Communications

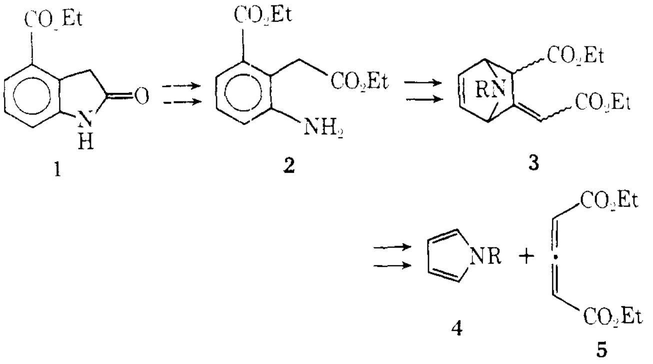
A Novel Potassium Hydride Induced Reorganization Reaction. Synthesis of Condensed Heterocycles

Summary: The potassium hydride induced β elimination of the heteroatom bridge of specifically substituted 7-heterobicyclo[2.2.1]heptenes has been examined as a new route to condensed heterocycles.

Sir: The Diels–Alder reaction is one of the most powerful tools available for the construction of complex organic molecules.[1] We now report an efficient method for the preparation of fused-ring heterocycles by base-induced heterolysis of the 7-heterobicyclo[2.2.1]heptenes available from the Diels–Alder reaction of furans and pyrroles with 1,3-dicarboethoxyallene.[4]

The primary objective of this investigation was the development of a direct process for the preparation of 4-carboethoxyoxindole (1). This product was deemed a valuable precursor for the synthesis of various ergot alkaloids.[2] These compounds have aroused renewed interest because of their possible use as prolactin inhibitors and anti-Parkinsonian drugs.[3]

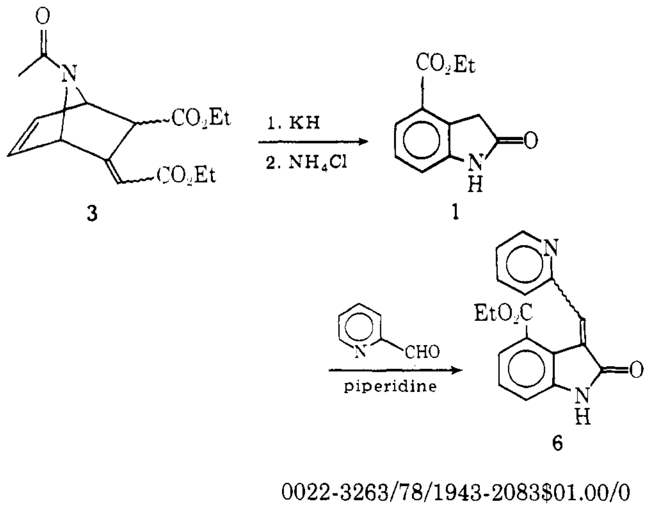
Structural analysis of the target 1 suggested its derivation from the aminohomophthalate 2, which in turn could be generated from an intermediate of structure 3, the cycloadduct of a pyrrole 4 and 1,3-dicarboethoxyallene (5).



1 2 3

4 5

That cycloadduct 3 does indeed possess all the structural features required for conversion to oxindole 1 was readily demonstrated. The azabicyclo[2.2.1]heptene 3 (R = COCH$_3$), available in 70% yield from the Diels–Alder reaction of *N*-acetylpyrrole and 1,3-dicarboethoxyallene (5),[4] was treated with a large excess of potassium hydride (4–5 equiv) in tetrahydrofuran for 1 h at room temperature. The reaction mixture was then quenched with aqueous ammonium chloride and extracted with chloroform. The solid residue obtained after concentration was recrystallized from methanol to afford 4-carboethoxyoxindole (1) (mp 184–185 °C) in 60–75% yield.

