# The Action of Nitrogen Dioxide and Nitric Oxide on Humulene, $C_{15}H_{24}$. Isolation and Characterization by *X*-Ray Crystallography of Two Distinct Conformers of Humulene Nitrosite. Molecular Mechanics Calculations for 1,4,4,8,8,9-Hexamethylcycloundeca-1,4-diene

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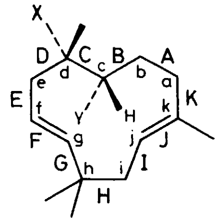
Two conformational isomers of humulene nitrosite have been isolated as distinct crystalline forms, needles and platelets. The conformations have been characterized by *X*-ray diffraction studies and molecular mechanics calculations. Crystallographic data for the platelet form are: $a = 7.873(6)$, $b = 16.660(9)$, $c = 12.140(6)$ Å, $\beta = 101.94(5)°$, $Z = 4$, space group $P2_1/c$. *X*-Ray intensity measurements were made on an automatic four-circle diffractometer and least-squares adjustment of the atomic parameters converged at $R$ 0.059 for 2 690 $|F_o|$ values.

The co-existence of conformational isomers in the gaseous and liquid phases is commonplace but generally only limited characterization of the conformational geometries is possible.[1] In the solid state it is usual to find a single preferred conformation, though occasionally two or more distinct conformers may co-exist. Crystals of cyclo(hexaglycyl), for example, have four different conformers in an ordered arrangement in the unit cell.[2] Crystals of 1,1,5,5-tetramethylcyclodecane-8-carboxylic acid, on the other hand, contain a random mixture of two conformers and the resultant superposition of molecules in the averaged unit cell prevents accurate definition and comparison of the molecular geometries.[3] Antibiotic ligands, such as nonactin or valinomycin, and macrocyclic polyethers have distinctly different conformations in the free state and in complexes with metal ions and in such cases *X*-ray studies have yielded details of the conformational changes.[4] A more novel route to conformational comparisons is provided by the discovery that a guest molecule accommodated in the cavity or channel of an inclusion compound can adopt a conformation that differs from the minimum-energy conformation of the free compound, because of the constraints imposed by the host–guest interactions.[5]

Conformational isomers can be isolated when there is a substantial barrier to their interconversion. Newton and Whitham have reported the syntheses of two conformational isomers of bicyclo[6.4.0]dodeca-*trans*-4-*cis*-10-diene, in which the cyclo-octene ring is locked into twist and chair forms by *trans*-fusion to the six-membered ring. Interconversion between the isomers by rotation of the cyclo-octene double bond through the eight-membered ring is a fairly high-energy process with a free-energy barrier of 131 kJ mol$^{-1}$ at 150 °C.[6]

We recently observed that humulene nitrosite (1) exists in two crystalline forms. Needles are obtained when the compound is recrystallized rapidly from ethanol but if the crystallization takes place slowly platelets are also formed. These forms have virtually identical spectroscopic properties but they show some differences in photochemistry when irradiated with red light and so we considered that the conformation of the cycloundecadiene ring in the platelet crystals might differ from that in the needles.[7]

*X*-Ray studies of dinitrohumulene (2), nitronitratohumulene (3), and the needle form of humulene nitrosite (1), revealed a common ring conformation shown in Figure 1 (conformation I).[8] The platelet form of humulene nitrosite has now also been subjected to *X*-ray crystallographic analysis and we find that it does indeed contain a different conformer, shown in Figure 2 (conformation II). The interconversion of conformers I and II involves rotation of the double-bond segments at C(6),C(7) and C(9),C(10) through 180°. This is similar to the basic mechanism for racemisation of medium-ring *trans*-cycloalkenes [6] and *trans*-lactones.[9]



(1) X = NO, Y = $NO_2$
(2) X = Y = $NO_2$
(3) X = $ONO_2$, Y = $NO_2$
(4) X = Y = $CH_3$

The torsion angles describing the ring conformations are listed in Table 1. The cycloundecadiene ring in conformation II has approximate $C_2$ symmetry and resembles closely a conformation found for cycloundec-1-enecarboxylic acid.[10] Anet and Rawdah have derived six low-energy conformations for cycloundecane by force-field calculations [11] and one of these conformations, the [12314], has the same pattern of torsion-angle signs as conformation II; conformation I, however, does not correspond to any of the six low-energy conformations of cycloundecane.

