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# 1,2-DIALKOXYCARBONYLHYDRAZINE DERIVATIVES OF PYRROLES AND INDOLIZINES. A NEW SYNTHESIS OF CYCL[3.2.2]AZINES

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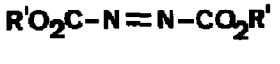
Summary: The reaction of pyrroles 1 with diisopropyl azodicarboxylate 2 yields 2- and 2,5-substituted derivatives. 3- and 1,3-substituted indolizines 5 and 6 are formed by the same route. Cycl[3.2.2]azines 7 have been obtained from 5 and 6 with dimethyl acetylenedicarboxylate.

The reaction of pyrroles and diethyl azodicarboxylate has been reported to lead to no isolable products (1). Using chromatographic techniques, however, we have been able to isolate substituted derivatives 3 and 4 from 1 and 2 (R = i-$C_3H_7$) in moderate yields from a reaction in methanol at room temperature (2,3). Extensive decomposition taking place simultaneously may originate from an oxidation of the pyrroles by the azo compound 2 (4). An indication for this comes from the reaction of 2,5-dimethyl pyrrole with 2 (R = i-$C_3H_7$) under the same reaction conditions which, besides decomposition, leads only to diisopropyl hydrazino-1,2-dicarboxylate (48 %).

The constitution of 3 and 4 follows unabiguously from the $^1$H-NMR-spectra (5), and the formation of 4 (R = $CH_3$) from 3 (R = $CH_3$).

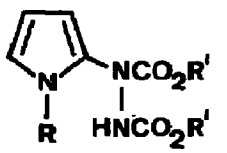
1



2

R = H, Me

R' = i-$C_3H_7$



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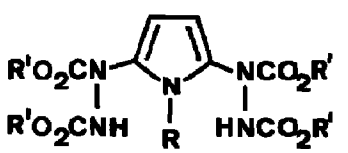
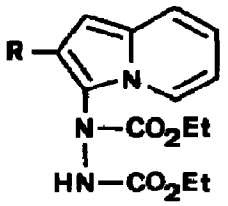


4

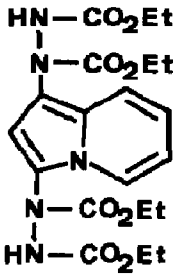
A substitution which is similar to that of pyrrole proceeds with indolizines in better yields. The formation of 3- and 1,3-hydrazino derivatives of type 5 and 6 has been described, the latter compounds being formed in a two-step reaction (6,7). We obtained 5a (45.2 %) and 6 (17 %) in one operation from a reaction of indolizine and 2 (R' = $C_2H_5$) in tetrahydrofurane at room temperature (2,5).

Attempts to achieve substitution into the 1-position of 5b using dimethyl acetylenedicarboxylate have been reported to result in the formation of a complex mixture from which no product was isolated (7). Refluxing the educts in benzene for 5 hours we have been able however to obtain 5.6 % of the previously described cycl[3.2.2]azine derivative 7c (8). The analogous reactions of 5a to give 7a (8) (32 %) and 6 to give 7b (2,5) (66 %) are more efficient.

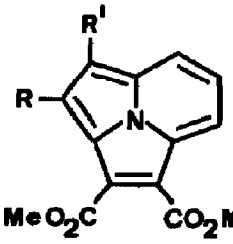


5a R = H

b R = $C_6H_5$



6



7a R = H, R' = H

b R = H, R' = N($CO_2$Et)NH$CO_2$Et

c R = $C_6H_5$, R' = H

Since 3-hydrazinoindolizine derivatives are readily accessible the (8 + 2)$\pi$ cycloaddition to electron deficient acetylenes nicely complements Boekelheide's method in which 3-unsubstituted indolizines have functioned as 8$\pi$ components (8).

It has been reported briefly that 3-cyano indolizine on reaction with dialkyl acetylenedicarboxylate also yields the cycl[3.2.2]azine 7a (9). The insensibility of the reaction to substituents in position 3 of the indolizines is noteworthy (10). This observation will be discussed in details in a future communication.

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## REFERENCES AND NOTES

(1) O. Diels and K. Alder, Liebigs Ann. Chem. 450, 237 (1926).

(2) All new compounds showed satisfactory C,H,N-analyses and spectral data.

(3) 3 (R = H): 5.6 %; 3 (R = $CH_3$): 3.9 %; 4 (R = H): 3.8 %; 4 (R = $CH_3$): 11.5 %.

(4) Other oxidation reactions of alkyl azodicarboxylates are known. For the oxidation of hydroquinones see: O. Diels and P. Fritsche, Ber. 44, 3018 (1911).