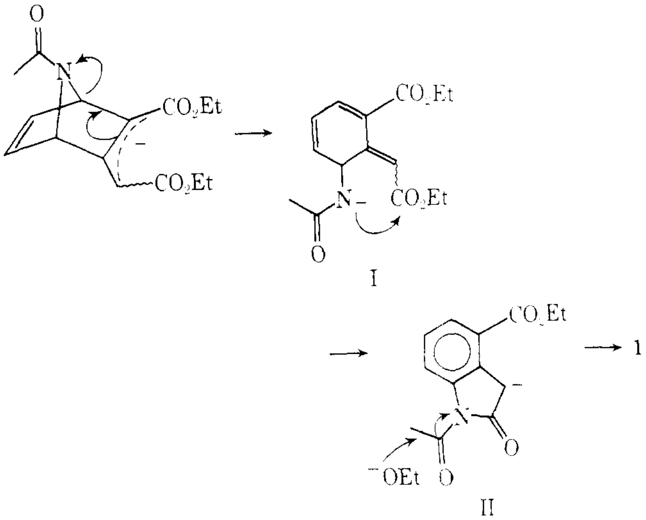


3 1

6

The structure of this product was confirmed by spectral analysis [IR (CHCl$_3$) 3450, 3200, 1705 (overlapping C=O groups) cm^{-1}; NMR (CDCl$_3$) δ 9.33 (br s, 1 H), 7.00–7.90 (m, 3 H), 4.43 (q, J = 7 Hz, 2 H), 3.90 (s, 2 H), 1.40 (t, J = 7 Hz, 3 H); M$^+$ *m/e* 205.07390] and by its facile base-catalyzed condensation with pyridine-2-carboxaldehyde to give the crystalline derivative 6.[5]

A possible mechanism for this novel molecular reorganization is shown below. The first two steps of this process are envisioned to involve carbanion formation followed by carbon–nitrogen bond cleavage to yield intermediate I. An analogous base-induced β elimination of a heteroatom bridge has previously been recorded by Stork and co-workers in some of their initial attempts to synthesize cantharidin.[6]



I

II

Intermediate I is now transformed by lactamization and aromatization (the timing of these steps is uncertain and, of course, will depend on the olefin geometry of I) to intermediate II.[7] Subsequent deacetylation of II by the ethoxide ejected during the course of this reaction affords 1 on acidic workup.

This methodology was also shown to be applicable to the synthesis of 5-methyl-4-carboethoxyoxindole (8) [IR (CHCl$_3$) 3450, 3200, 1720, 1710 cm^{-1}; NMR (CDCl$_3$) δ 8.45 (br s, 1 H), 6.93 (ABq, 2 H, J = 8 Hz, ν_{AB} = 13.86), 4.33 (q, J = 7 Hz, 2 H), 3.70 (s, 2 H), 2.48 (s, 3 H), 1.40 (t, J = 7 Hz, 3 H); M$^+$ *m/e* 219.08879] and 4-carboethoxy-2-oxo-2,3-dihydrobenzofuran (10) [IR (CHCl$_3$) 1810, 1720 cm^{-1}; NMR (CDCl$_3$) δ 7.07–7.83 (m, 3 H), 4.33 (q, J = 7 Hz, 2 H), 4.00 (s, 2 H), 1.40 (t, J = 7 Hz, 3 H); M$^+$ *m/e* 206.05580] from the precursor cycloadducts 7[8] and 9,[4] respectively.

The potassium hydride induced β elimination of a heteroatom bridge was also examined with cycloadduct 11 as substrate. Subjection of this oxabicycloheptene, prepared from the Diels–Alder reaction of 4-methyl-2,3-pentadienenitrile and furan, to excess potassium hydride in tetrahydro-

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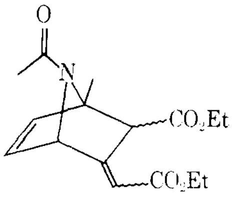

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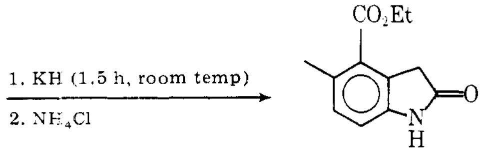
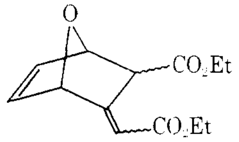


8 (55% isolated yield)



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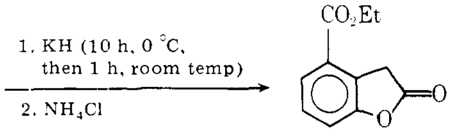
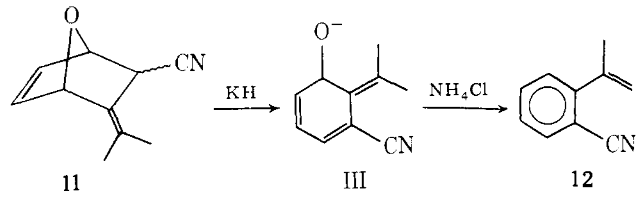


10 (45% isolated yield)

furan afforded isopropenylbenzonitrile (12) on ammonium chloride workup.



This product results from the acid-catalyzed dehydration of III, an intermediate which cannot aromatize in the basic milieu.

The heterolytic scission reaction reported herein thus provides a convenient method for the synthesis of fused heterocycles. This method is, however, limited to the use of allenes bearing specific electron-withdrawing groups in both the 1 and 3 positions.