In view of the ease of isolation of conformers I and II, it is likely that they do not differ appreciably in stability. Empirical force-field (molecular mechanics) calculations would provide a test of this but suitable parameters for NO and $NO_2$ groups are not yet available and the use of a poorly parameterized force field can lead to unreliable results.[12] On the other hand, several well tested and reliable hydrocarbon force fields are available [13] and we therefore chose to perform molecular mechanics calculations for the hydrocarbon analogue (4) with the force field developed by White and Bovill.[13] Conformations considered were I and II of humulene nitrosite and the two intermediate conformations obtained by 180° rotation of the C(6),C(7) or C(9),C(10) segment. The generation and initial optimization of the conformations were performed with a high-performance refreshed graphics system (Megatek MGS-7000). Energy minimization was accomplished by pattern search, block-diagonal and full-matrix iterative Newton–Raphson procedures.[14] The results of these calculations are shown in Table 2.

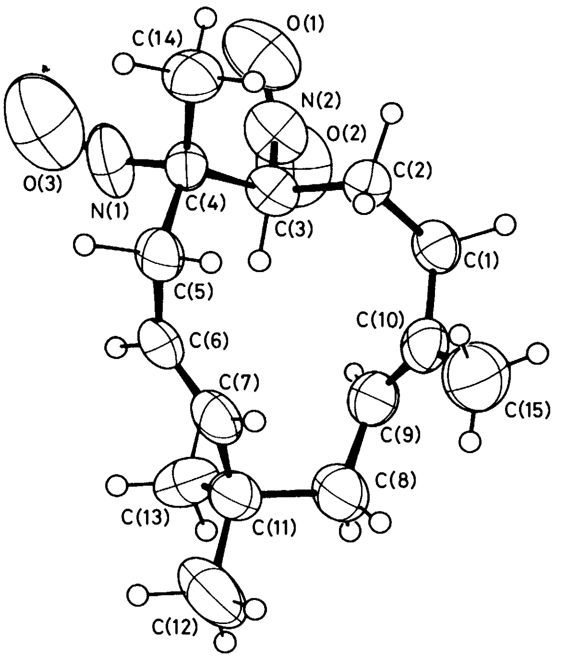


**Figure 1.** Conformer I of humulene nitrosite. The thermal ellipsoids of the C, N, and O atoms are drawn at the 50% probability level. The H atoms are represented by spheres of radius 0.1 Å. The numbering system for the C atoms is based on that commonly used for germacranolide sesquiterpenoids

**Table 1.** Torsion angles (°) in the two conformers of humulene nitrosite (1)

| Torsion angle about bond | I | II |
|---|---|---|
| A | −78 | −63 |
| B | 154 | 160 |
| C | −80 | −99 |
| D | −47 | 56 |
| E | 119 | −115 |
| F | −168 | 177 |
| G | 120 | −112 |
| H | −45 | 53 |
| I | 104 | −110 |
| J | −166 | 164 |
| K | 95 | −67 |

