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SYNTHESIS, ISOLATION AND CHARACTERIZATION OF CIS- AND TRANS-2,7-DIMETHYL-3,5-CYCLOHEPTADIENONE

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Abstract: The title compounds have been synthesized and separated and their configurations established through their Diels-Alder adducts with PTAD.

The synthesis of *cis*- and *trans*-2,7-dimethyl-3,5-cycloheptadienone has been a subject of study in this laboratory for many years. An earlier report[1] on the synthesis of 2,7-dimethyl-3,5-cycloheptadienone could not be reproduced in our laboratory. We wish to report a new synthesis, as well as stereochemical characterization of *cis*-2,7-dimethyl-3,5-cycloheptadienone (1) and its *trans* isomer (2). The synthetic scheme is shown in Chart I.

Methylation of tropone (3)[2,3] with MeMgI in dry ether gave 2-methyl-3,5-cycloheptadienone (4) contaminated by 2-methyl-2,4-cycloheptadienone (5) (yield 41%, lit. 39%)[4]. Bromination of this mixture in CCl_4 followed by debromination with aqueous NH_3 gave 2-methyl-2,4,6-cycloheptatrienone (2-methyltropone) (6) in a yield of 51% (purity 96%). Methylation of 2-methyltropone by Me_2CuLi at temperatures below 0°C gave 34% of 2-methyl-3,5-cycloheptadienone (4), 54% of 2,7-dimethyl-3,5-cycloheptadienone (Fraction A: 60%; Fraction B: 33%) and 9% of 2,7-dimethyl-2,4-cycloheptadienone (7) along with 3% of recovered starting material (6), based on glpc analysis with an internal standard.

The difficult separation of *cis*-(1)- and *trans*-2,7-dimethyl-3,5-cycloheptadienone (2) was finally achieved by high pressure liquid chromatography using 2% ethyl acetate in hexane as the eluent. Both fractions collected (F-A and F-B) were structural isomers of 2,7-dimethyl-3,5-cycloheptadienone based on their spectral data (see below). Both (1) and (2) readily isomerize to (7) to varying extents on treatment with acid or base, on column chromatography or vapor chromatography, and even on prolonged standing in the dark in a refrigerator; on mild heating for 2-3 hours, both (1) and (2) completely isomerize to (7).

The IR spectra of (1) and (2) exhibit peaks at 1705(s) and 1710 cm^{-1} (s), respectively and both show $\lambda^{max}_{cyclohexane}$ at 234 nm and 290 nm. (lit.[1] IR and UV spectra of