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References and Notes

(1) A. S. Onishchenko, "Diene Synthesis", Daniel Davey and Co., New York, N.Y., 1964; W. Oppolzer, *Angew. Chem., Int. Ed., Engl.*, **16**, 10 (1977), and references cited therein.
(2) A. Hofmann, "Die Mutterkornalkaloide", Ferdinand Enke Verlag, Stuttgart, Germany, 1964; H. G. Floss, *Tetrahedron*, **32**, 873 (1976).
(3) H. G. Floss, J. M. Cassady, and J. E. Robbers, *J. Pharm. Sci.*, **62**, 699 (1973); J. M. Cassady, G. S. Li, E. B. Spitzner, H. G. Floss, and J. A. Clemens, *J. Med. Chem.*, **17**, 300 (1974).
(4) A. P. Kozikowski, W. C. Floyd, and M. P. Kuniak, *J. Chem. Soc., Chem. Commun.*, 582 (1977). *N*-Acetylpyrrole, prepared by the method of G. S. Reddy, *Chem. Ind.*, 1426 (1965), was reacted with 1,3-dicarboethoxyallene in refluxing benzene for 84 h to afford cycloadduct **3**.
(5) G. N. Walker, R. T. Smith, and B. N. Weaver, *J. Med. Chem.*, **8**, 626 (1965).
(6) G. Stork, E. E. van Tamelen, L. J. Friedman, and A. W. Burgstahler, *J. Am. Chem. Soc.*, **75**, 384 (1953), footnote 10.
(7) TLC analysis of cycloadduct **3** reveals three separable components (two are major). Although definitive assignments of stereochemistry to these products have not been made, NMR analysis of the isomers indicates that the major components probably have the same stereochemical features as found for the cycloadducts of pentadienedioic acid and cyclopentadiene: W. C. Agosta, *J. Am. Chem. Soc.*, **86**, 2638 (1964). Also see H. Hauth, D. Stauffacher, P. Niklaus, and A. Melera, *Helv. Chim. Acta*, **48**, 1087 (1965) for the effect of the olefin geometry of an α,β-unsaturated acid on the chemical shift of neighboring protons. Since isomerization is likely to occur under these reaction conditions, the olefinic geometry of the starting materials is apparently not crucial to the success of this process.
(8) *N*-Acetyl-2-methylpyrrole, prepared from the potassium salt of 2-methylpyrrole [J. L. Rainey and H. Adkins, *J. Am. Chem. Soc.*, **61**, 1104 (1939)] and acetyl chloride, was transformed to cycloadduct **7** by refluxing with 1,3-dicarboethoxyallene in benzene for 3 days.
(9) The 4-methyl-2,3-pentadienenitrile was prepared by the method of P. M. Greaves, S. R. Landor, and D. R. J. Laws, *Chem. Commun.*, 321 (1965), and reacted with furan at 120 °C for 30 h to afford **11**. Attempts to prepare the cycloadduct of diethyl 3-methyl-1,2-butadienylphosphonate [V. Mark, *Tetrahedron Lett.*, 281 (1962)] and furan were unsuccessful.

Alan P. Kozikowski,* Michael P. Kuniak
Department of Chemistry, University of Pittsburgh
Pittsburgh, Pennsylvania 15260

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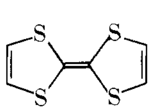
p-Quinobis(benzo-1,3-dithiole)

Summary: The synthesis and characterization of *p*-quinobis(benzo-1,3-dithiole) (**4**) is described. Compound **4** represents the first isolable *p*-quinodimethane derivative substituted by electron-donating groups at the *exo*-methylene groups.

Sir: The unusually high solid-state electrical conductivity of the charge-transfer complex of tetrathiafulvalene (TTF, **1**) with tetracyanoquinodimethane (TCNQ, **2**)[1] has provided the impetus for the synthesis of a variety of derivatives of TTF.[2] One of our recent goals has been the synthesis of derivatives of the unknown *p*-quinodimethane analogue of TTF, *p*-quinobis(1,3-dithiole) (**3**).[3] We now report the synthesis in pure crystalline form of the dibenzo derivative of **3**, namely *p*-quinobis(benzo-1,3-dithiole) (**4**), which also represents the first isolable *p*-quinodimethane substituted by electron-donating groups at C_7 and C_8.



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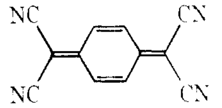

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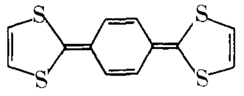

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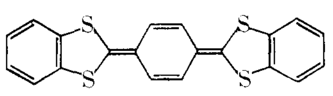
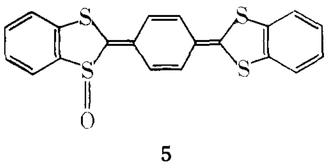


4

The recently described push-pull stabilized sulfoxide **5**,[4] as well as the stable bis(dithiolium)fluoborate **6**[4] should be convertible to **4** by chemical reduction; however, our attempts



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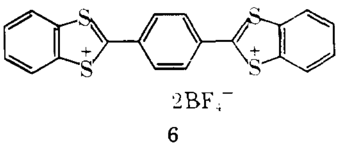

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