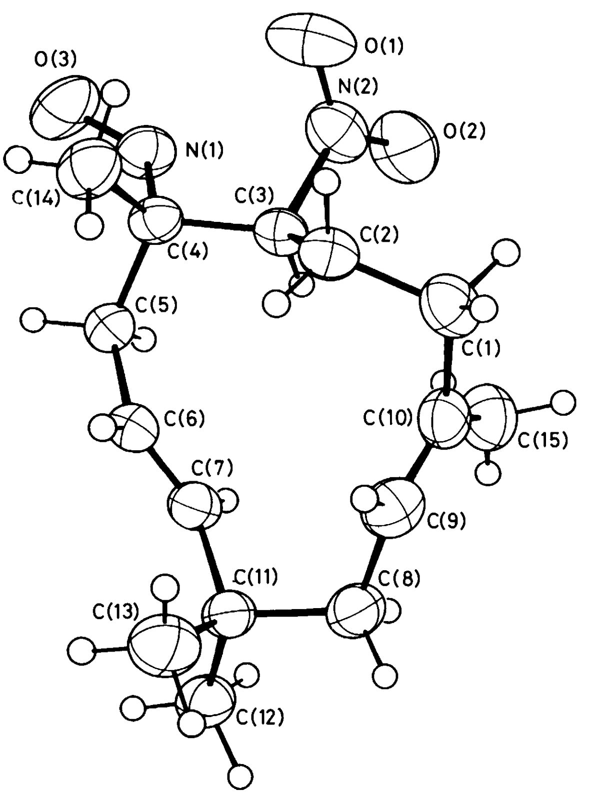


**Figure 2.** Conformer II of humulene nitrosite. Thermal ellipsoids as in Figure 1

**Table 2.** Torsion angles (°) and steric energies (kJ mol$^{-1}$) for four calculated conformers of 1,4,4,8,8,9-hexamethylcycloundeca-1,5-diene (4). Torsion angles for I have been reported in ref. 8

| Torsion angle about bond | I | II | III | IV |
|---|---|---|---|---|
| A | −84 | −70 | −97 | −74 |
| B | 147 | 151 | 153 | 146 |
| C | −67 | −88 | −92 | −93 |
| D | −48 | 56 | 48 | 39 |
| E | 130 | −124 | −123 | 102 |
| F | −170 | 178 | 175 | 180 |
| G | 110 | −103 | −103 | 27 |
| H | −42 | 51 | 34 | 44 |
| I | 101 | −104 | 91 | −124 |
| J | −169 | 168 | −167 | 165 |
| K | 95 | −72 | 81 | −62 |
| Steric energy | 65.9 | 67.3 | 81.0 | 84.3 |

The effect of performing the molecular mechanics calculations on the hydrocarbon analogue (4) is to neglect electrostatic interactions between the adjacent NO and $NO_2$ groups. This neglect should primarily distort the local geometry in the vicinity of C(3) and C(4), rather than the global geometry of the molecule, and should have little effect on the relative energies of conformers I—IV.

Conformers I and II of the hydrocarbon (4) differ in energy by only 1.4 kJ mol$^{-1}$ and are substantially lower in energy than conformers III and IV. On the basis of Table 2, compound (4) in the gas phase at 295 K should contain *ca.* 64% I, 36% II, and only very minor amounts of III and IV. Rotation of the C(6),C(7) and C(9),C(10) segments for interconversion of conformers I—IV requires passage of hydrogen atoms through the eleven-membered ring but the energy barrier to this process is not expected to be large. A recent study of humulene with an alternative set of force-field parameters suggested a relatively small barrier for the rotation of hydrogen atoms through that ring.[15] If these results can be extrapolated to humulene nitrosite (1) in solution, the ready isolation of conformers I and II and the failure to detect III or IV are explicable. The isolation of conformational isomers may be possible for other compounds where two or more conformers are of similar energy. The obvious analogy is to the spontaneous resolution of enantiomers.

The seven C–C($sp^3$)–C angles in the nitrosite range from 107.7 to 116.5°, indicating some degree of steric strain, and the four C–C=C angles range from 118.2 to 128.0° with the C–C(C)=C angle k smaller than the C–C(H)=C angles f, g, and j. The force-field calculations for conformer II of compound (4) reproduce these variations in a satisfactory manner (Table 3).

**Table 3.** Comparison of bond angles (°) in conformers I and II of compound (1) with force-field results for conformers I and II of compound (4). The standard deviations of the experimental results for (1) are *ca.* 0.4° for conformer I and 0.2° for conformer II

| Bond angle | I(1) | II(1) | I(4) | II(4) |
|---|---|---|---|---|
| a | 110.8 | 110.8 | 111.2 | 110.3 |
| b | 112.7 | 113.8 | 114.0 | 114.8 |
| c | 116.5 | 116.5 | 114.6 | 114.9 |
| d | 109.0 | 109.3 | 112.1 | 111.7 |
| e | 114.0 | 114.7 | 113.2 | 117.3 |
| f | 123.3 | 123.7 | 123.2 | 122.8 |
| g | 127.8 | 127.9 | 125.1 | 125.9 |
| h | 105.8 | 107.7 | 108.3 | 109.6 |
| i | 112.7 | 111.4 | 111.7 | 110.6 |
| j | 127.2 | 128.0 | 125.8 | 125.7 |
| k | 121.7 | 118.2 | 120.4 | 118.9 |

