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DIPOLAR ADDITION AND ACYL MIGRATION IN REACTIONS OF BENZYNE AND ACETYLENES WITH 5-MEMBERED RING α-DIAZO KETONES

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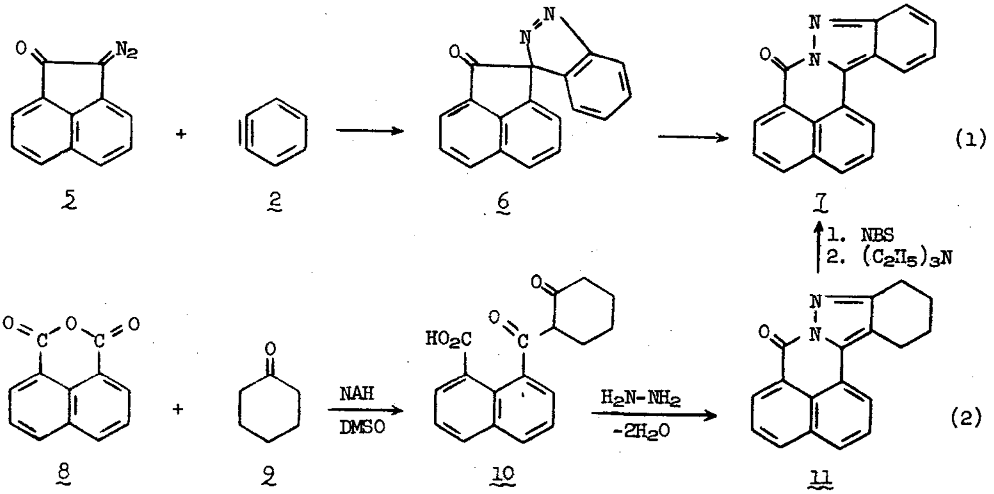
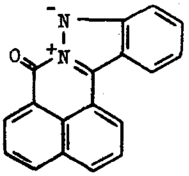
Azibenzil (1) reacts with benzyne[1a] (2) to give 1-benzoyl-3-phenylindazole (4)[1b] instead of 3-benzoyl-3-phenylindazole (3),[1c] the expected 1,3-dipolar adduct. The facile isomerization of 3 is intriguing in that 1,3- and/or successive 1,2-rearrangement processes may be involved. A study is now reported of reactions of 5-membered ring α-diazo ketones with benzyne and various acetylenes. The systems were investigated because, in the 3,3-disubstituted spiroindazoles and pyrazoles possibly initially formed, migration of a carbonyl moiety to nitrogen is restricted to 1,2-rearrangement.[1d]

Diazoacenaphthenone (5) and 2[1a] in refluxing dichloromethane give N-acylindazole 7[1e-g] (Eq 1, red, 57%, mp 219°). Sigmatropic rearrangement after dipolar addition apparently



occurs so rapidly that 6 could not be detected. Indazole 7 is thermally and photochemically inert. Synthesis of 7 via 10, as prepared from 1,8-naphthalic anhydride (8), cyclohexanone (9) and sodium hydride, and 11 (Eq 2) establishes its structure. Carbonyl absorption at 1705 cm^{-1} indicates the strong contribution of 12 to the structure of 7. Aqueous sodium hydroxide and excess hydrazine effect ring opening of 7 by attack at its amido function to give 13 and 14 (>C=O at 1650 cm^{-1}), respectively. The facile regeneration of 7 (~ 100%) by acidification of 13 or warming (35°) 14 indicates the ease of synthesis of the new heterocyclic system.



