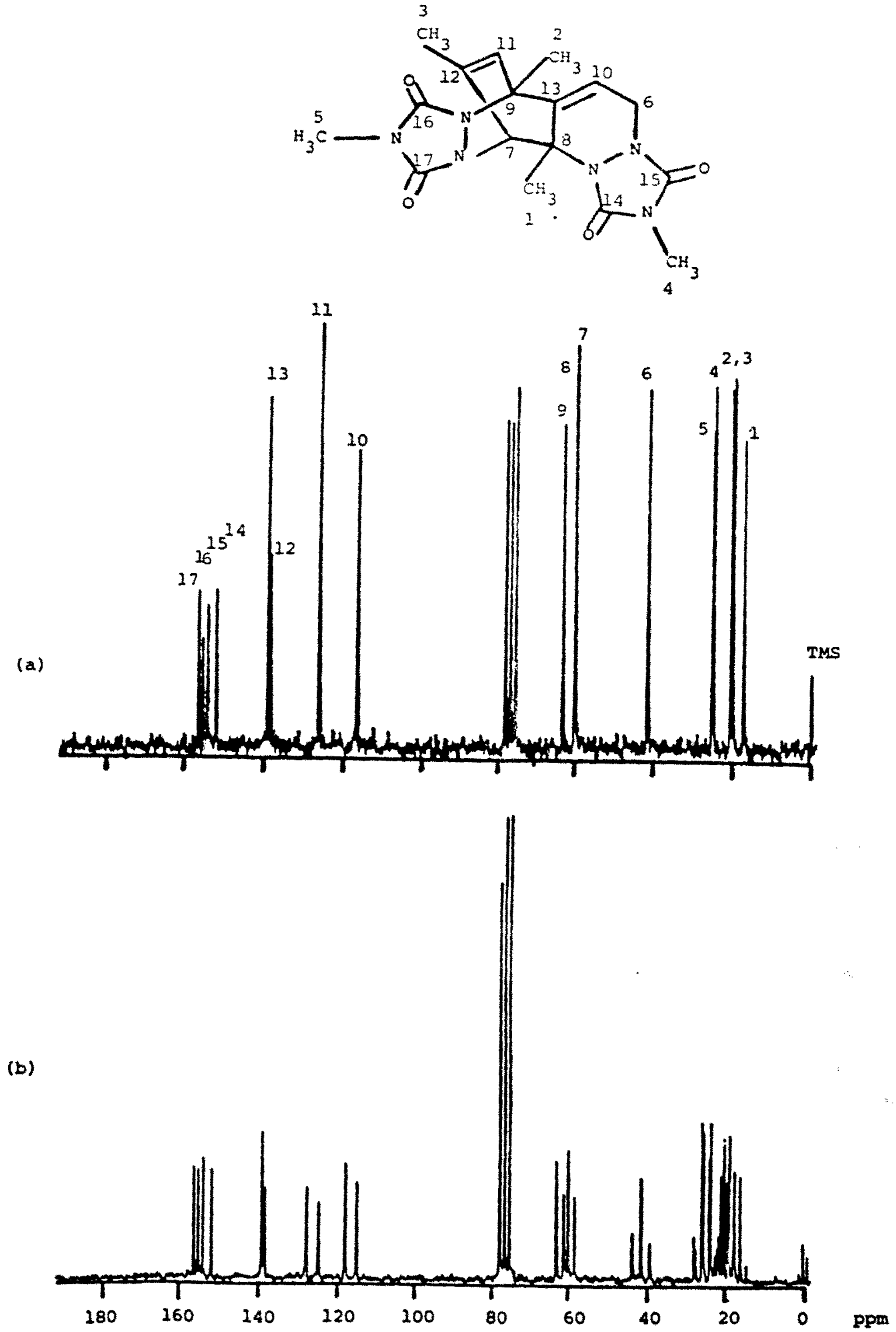


Figure 3. ^{13}C-NMR (25 MHZ) spectrum of compound (10) in $CDCl_3$ at 25°C. (a) complete decoupled, (b) off-resonance.

