Heteroatom Chemistry
Volume 7, Number 4, 1996

Regiochemistry of the Cycloaddition of Nitrilium N-Phenylimides to Dibenzalacetone: A Reinvestigation

Hassan A. Albar

Department of Chemistry, Faculty of Science, King Abdulaziz University, Jeddah 21413, Saudi Arabia

Magda A. Abdallah, Mosselhi A. N. Mosselhi, and Ahmad S. Shawali*

Department of Chemistry, Faculty of Science, University of Cairo, Giza, Egypt

Received 26 September 1995; revised 29 December 1995

ABSTRACT

Reaction of benzonitrilium N-phenylimide **3a** *with dibenzalacetone* **1** *yielded a mixture of the mono- and biscycloadducts* **8a** *and* **11a** *in a 1:1 ratio. A similar reaction of* **1** *with ethoxycarbonylnitrilium N-phenylimide* **3b** *afforded a mixture of the cycloadducts* **7b**, **8b**, *and* **12b** *in a 1:3:6 ratio, respectively. The structures of these products were established by spectral analyses and chemical transformations. The results invalidate the previously reported structure* **4a** *assigned for the biscycloadduct isolated from the reaction of* **3a** *with* **1**. © *1996 John Wiley & Sons, Inc.*

Ten years ago, Tsatsaroni [1] described the 1,3-dipolar cycloaddition of dibenzalacetone **1** with some 1,3-dipoles with the objective of studying the regiochemistry of the process. In his report, it was indicated that the reaction of **1** with benzonitrilium N-phenylimide **3** afforded only the biscycloadduct, bis-5,5'-pyrazolyl ketone, **4a** in 13% yield [1]. The regiochemistry of this product was assigned on the basis of comparison of the chemical shifts of its H-4 and H-5 protons with those reported for 1,3,4-triphenyl-5-benzoyl-2-pyrazoline **5a** obtained from the reaction of **3a** with benzalacetophenone [2]. Finally, the proposed regiochemistry of **4a** was rationalized in terms of the frontier molecular orbital (FMO) theory [3].

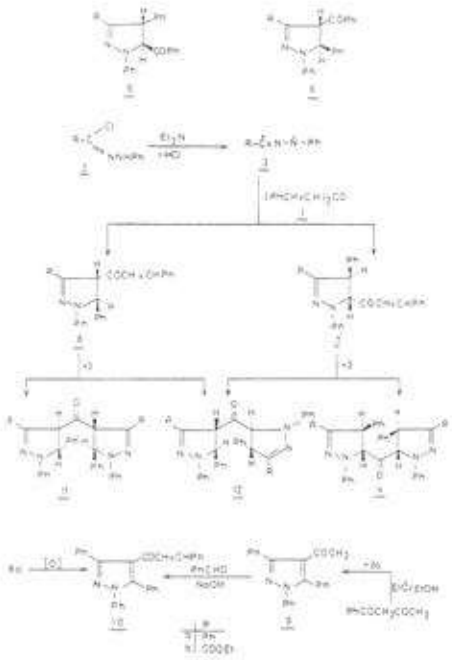
In our opinion, the comparison of **4a** with **5a** is unjustified. This is because while the chemical shifts of H-4 and H-5 protons of **5a** were reported to be δ 4.61 and 5.61 with $\Delta\delta_{4,5}$ = 1.0 [2], the H-4 and H-5 protons of **4a** resonate at δ 4.55 and 4.85 with $\Delta\delta_{4,5}$ = 0.3 [1]. Furthermore, our previous ^{1}H NMR study of an extensive series of 5- and 4-aroyl-2-pyrazoline regioisomers **5b** and **6b** indicates that $\Delta\delta_{4,5}$ values of 1.0–1.29 and 0.1–0.3 are characteristic of these two regioisomers, respectively [4]. Thus, the value of $\Delta\delta_{4,5}$ = 0.3 is incompatible with structure **4a** assigned for the product isolated from reaction of **1** with **3a** [1]. In addition, the FMO theory does not always give results in good agreement with experiment [5].

On the basis of the foregoing arguments, we reinvestigated the cycloaddition of **3a,b** to **1** to elucidate its regiochemistry and to see if the corresponding monocycloadducts **7** and **8** and also the biscycloadducts **11** and **12** are formed.

The cycloaddition of **3a**, prepared in situ by the

*To whom correspondence should be addressed.