Conformational isomers necessarily differ in some torsion angles but need not differ in bond lengths or angles. Since steric energies depend on all these parameters, some differences are to be expected. Changes in bond lengths are energetically expensive and will not be easily observed. Changes in bond angles should be more readily detected and the observed bond angles for (1) in conformers I and II are compared with the calculated angles for (4) in Table 3. The larger changes in the observed values (for angles b, h, i, and k) are matched in sign by the changes in the calculated results for these angles. The correlation coefficient for all values of $\Delta_{obs}$ and $\Delta_{calc}$ is 0.59 and the probability of obtaining a correlation coefficient of this magnitude from a purely random sample of eleven pairs is $P = 0.055$.[16] This result suggests that the changes in bond angles between conformers I and II of humulene nitrosite may well be genuine and not simply the result of experimental errors or crystal forces.

## Experimental

*Crystallographic Measurements.*—Cell dimensions were derived from least-squares treatment of the setting angles of 25 reflections measured on an Enraf–Nonius CAD4 diffractometer with Mo-$K_\alpha$ radiation. For intensity measurements, reflections were surveyed in the range $\theta < 27°$ and 2 690 satisfied the criterion $I > 2.5\sigma(I)$ and were used in the subsequent calculations.

*Structure Analysis.*—The crystal structure was elucidated with a direct-phasing program developed by Dr. C. J. Gilmore. After preliminary adjustment of the positions of the C, N, and O atoms, the H atoms were located in a difference electron-density distribution. Thereafter several cycles of block-diagonal least-squares calculations were carried out with anisotropic thermal parameters for the C, N, and O atoms and isotropic thermal parameters for the H atoms and convergence was reached at $R$ 0.059, $R_w$ 0.084, with weights given by $w = 1/\sigma^2(F)$. These calculations were performed on an SEL 32/27 computer with an integrated system of programs developed by Drs. C. J. Gilmore, P. R. Mallinson, and K. W. Muir.

Atomic co-ordinates are listed in Table 4. Observed and calculated structure amplitudes, thermal parameters, and full details of bond lengths and angles are listed in Supplementary Publication No. SUP 23603 (20 pp.).*

**Table 4.** Fractional atomic co-ordinates with standard deviations in parentheses

|  | *x* | *y* | *z* |
|---|---|---|---|
| C(1) | −0.179 7(2) | 0.148 1(1) | 0.760 5(2) |
| C(2) | −0.018 1(2) | 0.198 8(1) | 0.803 1(1) |
| C(3) | 0.075 0(2) | 0.178 7(1) | 0.924 0(1) |
| C(4) | 0.267 8(2) | 0.205 7(1) | 0.959 2(1) |
| C(5) | 0.388 4(2) | 0.133 0(1) | 0.950 3(1) |
| C(6) | 0.356 6(2) | 0.093 2(1) | 0.836 7(1) |
| C(7) | 0.301 0(2) | 0.019 1(1) | 0.818 5(1) |
| C(8) | 0.057 8(3) | −0.039 3(1) | 0.677 0(2) |
| C(9) | −0.039 2(3) | 0.037 5(1) | 0.680 5(2) |
| C(10) | −0.132 7(2) | 0.060 0(1) | 0.755 3(1) |
| C(11) | 0.258 1(3) | −0.025 5(1) | 0.706 6(2) |
| C(12) | 0.346 0(3) | −0.108 6(1) | 0.723 3(2) |
| C(13) | 0.318 8(3) | 0.019 5(1) | 0.613 0(2) |
| C(14) | 0.315 3(3) | 0.280 3(1) | 0.902 0(2) |
| C(15) | −0.181 6(3) | 0.005 6(1) | 0.841 7(2) |
| N(1) | 0.298 2(2) | 0.216 5(1) | 1.086 9(1) |
| N(2) | −0.033 1(2) | 0.215 6(1) | 1.000 7(1) |
| O(1) | −0.028 5(3) | 0.288 7(1) | 1.012 3(1) |
| O(2) | −0.121 7(2) | 0.171 3(1) | 1.045 0(1) |
| O(3) | 0.413 7(2) | 0.261 1(1) | 1.125 0(1) |

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