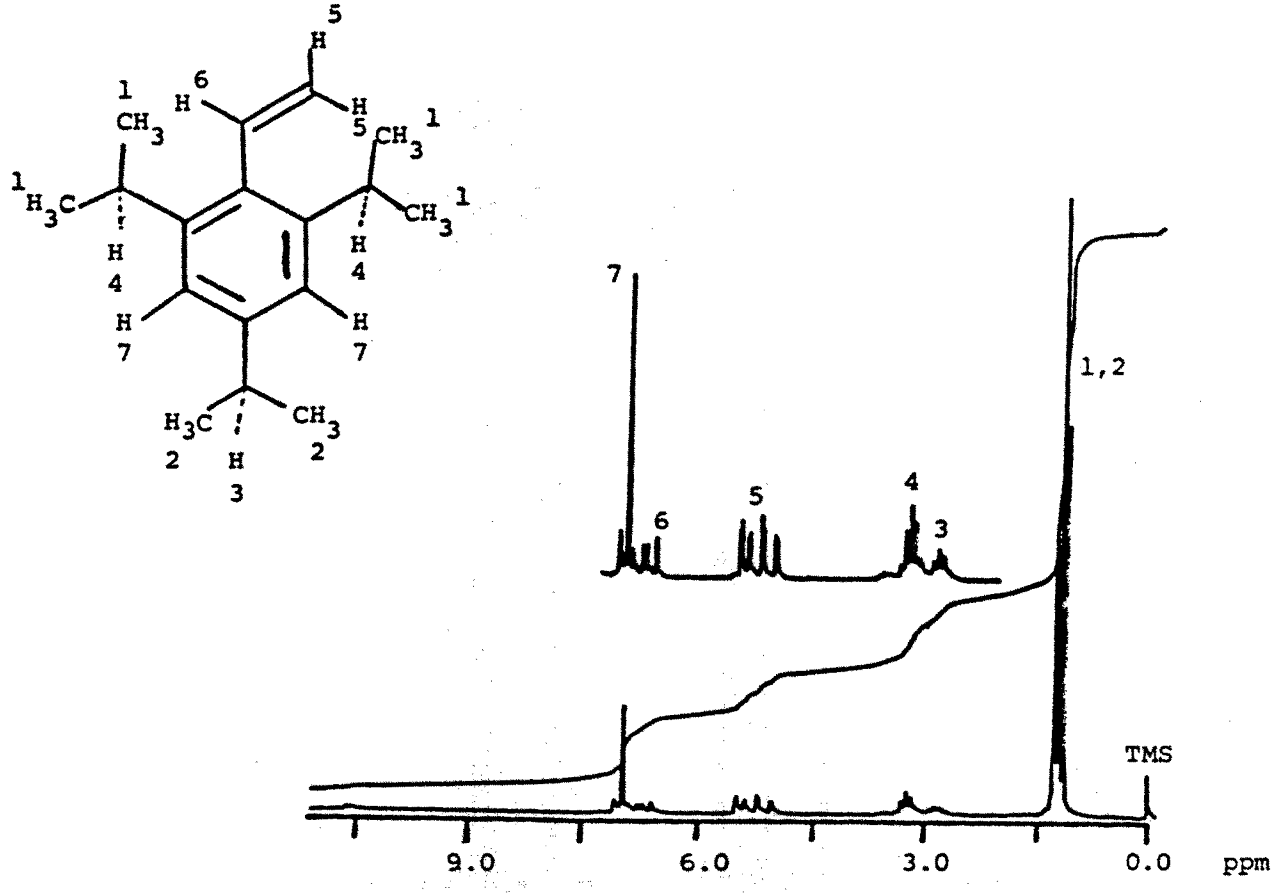


Figure 4. ^{1}H-NMR (100 MHZ) spectrum of 2,4,6- triisopropylstyrene in $CDCl_3$ at 25°C.

compound (11) showed all peaks which are in agreement with the assigned structure (11).

The reaction of 2,4,6-triisopropyl (11) with MeTD (2) was performed in methylene chloride solution at room temperature (1:1 mole ratio). The reaction is very fast and leads to the formation of 1:2 adduct (12) via (4+2) double Diels-Alder reactions. The elemental analysis of compound (12) is in agreement with 1:2 adduct. No allylic type of alkyl rearrangement was observed.