1042-7163/96/040225-04



SCHEME 1

action of triethylamine on N-phenyl benzenecarbohydrazonoyl chloride **2a** in benzene, to **1** was carried out at reflux for 2 hours. The crude reaction product, isolated after removal of the solvent, was subjected to column chromatography, two products being obtained, A and B, the former being the one that eluted first from the column. The mass spectra of such products indicated that product A is a biscycloadduct (m/z = 622), whereas the second product B is a monocycloadduct (m/z = 428). The yields of A and B, after being crystallized from ethanol, were 38% and 35%, respectively.

The ^{1}H NMR spectrum of product B showed two doublets at δ 4.70 and 4.88 (J = 6 Hz). On the basis of these chemical shift values, this product was assigned structure **8a**. Such an assignment was confirmed by its chemical transformations outlined in Scheme 1. Thus, dehydrogenation of the monocycloadduct **8a** with chloranil gave a product identified as 1,3,5-triphenyl-4-cinnamoylpyrazole **10** by comparison with an authentic sample prepared by the reaction of benzaldehyde with 1,3,5-triphenyl-4-acetylpyrazole **9** in ethanol in the presence of sodium hydroxide. Furthermore, on the basis of the value of the coupling constant (J = 6 Hz) between H-4 and H-5, the monocycloadduct **8a** was assigned the *trans*-configuration indicated. This is because the coupling constant between *trans*- and *cis*-H-4 and H-5 protons of 2-pyrazoline derivatives were reported to be 6 and 12 Hz, respectively [6].

Three possible regioisomeric structures, namely, **4a**, **11a**, and **12a**, can be written for the biscycloadduct A. Both structures **4a** and **12a** were discarded from further consideration. This is because, on the one hand, structure **12a** is expected to give in its ^{1}H NMR spectrum two pairs of doublets assignable to the magnetically nonequivalent protons H-4, H-4', H-5, and H-5' with $\Delta\delta_{4,4'}$ = 1.3 and $\Delta\delta_{5,5'}$ = 0.3 [4], and, on the other hand, structure **4a** is expected to show only one pair of doublets with $\Delta\delta_{4,4'}$ = 1.3 [4]. Contrary to these expectations, the ^{1}H NMR spectrum of the biscycloadduct **11a** isolated revealed only one pair of doublets (J = 6 Hz) at δ 4.9 and 4.6 assignable to H-5 and H-4 protons, respectively. Such data are compatible with structure **11a**, and based on the value of the coupling constant (J = 6 Hz), the biscycloadduct was also assigned the *trans*-configuration indicated [6].

^{13}C NMR spectra provide additional evidence for the assigned structures **8a** and **11a**. Each of the cycloadducts exhibits two signals characteristic of the C-4 and C-5 of the 2-pyrazoline ring residue near δ 57–58 and δ 76–77. The former signal is assigned to the C-4 atom; this assignment is in good agreement with that reported for an sp^3 carbon flanked by an acyl and sp^2 carbon atom. The lower field signal at δ 76–77 is assigned to the C-5 atom, which is flanked by a nitrogen atom and a phenyl group [7].

In the mass spectra of both **8a** and **11a**, the molecular ion peak is not the base peak. However, the base peak in both cases corresponds to a fragment having an m/z value of 297 assignable to the triphenyl-2-pyrazoline cation. This latter fragment undergoes retrocycloaddition affording diphenylnitrilimine and a phenylvinyl fragment, as the corresponding peaks at m/z 194 and 103, respectively, were common in the spectra of both cycloadducts.

In conclusion, the 1,3-dipolar cycloaddition of **3a** to **1** is regioselective, the carbon atom in the latter, which is substituted by a phenyl group, being the one that bonds to the nitrogen atom of **3a**. This result indicates that cross conjugation, as in dienone **1**, reverses the regiochemistry of the cycloaddition of the nitrilium imide **3a**.

In order to substantiate this conclusion, we studied also the reaction of **1** with ethoxycarbonylnitri-

lium N-phenylimide **3b**. In our hands, the latter reaction of **1** with **3b**, generated in situ by the action of triethylamine on **2b** in benzene at reflux for 2 hours, furnished three products, (C, D, and E), as evidenced by thin-layer chromatography (TLC) analysis of the crude reaction product. The formation ratios of the latter were determined by ^{1}H NMR analysis and found to be 1:3:6, respectively. These were separated by column chromatography (see Experimental).

