THE REGIOSELECTIVITY OF THE CYCLOADDITIONS OF KETENES WITH N-ALKYL- AND N-ARYLNITRONES

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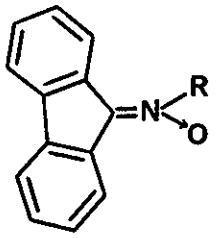
Cyclopentamethyleneketene, tert-butylcarbethoxyketene, and tert-butylcyanoketene react with N-arylnitrones to form oxazolidinones while tert-butylcyanoketene reacts with N-methyl- and N-ethylnitrones to afford isoxazolidinones.

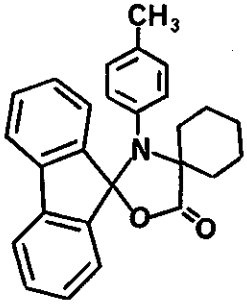
Our interest in the reactions of ketenes with N-arylimines, ketenimines, azines and N-alkylimines[1] led us to investigate the cycloadditions of ketenes and nitrones. We recently reported a general method for preparing N-methylnitrones as stable trans forms from aldehydes or ketones and N-methylhydroxylamine-O-sulfonic acid.[2] We would now like to report the reaction of N-aryl- and N-alkylnitrones with various ketenes.

The reactions of diphenylketene and dimethylketene with N-alkylnitrones are known to afford both azetidinones and oxazolidinones.[3-5] Similarly, we found that the reactions of cyclopentamethyleneketene, tert-butylcarbethoxyketene, and tert-butylcyanoketene with N-arylnitrones (1a-d), in dry toluene, yielded oxazolidinones (2,3a-e), but we did not observe the formation of azetidinones. N-Alkylnitrones (1e,f), on the other hand, reacted with tert-butylcyanoketene (110°C, 12 hr) to afford the corresponding isoxazolidinones (4a,b). The physical and spectral properties of compounds 2, 3a,d,e and 4a,b are summarized in Table 1.



1

a R = p-$CH_3C_6H_4$
b R = p-$OCH_3C_6H_4$
c R = p-FC_6H_4
d R = p-$CF_3C_6H_4$
e R = CH_3
f R = C_2H_5



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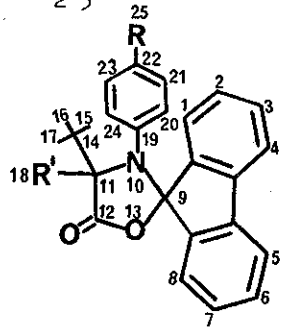
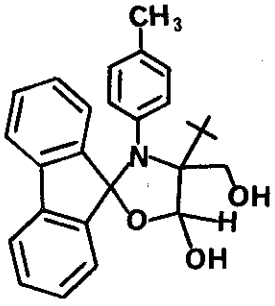


3

a R = CH_3, R' = $CO_2C_2H_5$
b R = OCH_3, R' = CN
c R = F, R' = CN
d R = CF_3, R' = CN
e R = CH_3 R' = CN



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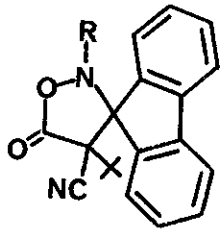

4

a R = CH_3
b R = C_2H_5

Table 1
Physical and Spectral Properties of Selected
Oxazolidinones and Isoxazolidinones