Chart I

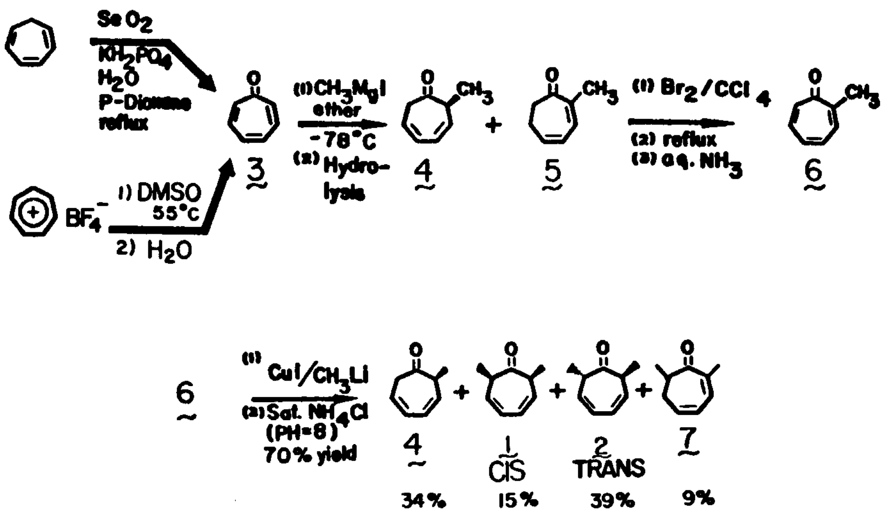


Chart II

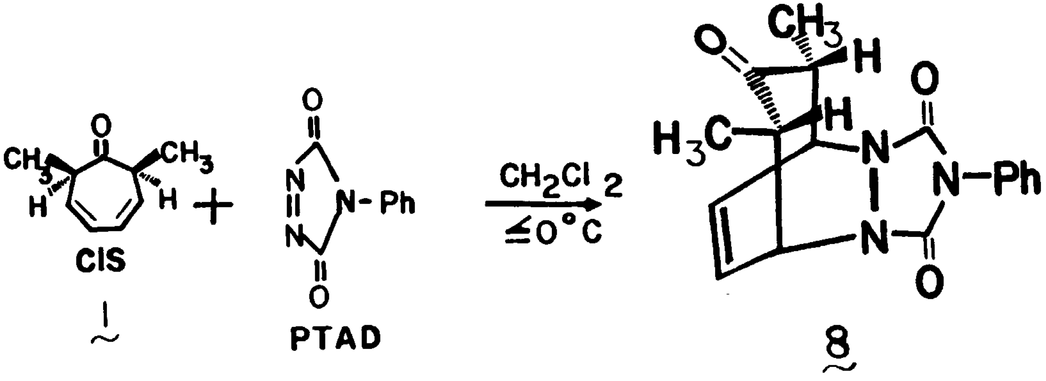
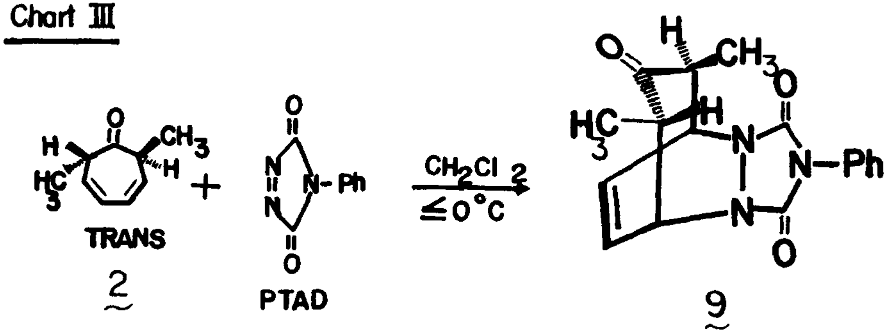


Chart III



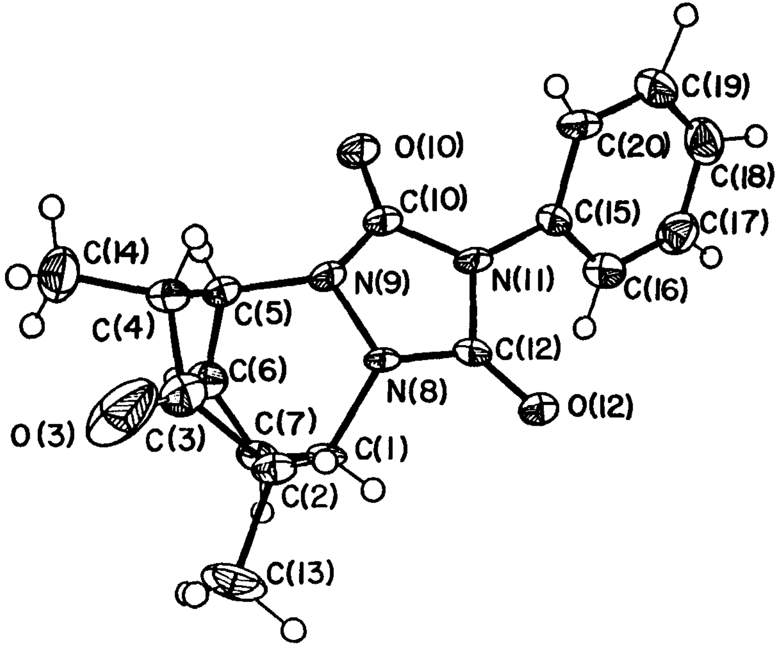


Figure 1 ORTEP drawing of 8 showing the atomic numbering scheme.