(5) $^1$H-NMR-spectra:

3 (R = H) $CDCl_3$: $\delta$ = 7.02 (s, 1H); 6.87 (t, 1H, J = 2.6 Hz); 6.00 (m, 2H); 4.92 (m, 2H); 1.30 (d, 6H, J = 6.5 Hz); 1.18 (d, 6H, J = 6.5 Hz). 4 (R = H) $CDCl_3$: $\delta$ = 6.82 (s, 1H); 6.01 (s, 2H); 4.92 (m, 4H); 1.23 (d, 12H, J = 6.5 Hz); 1.12 (d, 12H, J = 6.5 Hz). 3 (R = $CH_3$) $CDCl_3$: $\delta$ = 6.92 (s, 1H); 6.52 (t, 1H, J = 2.4 Hz); 6.06 (d, 2H, J = 2.4 Hz); 4.99 (m, 2H); 3.59 (s, 3H); 1.27 (d, 6H, J = 6.2 Hz); 1.20 (d, 6H, J = 6.2 Hz). 4 (R = $CH_3$) $CDCl_3$: $\delta$ = 6.94 (s, 2H); 6.06 (s, 2H); 4.99 (m, 4H); 3.50 (s, 3H); 1.27 (d, 12H, J = 6.2 Hz); 1.20 (d, 12H, J = 6.2 Hz). 5a $d_6$-Acetone: $\delta$ = 8.76 (s, NH); 8.25 (d, $H_5$, J = 6.8 Hz);

7.39 (d, $H_8$, J = 8.8 Hz); 6.74 (m, $H_2$, $H_7$); 6.61 (t, $H_6$, J = 6.8 , J = 6.6 Hz); 6.38 (d, $H_1$, J = 4.2 Hz); 4.19 (q, 2H, J = 7.0 Hz); 4.17 (q, 2H, J = 7.0 Hz); 1.25 (t, 3H, J = 7.0 Hz); 1.19 (t, 3H, J = 7.0 Hz). 6 $d_6$-Acetone: $\delta$ = 8.85 (s, NH); 8.63 (s, NH); 8.22 (d, $H_5$, J = 7.5, J = 0.9 Hz); 7.56 (d, $H_8$, J = 9.4, J = 1.2 Hz); 6.85 (s, $H_2$); 6.81 (m, $H_7$); 6.64 (m, $H_6$); 4.17 (m, 8H); 1.12 (m, 12H). 7b $d_6$-Acetone: $\delta$ = 8.46 (m, $H_5$, $H_7$); 8.05 (q, $H_6$, J = 7.8 Hz); 7.89 (s, $H_3$); 4.24 (m, 4H); 4.05 (s, 3H); 4.00 (s, 3H); 1.28 (m, 6H).

(6) P. Bonin and A. Monti, Gazz. Chim. Ital. 94, 509 (1964); C.M. Gupta and R.K. Rizvi, Ind. J. Chem. Sect. B. 1976, 14B, 57.

(7) M. Masumura and Y. Yamachita, Heterocycles 12, 787 (1979).

(8) The synthesis of 7a from indolizine and dimethyl acetylenedicarboxylate has been reported, a dihydroderivative being an intermediate of the reaction: A. Galbraith, Th. Small, R.A. Barnes and V. Boekelheide, J. Am. Chem. Soc. 83, 453 (1961). The chemistry of cycl[3.2.2]azines has been reviewed: A. Taurins: The Chemistry of Heterocyclic Compounds (A. Weissberger and E.G. Taylor), Vol. 30, p. 246, 1977, J. Wiley and Sons, N.Y. - K. Matsumoto, T. Uchida and J. Yamanichi, Yuki Gosei Kagaku Kyokai Shi 35, 739 (1977) [Chem. Abstr. 88, 3764d (1978)]. - W. Flitsch and U. Krämer, Adv. Heterocycl. Chem. 22, 322 (1978).

(9) K. Matsumoto, T. Uchida and L.A. Paquette, Synthesis 1979, 746 and K. Matsumoto, Y.B. Kemi-Kono, T. Uchida and L.A. Paquette, Heterocycles 14, 103 (1980).

(10) The yields of the (8 + 2)$\pi$ cycloaddition reaction to electron deficient acetylenes and ethylenes depend strongly on the substitution pattern of the indolizines (8). See also: S. Ikeda, S. Kajegaeshi and S. Kanemasa, Chem. Lett. 1976, 367. - E.K. Pohjola, J. Heterocycl. Chem. 15, 955 (1978).

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