Mass spectral and elemental analyses of the latter products indicated that C and D are both 1:1 cycloadducts, whereas E is a 1:2 cycloadduct. The former monocycloadducts C and D proved to be the regioisomeric 5- and 4-cinnamoyl-2-pyrazoline derivatives **7b** and **8b**, respectively. The distinction between these two regioisomers was made on the basis of their ^{1}H NMR spectra. Thus, each of these two monocycloadducts exhibits two doublets (J = 6 Hz) assignable to the H-4 and H-5 ring protons in addition to two other doublets (J = 15 Hz) assignable to the vinylic protons of the cinnamoyl moiety. The difference of the chemical shift values ($\Delta\delta_{4,5}$) of the pyrazoline ring protons of **7b** and **8b** were 1.2 and 0.5, respectively. The similarity between these values and those reported [4] for the 5-benzoyl- and 4-benzoyl-2-pyrazoline regioisomers **5b** and **6b** ($\Delta\delta_{4,5}$ = 1.29 and 0.34), respectively, seems to be in support of the assigned structures **7b** and **8b** for the 1:1 cycloadducts isolated. On the basis of the coupling constant (J = 6 Hz), both products were assigned the *trans*-configuration indicated [4] (Scheme 1).

The ^{1}H NMR spectrum of the cycloadduct E revealed two pairs of doublets with $\Delta\delta_{4,5}$ of 0.15 and 1.0. On this basis, it was assigned the 4,5'-bipyrazolyl ketone structure **12b**. The other two possible isomeric structures **4b** and **11b** were thus discarded since each of them is expected to exhibit only one pair of doublets in its ^{1}H NMR spectrum due to the H-4 and H-5 ring protons. A further evidence for structure **12b** is provided by the appearance of three singlet signals in its ^{13}C NMR spectrum at δ 161.5, 162.0, and 191.5 assignable to the three magnetically nonequivalent carbonyl carbons. The ^{13}C NMR spectrum of **7b** showed two singlets at δ 161.0 and 199.8, whereas that of **8b** revealed two singlets at 161.5 and 195.0.

EXPERIMENTAL

Melting points were determined on a Galenkamp apparatus and are uncorrected. ^{1}H NMR spectra were recorded in deuterated chloroform on a Varian EM-390-90MHz spectrometer; Chemical shifts are given in δ from tetramethylsilane (TMS) as the internal reference (J in Hz). ^{13}C NMR spectra were recorded on a Bruker WM 360 (90.56 MHz) pulsed Fourier Transform spectrometer. Mass spectra were recorded on a V.G. Micromass 7070E double-focusing mass spectrometer at the University of Wales, College of Cardiff. Infrared spectra were measured on a Perkin Elmer 1430 spectrophotometer. Silica gel used for column chromatography was Merck Kieselgel 60 (70-230 ms ASTM). The TLC analysis was carried out using fluka silica gel cards with fluorescent indicator 254 on aluminum cards, and the spots were detected under 254 nm UV light. The hydrazonoyl chlorides **2a,b** [8,9] and dibenzalacetone **1** [10] were prepared as described in the literature. Elemental analyses were carried out with a Perkin Elmer elemental analyzer, model 240-B at King Abdulaziz University.

Reaction of 1 with 2a,b. General Procedure. To a stirred equimolar mixture of dibenzalacetone (**1**) and the appropriate hydrazonoyl chloride (**2**) (2 mmol each) in benzene or tetrahydrofuran (50 mL) was added triethylamine (0.5 mL, 4 mmol), and the mixture was refluxed for 2 hours. The precipitated triethylamine hydrochloride was filtered off, the solvent was evaporated, and the residue was subjected to ^{1}H NMR analysis, which showed the presence of more than one cycloadduct. The latter were separated by column chromatography using Flash silica gel as adsorbent and petroleum ether (40/60°)-ethyl acetate (1:1 v/v) as eluent. The separation of the cycloadducts was followed by ^{1}H NMR analysis of the fractions collected. The solvent in the fractions was evaporated, and the remaining solid was collected and crystallized twice from ethanol.