2,7-dimthyl-3,5-cycloheptadienone reported as 1705 cm^{-1} and λ^{max}_{EtOH} 236 mμ, respectively). PMR, ^{13}CMR and mass spectral data of both isomers: compound (1) ^{1}H NMR (CCl_4, δ) 6.1-6.4 (m, 2H), 5.5-5.7 (m, 2H), 2.8-3.4 (br, s, 2H), 1.2-1.4 (d, 6H) and ^{13}CMR ($CDCl_3$, δ) 202.3, 133.6, 128.4, 47.8 and 15.4 ppm; compound (2) ^{1}H NMR (CCl_4, δ) 5.9-6.4 (m, 2H), 5.4-5.7 (m, 2H), 2.9-3.4 (m, 2H), 1.2-1.4 (d, 6H) and ^{13}CMR ($CDCl_3$, δ) 202.7, 131.4, 126.3, 48.4 and 15.5 ppm. This spectral similarity is a result of the rapid ring inversion of (1) and (2) around the C_2 axis. The assignment of configurations to (1) and (2) was achieved through their Diels-Alder adducts (8) and (9), with 4-phenyl-1,2,4-triazolin-3,5-dione (PTAD), as shown in Charts II and III. PMR and CMR spectra clearly indicated the methyls are structurally equivalent in (8) but not in (9).

The cis-methyl relationship in (8) was confirmed by single-crystal X-ray analysis. Crystal data for (8): $C_{17}H_{15}N_3O_3$, M = 309.4, orthorhombic, space group $P2_12_12_1$, a = 7.230 (3), b = 9.301 (3), c = 21.854 (7) A, $\alpha = \beta = \gamma = 90.00^o$, Z = 4. Crystal dimensions 0.30 x 0.40 x 0.85 mm. X-ray data were collected on a computer-controlled Four-Circle Nicolet Autodiffractometer using graphite-monochromated Mo-Kα radiation in the ω-scan mode for $2\ \theta > 55^o$. The structure was solved by direct methods using MULTAN-80.[5] Twenty of the 23 non-hydrogen atoms appeared on the first Fourier map. The structure was completed with one structure Factor-Fourier cycle using all the data.[6] An ORTEP[7] drawing of the final structure of this adduct (8) from its x-ray data is shown in Figure I. This structure exhibits a plane of symmetry which runs through the C=O group, and the two methyl groups are clearly on the same side of the carbonyl group, which requires that fraction B is cis-2,7-dimethyl-3,5-cycloheptadienone (1).

The interesting photochemistry of (1) and (2) will be reported elsewhere.

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REFERENCES

1. G.L. Closs and L.E. Closs, J. Am. Chem. Soc., 1961, 83, 599.
2. P. Radlick, J. Org. Chem., 1964, 29, 960.
3. E. Garfunkel and I.D. Reingold, J. Org. Chem., 1979, 44, 3725.
4. a) T. Nozoe, T. Mukai and T. Tezuka, Bull. Chem. Soc. Japan, 1966, 31, 4281.
   b) O.L. Chapman, D.J. Pasto and A.A. Griswold, J. Am. Chem. Soc., 1962, 84, 1218.
5. P. Main, Dept. of Physics, University of York, York, England, January 1980.
6. The X-ray System-Version of 1976, J.M. Stewart, Editor, Technical Report TR-446 of the Computer Science Center, University of Maryland, College Park, Maryland.
7. ORTEP-11, C.K. Johnson, ORNL-5138, Oak Ridge National Laboratory, Oak Ridge, Tennessee 37830.

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