Compound No.	Yield, %	mp, °C	Spectral Data
2	52	188-189	IR (KBr) 1775 cm^{-1}(CO); ^{1}HNMR ($CDCl_3$) δ 1.10-2.40 (m, 10H), 2.14 (s, 3H), 6.63-6.93 (m, 4H), 7.10-7.74 (m, 8H); ^{13}CNMR, 101.8 (C-9).
3a	55	159-161	IR (KBr) 1775 cm^{-1}(CO); ^{1}HNMR (DMSO-d_6) δ 1.21 (s, 9H), 1.32 (t, 3H), 2.06 (s, 3H), 4.46 (q,2H) 6.68-6.76 (m, 4H), 7.23-7.63 (m, 8H); ^{13}CNMR 102.4 (C-9).
3d	65	169-170	IR (KBr) 1800 cm^{-1}(CO); ^{1}HNMR ($CDCl_3$) δ 1.25 (s, 9H), 7.30-8.00 (m, 12H); ^{13}CNMR; 102.8 (C-9).
3e	65	189-190	IR (KBr) 1778 cm^{-1}(CO); ^{1}HNMR ($CDCl_3$) δ 1.30 (s, 9H), 2.15 (s, 3H), 6.52-8.30 m (12H); ^{13}CNMR 102.7 (C-9).
4a	72	178-180	IR (KBr) 1765 (CO); ^{1}HNMR ($CDCl_3$) δ 0.85 (s, 9H), 2.40 (s, 3H), 7.30-8.40 (m, 8H); ^{13}CNMR 83.7 (C-9).
4b	65	161-163	IR (KBr) 1770 cm^{-1}(CO); ^{1}HNMR ($CDCl_3$) δ 0.80 (s, 9H), 0.98-1.25 (t, 3H), 1.90-2.70 (m, 2H), 7.20-7.70 (m, 7H), 8.20-8.40 (m, 1H); ^{13}CNMR 82.7 (C-9).
5	67	191	IR (KBr) 3300 cm^{-1}(OH); ^{1}HNMR (DMSO-d_6) δ 1.00 (s, 9H), 2.00. (s, 3H), 3.20 (s, 1H, exchanged with D_2O),4.08-4.20 (m, 3H; after D_2O:q, 2H), 6.00 (d, 1H, J=6 Hz; after D_2O,appeared as singlet),6.70 (q,4H), 7.00-8.40 (m,8H);^{13}CNMR 101.4 (C-9).

Treatment of 2 with lithium aluminum hydride gave 9-fluorenol, presumably via a sequence involving reduction of the oxazolidinone function and decomposition of the resulting hydroxy ether to fluorenone which subsequently reacts with additional lithium aluminum hydride to yield the final product. The reduction of 3a with lithium aluminum hydride, however, afforded a stable diol, (5), further supporting the oxazolidinone structure of 3a. The physical properties of 5 are included in Table 1.

Distinction between the oxazolidinone and isoxazolidinone structures is provided by the ^{13}C chemical shift of the C-9 spiro carbon: $\sim$ 83-84 ppm for isoxazolidinones and $\sim$ 102-103 ppm for oxazolidinones.[6] The latter value is indicative of a carbon between two electronegative elements. In addition, the pmr resonance of the tert-butyl group appears at $\sim$ 1.25 ppm in the oxazolidinones but at $\sim$ 0.80 ppm in the isoxazolidinones. This shift difference can be ascribed to the proximity of the tert-butyl group to the fluorene system in isoxazolidinones but not in the oxazolidinones and, correspondingly, the influence of the diamagnetic fluorene ring current. Further evidence for the oxazolidinone structure is provided by the $^{1}HNMR$ spectrum of 3a. The broadened AA'BB' pattern observed for the protons of the N-phenyl group at room temperature undergoes considerable change as the temperature is decreased (Figure 1). This effect may be attributed to restricted rotation of the phenyl group which results from its interaction with the tert-butyl substituent on C-11. Further confirmation is provided by the low temperature[7] ^{13}C nmr spectrum of 3a which exhibits four different resonances for C-20, C-21, C-23, and C-24. In accord with these results, the $^{1}HNMR$ spectrum of 2 showed no major temperature dependence, with the exception of the cyclohexyl ring protons, as would be expected in the absence of steric interactions.