The ^{1}H-NMR spectrum of compound (12) (Fig. 6) showed a multiple peak between 0.76-1.52 ppm which was assigned to the methyl protons of three isopropyl groups. Two single peaks at 2.86 and 3.10 ppm were assigned to the methyl protons attached to the nitrogen atoms. All other peaks are in agreement with the assigned structure (12).

The ^{13}C-NMR spectrum of compound (12) (Fig. 7) showed peaks which are in agreement with the assigned structure (12).

Experimental Section

Materials and Equipment. Reagents were purchased from Fischer Scientific Co. or Aldrich Chemical Co., unless otherwise noted. 2,6-Dimethylstyrene from Polysciences was purified by distillation under reduced pressure of 21 mm Hg b.p. 80-81°C. 2,4,6-Triisopropyl benzene was used without further purification. 2,4,6-Trimethylstyrene was purified by distillation under reduced pressure of 12 mm Hg b.p. 83°C. Deuterated NMR solvent was obtained from Merck & Co., Inc. All solvents used for general application were of reagent grade or ACS grade quality.

4- Methyl-1,2,4-trizzoline-3,5-dione (2) and 2,4, 6-triisopropylbenaldehyde were synthesized according to published procedures [7,18].

All temperatures are uncorrected and are reported in degrees centigrade. Melting points are determined in open capillary tubes using a Thomas-Hoover melting apparatus. Pressure is expressed as millimeters (mm) of mercury. Elemental analysis was performed by Dr. R.