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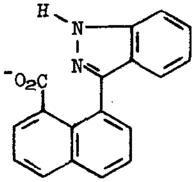

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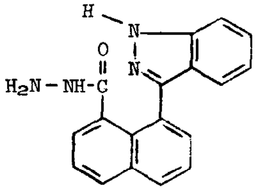
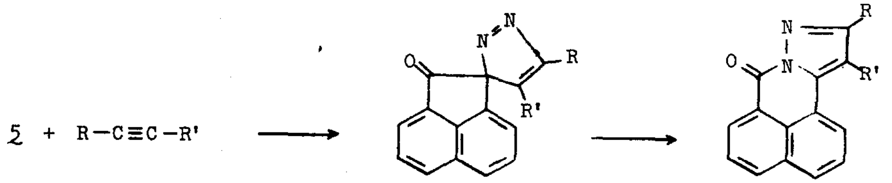


14

Reactions of 5 with phenylacetylene (15) and with dimethyl acetylenedicarboxylate (18) are reported[1h] to yield 16 and 19. The products are however 17 and 20, and thus their thermal and photolytic stabilities are now understandable.[1h] The isomerizations of 16 and 19 are



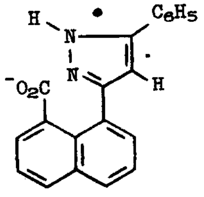
(3)

15; $R=C_6H_5$, R'=H
18; $R=R'=CO_2-CH_3$

16; $R=C_6H_5$, R'=H
19; $R=R'=CO_2-CH_3$

17; $R=C_6H_5$, R'=H
20; $R=R'=CO_2-CH_3$

analogous to those of 6 and of dimethyl 5-acetyl-5-methylpyrazolenine-3,4-dicarboxylate.[1e] The structure of 17 is revealed by its carbonyl absorption (1710 cm^{-1}), saponification to 21,[1i] and regeneration upon acidification of 21. Synthesis of 17 (>C=O at 1710 cm^{-1}) was effected by condensation of 8 and acetophenone with sodium hydride in dimethylsulfoxide to give 8-benzoacetyl-1-naphthoic acid (22) in situ, reaction of 22 with hydrazine, and ring closure similar to that of Eq 2. Dimethyl ester 20 is assigned as indicated because of its spectral properties (>C=O at 1740 cm^{-1}), its saponification with ring opening to 23,[1i] which upon acidification closes to 24 (yellow, mp 298°), and its resynthesis from 24 and diazomethane.



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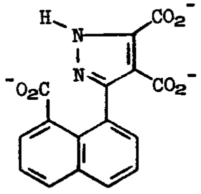

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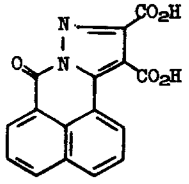

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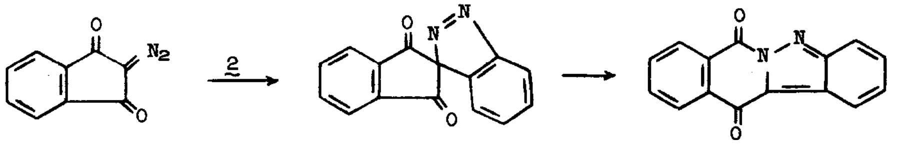
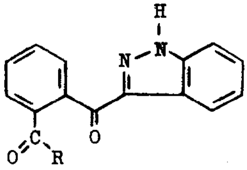
2-Diazo-1,3-indanedione (25) and 2 yield 27 (Eq 4, red, 73%, mp 266.5-267.5°; $>C=O$ at 1660 and 1730 cm^{-1}), presumably via sigmatropic rearrangement of the initial dipolar adduct, 26. The behavior of 25 and of 5 with 2 are thus similar. Naphthoquinone 27 is very sensitive to nucleophiles. Ring opening of 27 occurs upon saponification and acidification to give 28 (white, mp 216°). The structure of 28 (and thus 27) is demonstrated by its oxidative-cleavage by alkaline hydrogen peroxide to phthalic acid (43%), benzoic acid (40%) and nitrogen, presumably by peroxidation of the ketone (28) involving migration of the 3-indazolyl group, and hydrolysis of the monophthalate to phthalic acid and to 3(H)-indazolone which is subsequently oxidized.[1j] Cleavage of 27 also occurs upon reactions with

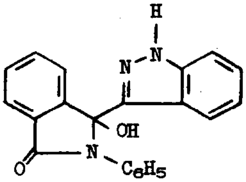


25 26 27

(4)