Compound **8a** (0.30 g, 35%): mp 184–185°C; IR (KBr) 1690 cm^{-1} (CO); ^{1}H NMR δ 4.7 (d, 1H, J = 6 Hz), 4.88 (d, 1H, J = 6 Hz), 6.9 (d, 1H, J = 15 Hz), 7.2–7.8 (20H, m), 7.9 (d, 1H, J = 15 Hz); m/z 428, 297, 236, 194, 177, 136, 103, 91, 77. Found: C, 83.95; H, 5.60; N, 6.38; calcd. for $C_{30}H_{24}N_2O$: C, 84.08; H, 5.64; N, 6.54%.

Compound **11a** (0.47 g, 38%): mp 225–226°C; IR (KBr) 1715 cm^{-1} (CO); ^{1}H NMR δ 4.6 (d, 2H, J = 6 Hz), 4.9 (d, 2H, J = 6 Hz), 6.7–7.7 (30H, m); m/z 622, 297, 236, 194, 116, 103, 91, 77. Found: C, 82.80; H, 5.45; N, 8.90; calcd. for $C_{43}H_{34}N_4O$: C, 82.93; H, 5.50; N, 8.99%.

Compound **7b** (0.06 g, 7%): mp 159–160°C, m/z 424. IR (KBr) 1705, 1694 cm^{-1} (CO); ^{1}H NMR δ 1.3 (t, 3H, J = 7 Hz), 4.3 (q, 2H, J = 7 Hz), 4.5 (d, 1H, J = 6 Hz), 5.7 (d, 1H, J = 6 Hz), 7.05 (d, 1H, J = 15 Hz), 7.70 (d, 1H, J = 15 Hz), 7.1–7.5 (m, 15H). Found: C, 76.20; H, 5.86; N, 6.71; calcd. for $C_{27}H_{24}N_2O_3$: C, 76.40; H, 5.70; N, 6.60%.

Compound **8b** (0.18 g, 21%): mp 131–132°C,

m/z 424. IR (KBr) 1700, 1685 cm^{-1} (CO); ^1H NMR δ 1.2 (t, 3H, J = 7 Hz), 4.2 (q, 2H, J = 7 Hz), 4.55 (d, 1H, J = 6 Hz), 5.10 (d, 1H, J = 6 Hz), 6.85 (d, 1H, J = 15 Hz), 7.8 (d, 1H, J = 15 Hz), 7.0–7.5 (m, 15H). Found: C, 76.16; H, 5.85; N, 6.26; calcd. for $C_{27}H_{24}N_2O_3$: C, 76.40; H, 5.70; N, 6.60%.

Compound 12b (0.5 g, 41%): mp 187–188°C, *m/z* 614. IR (KBr) 1705, 1687 cm^{-1} (CO); ^1H NMR δ 1.2 (t, 3H, J = 7 Hz), 1.35 (t, 3H, J = 7 Hz), 4.15 (q, 2H, J = 7 Hz), 4.25 (q, 2H, J = 7 Hz), 4.3 (d, 1H, J = 6 Hz), 4.45 (d, 1H, J = 6 Hz), 4.50 (d, 1H, J = 6 Hz), 5.5 (d, 1H, J = 6 Hz), 7.0–8.0 (m, 20H). Found: C, 71.90; H, 5.22; N, 9.02; calcd. for $C_{37}H_{34}N_4O_5$: C, 72.30; H, 5.58; N, 9.11%.

Repetition of the above procedure using a double ratio of 1 to 2 and increasing the time of reflux to 24 hours did not change the yields of the above-mentioned cycloadducts.

1,3,5-Triphenyl-4-acetylpyrazole (9): Benzoylacetone (1.62 g, 0.01 mol) was added to an ethanolic sodium ethoxide solution (prepared from sodium metal (0.23 g, 0.01 g atom) and absolute ethanol (50 mL). After the mixture had been stirred for 10 minutes, the hydrazonoyl chloride (2a) (2.3 g, 0.01 mol) was added, then stirring continued for 5 hours and the mixture was left overnight at room temperature. The solid product that separated was collected, washed with water, and dried. Crystallization from acetone gave 9 (2.5 g, 75%): mp 149°C (Ref. [11] mp 124°C). IR (KBr) 1675 cm^{-1} (CO); ^1H NMR 2.45 (s, 3H), 7.1–7.8 (m, 15H). Found: C, 81.36; H, 5.40; N, 8.19; calcd. for $C_{23}H_{18}N_2O$: C, 81.63; H, 5.36; N, 8.28%.