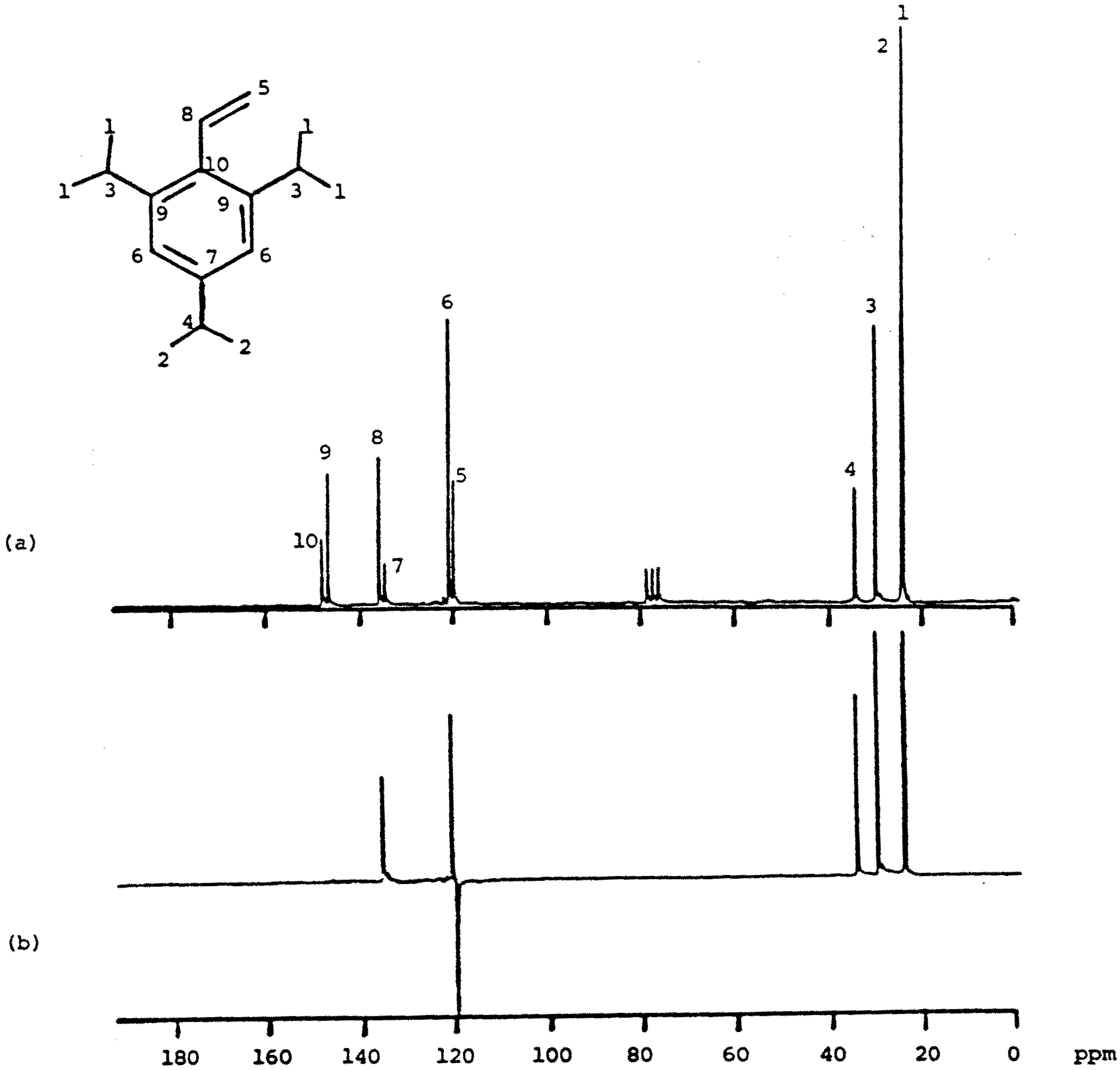


Figure 5. ^{13}C-NMR (25 MHZ) spectrum of 2,4,6- triisopropylstyrene in CDCl$_3$ at 25°C, (a) complete decoupled, (b) inept (CH$_2$, negative; CH$_3$, CH, positive; $-\overset{|}{\underset{|}{C}}-$ supresses).

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Proton nuclear magnetic resonance (NMR) spectra were obtained with a JEOL J NM- fx- 100 spectrometer. Carbon-13 (25.0 MHZ and 75.0 MHZ) spectra were obtained on JEOL J NM- fx- 100 and Nicolet UT- 300 instruments, respectively.

Reaction of MeTD and 2,6-Dimethylstyrene. Into a 250ml round-bottomed flask was placed 4.68 g (0.0354 mol) of 2,6-dimethylstyrene and 40 ml of methylene chloride. The flask was fitted with a magnetic stirring bar and an additional funnel. The stirrer was started and a solution of 2.00 g (0.0177 mol) of MeTD in 100 ml of methylene chloride was added in 15 portions at room