28, R=OH; 29, R=OCH$_3$
30, R=N(C$_2$H$_5$)$_2$
31, R=N(CH$_3$)-C$_6$H$_5$



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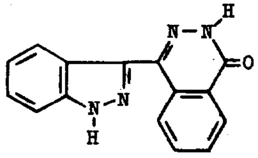

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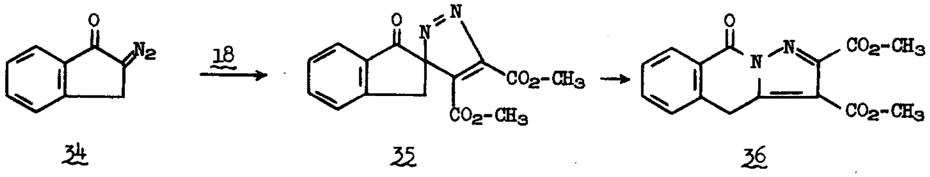
sodium methoxide, diethylamine, and N-methylaniline to give 29 (white, mp 163-165°), 30 (white, mp 198°), and 31 (white, mp 190-191°), respectively. Of note is that aniline, a primary amine, effects ring opening of 27 and subsequent ring-chain tautomerization to 32 (white, mp 223-224°).[1k] On heating, 28-32 all revert essentially quantitatively to 27.

Ring opening of 27 is also effected by hydrazine; subsequent ring closure and dehydration yield 33 (white, mp 277-278°).

2-Diazoindanone (34) adds effectively to 18 to give the rearrangement product 36 (Eq 5, white, 91%, mp 185-186°, >C=O at 1720 and 1750 cm^{-1}). The present study thus reveals that 5-membered ring α-diazo ketones react with 2 and acetylenes to give 3-acyl-3-substituted spiroindazoles and pyrazoles which undergo 1,2-migration of their 3-acyl groups to N-2 of the heterocyclic moieties rather than loss of nitrogen and subsequent carbenic processes. The ease of formation of these 2-acylindazole and pyrazole derivatives and their facile ring-opening reactions with nucleophiles are of importance synthetically and are suggestive that conversion of 3 to 4 involves successive 1,2-rearrangements.



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1. (a) As generated from benzenediazonium carboxylate, L. Friedman and F. M. Logullo, Org. Syn., 48, 12 (1968); (b) G. Baum, Ph.D. Thesis, The Ohio State University, Columbus, Ohio, 1965; Diss. Abstr., 27, 97B (1966); Chem. Abstr., 65, 20071g (1966); (c) W. Ried and M. Schön, Ann., 689, 141 (1965); (d) based on orbital symmetry, such 1,2-rearrangements are 1,5-sigmatropic processes; R. B. Woodward and R. Hoffmann, "The Conservation of Orbital Symmetry," Academic Press, Inc., 114 (1970); (e) after the present work was complete, M. Franck-Neumann and C. Buchecker, Tetrahedron Lett., 937 (1972) reported that 3-diazo-2-butanone and dimethyl acetylenedicarboxylate give dimethyl 1-acetyl-5-methylpyrazole-3,4-dicarboxylate by rearrangement of the presumed dipolar adduct, dimethyl 5-acetyl-5-methylpyrazolenine-3,4-dicarboxylate. R. Yeater of this laboratory also made this observation (1971) independently; (f) reaction of 3 and 2 was first reported by J. C. Fleming, Ph.D. Thesis, The Ohio State University, Columbus, Ohio, 1964; (g) all new isolable compounds of the present work gave proper analyses and appropriate ir, uv, and nmr absorptions and mass spectra; (h) O. Tsuge, I. Shinkai, and M. Koga, J. Org. Chem., 36, 745 (1971); (i) the position of hydrogen on nitrogen in the pyrazole moiety is not known with certainty; (j) 3(H)-indazolone is converted to benzoic acid by hydrogen peroxide; (k) the structure of 32 is based on its ir and uv absorptions and comparison with model compounds.