1,3,5-Triphenyl-4-cinnamoylpyrazole (10): To a solution of 1,3,5-triphenyl-4-acetylpyrazole (9) (1.69 g, 5 mmol) in ethanol (40 mL) was added aqueous sodium hydroxide solution (2.8 mL, 10%). The resulting solution was cooled in an ice bath, benzaldehyde (0.53 g, 5 mmol) was added, and the mixture was stirred for 3 hours, then kept overnight in a refrigerator. The solid that precipitated was filtered off, washed with water, then dried. Crystallization of the crude product from aqueous dimethylformamide gave 1,3,5-triphenyl-4-cinnamoylpyrazole (10) (1.29 g, 90%): mp 209–210°C; IR (KBr) 1700 cm^{-1} (CO); ^1H NMR δ 6.9 (d, 1H, J = 15 Hz), 7.2–7.8 (m, 20H), 7.95 (d, 1H, J = 15 Hz); Found: C, 84.39; H, 5.15; N, 6.60; calcd. for $C_{30}H_{22}N_2O$: C, 84.48; H, 5.20; N, 6.56%.

Dehydrogenation of 8a: A mixture of 8a (0.43 g, 1 mmol) and chloranil (0.25 g, 1 mmol) in xylene (30 mL) was refluxed for 20 hours. The solution was diluted with ether, washed with aqueous sodium hydroxide solution and water, dried over anhydrous sodium sulfate, then filtered. The solvent in the filtrate was evaporated under reduced pressure, and the crude solid left was crystallized from aqueous dimethylformamide to give 10 (0.34 g, 80%) identical in all respects (mp, mixed mp, IR spectra) with 1,3,5-triphenyl-4-cinnamoylpyrazole obtained previously.

REFERENCES

[1] E. G. Tsatsaroni, *Chim. Chron., 13,* 1984, 185.
[2] G. Bianchi, R. Gandolfi, and C. deMicheli, *J. Chem. Res.,* 1981, (S) 6; (M) 135.
[3] K. N. Houk, J. Sims, C. R. Watts, and L. J. Luskus, *J. Am. Chem. Soc., 95,* 1973, 7301.
[4] A. S. Shawali, S. T. Ezmirly, and A. M. Bukhari, *Spectrochimica Acta, 48A,* 1992, 1165.
[5] B. Laude, M. Soufaoui, and J. Arriau, *J. Heterocycl. Chem., 14,* 1977, 1183.
[6] R. Sustman, R. Huisgen, and H. Hubet, *Chem. Ber., 100,* 1967, 1802.
[7] D. W. Brown, *J. Chem. Educ., 62,* 1985, 209.
[8] P. Wolkoff, *Can. J. Chem., 53,* 1975, 1333.
[9] M. O. Loziniskii, S. N. Kukota, and P. S. Pel'kis, *Ukr. Khim. Zh., 33,* 1967, 1295; *Chem. Abstr., 69,* 1968, 51762g.
[10] J. Finkelstein and R. C. Elderfield, *J. Org. Chem., 4,* 1939, 371.
[11] I. Grandberge, S. V. Taback, N. I. Bobrova, A. N. Kost, and L. G. Vasina, *Khim. Geterotsikl. Soedin. Akad. Nauk. Latv. SSR,* 1965, 407; *Chem. Abstr., 63,* 1965, 16332f.

THE BRITISH LIBRARY

Copyright Declaration to be retained by the registered BL Customer

This document has been produced and supplied by the British Library under the terms of its Library Privilege Photocopy Services. Unless a declaration has already been obtained the following Declaration, signed in person by the end user, must be obtained by the Librarian of the user library before the document is handed over.

To the Librarian of the [ ] Library

(name of User Library or Library Stamp)

1. I hereby request you to supply me with a copy of the item specified on Request Number _____ which I require for the purpose of research or private study.
2. I have not previously been supplied with a copy of the same material by you or by any other librarian.
3. I will not use the copy except for research or private study and will not supply a copy of it to any other person.
4. To the best of my knowledge, no other person with whom I work or study has made, or intends to make at about the same time as this request, a request for substantially the same material for substantially the same purposes.
5. If this item was delivered by an electronic method (which includes facsimile transmission), I will retain only a single paper copy and destroy any electronic copies after printing.
6. I understand that if this declaration is false in a material particular the copy supplied to me by you will be an infringing copy and that I shall be liable for infringement of copyright as if I had made the copy myself.

Signature _____ Address _____

Name (CAPITALS) _____

Date _____