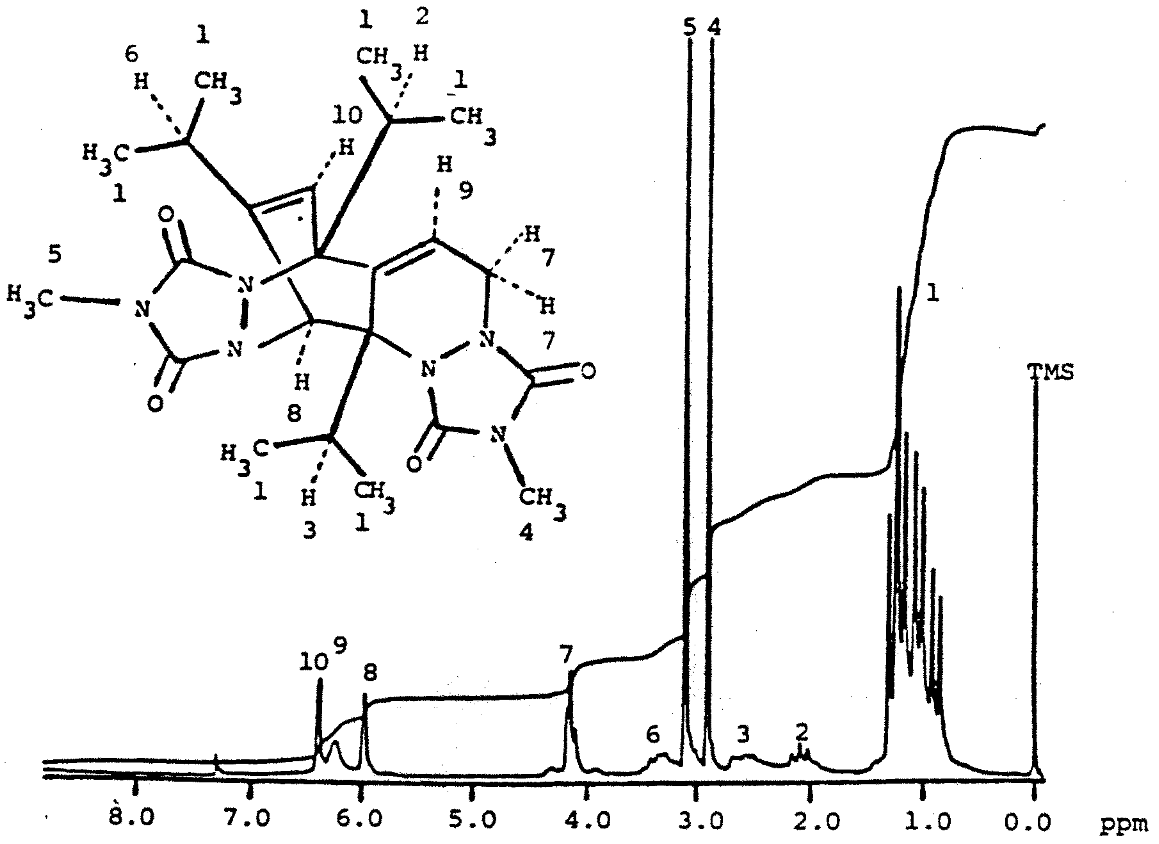

Figure 6. ^{1}H-NMR (100 MHZ) spectrum of compound (12) in $CDCl_3$ at 25°C.

temperature. Each portion was added after complete disappearance of the pink color. The colorless solution was stirred at room temperature for 30 min. At the end of reaction the solvent was removed with a rotary evaporator under vacuum. The white solid obtained was washed with 200 ml of n-hexane, dried in a vacuum oven at 60 °C to give 3.02 g (95.2%) of white solid, m.p. 208°C (d).

^{1}H-NMR ($CDCl_3$, TMS):δ 1.30 (S,3H), 2.10 (S,3H), 2.96 (S,3H), 3.10 (S,3H) 4.33 (q,q,ABX, 2H), 6.38 (m, 4H).

^{13}C-NMR ($CDCl_3$, TMS, int.ref. $CDCl_3$):δ 17.30, 20.91, 25.00, 25.34, 42.06, 56.14, 59.94, 63.45, 117.50, 128.76, 134.17, 138.51, 151.81, 153.76, 155.13, 156.34.

ANAL. Calcd. for $C_{16}H_{18}N_6O_4$: C, 53.62; H, 5.06; N, 23.45. Found: C, 53.36; H, 5.01; N, 23.51.

Mass spectrum calcd m/e for $C_{16}H_{18}N_4O_4$ 358. 1389, obsd, 358.1389.

Reaction of MeTD with 2,4,6-Trimethylstyrene. MeTD (0.72 g, 0.0068 mol) was dissolved in 40 ml of methylene chloride. This pink solution was added dropwise to a solution of 2,4,6-Trimethylstyrene (1.00g, 0.006838 mol) in 20 ml of methylene chloride over a period of 30 min. at room temperature. At the end of reaction a colorless solution was obtained. The mixture was stirred at room temperature for two hours. The solvent was removed with a rotary evaporator under vacuum. A white solid was obtained, washed with 150 ml of pentane, dried to yield 1.20 g (94.5%) of white solid m.p. 198.5- 199.5 C (d).

^{13}C-NMR ($CDCl_3$, TMS, int.ref. $CDCl_3$):δ 16.62, 20.08, 20.77, 24.24, 24.93, 41.55, 59.47, 60.39, 63.57, 116.34, 126.03, 138.08, 139.18, 151.66, 153.73, 155.12, 156.23.