3e in $CDCl_3$

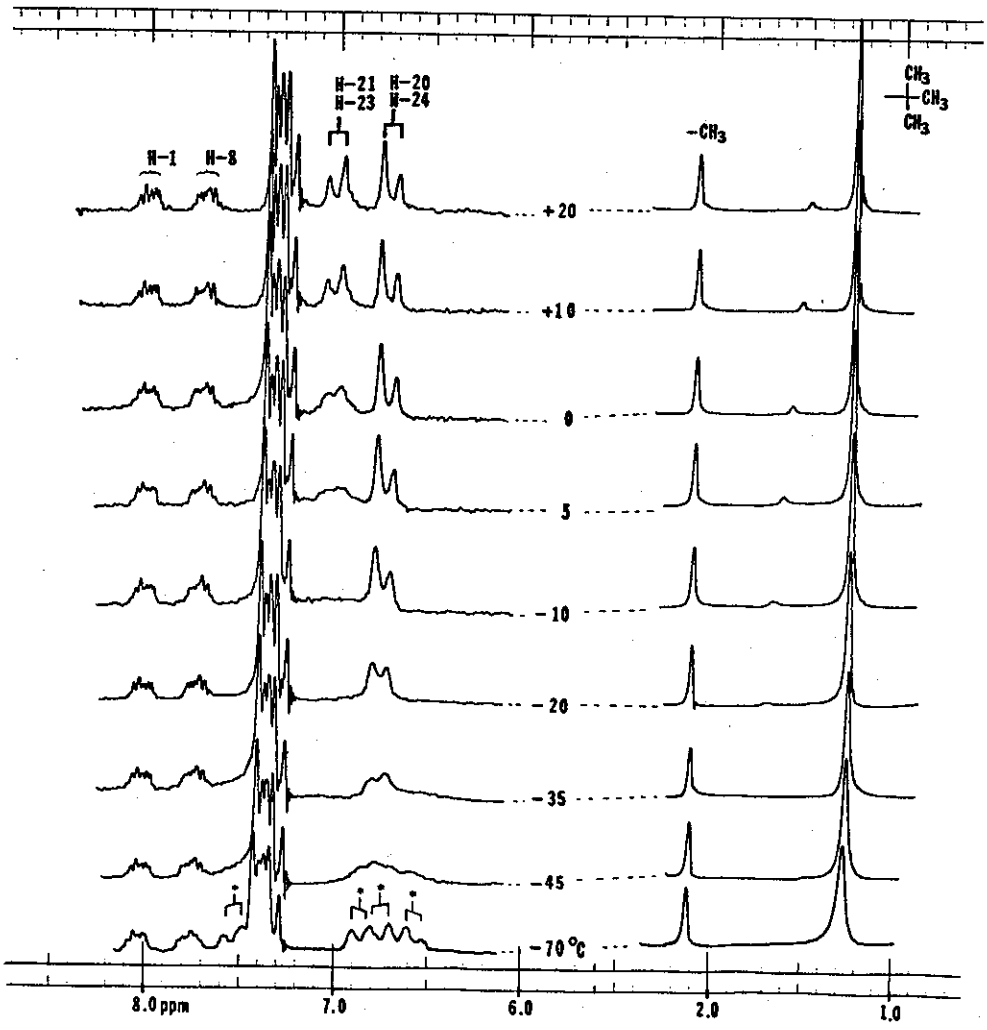

Figure 1

References and Notes:

1. A. S. Gomes and M. M. Joullié, J. Heterocycl. Chem., 1969, 6, 729; J. M. Bohen and M. M. Joullié, J. Org. Chem., 1973, 38, 2652; Z. Lysenko and M. M. Joullié, J. Org. Chem., 1976, 41, 3925; Z. Lysenko, M. M. Joullié, I. Miura and R. Rodebaugh, Tetrahedron Lett., 1977, 1705.
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4. D. S. C. Black, R. F. Crozier and V. C. Davis, Synthesis, 1975, 4, 205.
5. R. Nigel Pratt, D. P. Stokes, and G. A. Taylor, J. C. S. Perkin I, 1975, 498.
6. The assignment of ^{13}C chemical shifts was made on the basis of shift comparisons with C-9 substituted fluorenes, selective proton decoupling experiments and low temperature nmr studies.
7. Low temperature ^{1}HNMR studies were carried out both in acetone-d_6 (+ 10 to -80°C) and $CDCl_3$ (+ 30 to -70°C).

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