ANAL. Calcd. for $C_{17}H_{20}N_6O_4$: C, 54.83; H, 5.41; N, 22.58. Found: C,54.24; H, 5.36; N, 22. 34.

Preparation of 2,4,6-Triisopropylstyrene. Into a 1000 ml three-necked round-bottomed flask was placed 16.89 g (0.0473 mol) of methyltriphenylphosphoniumbromide and 500 ml dry

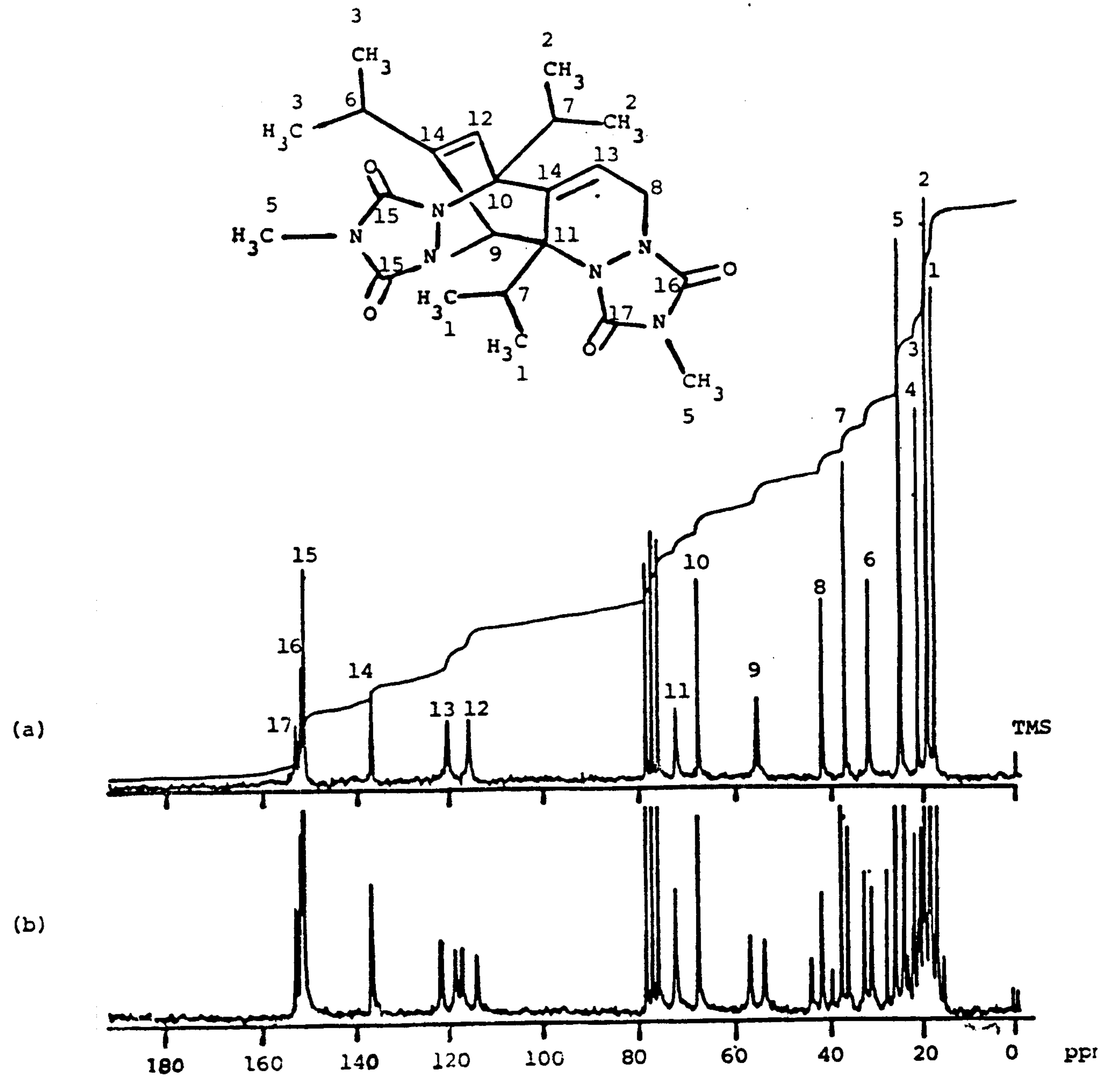

Figure 7. ^{13}C-NMR (25 MHZ) spectrum of compound (12) in $CDCl_3$ at 25°C. (a) complete decoupled. (b) off- resonance.

diethylether. The flask was equipped with a mechanical stirrer, addition funnel, a gas inlet tube and water-cooled condenser. Nitrogen gas was allowed to pass through the mixture and 36.5 ml of methyllithium (1.33 M) in ether was added all at once. The yellowish suspension was stirred for 5 hours. A solution of 9.00 g (0.0387 mol) of 2,4,6-Triisopropylbenzaldehyde in 200ml of dry diethylether was added dropwise. A white precipitate formed and the mixture was refluxed for 4 days. The reaction mixture was cooled, filtered and the filtrate was washed with two portions each of 100 ml of water. The ether layer was collected and dried over $MgSO_4$. The solvent was removed via rotary evaporation to give 7.60 g (85.2%) of pale yellow liquid. Distillation under vacuum gave colorless liquid: b.p. 67-70°C/ 0.35 mm Hg.

^{1}H-NMR ($CDCl_3$, TMS): δ 1.10 (s,6H), 1.20 (s,12H), 2.85 (septet, 2H), 4.90-5.50 (q,q, ABX, 2H), 6.50-7.10 (m,1H), 6.90 (s,2H).

^{13}C-NMR ($CDCl_3$, TMS, int.ref. $CDCl_3$): δ

23.99, 24.65, 29.98, 33.97, 119.33, 121.33, 133.96, 135.29, 146.65, 148.64.

Reaction of MeTD with 2,4,6-Triisopropylstyrene: Into a 100 ml round-bottomed flask equipped with a magnetic stirring bar and an additional funnel was placed 1.00 g (0.0043 mol) of 2,4,6-Triisprpylstyrene and 10 ml of methylene chloride. A pink solution of 0.49 g (0.0043) of MeTD in 20 ml of methylene chloride was added in five portions. Each portion was added after the pink color had completely disappeared. The colorless solution was stirred at room temperature for 1hr. The solvent was removed with a rotary evaporator under vacuum. The white solid obtained was washed with 100 ml of n-hexane, dried to give 1.00g (100 %) of white solid. Recrystallization from ether gave white crystals m.p. 162-164°C.

^{1}H-NMR ($CDCl_3$, TMS): δ 0.76-1.52 (m, 18H), 2.10 (m, 1H), 2.62 (m, 1H), 2.86 (s, 3H), 3.10 (s, 3H) 4.14 (m, 2H), 5.96 (s, 1H), 6.24 (m, 1H), 6.41 (s, 1H).

^{13}C-NMR ($CDCl_3$, TMS, int. ref. $CDCl_3$): δ 17.37, 18.76, 19.04, 21.54, 25.02, 31.97, 36.83, 41.98, 55.60, 67.41, 68.80, 115.60, 120.46, 137.14, 151.04, 151.74, 153.13.

ANAL. Calcd for $C_{23}H_{32}N_6O_4$: C, 60 50: H; 7.07; N, 18.41. Found: C, 59.67; H, 7.27; N, 18.33.

Conclusion

From the result obtained, it is clear that the reaction of 2,6-dimethylstyrene, 2,4,6-trimethylstyrene and 2,4,6-triisopropylstyrene with 4-methyl-1,2,4-triazoline-3,5-dione is very fast at room temperature and gives double Diels-Alder adducts in high yield. The first step of the reaction is the formation of 1:1 Diels-Alder adduct, which is extremely reactive and cannot be isolate readily undergoes a second Diels-Alder reaction MeTD. Although this reactive intermediate has potential to undergo an allylic type rearrangemen alkyl migration, such a rearrangement was not obse The reaction of di and tri- alkyl substituted-styrene bistriazoline dione should give new type polymer double Diels-Alder reactions. Work in this area ir laboratory is under investigation.

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